ISSN 2545-4366
www.e-mja.finki.ukim.mk

MJA

Macedonian Journal of Anaesthesia

A Journal on Anaesthesiology, Resuscitation, Analgesia and Critical Care

Vol. 8 No 4, December 2024

Journal of the Macedonian Society of Anaesthesiologists
and Macedonian Society of Critical Care Medicine

Publisher:
Department of Anaesthesia and Reanimation Faculty of Medicine,
"Ss. Cyril and Methodius" University, Skopje, R.N.Macedonia

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I.V. Paracetamol

БЕЗБЕДНА АНАЛГЕЗИЈА

менаџирање на болка кога сте загрижени за безбедноста

I.V. paracetamol за прв пат во Европа е применет во 2001 година, а денес поради неговата докажана безбедност и ефикасност е прв од избор **аналгетик и антипиретик.**

Предоперативна и Интраоперативна Аналгезија:
Предоперативна анелгезија е дефинирана како третман кој што започнува пред оперативниот зафат се со цел да се превенира воспоставувањето на централна сензибилизација на болка.
i.v. paracetamol е безбеден, добро толериран лек со докажана ефикасност како **предоперативна и интраоперативна анелгезија** за умерена до средна болка при оперативни зафати.
Голем број на клинички студии ја докажуваат ефикасноста на **i.v. paracetamol** како **преодоперативна и интраоперативна анелгезија**.

КЛИНИЧКА СТУДИЈА:
Ефект од **предоперативен i.v. paracetamol** за постоперативни аналгетски потреби кај пациенти кои се подлежни на оперативни зафати. A Sreenivasulu , R Prabhavathi, 2015
Цел: Да се утврди ефикасноста на **предоперативната употреба на 1000mg i.v. paracetamol** кај постоперативните болки и анелгетски потреби кај пациенти подлежни на хируршки зафати.
Метод: 60 пациенти беа поделени во две рандомизирани групи од по 30 пациенти.
На I. Група им беше администриран**о ампула од 1000mg i.v. paracetamol разредена 0,9%NaCl** р-ор 30 минути пред индукција **(ГРУПА П)**,
На II. Група им беше администрирано **i.v. 0,9% NaCl р-ор 100мл** 30 минути пред индукција **(ГРУПА НС)**
Сите пациенти беа индуцирани со i.v. thiopentone 5mg/kg, i.v. fentanyl 2µg/kg, i.v. vecuronium 0.1mg/kg
Постоперативниот резултат на болка беше мерен со **Визуелна Аналогна Скала (ВАС) од "0-10"**. Исто така беше забележувана и **постоперативната употреба на tramadol** како спасувачки аналгетик. Инциденцата на **постоперативно гадење и повраќање (ПОГП)** и други компликации исто така беа забележувани во пост оперативниот период.
Резултатот на постоперативната болка беше забележуван во интервали 15 мин, 30 мин, 1 час, 2 часа, и 6 часа.

Резултат:
Табела 1: *Споредба на средниот резултат на болка (ВАС) помеѓу двете групи*

Интервали	I Група П	II Група НС	*P вредност*
15 мин	2.06 ± 0.63	2.61 ± 0.56	0.0006
30 мин	2.35 ± 1.17	3.84 ± 1.55	0.0001
1 час	2.42 ± 1.12	2.87 ± 0.99	0.0989
2 часа	2.13 ± 1.06	2.52 ± 0.89	0.1219
6 часа	2 ± 0.52	2.52 ± 0.89	0.0549

Табела 2: *Споредба за потребите од tramadol помеѓу двете групи*

Интервали	I Група П	II Група НС	*P вредност*
До 1 час	4 (12.90%)	15 (50%)	0.0002
1-2 часа	3 (9.68%)	2 (6.45%)	0.64
2-6 часа	1 (3.23%)	3 (9.68%)	0.301
Вкупно	**8 (25.81%)**	**20 (64.52%)**	**0.002**

Табела3: *Споредба на ПОПГ помеѓу двете групи*

ПОГП	
I Група П	II Група НС
0	4

Заклучок: Предоперативна администрација на **1000mg i.v. paracetamol** кај пациенти подлежни на оперативен зафат обезбедува **статистички задоволителна анелегизија**, и ја **намалува постоперативната употреба на tramadol**. Оттука **1000mg i.v. paracetamol** може безбедно да се администитрира како превенција при оперативни зафати.

i.v. Paracetamol + јак опоид	МНОГУ ЈАКА БОЛКА
i.v. Paracetamol + слаб опоид	ЈАКА БОЛКА
i.v. Paracetamol + NSAID i.v. Paracetamol + rescue medicine	УМЕРЕНА БОЛКА
i.v. Paracetamol + rescue medicine	СЛАБА БОЛКА

Мултимодално менаџирање на постоперативна болка
I.V. Paracetamol е атрактивна компонента за мултиодално менаџирање на болка.

- **Синергистичко делување**
- **Зголемување на аналгетски ефект**
- **Значително намалување на болка**
- **Редукција на дозата на опоидни лекови за - 40% во првите 24 часа**
- **Намалување на несаканите ефекти поврзани со монотерапија на NSAID и опоидни лекови**
- **Ублажување на акутна и хронична болка**

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CONTENT

EDITORIAL *UDK: 616.24-089.168-06*

www.doi.org/10.55302/MJA2484011gb

DO WE NEED TO PERFORM A SINGLE-STEP, MULTI-STEP, OR NO ALVEOLAR RECRUITMENT MANEUVER AT ALL?

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On one hand, postoperative pulmonary complications (PPCs) have been associated with increased early postoperative mortality, ICU readmission and length of hospital stay. On the other hand, general anesthesia disrupts the natural sigh reflex and contributes to alveolar collapse, significantly impairing oxygenation and gas exchange during surgery. Alveolar collapse or atelectasis affects nearly all patients under general anesthesia, leading to hypoxemia, postoperative pulmonary complications and prolonged recovery time (1-4). Thus, we must avoid PPCs throughout the perioperative phase (5-8). A lot of research has been done on the benefits of pulmonary-protective ventilation techniques, like positive end-expiratory pressure (PEEP) ventilation and low tidal volume ventilation, to lower PPCs (9). However, there is still disagreement and no set guidelines to abide by when it comes to the alveolar recruitment maneuver (RM). In order to open collapsed alveoli, a recruitment procedure involves a prolonged increase in airway pressure. Then sufficient PEEP is administered to maintain the alveoli open (10). RM aims to increase oxygenation and function as a component of a lung protection strategy. Through increased airway pressure, the RM can partially reverse pulmonary atelectasis and preserve the alveolar aperture. The clinical community is actively investigating the technique that optimally balances efficacy and safety, and this editorial assesses recent evidence for alveolar RM, integrating new findings and insights from key studies.

Recruitment maneuvers vary widely in their application, encompassing various approaches in terms of timing, pressure settings and repetition (4, 11-31). Based on the variation in airway pressure, we can separate RMs into stepwise (multistep) and persistent categories (single step). A stepwise increase in PEEP plus a gradual increase in tidal volume make up the stepwise RM (4). According to earlier systematic studies, RM enhances oxygenation and lowers PPCs in patients under general anesthesia (11). Nevertheless, the analysis only covered a small number of included papers and it did not differentiate between different types of surgery. A large multicenter randomized controlled study (RCT) found that the open-lung ventilation technique was not as good at lowering the incidence of PPCs as conventional protective ventilation (12). In order to address the impact of the RM on PPCs, respiratory mechanics and hemodynamics during surgery, Pei and coauthors conducted high-quality evidence of systematic review and meta-analysis of RCTs (13). The initial studies they found included 209 from PubMed, 532 from Web of Science, 421 from Embase, 926 from the Cochrane Library database and 81 from the Clinicaltrials.gov registry. These sources collectively yielded a total of 2,160 likely associated studies. Out of them, 1,087 were duplicate. After a careful analysis of the titles and abstracts of the remaining literature, 873 publications were deemed irrelevant and removed. After screening 200 full-text papers, only 17 of them met the criteria for inclusion. Ultimately, a total of 3,480 individuals from 17 RCTs were analyzed (13). PPCs with a general incidence of roughly 21.9% were observed (448/1734 in the non-RM group and 314/1746 in the RM group). With minimal

variability, RMs dramatically decreased PPCs in comparison to the control group in obese and non-obese patients, as well. Only one study included participants who were over 65 years old. In individuals who were not elderly, RMs reduced the incidence of PPCs, but they had no effect on elderly patients. The results were tested for heterogeneity as well > 0.10; I2 = 5%. Because there isn't enough research on the effects of RMs on the elderly, we should exercise caution when treating elderly patients (age ≥ 65) (13).

Another question to be raised is the use of one or repeated RMs. According to the evidence, one RM has a much higher incidence of lowering PPCs than repeated RMs. To be more precise, although repeated RMs also decreased the incidence of PPC, they were less effective than a single RM, and there was heterogeneity. The statistical analysis also shows a big difference in heterogeneity between the two methods (p for heterogeneity <0.05), which suggests that a single RM may work better than repeated RMs (14–30).

The data clearly shows that single RMs are effective in reducing PPCs, but the optimal timing for performing these maneuvers remains unclear. Although the literature highlights the advantages of both single and repeated RMs, it fails to offer definitive recommendations on the optimal timing of these maneuvers during the procedure.

For single RMs, it is still uncertain whether there is an ideal time point for maximum effectiveness. For repeated RMs, there is similarly no definitive answer regarding the frequency or timing of each maneuver that would offer the best outcomes. The available data lacks sufficient evidence to make firm recommendations on the precise timing or frequency of recruitment maneuvers in clinical practice.

Another ongoing debate is the sustained or stepwise RMs. Nine researchers applied sustained RMs, while eight applied stepwise RMs. The findings demonstrated that sustained RMs had a more notable impact on reducing the incidence of PPCs than stepwise RMs. With no evidence of heterogeneity in either grouping (14–30).

According to Rothen and colleagues, a recruited pressure of more than 40cm H_2O is necessary in order to guarantee opening in pulmonary atelectasis (31). There are investigations, which, based on the recruited pressure, are divided into two groups. While one used recruited pressure <40cm H_2O, other studies used pressure ≥ 40cm H_2O. The findings showed a decrease in the incidence of PPCs when the recruiting pressure was less than 40cm H2O. However, when the recruited pressure was greater than 40cm H_2O, the results were not improved, and other issues could arise (14–31).

Recruitment, however, is not without its risks. The balance between adequate recruitment and the potential for barotrauma, volutrauma or hemodynamic instability, must be carefully managed by a multidisciplinary team. Notable is the hemodynamic stability throughout the RM. On the other hand, this does not mean that the RM has no effect on the circulatory system. The time at which each study recorded its data varied greatly; some studies reported their data 60 minutes after initiation, while others recorded their data prior to the conclusion of surgery. The right and left ventricular ejection fractions temporarily decrease during RMs as a result of the elevated transpulmonary pressure during RMs. This is actually due to increases in the central venous pressure, pulmonary vascular resistance index and pulmonary artery pressure. According to Celebi et al., the right ventricle was temporarily affected by the RM, and when the high airway pressure was released, the hemodynamics restored to normal (32). It was also shown in

other studies that the right ventricular work increases only in the initial two minutes following intervention (33). Future research should concentrate on enhancing personalized strategies by considering patient-specific factors, including lung compliance, body habitus and pre-existing medical comorbidities and respiratory conditions.

RMs are frequently utilized in pediatric patients as well, to address conditions such as pulmonary atelectasis, particularly in critically ill or ventilated patients. In pediatric patients, recruitment maneuvers enhance lung function by reopening collapsed alveoli, thereby improving oxygenation and decreasing complications associated with ventilation. The application of respiratory techniques in pediatric populations necessitates meticulous oversight and personalized strategies, taking into account variables such as lung compliance, pre-existing disorders and hemodynamic stability. Research indicates that RMs effectively enhance respiratory outcomes in pediatric patients when applied correctly (34-38).

While standardized protocols provide a foundation, clinical judgment, combined with continuous monitoring and advanced imaging techniques, plays a critical role in optimizing outcomes. We expect ongoing trials and new studies to further refine these approaches, but until such data is available, careful clinical application and collaboration remain at the forefront of successful mechanical ventilation.

As we continue to learn and adapt, recruitment maneuvers will likely evolve, driven by innovations in ventilation technology and deeper insights into lung mechanics. For now, the focus should remain on multidisciplinary teamwork, rigorous patient monitoring and a personalized approach to each patient's ventilatory needs.

In conclusion, we must emphasize that the optimization of patients' outcomes in contemporary anesthesiology depends on the integration of advanced techniques and the rigorous reassessment of traditional approaches. Alveolar RMs have emerged as a key intervention in mitigating perioperative atelectasis. Despite their widespread adoption, the precise timing and frequency of alveolar RMs remain subjects of ongoing debate. This underscores the need for a more refined, evidence-based application of these maneuvers to enhance their efficacy and ensure superior clinical outcomes. Future research must focus on establishing standard protocols that tailor the use of alveolar RMs to individual patients' profiles, ultimately advancing the quality of perioperative care.

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ORIGINAL ARTICLE *UDK: 616.728.3-018.2-072.1-089.5(497.7)"2021/2022"*

www.doi.org/10.55302/MJA2484017a

PATIENT SATISFACTION WITH KNEE ARTHROSCOPY UNDER LOCAL ANESTHESIA AND SEDATION

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Abstract

Introduction: Knee arthroscopy can be performed under general, regional (spinal or epidural) or local anesthesia with different patients' satisfaction after surgery.

Purpose: The aim of our study was to evaluate the level of satisfaction in patients after knee arthroscopy under local anesthesia.

Patients and methods: The study included 52 patients where knee arthroscopy under local anesthesia was performed at the University Clinic for Orthopedic Surgery in Skopje, North Macedonia in the period from February 2021 to February 2022. The study did not include patients with allergy to the used drugs, infection at the portal sites of injection, any previous surgery to the knee, patients with chronic extensive synovitis or gross deformity of the knee (severe varus or valgus knee), as well as those with psychological problems, severe systemic disease, consumption of analgesics or non-steroidal anti-inflammatory drugs within 24 h of surgery, bleeding diathesis or coagulopathy. Evaluation of patients' satisfaction after surgery was done one to three months later by determining the level of satisfaction, pain during surgery, anesthesia-related postoperative complications and preference of this anesthetic technique in the future.

Results: The majority of patients were either very satisfied (84.6%) or satisfied (9.6%) with local anesthesia for knee arthroscopy. Only 1.9% of them were not satisfied at all. Most of the patients reported no pain (80.8%) or mild pain (11.5%) during knee arthroscopy under local anesthesia. Only 1.9% of patients complained of strong or very strong pain during arthroscopy. Of all patients, 51 (98%) had no anesthesia-related problems after surgery except one patient who had redness, pain, swelling and blisters formation on the portal where local anesthetic and adrenaline were previously injected. Most of the patients (96%) reported that they would choose local anesthesia for knee arthroscopy again.

Conclusion: Our study showed that most patients had no pain, were very satisfied and would choose local anesthesia for knee arthroscopy again.

Key Words: *knee arthroscopy; local anesthesia; patients' satisfaction.*

Introduction

Knee arthroscopy is a minimally invasive surgical technique that can be performed under general, regional (spinal or epidural) or local anesthesia. Although local anesthesia for knee arthros-

copy is less preferred compared to regional and general anesthesia, it offers several advantages such as decreased hospital and recovery time, prolonged postoperative analgesia, low cost and rare side effects and complications seen in spinal and general anesthesia such as nausea, vomiting, drowsiness, and urine retention (1). Fear of insufficient anesthesia with patient discomfort and unsuccessfully performed arthroscopy with an increased number of rearthroscopies could be some of the reasons why some orthopedic surgeons do not prefer this type of anesthesia for knee arthroscopy. Studies by Forssblad et al. (2) and Jacobson et al. (3) showed that only 0.9% of the primary arthroscopies under local anaesthesia could not be performed safely due to patient discomfort and that patients with gross knee deformity (severe varus or valgus) as well as those with extensive hypertrophic synovitis of the knee are not good candidates for knee arthroscopy under local anesthesia. A study by Iossifidis (4) showed no discomfort or mild discomfort in 94% of patients during knee arthroscopy under local anesthesia, mostly experienced during knee manipulation and introduction of instruments inside the knee. A study by Inam (5) reported discomfort in 20% of patients where knee arthroscopy under local anesthesia was performed. The satisfaction rate in patients where knee arthroscopy under local anesthesia was performed varies according to the literature. The studies by Maldini (1), Iosifidis (4), Kan-Yip Law (6) and Kozlowski (7) showed that more than 93% of patients were either satisfied or very satisfied with their knee arthroscopy under local anesthesia and agreed to have the same procedure in the future. Opposite to these studies, there are other like those by Inam (5) and Eriksson (8), which showed lower satisfaction rate (70% and 77% retrospectively).

The aim of our study was to evaluate the level of satisfaction in patients after knee arthroscopy under local anesthesia.

Material and methods

The study included 52 patients where arthroscopic knee surgery under local anesthesia was performed in the period from February 2021 to February 2022 at the University Clinic for Orthopedic Surgery in Skopje, North Macedonia. Preoperative assessment included medical history, clinical examination, detailed laboratory investigations, radiography (RTG) and magnetic resonance imaging (MRI) of the knee and electrocardiogram (ECG). Exclusion criteria were: allergy to the used drugs, infection at the portal sites of injection, any previous surgery to the knee, patients with chronic extensive synovitis or gross deformity of the knee (severe varus or valgus knee), psychological problems, severe systemic disease, consumption of analgesics or non-steroidal anti-inflammatory drugs within 24 h of surgery, bleeding diathesis or coagulopathy. Prior to surgery, a document for informed consent was obtained by all patients.

Knee arthroscopy was performed without a tourniquet. Knee portal sites were anesthetized with 10 ml solution of 2% lidocaine with adrenaline 1:200,000 (5 ml at each portal site) and 10 ml of 0.5% bupivacaine with adrenaline plus 4 mg morphine were injected inside the knee. After 15 to 20 minutes, knee arthroscopy was performed. Intravenous sedation with propofol was used in apprehensive patients to manage their anxiety and irritability. In some patients who experienced marked knee pain during the surgery fentanyl (0.05 – 0.15 mg) was also added intravenously.

In order to evaluate patients' perception of the technique, one to three months after the surgery patients were contacted and asked to fill in a questionnaire (Table 1) describing the level of satisfaction, pain during surgery, anesthesia related postoperative complications and preference of this anesthetic technique in the future.

Table 1. Questionnaire for evaluation of patients' satisfaction after knee arthroscopy under local anesthesia

How satisfied were you by the anesthesia during knee arthroscopic procedure? (range 1 – not satisfied at all to 5 – very satisfied)
Did you experience pain during the arthroscopic procedure? (range 1 – no pain to 5 – very strong pain)
Did you have anesthesia-related side effects and complications after the arthroscopic procedure?
Do you prefer local anesthesia for knee arthroscopy in the future?

We used descriptive statistics and multiple regression analysis to assess the impact of age, sex, intraoperative pain, type of procedure, postoperative complications and revision surgery on patient satisfaction. We used XLSTAT Statistical Software for Excel for data analysis. The alpha level was set at 0.05.

Results

Of the 52 patients who underwent knee arthroscopy under local anesthesia in this study, 20 patients (38.5%) were female and 32 (61.5%) were male. The average age of patients was 39.1 years (range 15 – 71). Distribution according to type of performed arthroscopic procedure is shown in Figure 1. Three arthroscopies (5.8%) were revision procedures and the rest were primary procedures. Arthroscopic surgery was successfully performed in 49 (94%) of patients. In 1 patient we had poor visibility because of intra-articular bleeding and in 2 patients it was difficult to access the menisco-capsular part of the medial meniscus due to the tightness of the knee joint. In some patients there was poor visibility caused by inadvertent infiltration of anterior fat pad, but we used shaver to clean it and obtain better visualization. There were no conversions from local to other type of anesthesia during surgery in none of these patients. No side effects of local anesthetics were noted. The average hospital stay was 3.2 hours (range 2 – 5).

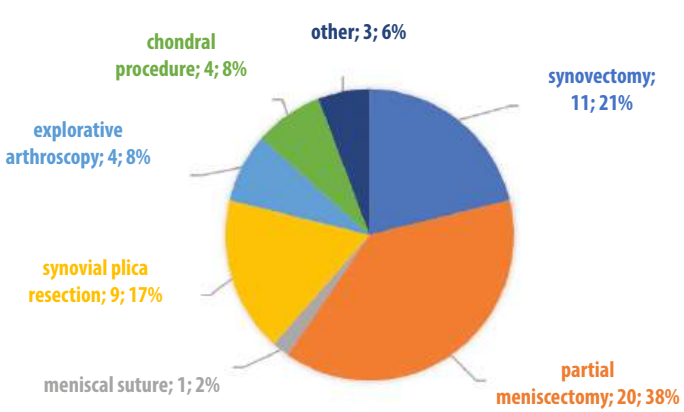

Figure 1. Distribution of performed arthroscopic procedures

Most of the patients were either very satisfied (84.6%) or satisfied (9.6%) with local anesthesia for knee arthroscopy (Table 2). Only 1.9% of them were not satisfied at all.

Table 2. Patients' satisfaction after knee arthroscopy under local anesthesia

Answer	No. of patients	Percentage of patients (%)
1 – not satisfied at all	1	1.9
2 – a little satisfied	0	0
3 – moderately satisfied	2	3.9
4 – satisfied	5	9.6
5 – very satisfied	44	84.6

Most of the patients reported no pain (80.8%) or mild pain (11.5%) during knee arthroscopy under local anesthesia (Table 3). Only 1,9% of the patients complained of strong or very strong pain during arthroscopy.

Table 3. Pain during knee arthroscopy under local anesthesia

Answers	No. of patients	Percentage of patients (%)
1 - no pain	42	80.8
2 - mild pain	6	11.5
3 - moderate pain	2	3.8
4 - strong pain	1	1.9
5 - very strong pain	1	1.9

Of all patients, 51 patients (98%) had no anesthesia-related problems after surgery and only one patient reported problems after the procedure. He had redness, pain, swelling and blisters formation on the portal where local anesthetic and adrenaline were previously injected.

According to the preference of local anesthesia for knee arthroscopy, 50 patients (96%) would choose local anesthesia for knee arthroscopy again in the future and 2 patients (4%) would not choose the same type of anesthesia. One of these patients had very strong pain during the procedure and the second one had moderate pain. None of them experienced anesthesia-related problems after surgery.

Multiple regression analysis showed that only the level of pain significantly affected patient satisfaction by anesthesia ($p<0.0001$), while sex, type of surgical procedure, revision surgery and postoperative complications related to anesthesia did not have significant influence on the satisfaction ($p>0.05$). Pain during surgery was also the main factor that affected patients' willingness to undergo the same type of anesthesia for knee arthroscopy in the future ($p<0.0001$).

These results show that most patients have no pain and are very satisfied with the use of local anesthesia for knee arthroscopy. The level of pain is the main predictor of patient satisfaction.

Discussion

There is no patient that is fully satisfied with any surgical procedure under any anesthesia since each and every patient expects the procedure to be pain- free and he/she wants be able to do

routine work immediately after surgery. Although these expectations in ambulatory surgery under local anesthesia can be fulfilled in majority of patients, there are also patients who are not completely satisfied. Most of the studies (1, 2, 3, 4, 6, 7) showed high patient satisfaction rate after knee arthroscopies under local anesthesia. There are also studies (5, 8) which showed low satisfaction rate (70% and 77% retrospectively) compared to previous studies.

In our study we found high satisfaction rate in patients where knee arthroscopy under local anesthesia was performed. Most of the patients were either very satisfied (84.6%) or satisfied (9.6%) with local anesthesia for knee arthroscopy. Multiple regression analysis showed that the level of pain was the main predictor of patient satisfaction. In our study, most of the patients reported no pain (80.8%) or mild pain (11.5%) during surgery. According to Takahashi et al. (9), in patients where knee arthroscopy under local anesthesia was performed more knee pain was experienced at the time of injection of local anesthetic as well as when synovectomy, anterior cruciate ligament remnant or plica resection was done. In our study, synovectomy was done in 21%, plica resection in 17%, meniscal suture in 2% and anterior cruciate ligament remnant resection in 3.5% of the patients, but the type of surgical procedure did not show significant influence on the level of pain during surgery or patient satisfaction after surgery. This was probably due to the sedation with propofol and analgesia with fentanyl performed in some patients.

In our study, we did not investigate the influence of other factors on patients' satisfaction such as poor communication skills of the operation theatre personnel, poor discipline, noise, increased trafficking, prolonged surgery etc., and this was the limitation of our study.

Conclusion

Our study showed that most patients had no pain and were very satisfied with the use of local anesthesia for knee arthroscopy. The level of pain was the main predictor of patient satisfaction in our study. Intravenous sedation with propofol should be used in apprehensive patients to manage their anxiety and irritability. More studies that investigate the influence of other factors on patients' satisfaction should be performed in the future.

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ORIGINAL ARTICLE *UDK: 616.7:621.315.027.7-057.16*

www.doi.org/10.55302/MJA2484023a

PREVALENCE AND RISK FACTORS OF WORK-RELATED MUSCULOSKELETAL DISORDERS AMONG WORKERS IN HIGH-VOLTAGE TRANSMISSION LINE NETWORK AND SUBSTATIONS

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Abstract

Introduction: There is a high risk of developing work-related musculoskeletal disorders (WMSDs) among workers in high-voltage transmission line network and substations. Most WMSDs are cumulative disorders resulting from repeated exposure to one or more harmful factors over a long period of time.

Aim of the Study: The aim of this study is to determine the occurrence and frequency of symptoms of WMSDs among workers in high-voltage transmission line network and substations.

Material and Methods: This cross-sectional study involves 100 workers from a high-voltage transmission line network and substations, all males aged 20 to 63, classified as electricians - group F06, electricians - group F07 and substation workers. The research methodology includes a standardized questionnaire "Symptoms Survey for Work-Related Musculoskeletal Disorders (WMSDs)". The results obtained are statistically processed by descriptive and analytical methods.

Results: The frequency of symptoms of WMSDs among workers from a high-voltage transmission line network and substations that lasted two or more days in the last year, and was caused by their work is 32% and it refers to pain or discomfort in any region. The most common localizations are determined on the lower back (14%), knee (11%) and shoulder (9%). No upper back pain was registered in any of the subjects. A significantly higher number of electricians reported that their working body position was combined compared to substation workers, and that they often had to reach further from their body compared to substation workers. On the other hand, a significantly higher number of substation workers declared that they do not reach beyond their body compared to electricians. There is no significant difference between substation workers and electricians in terms of performing repetitive movements.

Conclusion: WMSDs are often regularly occurring among workers in high-voltage transmission line network and substations; therefore, it underlines the need for their early detection through preventive medical examinations and application of appropriate measures for protection of workers.

Key Words: *electricians; electrical industry;, musculoskeletal disorders; power lines; preventive measures; substations; substation workers; work capacity.*

Introduction

In order, the electricity produced by power plants and other producers, to reach all consumers, it is necessary to properly transmit it. The transmission of electricity to consumers is carried out through two interconnected systems: the transmission system and the electricity distribution system. The electricity transmission system consists of substations and a high-voltage transmission network, whose main task is to transmit electricity over long distances, sometimes exceeding several hundred kilometers. To accomplish this task, the system operates at voltage levels of 110,000 volts and 400,000 volts. The electricity distribution system is connected to the transmission system. Its task is to deliver electricity to all consumers. It consists of substations and a distribution network of electrical lines, which transmit electricity at various voltage levels depending on the consumers' requirements. These levels range from 110,000 volts to 35,000, 20,000, 10,000, 6,000 volts, and down to 240 volts (1).

Substations are located between the transmission and distribution systems and serve various functions, such as voltage transformation and regulation, acting as switching points in the transmission system, and serving as sources for distribution circuits.

Substation workers are responsible for tasks such as regular visual supervision of high-voltage and medium-voltage equipment across the entire substation, recording voltage and current levels, operating switches and fuses, and documenting technical characteristics, among other duties. The electricians, on the other hand, work on the construction, inspection and maintenance of other electrical power facilities. Their responsibilities include fixing defects both during and outside regular work hours, receiving, processing and organizing work-related documentation, providing data for updating network parameters, inspecting connections and measuring points, reading data from measuring devices, as well as interacting with electricity end users (e.g., replacing meters, reconnecting or disconnecting power, etc.). According to the conducted risk assessment, all these workplaces are classified as workplaces with increased risk.

Physical stress on specific parts of the musculoskeletal system can lead to disorders or injuries. These stresses can vary in nature and intensity, including short-term and intense, prolonged, repetitive (cyclical), or a combination of these. The factors influencing these physical loads are known as ergonomic factors. Ergonomics is a scientific discipline focused on designing work environments and tasks to align with the individual characteristics of workers. Ergonomics integrates knowledge from various scientific fields, including physiology, biomechanics, psychology, anthropometry, industrial hygiene and kinesiology. By adapting tasks, tools and equipment to the worker's needs and characteristics, physical stress on the body can be significantly reduced, minimizing the risk of work-related musculoskeletal disorders. For electricians, critical ergonomic factors include body posture, repeated application of force, the distance from the body at which tasks are performed, and the position and movement of joints (2).

Musculoskeletal disorders (MSDs) encompass a wide range of inflammatory and degenerative conditions affecting muscles, tendons, nerves, joints, ligaments and associated blood vessels (3). The term "disorder" reflects the multifactorial nature of these conditions, which do not fit neatly into the categories of "disease" or "injury". The health effects of MSDs vary widely in severity,

from mild discomfort or moderate pain that does not significantly impact daily life or work, to severe cases where pain and functional impairments make even basic activities difficult or impossible (4). When MSDs are caused or worsened by work conditions or the immediate environment in which work is performed, they are classified as work-related musculoskeletal disorders (WMSDs). Most WMSDs are cumulative, developing from repeated and prolonged exposure to one or more risk factors encountered during work activities and tasks (5).

Electricians and substation workers are exposed to various occupational hazards that contribute to the prevalence of musculoskeletal disorders among them. For substation workers, prolonged sitting is a significant factor, while electricians often face heavy physical tasks, poor posture, improper material handling, and changing weather conditions during fieldwork (6).

A significant amount of data confirms the harmful effects of specific occupational risks on the health of exposed workers, particularly electricians and substation workers, with special attention given to their impact on the musculoskeletal system. However, in our country, there are few studies examining the harmful effects of these occupational risks on this group of workers (7).

This research was motivated by the need to assess the extent to which occupational hazards faced by electricians and substation workers affect the musculoskeletal system and contribute to symptoms of work-related musculoskeletal disorders.

Objective of the Study

The main objective of this study is to determine the occurrence and frequency of symptoms of WMSDs among workers in the high-voltage transmission network and substations.

Material and Methods

Study Design and Setting

This is a cross-sectional study conducted under company's conditions during October–November 2021, coinciding with the regular preventive medical examinations of employees at an electricity distribution company. The study is based on data collected through interviews using a standardized and adapted questionnaire.

Subjects - Study Sample

The study includes workers from a high-voltage transmission network and substations from a company that distributes electricity from the producer to end consumers. All respondents were informed about the purpose and methodology of the research and verbal and written consent was obtained from them to participate in the research.

The research group consisted of 100 workers from high-voltage transmission network and substations, all male, aged 20-63 years. Based on their work tasks, they were classified into three groups: electricians - group F06, electricians - group F07, and substation workers (dispatchers).

Inclusion criteria: workers from the high-voltage transmission network and substations who spend all their working time at their current workplace and are over 18 years of age.

Exclusion criteria: workers from the high-voltage transmission network and substations who are under the age of 18 or over 65 years.

Questionnaire

For this study, was used a "Questionnaire on Symptoms of WMSDs". It was based on the standardized "Symptoms Survey for Work-Related Musculoskeletal Disorders" developed by the Canadian Centre for Occupational Health and Safety (CCOHS) (8), which was translated into Macedonian. Several additional questions were also included, such as initials, age, gender and place of residence.

The standardized questionnaire on symptoms of WMSDs, developed by CCOHS, consists of 46 questions divided into two parts. The first part, a general health survey, includes 10 questions and a diagram. The questions cover topics such as the current occupation, main work tasks and their duration, body posture, frequently used tools, the need to reach away from the body, whether objects or tools are often held above shoulder height or near the floor, the presence of repetitive movements, the most difficult work tasks, and any recent changes in work (e.g., tasks or tools). The diagram illustrates the body parts, and respondents are asked to mark areas where pain or discomfort lasting two or more days occurred in the past year due to their current work, excluding any pain related to traumatic injuries.

Statistical Analysis

Data from the questionnaire were entered electronically into Microsoft Excel 2007. The data obtained were processed with descriptive and inferential methods through the statistical program Statistica for Windows release 7. The databases were created using specific computer application programs for that purpose (MS Excel).

Continuous variables are expressed as mean values with standard deviation, and nominal variables as absolute numbers and percentages. The statistical processing of the data is performed with descriptive-statistical and inferential-statistical methods. Descriptive-statistical processing consists of tabular presentation of statistical series according to defined variables.

From the inferential-statistical analysis, the following methods were applied: structure analysis with measures of central tendency (average, median and mode) and measures of statistical dispersion (standard deviation and standard error), as well as analysis of relationships between separate statistical series with Pearson'sχ^2 test (or Fisher's exact test) for the attributive, that is, the t-test for independent samples for the numerical series. Statistical significance was determined for a p value of less than 0.05.

Results

Table 1. Percentage distribution of respondents by demographic characteristics (gender, age) and job characteristics (profile, work experience at the current workplace and night shift).

Variable		**Respondents (n=100)**
Gender	Male	100 (100%)
	Female	0 (0%)
Age (yrs.)		51.4 ± 10.1
Rank (yrs.)		20 - 63
Work experience at the current workplace (yrs.)		23.7± 11.1
Rank (yrs.)		1-41
Work profile	Substation workers	31 (31%)
	Electricians group F06	34 (34%)
	Electricians group F07	35 (35%)
Night shift	yes	98 (98%)
	no	2 (2%)

Numerical data are expressed as mean value with standard deviation, frequencies as number and percentage of study subjects with certain variables.

According to the data in Table 1, the average age of the respondents is 51.4 ± 10.1 years (range: 20–63 years), while the average work experience in the current position is 23.7 ± 11.1 years (range: 1–41 years). All respondents are male (100%), and 98 (98%) work night shifts. Regarding job profiles, 31 respondents (31%) work as substation workers, 34 (34%) are in the position of electrician group F06, and 35 (35%) hold the position of electrician group F07.

Table 2. Distribution of the examined groups by age.

Age (years)	**Work profile**							
	Substation workers (n=31)		Electricians F06 (n=34)		Electricians F07(n=35)		Total (n=100)	
	n	%	n	%	n	%	n	%
20 - 29 yrs.	/	/	7	20.6	1	2.9	8	8
30 - 39 yrs.	/	/	2	5.9	/	/	2	2
40 - 49 yrs.	2	6.4	9	26.5	6	17.1	17	17
50 - 59 yrs.	22	71	13	38.2	23	65.7	58	58
60 – 64yrs.	7	22.6	3	8.8	5	14.3	15	15

Data are given as number and percents of subjects with certain variable.

The table shows that the majority of respondents belong to the 50–59 age group (58%), while the fewest respondents are in the 30–39 age group (2%). Most of the substation workers are in the 50–59 age group (71%), as are the majority of electricians in group F07 (65.7%). Among electricians in group F06, the largest group is also in the 50–59 age range (38.2%). Notably, there are no substation workers in the 20–39 age range, and no electricians in group F07 in the 30–39 age range.

Table 3. Distribution of the examined groups by total work experience in the current position.

Work experience (years)	Work profile							
	Substation workers (n=31)		Electricians F06 (n=34)		Electricians F07(n=35)		Total(n=100)	
	n	%	n	%	n	%	n	%
0-9 yrs.	/	/	10	12	2	5.7	12	12
10-19yrs.	9	29	3	14	2	5.7	14	14
20-29 yrs.	10	32.3	11	37	16	45.7	37	37
30 - 39 yrs.	12	38.7	8	35	15	42.9	35	35
40 - 41 yrs.	/	/	2	2	/	/	2	2

Data are given as number and percents of subjects with certain variable.

From the table, it can be concluded that the majority of respondents have between 20–29 years of work experience at the current workplace (37%), while the fewest respondents belong into the 40–41 years of work experience group (2%). Most of the substation workers have 30–39 years of work experience (38.7%). Among electricians in group F06, the largest group has 20–29 years of experience (32.4%), while among electricians in group F07, the majority also have 20–29 years of experience (45.7%).

Table 4. Distribution of the examined groups by their working body positions.

How is your working position of the body?	Work profile								
	Substation workers (n=31)		Electricians F06 (n=34)		Electricians F07(n=35)		Total (n=100)		p-value (p<0.05)
	n	%	n	%	n	%	n	%	
Combined	4	12.9	25	73.5	25	71.4	54	54	**0.0017**
Sedentery	27	87.1	/	/	/	/	27	27	N/A*
Standing	/	/	9	26.5	10	28.6	19	19	N/A*

Data are given as number and percents of subjects with certain variable. *Tested by chi-square test or Fisher's exact test where appropriate. *N/A - non applicable.

The data show that a significantly larger proportion of electricians (73.5% in Group F06 and 71.4% in Group F07) reported having a combined working body position compared to substation workers (12.9%) ($p = 0.0017$).

Table 5. Distribution of the examined groups according to whether they often have to reach beyond their body.

Do you often have to reach beyond your body?	Work profile								
	Substation workers (n=31)		Electricians F06 (n=34)		Electricians F07(n=35)		Total (n=100)		p-value (p<0.05)
	n	%	n	%	n	%	n	%	
Yes	6	19.4	26	76.5	26	74.3	58	58	**0.0074**
No	25	80.6	8	23.5	9	25.7	42	42	**0.0097**

Data are given as number and percents of subjects with certain variable. *Tested by Chi-square test or Fisher's exact test where appropriate.

The data indicate that a significantly higher proportion of electricians (76.5% in Group F06 and 74.3% in Group F07) reported often reaching beyond their body compared to substation workers (19.4%) (p = 0.0074). Conversely, a significantly larger proportion of substation workers (80.6%) reported not reaching beyond their body compared to electricians (23.5% in Group F06 and 25.7% in Group F07) (p = 0.0097).

Table 6. Distribution of the examined groups according to whether they often hold objects or tools above shoulder height or near the floor.

Do you often hold objects or tools above shoulder height or near the floor?	Work profile								
	Substation workers (n=31)		Electricians F06 (n=34)		Electricians F07 (n=35)		Total (n=100)		p-value (p<0.05)
	n	%	n	%	n	%	n	%	
At body height	28	90.3	10	29.4	13	37.1	51	51	0.010
Above shoulder height	3	9.7	14	41.2	20	57.2	37	37	0.025
Near the floor	/	/	3	8.8	/	/	3	3	N/A*
Combined	/	/	7	20.6	2	5.7	9	9	N/A*

Data are given as number and percents of subjects with certain variable. *Tested by Chi-square test or Fisher's exact test where appropriate. *N/A – non applicable.

There is a significant difference in holding tools at body height between substation workers (90.3%) and electricians (29.4% in Group F06 and 37.1% in Group F07) (p = 0.010). Similarly, a significant difference is observed in holding tools above shoulder height, with electricians (41.2% in Group F06 and 57.2% in Group F07) reporting this more frequently than substation workers (9.7%) (p = 0.025).

Table 7. Distribution of the examined groups according to whether they make repetitive movements.

Do you make repetitive movements?	Work profile								
	Substation workers (n=31)		Electricians F06 (n=34)		Electricians F07(n=35)		Total (n=100)		p-value (p<0.05)
	n	%	n	%	n	%	n	%	
Yes	21	67.7	32	94.1	30	85.7	83	83	N/S**
No	10	32.3	2	5.9	5	14.3	17	17	N/S**

Data are given as number and percents of subjects with certain variable. *Tested by Chi-square test or Fisher's exact test where appropriate. **N/S - nonsignificant.

Table 7 shows that 83% of the respondents reported making repetitive movements, while only 17% reported not making them. Among the groups, 67.7% of the substation workers, 94.1% of the electricians in group F06, and 85.7% of the electricians in group F07 indicated they perform repetitive movements during work.

Table 8. Distribution of the examined groups according to whether they had pain or discomfort that lasted two or more days and was caused by their work in the last year.

In the last year, have you had pain or discomfort that lasted two or more days and was caused by your work?		Work profile								
		Substation workers (n=31)		Electricians F06(n=34)		Electricians F07 (n=35)		Total (n=100)		p-value (p<0.05)
		n	%	n	%	n	%	n	%	
In at least one region	No	25	80.6	24	70.6	19	54.3	68	68	N/S**
	Yes	6	19.4	10	29.4	16	45.7	32	32	N/S**
Neck	No	30	96.8	34	100	35	100	99	99	N/S**
	Yes	1	3.2	0	0	0	0	1	1	N/A*
Shoulder	No	30	96.8	32	94.1	29	82.9	91	91	N/S**
	Yes	1	3.2	2	5.9	6	17.1	9	9	N/S**
Elbow	No	31	100	34	100	34	97.1	99	99	N/S**
	Yes	0	0	0	0	1	2.9	1	1	N/A*
Forearm	No	31	100	34	100	33	94.3	98	98	N/S**
	Yes	0	0	0	0	2	5.7	2	2	N/A*
Wrist	No	30	96.8	31	91.2	32	91.4	93	93	N/S**
	Yes	1	3.2	3	8.8	3	8.6	7	7	N/S**
Upper back	No	31	100	34	100	35	100	100	100	N/S**
	Yes	0	0	0	0	0	0	0	0	N/A*
Lower back	No	29	93.6	29	85.3	28	80	86	86	N/S**
	Yes	2	6.4	5	14,7	7	20	14	14	N/S**
Knee	No	29	93.6	33	97.1	27	77.1	89	89	N/S**
	Yes	2	6.4	1	2.9	8	22.9	11	11	N/S**
Foot	No	30	96.8	33	97.1	33	94.3	96	96	N/S**
	Yes	1	3.2	1	2.9	2	5.7	4	4	N/S**

Data are given as number and percents of subjects with certain variable. *Tested by Chi-square test or Fisher's exact test where appropriate. *N/A – non applicable** N/S – nonsignificant.

According to the data from the table, 32% of respondents experienced musculoskeletal pain or discomfort during the past year that lasted for at least two consecutive days and was attributed to their work. The most commonly affected regions were the lower back (14%), knee (11%), and shoulder (9%). Notably, none of the respondents reported pain or discomfort in the upper back. Additionally, no electricians in groups F06 or F07 reported neck pain, and no substation workers or electricians in group F06 reported pain in the elbow or forearm.

Table 9. Distribution of examined groups according to the assessment of work ability at the current workplace.

Assessment of work ability		Work profile							
		Substation workers (n=31)		Electricians F06 (n=34)		Electricians F07(n=35)		Total (n=100)	
		n	%	n	%	n	%	n	%
Able to work without restrictions		30	96.8	33	97.1	32	91.3	95	95
Able to work with restrictions	Do not work at height and heavy physical work	/	/	/	/	1	2.9	1	1
	Do not work night shifts	1	3.2	1	2.9	/	/	2	2
	Do not do heavy physical work	/	/	/	/	1	2.9	1	1
	Do not lift weights	/	/	/	/	1	2.9	1	1
Unable to work		/	/	/	/	/	/	/	/

Data are given as number and percents of subjects with certain variable.

According to assessment of work ability, 95% of all respondents are able to work without restrictions, and just 5 respondents (5%) are able to work with restrictions. None of the respondents were classified as unable to work.

Discussion

The Occupational Safety and Health Administration (OSHA) defines musculoskeletal disorders as a broad spectrum of inflammatory and degenerative changes that affect the musculoskeletal system as well as the corresponding blood vessels and usually develop gradually over several weeks, months or years as a result of exposure to one or more risk factors that cause their appearance or worsening, and not as a result of a single accident or injury (3).

According to the Census of Fatal Occupational Injuries sponsored by the U.S. Bureau of Labor Statistics, in 2020, 126 workers died due to exposure to electrical energy, representing 5.3% of all incidents due to contact with electricity. This represents a decrease of 24% from the deaths reported in 2019 and the lowest annual number of fatal electrical injuries in the nearly 30 years

of data collected by CFOI. Non-fatal electrical injuries led to 2,220 hours of absenteeism during 2020 (9).

According to the U.S. National Safety Council (NSC), in 2020, 17% of all fatal workplace injuries, or 805 deaths, were caused by slips, trips and falls. Additionally, 211,640 workers sustained injuries that led to several days of absence from work (10). In the same year, the U.S. Bureau of Labor Statistics reported that 18% of the total 1,176,340 non-fatal work-related injuries resulting in several days of absenteeism were due to slips, trips and falls (11).

In our study, no fatal or non-fatal injuries caused by electricity were recorded in the past year. Furthermore, none of the respondents reported any workplace accidents or injuries during this period.

In a study conducted by Moriguchi et al. in Brazil, 26 out of 30 respondents (87%) employed as electricians reported experiencing discomfort in at least one body region. The most commonly affected areas were the shoulder, spine and knee. Among the 13 participants who reported spinal discomfort, 62% experienced pain in the lumbar region, 31% in the thoracic region, and 15% each in the neck and gluteal regions. The shoulder was identified as the most commonly affected area overall (12).

Similarly, a study by Hunting et al. in the USA surveyed 308 relatively young workers, 86% of whom were electricians. The study aimed to assess the prevalence of symptoms in the neck, shoulder, elbow, wrist, back and knee over the previous year. The results revealed a high prevalence of symptoms, with many participants reporting discomfort occurring more than three times or lasting for over a week. About half of the respondents experienced discomfort in the back or wrist, while only 15% reported issues with the elbow (13).

In 2012 study by Tankovic and Suljic-Beganovic, conducted on 246 respondents employed in an electric company in Novi Travnik (over 80% of whom were male), 10.97% were diagnosed with musculoskeletal disorders. In a follow-up study in 2013, which included 157 respondents (99.37% male), 17.83% were found to have diseases of the locomotor system (14).

In another study by Ćeranić et al. (2003), which aimed to assess the health status and common health issues among electricians in Novi Pazar, Republic of Serbia, musculoskeletal disorders were identified in 30 out of 86 electricians (55.5%) (15).

Our research revealed that 32% of the total respondents reported experiencing musculoskeletal pain lasting at least two days in one or more body regions in the past year. The most common areas affected were the lower back (14%), knee (11%) and shoulder (9%). Among substation workers, 19.4% declared that they have pain or discomfort in at least one region, and according to the frequency, the pain/ discomfort in the lower back and knee (6.4% respectively) stands out. Among the electricians in group F06, 29.4% of the respondents stated that they have pain or discomfort in at least one region, and according to the frequency, the pain/ discomfort in the lower back (14.7% of the respondents) stands out. Among the electricians in group F07, 45.7% of the respondents declared that they have pain or discomfort in at least one region, and according to the frequency, the pain/discomfort in the knee (22.9%), the lower back (20%) and in the shoulder (17.1%).

Just in England, it was estimated that in 2014/ 2015, 553,000 workers suffered from musculoskeletal disorders caused or aggravated by work (current or previous). Oot of these, about

233,000 suffered from back pain, 233,000 had neck and upper limb problems, and 97,000 had leg problems. For the same period, it was determined that 9.5 million working days were lost due to musculoskeletal disorders caused or aggravated by work (16).

In our study, a total of 77 workdays were lost due to pain or discomfort that caused subjects to take days off.

Regarding the assessment of work ability, 95 out of a total of 100 respondents (95%) were assessed as able to work without restrictions. 96.8% of substation workers were rated as capable of working without restrictions, with only one substation worker having a restriction on working night shifts. 97.1% of electricians in group F06 are rated as capable of working without restrictions, and one respondent was restricted from working night shifts. On the other hand, 91.3% of electricians in group F07 were rated as able to work without restriction, and the restriction of not doing heavy physical work, not lifting weights and not working at height and heavy physical work has one respondent for each. None of the respondents were assessed as unable to work.

Conclusion

Taking into account the purpose of this research and based on the analysis of the obtained results, it can be concluded that the frequency of work-related musculoskeletal disorder (WMSD) symptoms among workers from the high-voltage transmission network and substations, which lasted for two or more days in the past year and were caused by their work, is 32%. The most common affected areas are the lower back, knee and shoulder. Key risk factors in the work environment associated with the occurrence of musculoskeletal disorders among this group of workers include prolonged standing and sitting, lifting and carrying loads, repetitive movements, unnatural body positions, pressure on certain body parts and vibrations. Additionally, the rhythm and organization of the work process, work monotony, adverse weather conditions and psychosocial factors play significant roles in the development of musculoskeletal disorders. Based on these findings, there is a clear need to develop and implement a strategy for preventing musculoskeletal disorders among workers in the high-voltage transmission network and substations in Republic of North Macedonia, aimed at improving their health and work ability.

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ORIGINAL ARTICLE *UDK: 616.24-031.4-085.816.2:616.24-006.6-089.87-06*

www.doi.org/10.55302/MJA2484035k

ONE-LUNG VENTILATION AND ITS ROLE IN POSTOPERATIVE PULMONARY MORBIDITY FOLLOWING LUNG SURGERY

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Abstract

Introduction: On one hand, one-lung ventilation is a method intended to improve surgical access while guaranteeing enough oxygenation and is often required for thoracic surgery. On the other hand, one-lung ventilation increases the risk of pulmonary complications both during and after surgery. Because they raise morbidity, lengthen hospital stays and may have negative consequences, these complications are clinically significant. Our evaluation's goal was to determine the frequency and predictors of these complications, which are crucial for enhancing patient care and maximizing surgical results.

Material and Methods: In this retrospective analysis, we assessed 80 elective patients who had one-lung ventilation and lung resection as a result of cancer. The anesthetic protocol for all patients followed a standardized approach, ensuring consistency in perioperative management. The defined inclusion and exclusion criteria were used to determine which patients were included in the study. We looked at pulmonary complications after surgery, such as respiratory insufficiency, pneumonia and atelectasis in the first week after surgery.

Results: The study included 80 patients, with a postoperative pulmonary complication rate of 30.0%. Atelectasis, pneumonia and respiratory failure were the most commonly observed complications, with pneumonia being the leading cause. Pulmonary complications were significantly more prevalent in patients undergoing lobectomy (79.2%) and in those over 60 years of age (75.0%). Male gender, higher BMI (>25), reduced FEV_1% (<70) and FVC (<70) significantly increased the risk of pulmonary complications. Although oxygen saturation (SpO_2%) dropped during one-lung ventilation, this was more pronounced on the right side, though without statistical significance.

Conclusion: It is very common for pulmonary complications to happen after thoracic surgery. This is mostly because of the physiological changes that happen in the operating room and the use of one-lung ventilation. These factors significantly impact respiratory mechanics and gas exchange, underscoring the need for vigilant perioperative monitoring and tailored management strategies to mitigate these complications.

Keywords: *atelectasis; one-lung ventilation; pneumonia; pulmonary complications; respiratory failure*.

Introduction

Anesthesia in thoracic surgery is inconceivable without the use of one-lung ventilation (OLV), which facilitates optimal surgical exposure. Typically achieved through the insertion of a double-lumen endotracheal tube or a bronchial blocker, OLV allows ventilation of a single lung while maintaining perfusion in both. But this method makes big changes to the lungs' physiology, like a ventilation/perfusion (V/Q) mismatch and intrapulmonary shunting, which can compromise oxygenation and raise the risk of pulmonary complications like atelectasis, pneumonia, and respiratory failure after surgery (1).

Multiple factors, including proper tube placement, the use of a bronchoscope, the patient's underlying respiratory status, body positioning during surgery, the type of surgical procedure, ventilator settings and the anesthesiologist's expertise in thoracic surgery, influence the risk of pulmonary complications during OLV (2,3). Hypoxemia, which is a drop in arterial oxygen saturation (SpO_2) below 90% as measured by pulse oximetry, may also happen during OLV, making patients even more likely to have pulmonary complications and bad outcomes after surgery (4).

Patients undergoing thoracic surgery often have pre-existing pulmonary and systemic comorbidities, such as chronic obstructive pulmonary disease (COPD), coronary artery disease, or anemia. These conditions, combined with the physiological challenges of OLV, can increase the likelihood of complications, including prolonged mechanical ventilation, pneumonia, atelectasis and acute respiratory distress syndrome (ARDS). Such complications can significantly compromise recovery and increase morbidity and mortality rates (5).

Preoperative risk assessment is crucial for identifying patients at high risk of developing postoperative pulmonary complications. Functional evaluations, including spirometry and arterial blood gas analysis, remain essential tools to assess pulmonary reserve and gas exchange capacity. Nonetheless, preoperative testing is a cornerstone of thoracic surgical planning to optimize patients' outcomes (6-9). Our evaluation's goal was to determine the frequency and predictors of these pulmonary complications, which are crucial for enhancing patient care and maximizing surgical results.

Material and Methods

The Clinic for Thoracic and Vascular Surgery in Skopje conducted this retrospective/ prospective observational study over the course of a year (2022–2023). Eighty patients underwent standard lung resection procedures (segmentectomy, lobectomy, bilobectomy and pneumonectomy) to treat lung cancer. These procedures were done with a double-lumen endotracheal tube (DLT) and general anesthesia.

Patients who met the ASA I–III classification, had an ejection fraction (EF) of at least 50%, hemoglobin levels of at least 90g/L, and had not been through any chemotherapy or radiation cycles before were eligible to take part. Patients with endocrinopathies, pathological arrhythmias, metastatic abnormalities in the contralateral lung, or significant pre-existing pulmonary

impairment, such as a FEV_1 of less than 40% before surgery, were not eligible. The clinical ethics council granted ethical permission for the trial, and each participant gave their informed consent.

Every patient had the same anesthetic regimen. The thorough preoperative examinations included the patient's history, a clinical examination that focused on the respiratory and cardiovascular systems, a measurement of body weight and height, a measurement of non-invasive blood pressure (NIBP), and a computation of the optimal body mass index (BMI). A 12-lead electrocardiogram (ECG), preoperative echocardiogram, routine laboratory testing, imaging examinations such as chest computed tomography (CT), and a baseline pulmonary function assessment were among the other assessments. We performed standard preoperative procedures, including premedication with 5mg diazepam tablets and fasting.

We monitored all patients intraoperatively with standard parameters such as an arterial line, NIBP, pulse oximetry and ECG. We used an epidural catheter to provide postoperative analgesia. We used a consistent protocol to induce general anesthesia, administering 2mg midazolam, 3g/kg fentanyl, and 1-2mg/kg propofol. We then administered rocuronium bromide (0.6mg/kg) to relax the muscles and facilitate the placement of the DLT. We used auscultation and bronchoscopy to verify the correct positioning of the DLT.

We used a continuous infusion of propofol (6–7mg/kg/h), intermittent fentanyl (2g/kg), and rocuronium (0.3mg/kg/h) to maintain anesthesia during the procedure. Tidal volumes of 7ml/kg of ideal body weight during two-lung ventilation (TLV) were lowered to 5ml/kg during one-lung ventilation (OLV), with PEEP set to 5cmH2O and a FiO_2 of 0.5. We modified these ventilation parameters based on the stage of operation. We adjusted other ventilatory parameters, such as respiratory rates and inspiratory-to-expiratory ratios, as needed to maximize oxygenation.

Within the first 7 days postoperatively, we focused particularly on evaluating, tracking and recording postoperative pulmonary complications, such as respiratory failure requiring intubation and mechanical ventilation, pneumonia as defined by the European Perioperative Clinical Outcome (EPCO) criteria, and atelectasis. A decrease in peripheral oxygen saturation (SpO_2) to less than 90%, as determined by pulse oximetry with a FiO_2 of 0.5, was referred to as hypoxemia. We assessed pulmonary problems using clinical and radiological results.

In order to reduce the risk of unfavorable outcomes, this study sought to improve the preoperative and perioperative care of patients undergoing thoracic surgery by identifying characteristics linked to a higher incidence of complications.

Results

The study included 80 patients. The characteristics of the cohort are presented in Table 1. The percentage difference between genders was statistically significant and a significant association was observed between gender and lung malignancy at $p<0.05$. Male gender increased the likelihood of developing lung malignancy by four times (OR=4.333, 95% CI [2.12577–8.8337]). The average age of all participants was 62.9±8.2 years, ranging from 41 to 80 years. A total of 64.0% of participants were older than 64 years. The average age among male participants was 63.1±8.1 years, while the average age among female participants was slightly lower at 61.7±9.0 years.

The difference in mean values between genders was not statistically significant ($p>0.05$). The percentage difference between the two BMI groups was not statistically significant as well ($p>0.05$).

Table 1. Characteristics of the cohort.

Value	Age		Gender		BMI	
	£ 60 years	³ 60 years	Male	Female	³25	£25
%	37.5	62.5	81	19	56.25	43.75

We also analyzed the distribution of patients according to the ASA classification and comorbidities presented in Figure 1 and 2.

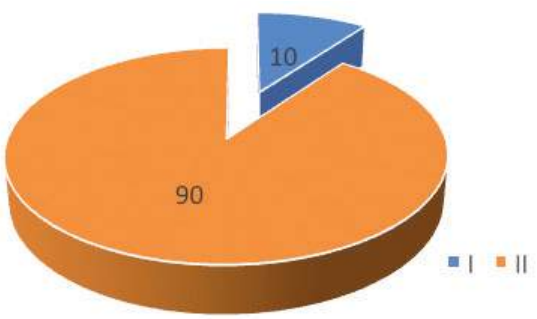

Figure 1. Graphical representation of the percentage distribution of ASA classifications.

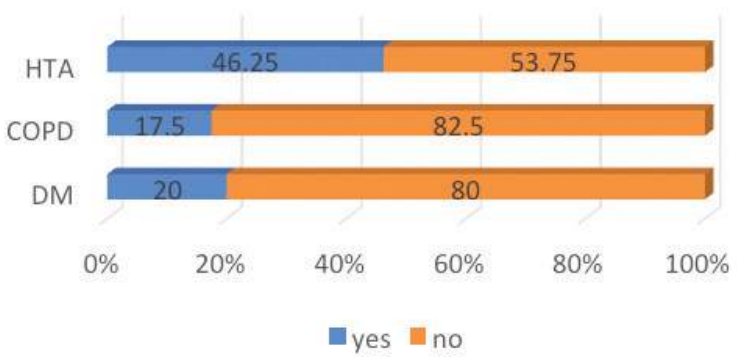

Figure 2. Graphical representation of the percentage distribution of diabetes mellitus (DM), hypertension (HTN) and chronic obstructive pulmonary disease (COPD).

Table 2 presents the characteristics of both the type of surgery and the surgical side. The percentage difference between lobectomy and other types of surgery is significant at $p<0.05$. The right side was affected in significantly higher percentage, with a significant difference at $p<0.05$. The average duration of single-lung collapse during surgery was 125.9±54.7 minutes, ranging from 20 to 285 minutes. In 50% of the patients, the duration of single-lung collapse during surgery exceeded 120 minutes, with a median of 120 minutes and an interquartile range (IQR) of 100–150 minutes.

Table 2. Characteristics of the surgery.

Surgery	**No**	**%**	**No**	**%**
Lobectomy	38	67.8	19	79.2
Pneumonectomy	11	19.6	0	0
Bilobectomy	4	7.1	3	12.5
Segmentectomy	3	5.4	2	8.3
Side of surgery				
Right	32	57.2	15	62.5
Left	24	42.8	9	37.5

The incidence of postoperative pulmonary complications in thoracic interventions with OLV in this study was 30.0%. The occurrence of complications, including atelectasis, pneumonia and postoperative respiratory insufficiency requiring mechanical ventilation, was observed in 30.0% of the patients, while 70.0% of the patients showed no complications. The percentage difference between patients with and without complications is significant at $p<0.05$ (Figure 3.).

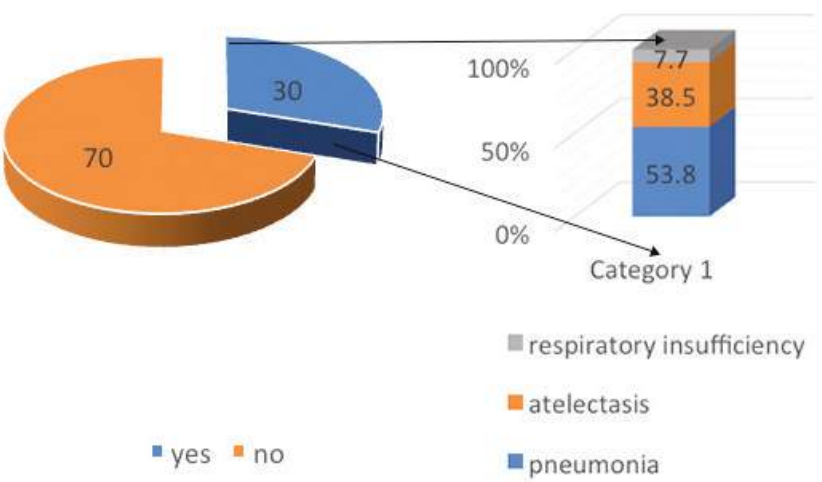

Figure 3. A graphical representation of the occurrence of complications and their types.

The percentage difference observed between pneumonia and atelectasis versus respiratory insufficiency is significant for p<0.05. The profile of patients experiencing postoperative complications during thoracic interventions with one-lung ventilation is significantly skewed towards males (87.5%) compared to females (12.5%), with a statistically significant difference of p<0.05. Postoperative pulmonary complications during thoracic interventions with OLV are observed in 75.0% of the patients aged over 60 years. The percentage difference compared to patients under 60 years old is statistically significant for p<0.05. Patients with complications have a mean age of 65.7±8.1 years. Complications are significantly more common in 79.2% of the patients who underwent lobectomy compared to other types of surgery. Among patients with complications, 65.4% had FEV_1% and FVC% values greater than or equal to 70. SpO2 % values were below 90 in 32.3% of the patients with complications, and 91.1% were smokers. An association was observed between the occurrence of complications and BMI (normal vs. overweight) for p<0.05.

A higher BMI above 25 (overweight) increases the likelihood of complications during thoracic interventions with one-lung ventilation by three times (OR=3.0, 95% CI [1.1138–9.0804]). For the other variables - gender, age, type of surgery, side, ASA classification, SpO2%, smoking, diabetes mellitus, COPD, hypertension and duration of lung collapse, no significant associations with the occurrence of complications were observed for $p>0.05$ in this group of patients.

Figure 4 presents the results we obtained for the oxygen saturation in our cohort of patients. A nonsignificant greater drop in oxygen saturation was observed during right-sided operations compared to left-sided ones. The values of oxygen saturation (SpO_2%) were lower on the right sided surgeries ($P<0.05$).

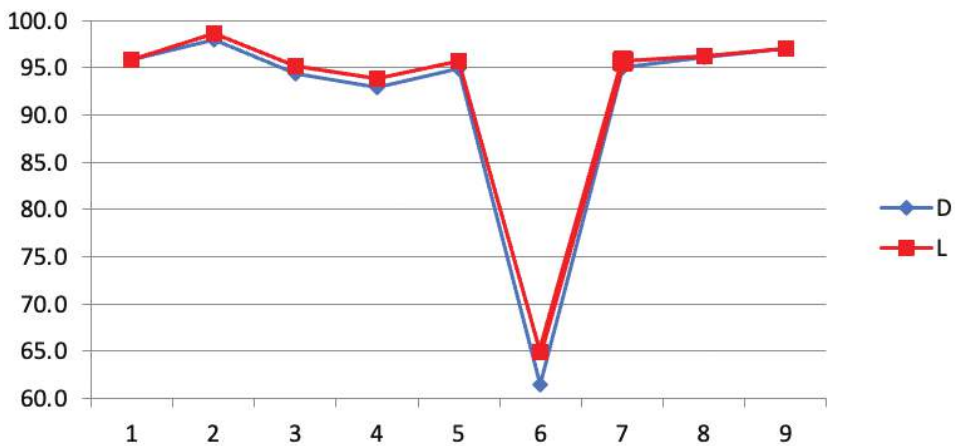

Figure 4. Line diagram of average SpO_2% values by side of the surgery.
*D - right, L – left.

Discussion

In our study, we observed a postoperative pulmonary complication (PPC) rate of 30.0%, aligning closely with findings reported in previous literature. The most common complications in our cohort were pneumonia (17.5%) and atelectasis (12.5%), with respiratory failure, necessitating mechanical ventilation, occurring in 2.5% of the patients. These findings emphasize the critical nature of PPC as significant contributors to postoperative morbidity. In one of the largest multicenter randomized clinical trials, 1,170 patients scheduled for lung resection were included, focusing, among other things, on postoperative complications depending on the type of ventilation (10,11). Pulmonary complications were reported in 40.5% to 42.8% of the patients, depending on the ventilation parameters. This is a higher incidence than observed in our study; however, Park et al. also considered hypoxemia (SpO_2 <90%) and empyema as postoperative complications, which were not included in our study (12). The higher reported incidence may also be attributed to differences in patients' demographics, surgical techniques, or intraoperative ventilation strategies employed across the two studies.

In the study by Fernandez et al., which analyzed 189 patients after lung resection (13), the incidence of PPC was reported at 34.3%, with pneumonia being the dominant complication, affecting 29.7% of the patients. This aligns with findings that pneumonia often represents the leading cause of morbidity following thoracic surgeries due to altered lung mechanics, immu-

nosuppression and impaired mucociliary clearance in the postoperative period. François and colleagues, in a study involving 266 patients, reported a slightly lower incidence of postoperative pulmonary complications, documented at 25% (14). This variation in incidence highlights the importance of standardized definitions and methodologies when assessing postoperative outcomes in thoracic surgery.

In our study, the incidence of postoperative pulmonary complications was 30.0%, aligning with previous studies. The postoperative complications analyzed in our study included atelectasis, pneumonia and respiratory failure (i.e., the need for mechanical ventilation), defined according to EPCO criteria (15). Consistent with the study by Fernandez et al., our findings show that pneumonia is the most common complication following lung surgery. In our cohort, pneumonia occurred in 17.5% of the patients, which aligns with data from the literature (16-18). This finding underscores the critical need for early recognition and management of pneumonia to improve postoperative outcomes, especially in high-risk patient groups.

Atelectasis was observed in 12.5% of patients in our study. This complication, although common, is often transient and resolves with appropriate postoperative care, including physiotherapy and respiratory support. However, persistent atelectasis can significantly impact postoperative recovery, particularly in patients with pre-existing pulmonary conditions or obesity (19). Development of atelectasis has been reported as one of the most frequent respiratory complications during the perioperative period, affecting nearly 90% of the patients (20,21). The persistence of atelectasis beyond the immediate postoperative phase may exacerbate local inflammation, impair gas exchange, and predispose patients to secondary infections, including pneumonia (22). Preventive strategies, such as the use of recruitment maneuvers, optimal intraoperative ventilation and early postoperative mobilization, remain crucial in minimizing the incidence and severity of atelectasis.

Respiratory failure, defined as the need for mechanical ventilation postoperatively, was noted in 2.5% of our patients. While less common than other complications, respiratory failure is associated with significant morbidity and prolonged hospitalization. Factors contributing to respiratory failure include inadequate pulmonary reserve, prolonged surgical duration, and intraoperative events such as hypoxia or hemodynamic instability. Identifying at-risk patients preoperatively and optimizing their condition can play a pivotal role in reducing this complication.

In literature, the incidence of PPC after lung resection varies widely across studies. Differences in patients' selection, comorbidities, surgical techniques and perioperative management likely contribute to this variability. For instance, studies utilizing advanced surgical techniques such as video-assisted thoracoscopic surgery (VATS) often report lower complication rates compared to traditional open thoracotomy approaches (23-27). Similarly, enhanced recovery protocols, including early ambulation and improved pain management, have been shown to mitigate the risk of PPC. Nonetheless, there is consensus that these complications are common.

Most of the studies agree that patients undergoing lung surgery often are presented with high burden of comorbidities during preoperative preparation, contributing to the elevated risk of postoperative pulmonary complications (24,28,29). Common comorbidities such as chronic obstructive pulmonary disease (COPD), diabetes mellitus and cardiovascular disease are known to increase susceptibility to PPC by reducing baseline pulmonary reserve and compromising immune function. Addressing these comorbidities through multidisciplinary preoperative assessment and tailored perioperative care is essential to improve surgical outcomes.

Finally, while variations in reported incidence rates exist, these studies underscore the importance of a comprehensive approach to the prevention, early detection and management of PPC in thoracic surgery. Future research should aim to harmonize definitions and methodologies to enable meaningful comparisons and develop evidence-based guidelines to optimize patient care.

Conclusion

Pulmonary complications are highly prevalent after thoracic surgery, primarily due to the physiological challenges introduced during the procedure and the use of one-lung ventilation. These challenges include significant alterations in respiratory mechanics, reduced lung compliance and ventilation-perfusion mismatch, all of which contribute to impaired gas exchange. The combination of surgical stress, anesthesia and mechanical ventilation further exacerbates the risk of complications. Effective perioperative strategies are essential to minimize these risks. Tailoring these interventions to the individual patient's risk profile can significantly enhance outcomes and reduce morbidity associated with thoracic surgery. By implementing a comprehensive and multidisciplinary approach to patient management, healthcare teams can mitigate the incidence and severity of pulmonary complications, thereby improving recovery and reducing hospital stay duration.

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ORIGINAL ARTICLE *UDK: 618.19-006.6-089.87-052(497.715)"2019/2023"*

www.doi.org/10.55302/MJA2484045d

SURGICALLY TREATED PATIENTS WITH BREAST CANCER IN PHI GENERAL HOSPITAL WITH EXTENDED ACTIVITY – GEVGELIJA IN THE PERIOD FROM 2019 TO 2023

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Abstract

We are presenting the analysis of surgically treated patients with breast cancer in PHI General Hospital with Extended Activity – Gevgelija in the period from 2019 to 2023. The data were taken from the diary of the performed surgical procedures and the patients' medical histories. The analysis consists of surgically treated patients' gender and age, place of residence, type of surgery applied, days of hospitalization, disease stage, histopathological diagnosis and immunohistochemical markers.

Keywords: *breast cancer; mastectomy; quadrantectomy; tumorectomy.*

Introduction

Breast cancer is the most common cancer in the female population worldwide, second in frequency in the general population (1). It is considered a systemic disease, with a tendency to metastasize in the early stages. There is a wide variety of therapeutic modalities that can be used for its treatment: surgical therapy, radiotherapy, chemotherapy, biological, hormonal and immunotherapy.

Breast cancer is the most common malignant disease in the female population (25 to 30% of malignancies in women are breast cancer) and is the leading cause of cancer-related death among women aged 20 to 59 years (2). The incidence of breast cancer has been increasing, especially in the last two decades (3). One in every twelve women will be diagnosed with breast cancer in their lifetime and one in seventy-one will die of it (4). The lifetime risk of developing breast cancer is 5-13% (30 to 100 cases per 100,000 inhabitants) (1). It is a global health problem, with more than 2 million cases diagnosed worldwide each year (5). The disease can occur at any age, but it most commonly affects women over the age of 50. The average age at diagnosis of breast cancer in women is 62 years (6). The incidence of breast cancer in men is 1 per 100,000 men (1). This is less than 1% of all breast cancers, less than 1% of all cancers in men, and 0.2% of cancer-related deaths in men (4).

Breast cancer is considered a systemic disease that has a tendency to metastasize even in the early stages. It is believed that even when the disease is localized only in the breast, there are subclinical metastases (which cannot be detected by available diagnostic methods). For this reason, the treatment should be multidisciplinary, involving the application of multiple therapeutic mo-

dalities. Surgical treatment is the initial therapy of choice for earlier stages. In the case of more advanced stages, systemic therapy is started, followed by other types of treatment. In metastatic disease (stage IV), only systemic therapy is used. For breast cancer, all therapeutic modalities are available: surgical therapy, radiation therapy, chemotherapy, hormonal therapy, biological therapy and immunotherapy. The therapeutic modalities that are used and their combination depend on many factors: the stage and grade of the disease, the patient's age, overall health condition, etc. The decision is individualized for each patient.

Surgical therapy is one of the most important components in the treatment of breast cancer. The primary goal of surgical therapy is locoregional control of the disease. Specifically, surgical treatment aims to remove the tumor and, in most cases, the locoregional lymph nodes in the axillary region.

Table 1. Surgical procedures for breast cancer treatment, sorted by radicality (1).

1. Superradical mastectomy (sec. Urban & Wangesten)
2. Radical Mastectomy (sec. Halsted)
3. Modified Radical Mastectomy (sec. Patey)
4. Modified Radical Mastectomy (sec. Madden)
5. Simple Mastectomy (Mastectomia Simplex)
6. Partial Mastectomy + Axillary Lymphadenectomy
7. Partial Mastectomy
8. Quadrantectomy + Axillary Lymphadenectomy
9. Quadrantectomy
10. Lumpectomy + Axillary Lymphadenectomy
11. Lumpectomy
12. Tumorectomy + Axillary Lymphadenectomy
13. Tumorectomy

As standard surgical procedures in the treatment of breast cancer today, modified radical mastectomy sec. Madden and quadrantectomy with axillary lymphadenectomy are commonly used. Tumorectomy is the most often used when there is suspicion of local recurrences or for establishing a definitive diagnosis.

Materials and Methods

In this study, surgically treated patients with breast cancer at the General Hospital with Extended Activity - Gevgelija were analyzed in the period from 2019 to 2023. Out of a total of 1,991 surgical procedures performed during this period, 123 were related to breast cancer surgery. The data were obtained from the registry of performed surgical procedures and patients' medical histories.

For each surgically treated patient, separate data were collected on age, gender, place of residence, type of surgical procedure and length of hospitalization. From the histopathological

findings of the removed tissues during the surgeries, data were collected on the pathological stage of the disease, the histopathological diagnosis and immunohistochemical analyses. All these data were analyzed, and the results are presented. Patients who were surgically treated due to suspicion of breast cancer, but whose pathological diagnosis was benign in nature, were not included in the study.

Results

The study includes 123 patients who were surgically treated at the General Hospital with Extended Activity in Gevgelija for breast cancer.

From January 1, 2019, to December 31, 2023, a total of 1,991 surgeries were performed at the General Hospital with Extended Activity in Gevgelija. Of these, 123 surgeries, or 6.2%, were for breast cancer.

Table 2. Total number of operations and operations for breast cancer in PHI GHEA Gevgelija from 2019 to 2023.

Year	Breast cancer surgeries	Total number of operations	Percentage
2019	22	409	5.4%
2020	19	329	5.8%
2021	34	364	9.3%
2022	24	398	6%
2023	24	491	4.9%
In total	123	1,991	6.2%

Table 2 presents data on the number of surgeries for each year separately. The highest percentage of breast cancer surgeries occurred in 2021 (34 surgeries, or 9.3% of the total number of surgeries for that year), while the lowest percentage was in 2023 (24 surgeries, or 4.9% of the total number of surgeries for that year).

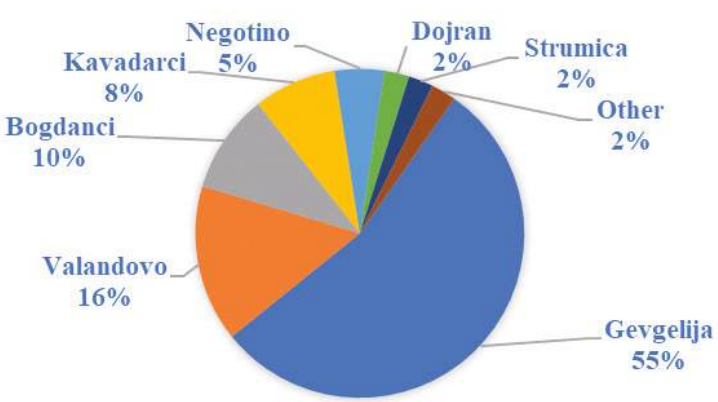

Diagram 1. Percentual representation by place of residence of surgically treated patients with breast cancer in PHI GHEA Gevgelija from 2019 to 2023.

Out of a total of 123 surgically treated breast cancer patients at the General Hospital with Extended Activity in Gevgelija over the last 5 years, the majority, 67 patients (55% of the total treated), are residents of Gevgelija. In addition to residents of Gevgelija, patients from other municipalities with breast cancer have also been treated at this institution, as shown in Diagram 1.

Diagram 2. Percentual representation by gender of surgically treated patients with breast cancer in PHI GHEA Gevgelija from 2019 to 2023.

Out of a total of 123 patients who were surgically treated for breast cancer in the last 5 years at the General Hospital with Extended Activity in Gevgelija, only 1 patient was male (around 1%). The remaining 122 patients (99%) were female.

Table 3. Average age of surgically treated patients with breast cancer in PHI GHEA Gevgelija from 2019 to 2023.

Year	Average age
2019	58.9
2020	61.5
2021	62.2
2022	53.2
2023	60.8
2019 - 2023	59.4

The average age of patients surgically treated for breast cancer in the last 5 years at the General Hospital with Extended Activity in Gevgelija is 59.4 years. Table 3 provides the average age for each year separately.

Table 4. Number and percentage of surgically treated patients with breast cancer in PHI GHEA Gevgelija from 2019 to 2023 by age groups.

Age groups	Patient number	Percentage
<19	1	0.8
20-29	2	1.6
30-39	6	4.9
40-49	18	14.6
50-59	28	22.8
60-69	41	33.3
70-79	19	15.4
80-89	8	6.5
In total	123	

Table 4 shows the number and percentage distribution of patients who were surgically treated for breast cancer according to age groups. The most common age group of patients is 60 to 69 years (33.3% of the total), while the least represented age group is under 19 years (only one patient).

Table 5. Days of hospitalization on average for each type of breast cancer surgery in PHI GHEA Gevgelija from 2019 to 2023.

Type of surgery	Patient number	Average days of hospitalization
Radical mastectomy sec. Madden	93	8
Quadrantectomy with axillary lymphadenectomy	12	7
Tumorectomy (wide local excision)	18	3.5

Table 5 shows the types of surgeries performed and the average hospitalization time for each type separately. The majority of breast cancer patients (75.6%) underwent Madden's radical mastectomy, with an average hospitalization time of 8 days. Approximately 15% were treated with wide local excision, with an average hospitalization time of 3.5 days. The smallest group, or 12 patients, underwent more extensive local procedure (quadrantectomy with axillary lymphadenectomy), with an average hospitalization time of 7 days.

Table 6. Histopathological types and their percentage representation in surgically treated patients with breast cancer in PHI GHEA Gevgelija from 2019 to 2023.

Histopathological type of carcinoma	Patient number	Percentage
Carcinoma ductale in situ (DCIS)	3	2.5 %
Carcinoma lobulare in situ (LCIS)	2	1.6 %
Carcinoma ductale invasivum mammae	92	74.8%
Carcinoma lobulare invasivum mammae	13	10.6%
Invasive breast carcinoma of no special type	3	2.5%
Mixed invasive lobular and ductal carcinoma	2	1.6%
Carcinoma colloides (mucinosum) mammae	3	2.5%
Carcinoma ductale invasivum et papillare	1	0.8%
Medullary carcinoma with lymphoid stroma	1	0.8%
Malignant Fibrous histrocytoma mammae (MFH)	1	0.8%
Benign (low grade) phylloides tumor	1	0.8%
Malignant phylloides tumor	1	0.8%

In the majority of cases (77%), the diagnosis is invasive ductal carcinoma. The second most common type is invasive lobular carcinoma, found in 10% of the cases.

Out of the 123 breast cancer patients analyzed, around 85% (105 patients) had a definitive pathological stage of the disease. In stage 0- 5 patients (4.1%) were diagnosed; in stage 1 - 18 patients (14.6%) were diagnosed, in stage 2 - 45 patients (36.6%) were diagnosed, and in stage 3 - 37 patients (30.08%) were diagnosed.

The available immunohistochemical reports of the patients were also analyzed. It was found that: Estrogen receptor positivity was present in 90% of the cases, Progesterone receptor positivity was found in 62%, HER2 positivity was observed in 30%, p53 positivity was present in 28%.

Table 7. Number, percentual representation and average age of non-invasive and invasive breast cancer among surgically treated patients in PHI GHEA Gevgelija from 2019 to 2023.

Type of carcinoma	Patient number	Percentage	Average age
Carcinoma In Situ	5	4%	49.8
Invasive Carcinoma	118	96%	59.9

Only a small portion, specifically 4% of the patients, were diagnosed with non-invasive, "in situ" carcinoma. Their average age is 10 years younger than that of patients diagnosed with invasive carcinoma (96% of the patients).

Discussion

According to statistics provided by the World Health Organization, 99% of those affected by breast cancer are women, while only 1% are men, which is consistent with the findings of this study (4). The average age of patients diagnosed with breast cancer is 62 years, according to the American Cancer Society. According to this research, the average age is 59.4 years. Numerous studies analyzing breast cancers for the expression of immunohistochemical markers indicate that: estrogen receptor positivity is found in over 70% of cases (90% in our study), progesterone receptor positivity is found in over 45% of cases (62% in our study), HER2 positivity occurs in 25% (30% in our study), p53 positivity is seen in 30% (28% in our study).

Conclusion

The analyzed patients treated for breast cancer were 99% women. This statistical data correlates with the statistics provided by the WHO. The average age of patients is 59.4 years, compared to an average age of 62 years found in literature.

The most common type of surgery performed is modified radical mastectomy sec. Madden. This procedure is the most radical compared to the other two procedures, and this radicality reflects in the number of hospitalization days. On average, tumorectomy requires 5 days of hospitalization less than the more radical procedures.

The histological type that predominates is invasive ductal carcinoma. The majority of patients are in pathological stage 2, positive for estrogen and progesterone receptor and negative for p53 and HER2 expression, which supports a better prognosis for overall survival. The average age of patients with "in situ" lesions is 10 years lower than that of patients with invasive carcinomas.

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ORIGINAL ARTICLE *UDK: 617.751-072.1-08*

www.doi.org/10.55302/MJA2484052nk

SUBRETINAL HYPERREFLECTIVE MATERIAL IN WET AGE-RELATED MACULAR DEGENERATION AS MONITORING BIOMARKER FOR DISEASE ACTIVITY AND THE RESPONSE TO ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY

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Abstract

Background and Objective: Hyper-reflective material can be considered as a surrogate Optical Coherence Tomography (OCT) biomarker in predicting disease activity and final visual outcome in patients with neovascular age-related macular degeneration (nARMD). The aim of this study was to assess the relationship between subretinal hyperreflective material (SHRM) morphological features, volume, response to anti-vascular endothelial growth factor (VEGF) therapy for choroidal neovascularization in wet age-related macular degeneration (AMD) and the best corrected visual acuity (BCVA).

Patients and Methods: The study is a prospective cohort. The study included 80 eyes with diagnosed wet form of AMD. The conducted study lasted for 1 year. 78 of the patients had finished the treatment regime. They were all previously untreated. A complete basic ophthalmological examination of both eyes was performed: BCVA was determined for the patient, intraocular pressure was measured according to the air puff method (non-contact air tonometry) and fundus examination. The diagnosis was confirmed using the non- invasive imaging method of OCT, DRI OCT Triton, Swept Source OCT device. OCT images and non-contrast angiography were also done in the region of the macula lutea of the retina. For measuring the SHRM weigh and high manual segmentation was performed.

Results: SHRM at the entry of our study is a present finding in 47 respondents (58%). The mean value of visual acuity in the patients in our study ranged from 3.95 at week 0 to 0.9 at week 52 from the start of treatment. We had foveal localization at the beginning in 13 eyes, parafoveal in 12 eyes and perifoveal in 2, while in 20 eyes it was absent as an initial parameter. At the 6th month, the location of SHRM was foveal in 29 eyes, parafoveal in 8 eyes and perifoveal in 4 eyes, in 47 the finding was absent. In month 12, SHRM was foveal in 28 eyes, parafoveal in 18 and perifoveal in 4 eyes, absent in 28. In 6th month the mean BCVA was 6.90, which was up to 2.95 lines higher than the base line. In 12 months, 63/78 (80%) respondents did not have SHRM, and 16 (20%) of the respondents had. The mean final best corrected visual acuity in month 12 was 0.9. In 12 months in 61, (78%) of the respondents there was no SHRM border, in 4 (5%) there was, and it was unclear in 12 (16%) of the respondents.

Conclusion: SHRM presence and reflectivity at base line, which correlated with the BCVA as one of the newest retinal biomarkers in wet AMD forms, carries important information about

the choroidal neovascularization (CNV) activity. SHRM reflectivity may be very useful for monitoring disease activity as well as important criteria for patient retreatment.

Keywords: *anti-vascular endothelial growth factor therapy; biomarker; macular degeneration; su bretinal hyperreflective material.*

Introduction

Age related macular degeneration (AMD) is the leading cause for severe and irreversible visual loss in patients aged 50 years and older in developed countries (1). Wet AMD changes progress rapidly if left untreated leading towards severe visual impairment and irreversible visual loss at the end (1). In the pathogenesis of the wet form of AMD, we have the creation of new blood vessels from the existing blood vessels that reach the subretinal space through Bruch's membrane and the retinal pigment epithelium. Newly growing blood vessels with discontinuous integrity release fluid, at first a transudate, and then an exudate that accumulates under the retinal pigment epithelium (RPE), and the neurosensory retina and is responsible for the disruption of the RPE and photoreceptor cells, with the ultimate consequence - damage to central vision. Classically, the abnormal blood vessels in wet AMD arise from the choroidal or choriocapillaris circulation. It is also one of the reasons why they have a pronounced fenestration and a large transudative potential, similar to small blood vessels of the choriocapillaris (2). Choroidal neovascularization (CNV) can be visualized with fluorescein angiography (FA). Although it is an imaging method that visualizes leakage from the vessels, the advent of spectral-domain optical coherence tomography (SD-OCT) allows more accurate visualization of all retinal layers (3). The two imaging methods provide different but complementary information for all retinal vascular disorders.

The hyper-reflective material (HRM) is retinal diagnostic monitoring biomarker for CNV in nAMD changes. The association of HRM with omission in active CNVs especially with a subretinal CNV network has been established (4). Additional studies show the presence of the so-called undefined HRM, ("gray" hyper-reflective material or subretinal hyper-reflective exudation) in untreated forms of nAMD (5). SHRM on OCT is defined as presence of hyperreflective deposition material located in the subretinal space and has been correlated with classic CNV on FA (6). Although SHRM typically correspondents to fibrovascular tissue as in CNV type 2, it can also be included fibrin, blood, lipid, fluid or scar as components that can change in time under anti-VEGF treatment (7). The presence of subretinal hyper-reflective material (SHRM) is of increasing relevance as new biomarker (8). Recent studies have indicated that the presence of this so called subretinal tissue may have stronger implications on visual acuity than the other retinal parameters, and thus may provide additional prognostic disease information (9). However, the anatomical response to anti-VEGF treatment and the functional outcomes can vary markedly among patients with n-AMD (10).

The introduction of anti-VEGF treatment in patients with retinal neovascularization little over a decade ago was the first revolutionary leap in treating patients with neovascular AMD and thus preserving their vision acuity (11). The same has reduced the incidence of legal blindness by more than 50% (12). It has been found that SHRM lesion size and location correlates with VA, and SHRM decreases in size with anti-VEGF therapy. The morphological features of SHRM have been studied previously, and it is important to characterize SHRM morphologic features

which will enable the treating physician to tailor treatment to provide adequate disease control, minimize recurrence and neurosensory damage, and limit the number of invasive and costly anti-VEGF injections (13).

Our purpose was to assess the response of SHRM on anti-VEGF therapy by monitoring its volume in correlation to visual acuity.

Material and Methods

The conducted study is a prospective cohort. All patients were treated and monitored over a period of one year. The study included 80 eyes that had established, diagnosed with wet AMD. All patients were previously untreated, newly diagnosed with nAMD, with present, developed CNV and reduced visual acuity, best-corrected visual acuity >20/200 according to Snellen optotype. When the patients were included in the study, at the beginning, a complete basic ophthalmological examination of both eyes was performed: the best corrected visual acuity (BCVA) was determined for the patient, intraocular pressure was measured according to the air puff method (non-contact air tonometry) and fundus examination. Imaging and monitoring of fundus changes was performed exclusively on the DRI OCT Triton, Swept Source Optical Coherence Tomography (OCT) device. OCT images and non-contrast angiography were done in both eyes in the macula lutea zone. Subretinal hyperreflective material was visualized and it was measured at the beginning of the treatment and during the treatment on the control period time during the study on week 12, 28 and 52. This was compared to patients' best corrected visual acuity. Patients were treated with the drug aflibercept, which is an inhibitor of vascular endothelial and placental growth factor. The drug was administrated by the so-called regime of treat and extend (T&E regime). All patients received three initial doses of 2mg aflibercept and the 4th dose on the 16th week. Also at this visit, OCTA was performed and BCVA determined and based on the finding (disease activity or inactivity), a further dosing regimen tailored to the needs of each patient was established with further follow-ups. If the activity of the disease was determined, it was continued with the 5th application of the preparation at an interval of 8 weeks. If inactivity of the disease was determined, the application interval was extended for another 2 or 4 more weeks (14). The drug was administrated into the eye vitreous cavity after topical anesthesia in clean and sterile conditions. For statistical processing of the data obtained during the research, a database was created in the statistical program SPSS 21.0. Categorical variables were presented with absolute and relative numbers, and descriptive statistics (mean, standard deviation) were used to describe quantitative variables. The student t-test was used to compare the analyzed variables between the studied and control groups. Paired sample test, Fisher exact test was used for comparison in 0, 12, 28 and 52 weeks. The x2 test and the McNeamar test were used to examine categorical variables. Values of $p<0.05$ were taken as statistically significant.

Results and Discussion

SHRM at the entry of our study was a present finding in 47 respondents (58%). The mean value of visual acuity in the patients in our study ranged from 3.95 at week 0 to 0.9 at week 52nd from the start of treatment. We had foveal localization at the beginning in 13 eyes, parafoveal in 12 eyes and perifoveal in 2, while in 20 it was absent as an initial parameter. At the 6th month, the location of SHRM was foveal in 29 eyes, parafoveal in 8 eyes and perifoveal in 4 eyes, in 47 the

finding was absent. In month 12, SHRM was foveal in 28 eyes, parafoveal in 18 and perifoveal in 4 eyes, absent in 28. When comparing localization with visual acuity, we obtained an increase in visual acuity at the 6th month of treatment compared to 0 week. On this section we had a drop in SHRM height below 175μm and width below 1500μm which was in favor of the obtained higher visual acuity values. In month 6, the mean BCVA was 6.90, that is up to 2.95 lines higher than the base line. At the end of the study, as a result of the progressive decrease in height and width, we also obtained a positive correlation with an increase in mean visual acuity. There was also an increase in the number of eyes where we obtained complete resorption of the deposit material under the retina in 6 and 12 months. In month 12, mean visual acuity was 0.9.

Table 1. Better 12 SHRM0 present

Cross table				
Number				
		SHRM0 presence		
		No	Yes	
Better12	No	11	20	
	Yes	21	26	
Total		32	46	

SHRM at the entry of our study was a present finding in 47 respondents (58%).

Table 2. Better12 SHRM0 limitation

Cross table					
Number					
		SHRM0 limitation			
		none	present	unclear	
Better12	No	11	17	3	
	Yes	22	23	2	
Total		33	40	5	

There was no SHRM border in 33 (42%) of the patients, 40 (51%) had a border, and 5 (7%) had an unclear border.

Table 3. Better12 SHRM0 high

Cross table					
Number					
		SHRM0high		
		negative	< 175µm	> 175µm
Better12	No	11	9	11
	Yes	21	13	13
Total		32	22	24

Table 4. Better12 SHRM0 width

Cross table					
Number					
		SHRM0 width		
		negative	< 1500µm	> 1500µm
Better12	No	12	11	8
	Yes	21	13	13
Total		33	24	21

Table 5. Better12 SHRM0 reflectivity

Cross table						
Number						
		SHRM0 reflectivity			
		none	Isodense RNFL	Isodense ONL	In between
Better12	No	12	4	13	2
	Yes	20	7	18	2
Total		32	11	31	4

Table 6. Better52 SHRM52 present

Cross table				
Number				
		SHRM52 present	
		No	Yes
Better52	No	10	6
	Yes	53	9
Total		63	15

At 12 months, 63/78 (80%) respondents did not have SHRM, and 16 (20%) of the respondents had.

Table 7. Better52 SHRM52 limitation

Cross table					
Number					
		SHRM52 limitation		
		none	present	unclear
Better52	No	10	0	6
	Yes	51	4	7
Total		61	4	13

In 61, (78%) of the respondents there was no SHRM border, in 4 (5%) there was, and it was unclear in 12 (16%) of the respondents.

Table 8. Better52 SHRM52 high

Cross table				
Number				
		SHRM52 high		
		none	< 175µm	> 175µm
Better52	No	10	6	0
	Yes	52	9	1
Total		62	15	1

Table 9. Better52 SHRM52 width

Cross table				
Number				
		SHRM52 width		
		none	<1500µm	1500µm
Better52	No	10	6	0
	Yes	52	9	1
Total		62	15	1

Table 10. Better52 SHRM52 reflectivity

Cross table						
Number						
		SHRM52 reflectivity			
		none	Isodense RNFL	Isodense ONL	In between
Better52	No	10	0	0	6
	Yes	46	1	3	12
Total		56	1	3	18

At 12 months from the start of the study, 56/78 or 71% of patients had no greater reflectivity, it was isodense at the RNFL in 1 (1%), isodense at the ONL in 3 (4%) and between the RNFL and ONL in 18 (23%) of the patients.

During the treatment over a period of 2 years in Comparison of Age-Related Macular Degeneration Treatments Trials (CATT), a reduction of subretinal material of up to 45% percent was determined. In another study SHRM was classified as a negative parameter for visual acuity where if the diameter of the expulsion is >1000 μm and involves the foveal center, studies show a difference of 14 letters seen in patients with and without SHRM (15).

In our subjects, the reduction or complete resorption of the drusenoid material after the 3 shock, initial doses of the anti-VEGF preparation was shown to be a positive parameter in correlation with the increase in VA, while further in the 6th and 12th month the presence of existing, persistent SHRM did not produce a statistically significant finding in terms of BCVA change. This finding of marked reduction in the undefined component of HRM by month 3 suggests that the subset of HRM that is diffuse and located in the subretinal space, is the result of an inflammatory reaction in early n-AMD. Regarding visual acuity, a statistically significant association was obtained between the thickness of the subretinal hyperreflective material and its reduction. Studies have found that eyes with undefined HRM at month 12 had the poorest vision which suggests a reactivation of the CNV complex and supports the recommendation to consider undefined HRM as a qualitative criterion for retreatment (16).

In another study, the subretinal deposit material is defined as a predictive parameter for the so-called "non-responders". This study has described the presence of subretinal hyperreflective material in patients with nAMD (17). Other features of HRM such as limitation, organization of SHRM seen on the OCT tomogram before the start of treatment, high reflectivity, zone of separation between HRM and outer retina, layered appearance, subretinal hyperreflective foci, thickness and width of HRM have been shown to correlate with poorer visual acuity outcome (18). In our study, we analyzed the limitation, the reflectivity of the deposited hyperreflective material, where at the beginning before the treatment we had an unclear limitation in 31 eyes (47%), while in 47 (60%) it was with a clear limitation. The reflectivity in week 0 was unclear in 31 eyes (39%), while we had increased reflectivity in the remaining 47 (60%). After treatment, we obtained SHRM resorption in 61 patients (78%), in 4 eyes (5%) there was a clear limitation, while in 13 eyes (17%) it remained unclearly limited. In week 52, we have resolution of the initial clearly defined HRM in 56 eyes (71%) while the remaining 22 (29%) have clearly defined

hyper-reflective material. SHRM as an initial finding according to the study by CATT and associates is associated with scar development and significant decline in visual acuity (19). Recurrence of scarring or atrophy is associated with persistent findings of drusenoid material during treatment. Bloch found a drop of 10 letters according to the ETDRS. El-Emam provided data on the significance of the location, i.e. the distance from the foveal center and the edge of the scar. SHRM as an initial finding, according to the study by CATT and associates, is associated with scar development and a significant decline in visual acuity. In our study the presence of SHRM was associated with worse VA, at all sites, regardless of height or width and when compared to a control group without a finding of HRM. In subgroup analysis, foveal SHRM involvement had worse visual acuity at baseline, 3, 6 and 12 months compared to eyes with absence of SHRM in the central 1mm2 of the fovea. There was a significant correlation between VA and SHRM such as height, width and area. The lowest, best-corrected visual acuity was obtained at baseline before starting treatment. SHRM was located in the fovea with an area greater than 0.24mm2 compared to SHRM outside the fovea region (20). VA was shown to be worse when SHRM included the fovea, and the baseline width was more than 1500 um compared to SHRM outside the fovea. When a foveal area involving SHRM greater than 175 ums in height was present, the baseline BCVA obtained was worse compared to SHRM outside the fovea. In our study, the disappearance of SHRM from the beginning to the 3rd month correlated with a better VA, but it did not show a statistically significant improvement at 6 and 12 months after the start of treatment. SHRM has been found to be a statistically more common finding in Type 2 and Type 3 choroidal neovascular lesions (21).

Conclusion

VA was shown to be worse when SHRM included the fovea, and the baseline width was more than 1500 um compared to SHRM localized outside the fovea. Initially vaguely circumscribed SHRM gave a better response to anti-VEGF treatment and visual acuity in 52 weeks of treatment compared to initially clearly circumscribed and increased reflectivity SHRM. In terms of visual acuity, a statistically significant correlation was obtained between the thickness of the subretinal hyperreflective material and its reduction. The unclearly defined SHRM had greater therapy response during the three initial doses of anti-VEGF. The fluctuations in its width and high have shown to be in correlation with disease activity and a biomarker for patient's retreatment. SHRM definitely can be used to better assess choroidal neovascular membrane activity which will promptly and correctly direct the treatment in patients with wet AMD and preserve satisfactory visual acuity necessary to perform daily activities.

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ORIGINAL ARTICLE *UDK: 616.24-002.7-073.756.8:004]:613.84*

www.doi.org/10.55302/MJA2484062d

IMAGING OF PULMONARY SARCOIDOSIS AND ITS CORRELATION WITH SMOKING - OUR EXPERIENCE

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Abstract

Introduction: Sarcoidosis is a multisystemic granulomatous disease that usually affects lung parenchyma with interstitial and granulomatous changes of varying intensity and expression, depending on the degree of the disease.

The aim of the study: To detect pulmonary changes of sarcoidosis on high-resolution CT (HRCT) and to correlate them with smoking.

Material and Methods: Computed tomography with high resolution was made on 128 slice CT scanner PHILIPS INCISIVE, using 1mm thin-slice thickness and high spatial frequencies algorithm for image reconstruction. A total of 50 patients diagnosed with sarcoidosis who came to our University Clinic of Pulmonology and Allergology - Skopje were included in this study and their HRCT findings were compared to smokers and non-smokers.

Results: The gender structure of the patients is predominantly made up of female patients 92% vs 8% male. Reticular opacities on HRCT were more often seen in smokers compared to non-smokers, with a statistically significant difference confirmed for their peripheral and subpleural localization (p=0.0034 and p=0.0014, respectively in the upper and middle lung zones, and in the lower lung zones). Smoking patients had insignificantly more often peribronchovascular localization of reticular opacities in the upper and middle lung zones (26.67% vs 10%, p=0.28) and in the lower lung zones (26.67% vs 20%, p=0.74). Regarding the smoking status, 16% of the patients declared themselves as current smokers, 56% as ex-smokers, with an average smoking experience of 14.9 ± 4.8 years.

Conclusion: HRCT is the method of choice in the evaluation of pathological changes in pulmonary sarcoidosis. It shows very precisely the characteristic findings of lymph nodes, micronodules and other lesions, their distribution, as well as atypical changes. Smoking plays a certain role in the interstitial changes of the patients with sarcoidosis, although we do not have data whether smoking has effects on the extent, course or outcome of the disease.

Keywords: *high-resolution computer tomography; interstitial disease; nonsmokers; sarcoidosis; smoking.*

Introduction

Sarcoidosis is a multisystemic granulomatous disease that usually affects the lung parenchyma with interstitial and granulomatous changes of varying intensity and expression, depending on the degree of the disease. Although many hypotheses have been proposed, the etiology of sarcoidosis remains unclear (1). Very often, hilar and mediastinal lymphadenopathy with changes of various types is seen, but peripheral groups of lymph nodes can also be involved, such as axillary, inguinal and cervical (1-3).

Sarcoidosis mainly affects adults under 40 years of age (with a peak in the third decade of life) and a second peak occurs in women over 50 years of age in countries such as Japan (4), but it can also occur at a younger age. The disease is diffusely distributed throughout the world and affects both genders almost equally with a slight predominance among women (3,5). The prevalence of the disease is higher among non-smokers than among smokers, and is more common in certain occupational groups, such as nurses, firefighters, transport and service workers, although the cause is unknown (5).

Imaging methods such as high-resolution computed tomography (HRCT) play key role in the diagnosis and monitoring of the patients. This is due to the fact that the plain radiograph of the lungs has many limitations, including insufficient resolution in the detection of pulmonary abnormalities and in the detection of hilar and mediastinal adenopathy.

HRCT has become a powerful tool and has greater superiority than conventional computed tomography in the detection and evaluation of subtle parenchymal lesions and abnormalities of lung structures (6). It helps us in the prognostic course and development of the disease, identification of irreversible changes, potentially reversible and the appropriate treatment.

In advanced stages of sarcoidosis, reticular opacities zones, tractional bronchiectasis, architectural distortion of the parenchyma, honeycomb lung, bullae, and paracicatricial emphysema are seen in the upper and middle lung zones. The lung bases are usually spared (7). On HRCT, 75–95% of the patients have mediastinal and hilar lymphadenopathy, and approximately 67–75% have hilar lymphadenopathy, usually bilateral, but not infrequently with a right-sided predominance (8,9). Lymph nodes are more often focally calcified than completely and dense, amorphous or nebulous, rod-like or eggshell-like in 3% of the patients within 5 years of diagnosis of the disease, or in 20% after 10 years (10).

Sarcoid nodules formed in the lung parenchyma are seen in nearly half of the patients, and in some studies up to over 90% of the patients (9, 11). They are typically predominant in the upper lobes but may also be seen with more diffuse distribution. The lower lobes are usually spared. Micronodules have dimensions below 1cm, and HRCT can detect changes up to 1-2mm in diameter. The presence of small, 1-5mm nodules clearly demarcated, or with irregular contours, is the most common and almost universal finding seen in the lung (12).

Although nodules appear as predominant finding in sarcoidosis, the parenchymal form of the disease includes opacities of different sizes (1-10cm) ground glass type, consolidation, reticulation. They predominate in the peripheral middle zones, while the costophrenic angles are spared.

Small nodules in sarcoidosis have a characteristic perilymphatic and symmetrical distribution. That distribution corresponds to nodules identified in the peribronchovascular interstitium,

interlobar septa, because the lymphatic tract lies along these two anatomical structures of the lungs. The subpleural zone, as well as the large and small fissures that are an extension of the pleura and belong to the lymphatic system are also often involved (13,14).

HRCT findings of fibrosis include reticulations, architectural distortion, tractional bronchiectasis and volume loss primarily in the upper or central lung. As fibrosis progresses, larger zones of mass-like consolidation occur in the perihilar regions.

Honeycomb lungs and lung cysts may also occur predominantly in the upper and middle lung lobes, in contrast to the basally predominant fibrosis and honeycombing in UIP and IPF.

Sarcoidosis mainly affects non-smokers, but in this article we will corelate the disease with smokers and past smokers and their HRCT changes, because in our country the dominant population is a smoker (15).

The aim of the study is to detect pulmonary changes of sarcoidosis on HRCT and to correlate them with smoking.

Material and Methods

Patients voluntarily participated in the study with a previously signed informed consent. The study was conducted with the consent of the Ethics Commission of the Faculty of Medicine in Skopje and was in accordance with the ethical principles of the Helsinki Declaration of the World Medical Association for medical research involving human subjects.

A total of 50 patients diagnosed with sarcoidosis came to our University Clinic of Pulmonology and Allergology-Skopje. HRCT was performed on a 128-slice PHILIPS INCISIVE computed tomography scanner, using 1mm thickness of sections and high spatial frequencies algorithm for image reconstruction.

The images were evaluated using appropriate lungs and mediastinal windows. Lymph nodes were classified as hilar and mediastinal with maximum short axis diameter (MSAD), more than 10mm taken as their enlargement.

Pulmonary changes (opacity) were classified as nodules (micronodules 1-3mm and macronodules greater than 5mm), reticular opacities, fibrous lesions, ground glass opacities and confluent consolidations. Nodular distribution was classified as perilymphatic, centrilobular and randomized. The predominant distribution of lesions in different zones of the lungs (upper, middle and lower zones) was also noted.

Results

This statistical analysis includes 50 patients diagnosed with sarcoidosis. The gender structure of the patients is predominantly made up of female patients – 46 (92%) vs 4 (8%) male.

The patients were aged from 30 to 73 years, with an average age of 52.6 ± 12.5 years, and with a place of residence mostly in an urban environment – 42 (84%) vs 8 (16%).

Reticular opacities on HRCT were more often seen in smokers compared to non-smokers, with a statistically significant difference confirmed for their peripheral and subpleural localization (p=0.0034 and p=0.0014, respectively in the upper and middle lung zones, and in the lower lung zones). Smoking patients had insignificantly more often peribronchovascular localization of reticular opacities in the upper and middle lung zones (26.67% vs 10%, p=0.28) and in the lower lung zones (26.67% vs 20%, p=0.74).

Regarding the smoking status, 8 (16%) patients declared themselves as current smokers, 28 (56%) as ex-smokers, with an average smoking experience of 14.9 ± 4.8 years. The time when they stopped smoking ranges between 4 and 27 years, on average ex-smokers stopped smoking 11.9 ± 7.1 years ago.

Due to lung disease, 16 (32%) patients were hospitalized, all with one hospitalization.

2 (4%) patients had a positive family history of lung disease.

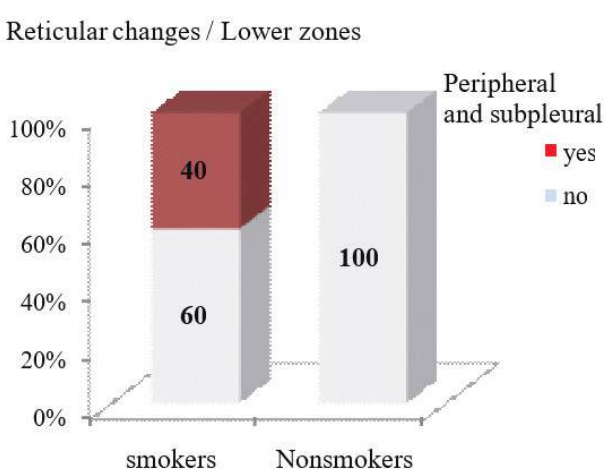
Table 1. Patients' characteristics.

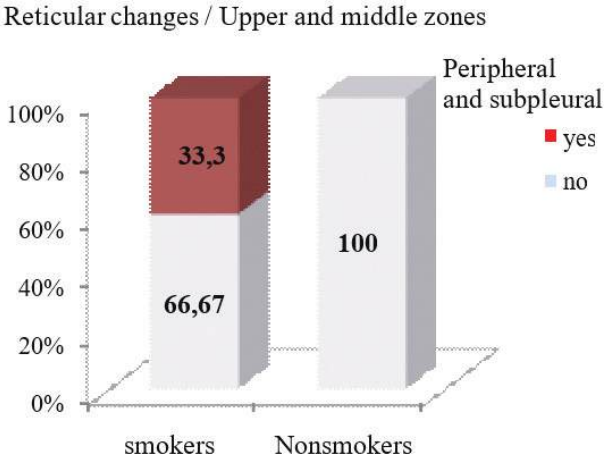
Variable	n (%)
Gender	
female	46 (92)
male	4 (8)
Age	
mean ± SD (min- max)	52.6 ± 12.5 (30 – 73)
Place of living	
town	42 (84)
village	8 (16)
Do you smoke	
yes	8 (16)
no	42 (84)
Have you ever smoked	
yes	28 (56)
no	22 (44)
How many years have you smoked	
(mean ± SD) (min- max)	14.9 ± 4.8 (7 – 20)
How many years ago did you stop smoking	
(mean ± SD) (min- max)	11.9 ± 7.1 (4 – 27)

Table 2. Distribution of reticular opacities depending on smoking status.

HRCT findings			Smokers		p-level
			yes n (%)	no n (%)	
Reticular changes					
Upper and middle zones	Peripheral and subpleural	yes	10 (33.33)	0	**p=0.0034
		no	20 (66.67)	20 (100)	
	Peribronchovascular	yes	8 (26.67)	2 (10)	p=0.28
		no	22 (73.33)	18 (90)	
Lower zones	Peripheral and subpleural	yes	12 (40)	0	**p=0.0014
		no	18 (60)	20 (100)	
	Peribronchovascular	yes	8 (26.67)	4 (20)	p=0.74
		no	22 (73.33)	16 (80)	

p (Fisher's exact test)



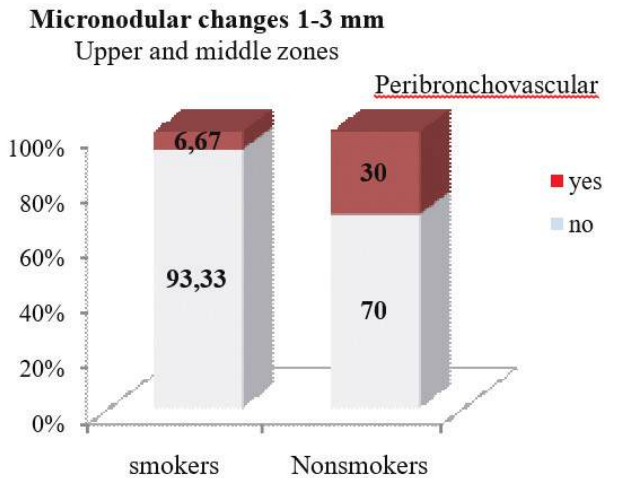


Micronodular opacities with a size of 1 to 3mm localized peribronchovascular in the upper and middle zones were significantly less frequent HRCT findings in smokers compared to non-smokers (6.67% vs 30%, p=0.047). Perilymphatic micronodular opacities with size of 1 to 3mm were diagnosed insignificantly more often in smokers, in the peribronchovascular regions of the upper and middle zones (33.33% vs 20%, p=0.353), in the subpleural regions of the upper and middle zones (26.67% vs 10%, p=0.28), in the peribronchovascular regions of the lower zones (6.67% vs 0%, p=0.51), and in the subpleural regions of the lower zones (6.67% vs 0%, p=0.51).

Table 3. Distribution of micronodular changes from 1-3mm depending on smoking status.

HRCT findings			Smokers		p-level
			yes n (%)	no n (%)	
Micronodular changes 1-3mm					
Upper and middle zones	Centrolobular	**yes**	0	0	
		no	30 (100)	20 (100)	
	Peribronchovascular	**yes**	2 (6.67)	6 (30)	*p=0.047
		no	28 (93.33)	14 (70)	
Lower zones	Centrolobular	**yes**	0	0	
		no	30 (100)	20 (100)	
	Peribronchovascular	**yes**	2 (6.67)	2 (10)	p=1.0
		no	28 (93.33)	18 (90)	
Micronodular changes (1-3mm) perilymphatic					
Upper and middle zone s	Peribronchovascular	**yes**	10 (33.33)	4 (20)	p=0.35
		no	20 (66.67)	16 (80)	
	Subpleural	**yes**	8 (26.67)	2 (10)	p=0.28
		no	22 (73.33)	18 (90)	
Lower zones	Peribronchovascular	**yes**	2 (6.67)	0	p=0.51
		no	28 (93.33)	20 (100)	
	Subpleural	**yes**	2 (6.67)	0	p=0.51
		no	28 (93.33)	20 (100)	

p (Fisher's exact test)
*Significance p<0.05

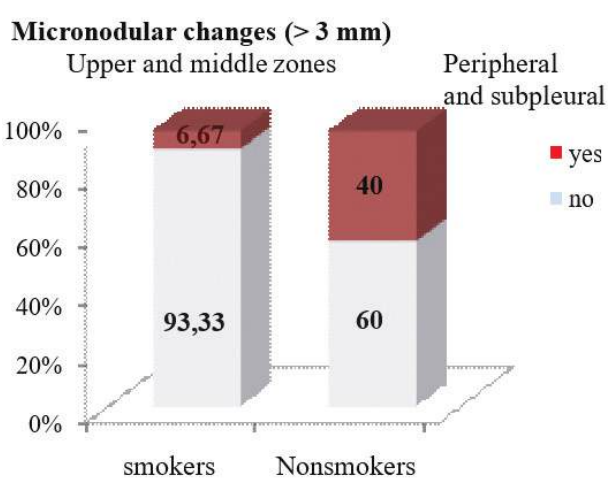


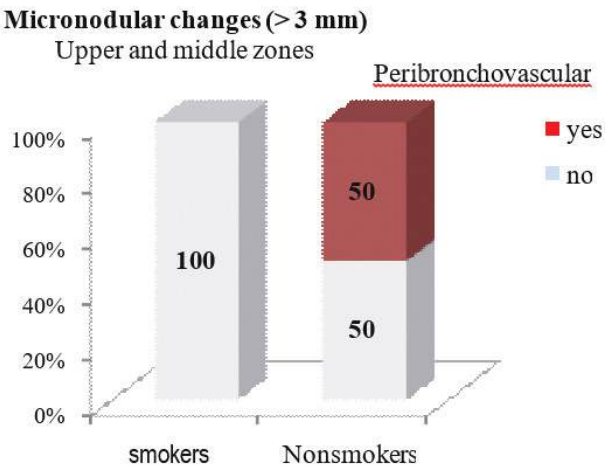
HRCT finding of micronodular changes greater than 3mm in the upper and middle lung zones was significantly associated with the smoking status of the patients ($p<0.05$). In non-smokers, micronodular changes greater than 3mm peripherally and subpleural, were significantly less often seen on HRCT (6.67% vs 40%, $p=0.0088$), while peribronchovascular localization of these changes in the upper and middle lung zones was seen only in 50% of the patients from the group of non-smokers ($p=0.00002$). Micronodular changes larger than 3mm in the lower lung zones were registered only in non-smokers (10%), but no statistically significant difference was confirmed between smokers and non-smokers in terms of the frequency of finding micronodular shadows larger than 3mm in the lower lung zones ($p=0.155$).

Table 4. Distribution of micronodular changes larger than 3mm depending on smoking status.

HRCT findings			Smokers		p-level
			yes n (%)	no n (%)	
Micronodular changes (>3mm)					
Upper and middle zones	Peripheral and subpleural	**yes**	2 (6.67)	8 (40)	**p=0.0088
		no	28 (93.33)	12 (60)	
	Peribronchovascular	**yes**	0	10 (50)	***p=0.00002
		no	30 (100)	10 (50)	
Lower zones	Peripheral and subpleural	**yes**	0	2 (10)	p=0.155
		no	30 (100)	18 (90)	
	Peribronchovascular	**yes**	0	2 (10)	p=0.155
		no	30 (100)	18 (90)	

p (Fisher's exact test)
**sig p<0.01, ***sig p<0.0001





GG opacities in the peripheral and subpleural regions of the lungs were detected only in smoking patients (6.67%), in 20% of the smokers in the central regions of the upper and middle zones, in 33.33% of the smokers and in 10% of the non-smokers in the central regions of the lower zones, without statistically significant difference in all localizations (p>0.05).

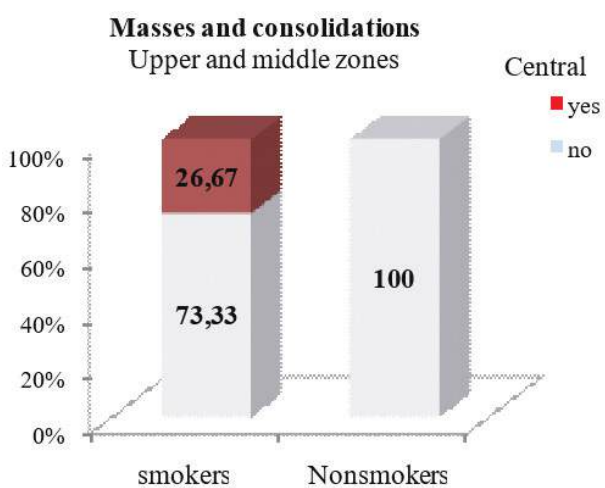
Masses and consolidations centrally localized in the upper and middle lung zones were observed only in smokers (26.67%), with a significant difference for p=0.015. Smokers and non-smokers did not differ significantly in terms of HRCT findings of hypoattenuation type changes (p>0.05). Smokers had insignificantly more often such changes in the upper and middle lung zones (13.33% vs 10%) in the peripheral and subpleural regions, (20% vs 10%) in the central regions.

Table 5. Distribution of GG opacities, masses, consolidations and hypoattenuation depending on smoking status.

HRCT findings			Smokers		p-level
			yes n (%)	no n (%)	
GG Opacities					
Upper and middle zones	Peripheral and subpleural	**yes**	2 (6.67)	0	p=0.51
		no	28 (93.33)	20 (100)	
	Central	**yes**	6 (20)	0	p=0.07
		no	24 (80)	20 (100)	
Lower zones	Peripheral and subpleural	**yes**	2 (6.67)	0	p=0.51
		no	28 (93.33)	20 (100)	
	Central	**yes**	10 (33.33)	2 (10)	p=0.09
		no	20 (66.67)	18 (90)	
Masses and consolidations					
Upper and middle zones	Peripheral and subpleural	**yes**	0	2 (10)	p=0.155
		no	30 (100)	18 (90)	
	Central	**yes**	8 (26.67)	0	*p=0.015
		no	22 (73.33)	20 (100)	

Lower zones	Peripheral and subpleural	**yes**	4 (13.33)	4 (20)	p=0.7
		no	26 (86.67)	16 (80)	
	Central	**yes**	0	0	
		no	30 (100)	20 (100)	
Hypoattenuation					
Upper and middle zones	Peripheral and subpleural	**yes**	4 (13.33)	2 (10)	p=1.0
		no	26 (86.67)	18 (90)	
	Central	**yes**	6 (20)	2 (10)	p=0.45
		no	24 (80)	18 (90)	
Lower zones	Peripheral and subpleural	yes	4 (13.33)	4 (20)	p=0.7
		no	26 (86.67)	16 (80)	
	Central	yes	0	2 (10)	p=0.155
		no	30 (100)	18 (90)	

p (Fisher's exact test)



According to the obtained results, lymphadenopathy was not presented as a significantly different HRCT finding in smokers and non-smokers (p>0.05). Bilateral hilar lymphadenopathy (66.67% of smokers and 70% of non-smokers) and right paratracheal lymphadenopathy (73.33% of smokers and 90% non-smokers) were predominant in both groups.

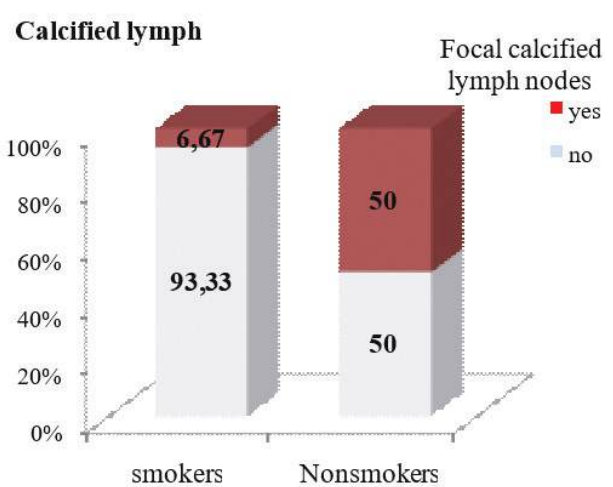
Focal large calcifications were significantly less frequently detected in smokers (6.67% vs 50%, p=0.0007).

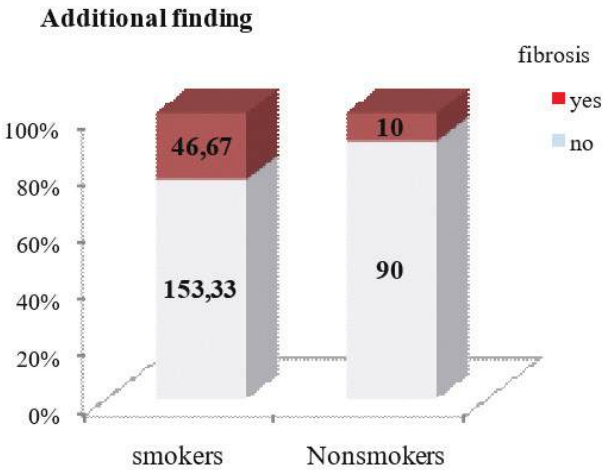
Smokers had significantly more frequent HRCT findings of traction bronchiectasis (40% vs 10%, p=0.026) and fibrosis (46.67% vs 10%, p=0.012).

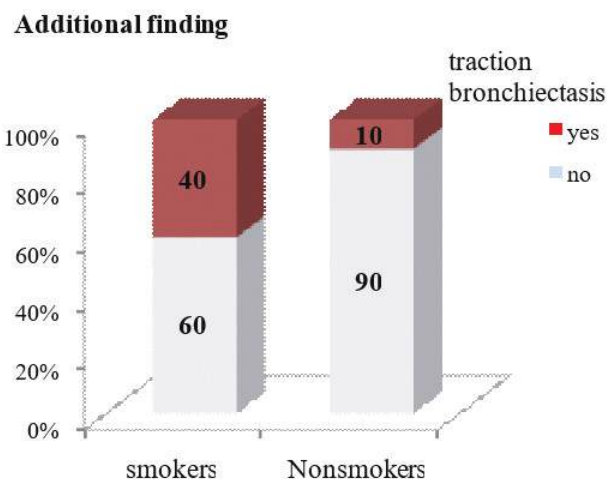
Only 6.67% of the smoking patients had a finding of honeycomb lung, but without statistically confirmed association with this group of patients (p=0.51).

Table 6. Distribution of lymphadenopathy, calcified lymph nodes and additional findings depending on smoking status.

Variable			Smokers		p-level
			yes n (%)	no n (%)	
Lymphadenopathy	Bilateral hilar	**yes**	20 (66.67)	14 (70)	p=1.0
		no	10 (33.33)	6 (30)	
	Right paratracheal	**yes**	22 (73.33)	18 (90)	p=0.28
		no	8 (26.67)	2 (10)	
	Others lymph nodes stations	**yes**	20 (66.67)	16 (80)	p=0.35
		no	10 (33.33)	4 (20)	
	Conglomerate lymph nodes	**yes**	4 (13.33)	6 (30)	p=0.17
		no	26 (86.67)	14 (70)	
Calcified lymph nodes	Focal calcified lymph nodes	**yes**	2 (6.67)	10 (50)	***p=0.0007
		no	28 (93.33)	10 (50)	
	Punctiform	**yes**	0	2 (10)	p=0.155
		no	30 (100)	18 (90)	
	Egg shell	**yes**	2 (6.67)	0	p=0.51
		no	28 (93.33)	20 (100)	
Additional finding	Bullae	**yes**	8 (26.67)	4 (20)	p=0.74







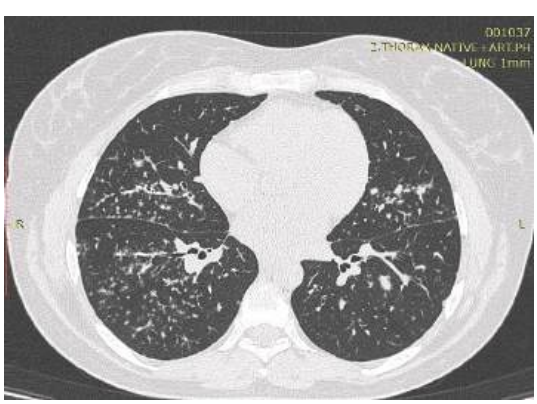


Image1. Perilymphatic distribution of sarcoidosis

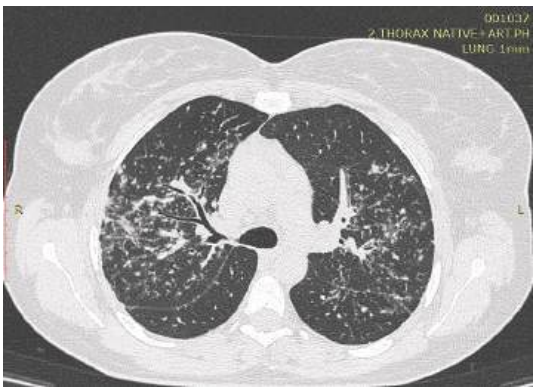


Image 2. Typical perilymphatic distribution of sarcoidosis

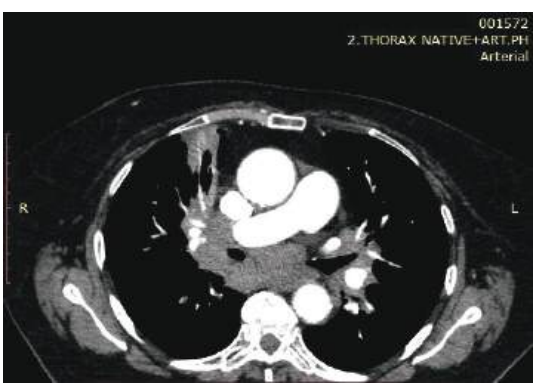


Image 3. Mediastinal Lymphadenopathy.

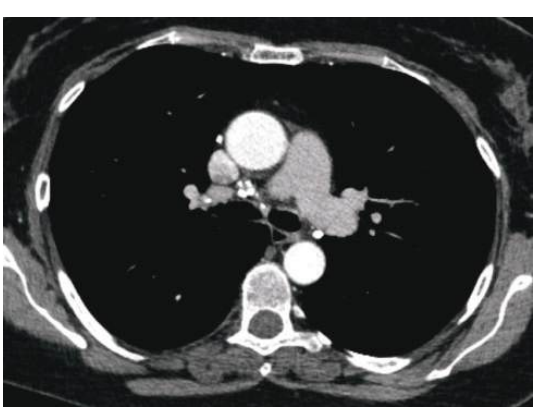


Image 4. Calcified lymph nodes.

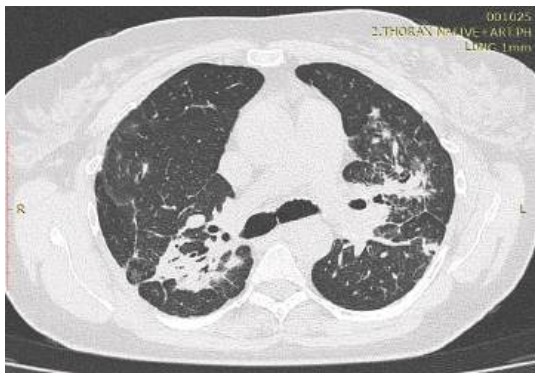


Image 5. Atypical manifestation of sarcoidosis.

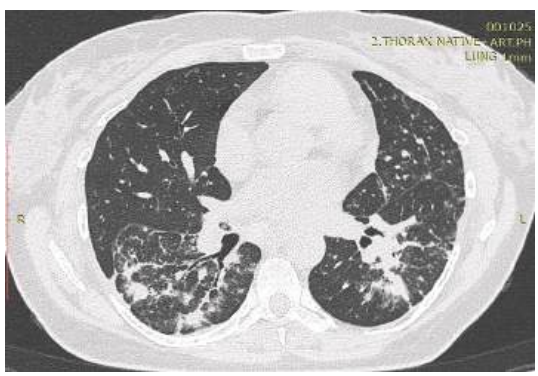


Image 6. Atypical manifestation of sarcoidosis.

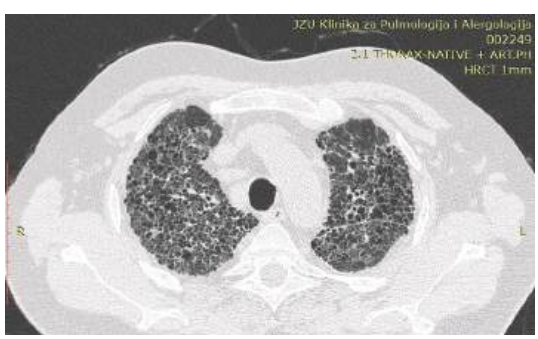


Image 7. End stage sarcoidosis-fibrosis.

Discussion

Sarcoidosis, with a total number of 50 patients analyzed in our study, is a multisystemic granulomatous disease of unknown etiology. Pulmonary involvement is the most common presentation of the disease with interstitial and granulomatous changes of different location, intensity and expression, depending on the stage of the disease. The staging of the disease is still done

according to the established radiological criteria of the conventional radiogram of the lungs, despite the great sensitivity of HRCT in detecting small changes in the lungs that are not visible on the ordinary radiogram. According to Lynch, the plain radiogram detects only 50-60% of the lymph nodes and 30-40% of the parenchymal abnormalities found with HRCT. Only in few cases, patients with transbronchial biopsy-confirmed sarcoidosis had a normal HRCT scan (16). Involvement of the hilar and mediastinal lymph nodes is seen in 50-90% of the patients, usually bilaterally. The disease affects both genders with a slight predominance in women, in whom a second peak can be seen after the age of 50 (Japan). Despite the fact that etiology is unknown, certain professions are still observed to increase the predisposition to this disease. These are nurses, hygienists, administrators in the chemical industry, dispatchers, firefighters. It mainly occurs in non-smokers with predominant symptoms of dry cough and dyspnea. Perilymphatic distribution of pulmonary granulomas is regularly detected by HRCT. A study by Herreaz from 2010 notes that the most common characteristic finding is small clearly circumscribed nodules between 2 and 5mm in size and with a lymphangitic distribution. Although these lesions are seen in the central lung zones, usually with a peribronchovascular and centrilobular distribution, they are more commonly seen in the peripheral lung, usually with a centrilobular and subpleural distribution along the fissures. The involvement is usually symmetrical, and the affected zones are mostly upper and middle lung parts (16). The perilymphatic distribution of micronodules, the interstitial changes as well as the additional (atypical) finding of sarcoidosis are analyzed in this article.

In this study, the patients are mainly female, i.e. 46 (92%) versus male with 4 (8%), aged 30-73 years, mostly living in an urban environment. Regarding the smoking status, 8 (16%) patients declared themselves as current smokers and 42 (84%) as non-smokers, but 28 (56%) of them were smokers in the past. The article compares the distribution of reticular shadows that were more often seen in smokers compared to non-smokers, with a statistically significant difference confirmed for their peripheral and subpleural localization (for p=0.0034 and p=0.0014), respectively in the upper and middle lung zones and in the lower lung zones.

HRCT findings of reticular opacities were not significantly associated with cough ($p > 0.05$).

Micronodular lung changes detected by HRCT and 1-3mm in size were more frequent compared to those of 3mm – 40 (80%) vs 24 (48%). Micronodules 1-3mm predominated in the upper and middle zones 32 (64%), while in the lower zones there were 8 (16%) patients. A statistical analysis and comparison of this type of micronodules in smokers and non-smokers was also made, where it was concluded that micronodular opacities with a size of 1-3mm localized peribronchovascular in the upper and middle lung zones were significantly less HRCT findings in smokers compared to non-smokers (6.67% vs 30%, p=0.047). Micronodules over 3mm also predominated according to localization in the upper and middle zones with 20 (40%) patients compared to the lower zones with 4 (8%) patients. HRCT findings of micronodular changes larger than 3mm in the upper and middle lung zones were significantly associated with the smoking status of the patients. In non-smokers, micronodular changes greater than 3mm peripherally and subpleural were seen significantly less often (6.67% vs 40%, p=0.0088), while the peribronchovascular localization of these changes in the upper and middle pleural zones was seen only in 50% of the patients from the non-smoking group (p=0.00002). The finding of GG opacities dominates in the lower zones, that is, in 14 (28%) of the patients compared to 8 (16%) patients who had this finding in the upper and middle lung zones.

Masses and consolidations easily predominated in the upper and middle zones with 10 (20%) vs 8 (16%) in the lower zones. Also, hypoattenuating lesions easily predominate in the upper and middle zones, compared to the lower, 11 (28%) versus 10 (20%). Regarding additional findings such as GG opacities, masses and consolidations and hypoattenuation-type changes, a significant difference for p=0.015 was observed in masses and consolidations centrally localized in the upper and middle lung zones only in smokers (26.67%). The stage of the disease had no significant effect on the frequency of findings of masses and consolidations (p> 0.05). Bilateral lymphadenopathy by HRCT was diagnosed in 34 (68%) patients, right paratracheal lymphadenopathy in 40 (80%), in the remaining nodal stations in 36 (72%) patients, and in 10 (20%) conglomerated lymph nodes were seen. Calcified lymph nodes were presented in 16 (32%) patients, out of which with focal large calcifications in 12 (24%) patients, punctiform in 2 (4%) and scaly also in 2 (4%) patients. The type of calcifications did not show significance in relation to the stage of the disease. Regarding the smoking status, according to the obtained results, lymphadenopathy was not presented as a significantly different HRCT finding in smokers and non-smokers (p> 0.05).

Focal large calcifications were significantly less frequently detected in smokers (6.67% vs 50%, p = 0.0007). Smokers have significantly more frequent HRCT findings of traction bronchiectasis (40% vs 10%, p=0.026) and fibrosis (46.67% vs 10%, p=0.012).

It is worth highlighting in our study that a correlation was made between the findings and the distribution of the reticular opacities according to the zones and the smoking status. In general, sarcoidosis is not associated with smoking, but since smoking causes an interstitial reaction, and there are a relatively large number of smokers and ex-smokers in the group, our goal was to see if there was significance in that regard. Reticular opacities on HRCT in sarcoidosis were more often seen in smokers compared to non-smokers with statistical significance. We confirm a difference for their presence in the upper middle as well as lower peripheral and subpleural zones. Reticular changes were present in 33.3% of smokers in the upper and middle zones, peripherally and subpleural in contrast to non-smokers where they were absent. While in the lower zones, reticular opacities were present in 40% of the smokers.

Conclusion

HRCT thin-section imaging capabilities and high spatial resolution to generate high-quality images result in better characterization and determination of abnormal changes in the lung parenchyma and interstitium. HRCT is superior to conventional CT for showing subtle parenchymal lesions and aids in the differentiation of active lesions from terminal changes. Pulmonary sarcoidosis shows spontaneous remission in approximately half of the cases within the first two years and an additional number within 5 years. However, it is estimated that for 20% of the patients it is progressive and chronic with the development of pulmonary fibrosis and significant functional insufficiency (3, 17), which leads to 5% mortality, which is why timely and accurate diagnosis is necessary. HRCT is the method of choice in the evaluation of pathological changes in pulmonary sarcoidosis, a disease that shows a wide range of radiological manifestations and is a challenge for radiologists. It shows very precisely the characteristic findings of lymph nodes, micronodules and other lesions, their distribution, as well as atypical changes.

It helps us to guide the therapy accordingly by differentiating active lesions from irreversible fibrosis, and knowing the key and characteristic signs of the disease in parallel with the clinical

symptomatology ensures that the radiologist can make a specific diagnosis.

Based on the results of this study we conclude that smoking plays a certain role in the interstitial changes of the patients with sarcoidosis detected on HRCT, although we do not have data whether smoking has effects on the extent, course or outcome of the disease.

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ORIGINAL ARTICLE *UDK: 616-089.5:615.216.5*

www.doi.org/10.55302/MJA2484079os

A COMPARATIVE STUDY BETWEEN DESFLURANE AND SEVOFLURANE INHALATIONAL ANESTHESIA IN ROCURONIUM CONSUMPTION DURING GENERAL ANESTHESIA WITH FENTANYL AND REMIFENTANIL

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Abstract

Introduction: Rocuronium is a non-depolarizing neuromuscular blocking agent commonly used in anesthesia for muscle relaxation during surgery. It is frequently administered in combination with inhalational anesthetics like sevoflurane or desflurane, as well as opioids like fentanyl or remifentanil. They have distinct pharmacodynamic effects that can alter the required dose of rocuronium to achieve optimal muscle relaxation.

Objectives: The purpose of this study is to compare the consumption of rocuronium in four common anesthetic combinations: desflurane with remifentanil, desflurane with fentanyl, sevoflurane with remifentanil and sevoflurane with fentanyl.

Material and methods: This study included ASA I and II patients undergoing surgery who were randomly assigned into four groups. We used standard hemodynamic monitoring, the Train of Four (TOF) and the Bispectral Index System (BIS) to determine the depth of the anesthesia. We recorded the consumption of neuromuscular relaxant rocuronium in milligrams from intubation until weaking of the patient.

Results: The results obtained in both patient groups demonstrate a significantly lower consumption of rocuronium in the patients who received a desflurane inhalation anesthetic with remifentanil compared to the patients who received a sevoflurane inhalation anesthetic with fentanyl. This is thought to be due to the faster pharmacokinetic profile of desflurane, leading to an accelerated elimination in the patients, in combination with remifentanil, a short-acting opioid.

Conclusion: This study contributed to an awareness of the differences in impact between the two inhalation anesthetics in the consumption of muscle relaxants for general anesthesia.

Key Words*: desflurane; sevoflurane; remifentanil; fentanyl; rocuronium***.**

Introduction

Rocuronium is a non-depolarizing neuromuscular blocking agent (NMBA) commonly used in anesthesia for muscle relaxation during surgery. It is frequently administered in combination

with inhalational anesthetics like sevoflurane or desflurane, as well as opioids like fentanyl and remifentanil. They have distinct pharmacodynamic effects that can alter the required dose of rocuronium to achieve optimal muscle relaxation. Understanding how these agents interact and influence rocuronium consumption is crucial for improving patient's outcomes, minimizing side effects and optimizing anesthetic management (1). Rocuronium is a non-depolarizing neuromuscular blocking agent that works by competitively inhibiting acetylcholine at the nicotinic receptors on the motor endplate of skeletal muscles. This blockade prevents muscle contraction, facilitating muscle relaxation required for various surgical procedures and it is preferred for its rapid onset of action (within 1-2 minutes) and intermediate duration of effect, making it ideal for situations where quick, controlled muscle relaxation is necessary. Its effects are reversible with the administration of acetylcholinesterase inhibitors like neostigmine (2).

Desflurane and sevoflurane are volatile anesthetic agents, and they belong to the halogenated ether class and are characterized by low blood-gas solubility, which allows for rapid onset and offset of anesthesia (3). Desflurane has the lowest blood-gas partition coefficient among modern volatile anesthetics, meaning it is quickly absorbed and eliminated from the body. This characteristic makes desflurane an ideal choice for outpatient surgeries where fast recovery is desired. In terms of its impact on rocuronium, desflurane enhances the action of neuromuscular blockers, often leading to a reduced requirement for rocuronium doses. Sevoflurane is a highly volatile anesthetic that is also less irritating to the airway compared to desflurane, making it a popular choice for general anesthesia in both adults and children. Sevoflurane is associated with potent muscle relaxation and like desflurane, can reduce the need for higher doses of neuromuscular blockers. Both desflurane and sevoflurane are known to have synergistic effects with neuromuscular blockers like rocuronium. The enhancement of neuromuscular blockade, during the administration of these volatile anesthetics, allows for lower doses of rocuronium to achieve the same level of muscle relaxation. Opioid like fentanyl and remifentanil provide potent pain relief and contribute to the overall depth of anesthesia (4). These drugs work primarily by binding to μ-opioid receptors in the central nervous system, inhibiting pain transmission pathways and reducing sympathetic nervous system activity. Fentanyl is a synthetic opioid with a long duration of action compared to remifentanil. It is commonly used in combination with volatile anesthetics to provide both analgesia and anesthesia during surgery. By decreasing the sympathetic response to surgery, fentanyl can indirectly reduce muscle tone and the need for higher doses of neuromuscular blockers like rocuronium. It is particularly useful for maintaining stable hemodynamics during surgery, especially in major procedures. Remifentanil is an ultra-short-acting opioid that undergoes rapid hydrolysis by nonspecific esterase in plasma and tissues. This effect is almost immediate but short-lived, making it highly useful for procedures that require precise control over analgesia and anesthesia depth. The rapid onset and offset of remifentanil help minimize opioid accumulation and reduce the risk of prolonged muscle relaxation or respiratory depression. Remifentanil also reduces the need for higher doses of rocuronium by suppressing the autonomic nervous system.

This study will compare the consumption of rocuronium in four common anesthetic combinations: desflurane and remifentanil versus desflurane and fentanyl versus sevoflurane and remifentanil versus sevoflurane and fentanyl.

Material and Methods

This prospective, randomized, interventional clinical study was carried out at University Clinic for Traumatology, Orthopedic Disease, Anesthesiology, Reanimation and Intensive Care Medi-

cine and Emergency Department, Skopje. We obtained approval from the Bioethics Committee of the Medical Faculty in Skopje. It took over a period of 24 months in which 120 respondents were included, 52 of whom received halogenated inhalational desflurane (MAC=0.7-1), while 68 respondents received halogenated inhalational sevoflurane (MAC=0.7-1) to administer general anesthesia. In the desflurane group, 26 subjects received fentanyl intraoperatively, while 26 subjects were maintained under anesthesia by remifentanil, and in the sevoflurane group, 34 received fentanyl, while 34 were maintained under anesthesia by remifentanil. Inclusion criteria for the study encompassed ASA 1.2 and 3 with BMI below 35 and an age limit of 18–65 years for both genders. The subjects received elective general anesthesia with an inhaled anesthetic desflurane or sevoflurane for colorectal pathology during an elective surgery lasting between 2 and 3 hours. The depth of anesthesia was monitored by the Bispectral Monitoring Index, which ranged from 45 to 55 in both groups, corresponding to stage 3 surgical anesthesia. Then the Rocuronium consumption was measured from intubation until weaking of the patient. The study's exclusion criteria were ASA over 3, age under 18 and over 65 years, morbid obesity, BMI over 35, existence of neuromuscular diseases, history of possible malignant hyperthermia, obstructive lung disease with regular use of bronchodilators and the presence of preoperative cognitive disorder, which originates from chronic opioid or benzodiazepine use, as well as cerebrovascular disorders.

In the operating room, patients were connected to a monitor to observe the ECG, non-invasive blood pressure, pulse oximetry, and Bispectral Index. A peripheral neurostimulator was installed to monitor The Train of Four (TOF). Patients were reoxygenated with 100% oxygen within 3 minutes with a flow of fresh gases of 6L/min and anesthesia was induced with a standardized induction approach using sedative midazolam 0.03mg/kg iv., fentanyl 1-2mcg/kg, propofol 2mg/kg and muscle relaxant rocuronium 0.6mg/kg. The respiratory pathway is secured with an adequately-sized endotracheal tube and connected to an anesthesiology ventilation machine with an inhaled anesthetic desflurane (3–6%), (1–2%) to MAC=0.7–1, with a flow of fresh gases of 2L/min, 50% air with 50% oxygen. Tidal capnography etCO2, the inspiratory faction (Fi) of anesthetic gases and the expiratory faction (FE) of volatile anesthetics are monitored. Minute ventilation is set with a respiratory volume of 6–8ml/kg, a 12/min respiratory frequency and an inhale exhale ratio of 1:2 to maintain a 30–40mmHg CO2 tidal. The dosage for maintenance of intravenous and inhaled anesthetic agents is titrated to maintain BIS from 45–55. Additional bolus doses of fentanyl at a dose of 0.5mcg/kg were given as needed. Remifentanil was given at a dose of 0.125–0.25mcg/kg/min. Muscle relaxation was maintained with intermittent doses of rocuronium at a dose of 0.15mg/kg. The volatile anesthetic was reduced 15 minutes before the surgery ended to MAC=0.5 and was interrupted after the last surgical stitch was placed. The flow of fresh gases was then increased to 6L/min with 100% oxygen. After achieving TOF ≥ 3, a reversion of the neuromuscular block with Neostigmine 0.03mg/kg and Atropine 0.01mg/kg was administered iv.

Results

The statistical analyses were performed using SPSS version 26. The significance threshold, for all statistical analyses, was set at $p<0.05$. To compare the data, a student's T test was employed. The sample size was 120 subjects. Both groups were comparable in demographic data. The patients were aged from 55.2 to 65 years, and the average age was 62±2.5 years. The gender structure of the patients consisted of 54 (45%) women and 66 (55%) men. According to the ASA value, 54 (45%) patients had score 3, 52 (43.33%) had score 2 and 14 (11.67%) had ASA 1. The body mass index ranged from 20.1 to 28.2kg/m2, on average was 23.8 ± 1.9kg/m2.

For p=0.000001, an overall statistically significant difference between the analyzed groups was confirmed in terms of Body Mass Index, which, with post-hoc analysis, was shown to be due to a significantly lower BMI in the desflurane remifentanil group versus the desflurane fentanyl group (22.33±1.4 vs 24.09±1.5kg/m2, p=0.0006), versus the sevoflurane remifentanil group (22.33±1.4 vs 24.06±2.1kg/m2, p=0.00075), and, versus the sevoflurane fentanyl group (22.33±1.4 vs 24.73±1.6kg/m2, p=0.00014) (Table 1, 1a, Figure 1).

Table 1. BMI of patients in the desflurane remifentanil, desflurane fentanyl, sevoflurane remifentanil and sevoflurane fentanyl groups.

Statistical parameters	Group			
	Desflurane Remifentanil	**Desflurane Fentanyl**	**Sevoflurane Remifentanil**	**Sevoflurane Fentanyl**
BMI (kg/m2)				
mean ± SD	22.33±1.4	24.09±1.5	24.06±2.1	24.73±1.6
min- max	20.1 – 25.1	21.8 – 27.1	21.1 – 28.2	21.3 – 27.1

F (Analysis of Variance)

Table 1a. Tested intergroup differences in patients' BMI

F=11.31 ***p=0.000001; Tukey HSD test			
Group	**Desflurane Fentanyl**	**Sevoflurane Remifentanil**	**Sevoflurane Fentanyl**
Desflurane Remifentanil	***p=0.0006	***p=0.00075	***p=0.00014
Desflurane Fentanyl		p=1.0	p=10.45
Sevoflurane Remifentanil			p=10.42

F (Analysis of Variance); post-hoc Tukey honest test.
***sig p<0.0001

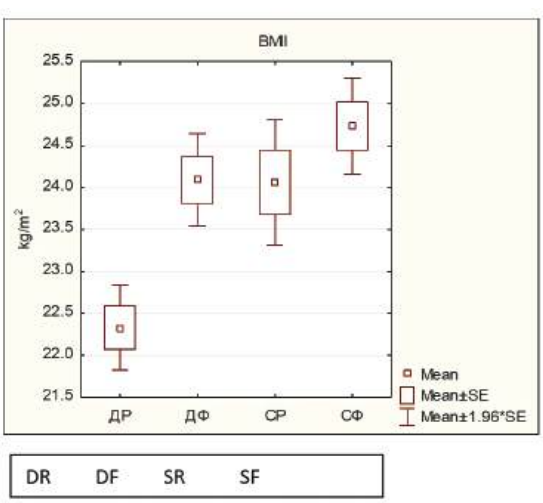

Figure 1. Mean BMI in the desflurane remifentanil, desflurane fentanyl, sevoflurane remifentanil, and sevoflurane fentanyl groups.

An overall statistically significant difference was confirmed in terms of the Rocuronium value (p<0.0001), which with post-hoc analysis, was shown to be due to significantly lower consumption of muscle relaxant given intraoperatively in the desflurane remifentanil group compared to the three other groups: desflurane fentanyl group (57.67±8.2 vs 66.67±10.9mg, p=0.025), sevoflurane remifentanil group (57.67±8.2 vs 73.0±13.4mg, p=0.000152) and sevoflurane fentanyl group (57.67±8.2 vs 79.0±14.9mg, p=0.000137), as well as significantly lower consumption in the desflurane fentanyl group compared to the sevoflurane fentanyl group. (66.67±10.9 vs 79.0±14.9mg, p=0.00092) (Table 2, 2a, picture 2).

Table 2. Consumption of rocuronium in desflurane remifentanil, desflurane fentanyl, sevoflurane remifentanil and sevoflurane fentanyl groups.

Statistical parameters	Group			
	Desflurane Remifentanil	**Desflurane Fentanyl**	**Sevoflurane Remifentanil**	**Sevoflurane Fentanyl**
Rocuronium/mg				
Mean ± SD	57.67±8.2	66.67±10.9	73.0±13.4	79.0±14.9
Min - max	50 – 70	50 – 90	50 – 90	50 – 100

Table 2a. Tested between-group differences in consumption of rocuronium.

F=16.95 p=0.000000 Tukey HSD test			
Group	**Desflurane Fentanyl**	**Sevoflurane Remifentanil**	**Sevoflurane Fentanyl**
Desflurane Remifentanil	*p=0.025	***p=0.000152	***p=0.000137
Desflurane Fentanyl		p=0.19	***p=0.00092
Sevoflurane Remifentanil			p=0.23

F (Analysis of Variance); post-hoc Tukey honest test.
*sig p<0.05, ***sig p<0.0001.

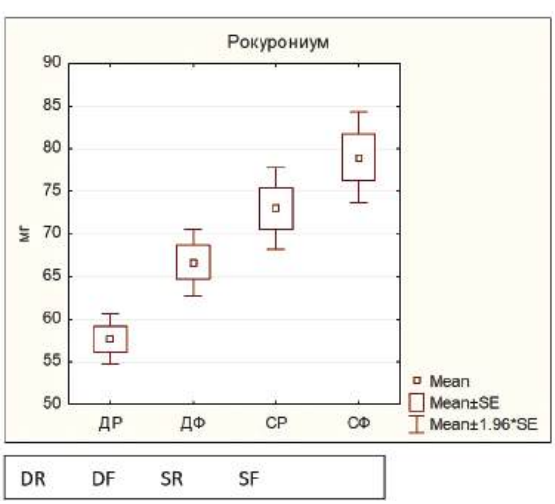

Figure 2. Mean consumption of rocuronium in the desflurane remifentanil, desflurane fentanyl, sevoflurane remifentanil and sevoflurane fentanyl groups.

Discussion

The consumption of rocuronium is influenced by various factors including the type and dose of anesthetics administered. Desflurane potentiates the effects of neuromuscular blocking agents like rocuronium and the exact mechanisms underlying this potentiation are not fully understood but is believed to involve interactions at both the spinal cord and neuromuscular junction. The use of remifentanil with its rapid onset and offset can provide a high degree of intraoperative control over anesthesia depth further reducing the need for larger doses of rocuronium. Rapid metabolism ensures that it does not accumulate and minimize prolonged muscle relaxation or respiratory depression following surgery. A comparable outcome was reported in the study of Maidatsi et al., that desflurane anesthesia significantly prolongs the duration of action of rocuronium at 0.9mg/kg −1 single bolus dose, compared to sevoflurane or propofol anesthesia maintenance regimens (5). Our findings suggest that the group desflurane remifentanil had significantly lower consumption of muscle relaxant given intraoperatively compared to the three other groups. Significant difference was shown to be due to lower consumption of rocuronium given intraoperatively in the desflurane remifentanil group 57.67±8.2mg compared to the sevoflurane fentanyl group 79.0±14.9mg. Same results were presented in the study of Moriyama et al., that neuromuscular relaxation effects were found to be stronger when using inhaled anesthesia, especially desflurane (6). Both desflurane-remifentanil and sevoflurane-fentanyl provide excellent hemodynamic stability during surgeries, but remifentanil, when used with desflurane, tends to offer slightly more precise control over hemodynamic fluctuations, especially in high-stress surgeries. This enables an overall decrease in the required doses of rocuronium, as muscle tone and autonomic responses are more finely tuned. Regarding their adjustment in dosage, ensured optimal muscle relaxation is attained, with a minimum of drug-related side effects such as postoperative residual neuromuscular blockade.

Conclusion

The resulting values obtained from this study showed a statistically significant difference. Desflurane combined with remifentanil has a lower consumption of rocuronium due to the synergistic effects of desflurane on neuromuscular blockade and the rapid metabolism of remifentanil. As showed in the results, sevoflurane combined with fentanyl results in a significantly higher dose of rocuronium. Intraoperative rocuronium consumption is influenced by the choice of anesthetic agents like the inhalational anesthetics and opioids used. This study contributed to an awareness of the differences in impact between the two inhalation anesthetics in the consumption of muscle relaxants for general anesthesia in clinical practice. Understanding the interactions between these anesthetics is essential for optimizing anesthesia management, minimizing drug-related side effects and ensuring safe and effective surgical outcomes. Further research into these interactions will continue to improve clinical protocols and enhance patients' outcomes.

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ORIGINAL ARTICLE *UDK: 616-089.5-032:611.819.59]:616-089.168*

www.doi.org/10.55302/MJA2484086ch

UNVEILING THE ADVANTAGES: REDUCED OPIOID REQUIREMENT WITH CONTINUOUS EPIDURAL ANALGESIA - PILOT STUDY

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Abstract

Introduction: Epidural anesthesia is particularly suitable for patients in older age brackets. While it was previously the predominant approach for postoperative analgesia across various procedures, alternative methods that are equally effective, potentially safer, and more cost-efficient have since emerged. This article will explore the advantages and drawbacks of continuous epidural analgesia intraoperatively, particularly its outcomes in specific surgical contexts.

Material and methods: The University Clinic for Traumatology, Orthopedics, Anesthesiology, Resuscitation, Intensive Care and Emergency Center, enrolled twenty patients in an observational clinical study over a six-months period to assess the comprehensive management of analgesia during the intraoperative and postoperative phases. After induction of GA, Bupivacaine 0.125% was administered by a continuous epidural infusion until the end of the surgery. Postoperative outcomes included assessing pain levels immediately after surgery, 3, 6, 12 and 24 hours later, as well as the incidence of postoperative complications, if any.

Results: The study enrolled twenty patients who underwent a combination of general anesthesia and epidural anesthesia. We measured the patients' postoperative pain, and the results showed that the most pain typically flares up three hours after surgery and then subsides over the next 24 hours. On the first day following surgery, the average VAS was 1.8. Postoperative nausea and vomiting occurred in every patient who had morphine administered as postoperative analgesia.

Conclusion: The study concludes that continuous epidural analgesia reduces the need for opioid use and mitigates the associated side effects.

Keywords: *epidural analgesia; postoperative nausea and vomiting; visual analogue scale.*

Introduction

Continuous epidural analgesia can be employed for managing postoperative pain following thoracic, abdominal or lower extremity surgery. While it was previously widely adopted as the standard approach for postoperative pain relief across various procedures, alternative methods that

are equally effective, potentially safer and more cost-efficient, have now become available (1). Continuous epidural analgesia is predominantly utilized in open surgeries, although it can also be employed in genitourinary or lower extremity procedures. Epidural catheters are typically reserved for patients expected to remain hospitalized for more than 24 hours post-surgery and are seldom utilized in minimally invasive procedures. Over time, the indications for and utilization of continuous epidural analgesia have diminished due to shorter hospital stays for many surgeries, increased adoption of minimally invasive techniques, and advancements in perioperative pain management strategies. Multimodal approaches focusing on sparing opioids with nonopioid analgesics, peripheral nerve blocks, local anesthetic infiltration and other methods, have emerged as viable alternatives. These strategies can provide equivalent pain relief to epidural analgesia for many procedures while mitigating the risks, side effects and costs associated with epidurals. Epidural analgesia remains part of some enhanced recovery after surgery protocols, sometimes offered alongside other regional anesthesia options as alternatives. Furthermore, epidural techniques are increasingly employed for diagnostic procedures, acute pain management and the treatment of chronic pain. Epidural blocks have been demonstrated to potentially decrease the surgical stress response, lower the risk of cancer recurrence, reduce the incidence of perioperative thromboembolic events, and potentially lower the morbidity and mortality related to major surgery (2,3). Neuraxial anesthesia, when compared to general anesthesia, offers several potential advantages. These include reduced intraoperative blood loss and transfusion requirements, a lower incidence of postoperative thromboembolic events, improved pain relief and postoperative mobility up to 9 weeks after surgery, quicker return of bowel function, and other debated benefits such as shorter hospital stays and reduced healthcare costs (4). During open surgeries, patients may require significant sedation if not undergoing a combined general-neuraxial approach. A sensory level typically around T6 is necessary, with catheter placement usually in the midthoracic region (5). The aim of this study was to evaluate the impact of continuous epidural analgesia on reducing the necessity for opioid use, mitigating their associated side effects, and improving overall patients' outcomes in the postoperative period. Additionally, to assess the benefits of this analgesic approach in enhancing patient's comfort, satisfaction, and recovery in comparison to traditional opioid-based pain management strategies.

Material and Methods

Since January 1, 2024, at the University Clinic for Traumatology, Orthopedics, Anesthesiology, Resuscitation, Intensive Care and Emergency Center - Skopje, a prospective database was maintained for patients undergoing radical cystectomy (RC), kidney transplantation, prostatectomy, Whipple surgery and nephrectomy (Chart 1). Approval from the Internal Hospital Ethics Committee and written informed consent from patients were secured prior commencing the study. The American Society of Anesthesiologists (ASA) score was evaluated for all patients and all of them abstained from eating or drinking after midnight on the night before surgery. Standard hemodynamic monitoring (including electrocardiogram, pulse oximetry and non-invasive blood pressure measurement) was performed before anesthesia induction. An epidural catheter was administered before anesthesia induction. The patients receiving epidural, were positioned sitting up, and the L1-L2 epidural space was located using an 18G Touhy needle with a loss of resistance technique. Subsequently, placement of the epidural catheter was confirmed by a negative aspiration test using 2ml of 0.5% bupivacaine. All patients were induced to general anesthesia, adequately with benzodiazepines, midazolam (0.02-0.04mg/kg), propofol (1.5-2.5mg/kg), rocuronium bromide (0.6-1mg/kg) and Fentanyl in range of 0 to 20mcg before laryngoscopy

and intubation. After the induction of general anesthesia, it was maintained with Sevoflurane (1/2%), and Bupivacaine 0.125% was administered by a continuous epidural infusion until the end of the operation.

Postoperative pain management relied on NSAIDs (non-steroidal anti-inflammatory drugs), Acetaminophen, Methimazole, based on sufficient measurement of pain intensity, according to VAS scale (The Visual Analogue Scale (VAS) measures pain intensity). The VAS consists of a 10cm line, with two end points representing 0 ('no pain') and 10 ('pain as bad as it could possibly be'). Postoperative outcomes included assessing pain levels immediately after surgery, 3, 6, 12 and 24 hours later, as well as the percentage of complications if any occurred.

All data were gathered by trained anesthesia staff who were not involved in patients' care to reduce bias. Patients' demographics, perioperative data and outcome metrics were among the information gathered. Statistical software was used to carry out statistical analyses. Categorical variables were displayed as frequencies and percentages, whereas continuous variables were given as means ± standard deviations.

Results

In this evaluation, 20 patients were recruited who were operated under combined general anesthesia and epidural anesthesia. Thirteen of the patients were males, seven females (Chart 2) and the age range of the group was between 37 and 79 years, with average age of 64.15 years. The body mass index varied between 21 and 32, an average of 26.15. Total administration of Bupivacaine 0.125% was in range of 20ml for Bricker surgery in duration of 200 minutes, to 150ml for Whipple in duration of 550 minutes (Chart 3).

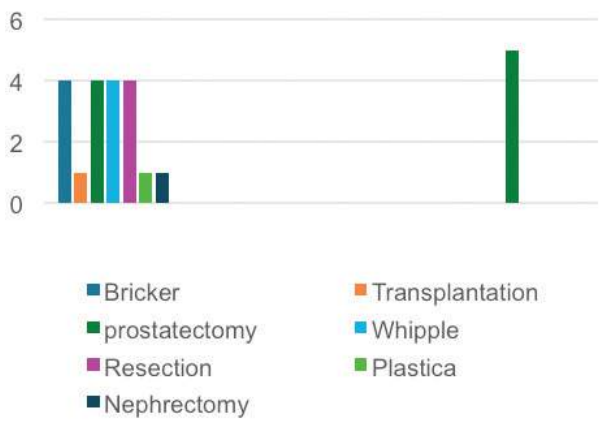

Chart 1. Types of surgeries.

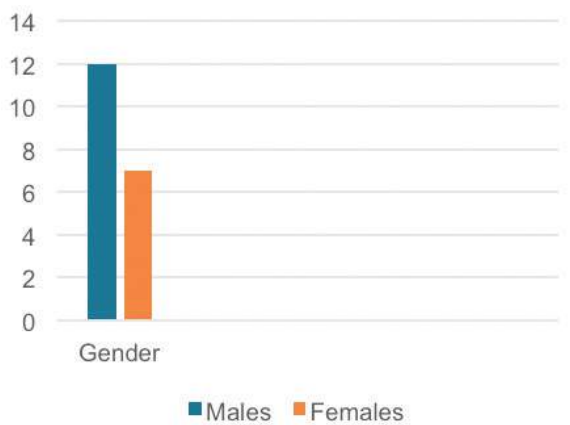

Chart 2. Gender of patients.

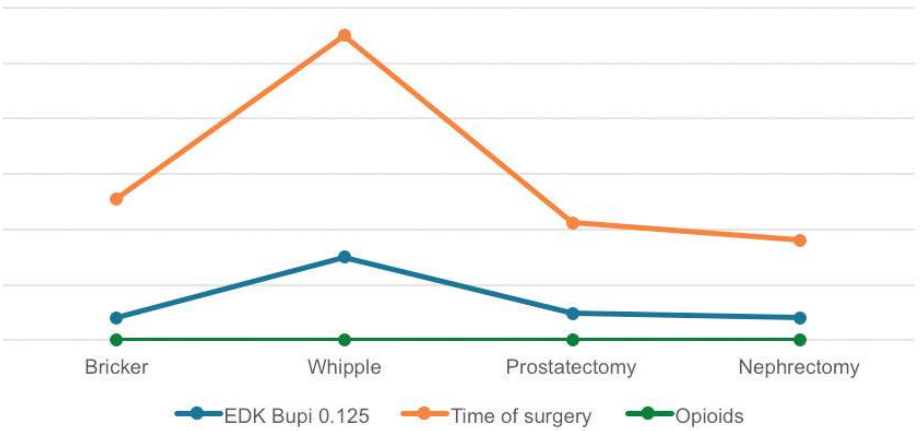

Chart 3. Average use of Bupivacaine 0.125%, use of Opioids and duration of surgery.

After reviewing the data, it was found that patients who received continuous epidural analgesia, with dosage adjusted based on surgery length and patients' needs, required less opioid pain relief. The patients with a greater body mass index (BMI) necessitated higher amount of pain relief medication. Postoperative outcomes included assessing pain levels immediately after surgery, 3, 6, 12 and 24 hours after surgery, and the incidence of postoperative nausea and vomiting. The patients experienced peak pain intensity 3 hours after surgery, with pain levels gradually decreasing over the next 24 hours. After surgery, the majority of patients relied on acetaminophen and methimazole for postoperative pain relief (Chart 4). Four out of twenty patients have a demand for postoperative analgesia with Morphine (2-3mg), according to VAS. Subsequently, all experienced postoperative nausea and vomiting.

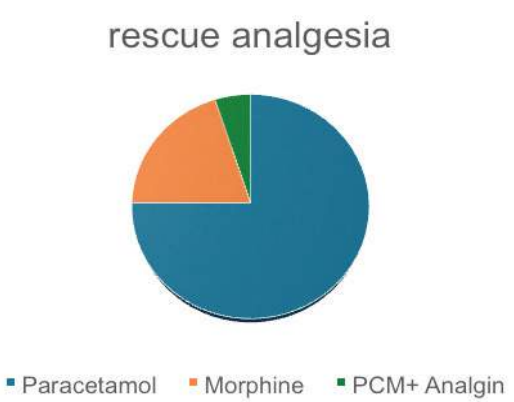

Chart 4. Rescue Analgesia

Discussion

The International Association for the Study of Pain (IASP) defines pain as an unpleasant emotional and sensory experience that is either described, or actually connected to potential tissue damage (5). The opioid system is a vital physiological mechanism that regulates pain, emotions, immune responses and various other bodily functions. It encompasses the interaction and coordination of numerous endogenous opioid peptides and various types of opioid receptors located

in both the central nervous system (CNS) and peripheral nervous system (6).

Opioids are commonly prescribed to treat moderate to severe acute and chronic pain. However, these medications have significant drawbacks, such as inducing tolerance to pain relief, addiction, and various behavioral side effects that frequently lead to patient's non-adherence (7). All opioids used in clinical practice act as agonists on the μ-opioid receptor, and the main adverse effects are either directly related to this receptor or potentially influenced by its activation. While opioids are highly effective in managing pain, it is crucial to acknowledge their associated side effects as well. Side effects are prevalent with opioid therapy, with between 50% and 80% of patients in clinical trials experiencing at least one side effect. In real-world usage, the incidence of side effects may be even higher (1). Respiratory depression is a significant concern linked to the use of opioids, particularly in acute pain management when patients have not yet developed tolerance. In cases of persistent pain, the risk is more likely to arise if there is a substantial, often unintended increase in dosage, or changes in the formulation or method of administration. Tolerance, which involves a diminishing response to opioids' pain-relieving effects, is a frequent complication of opioid therapy. This often results in the need for higher doses of opioids to achieve the same level of pain relief, ultimately reducing their effectiveness over time. The impact of opioid compounds on hormonal function is now well-documented and referred to as opioid endocrinopathy (OE) or opioid-induced androgen deficiency (OPIAD) in the case of androgen hormones. These hormonal effects occur in both men and women and have been observed with oral consumption, transdermal, intravenous and intrathecal administration of opioids. Hyperalgesia, also known as hypalgia, is a recently recognized adverse effect characterized by heightened pain sensitivity. This phenomenon manifests as escalating pain levels despite increasing doses of opioids. Prolonged and high-dose opioid use may lead to the development of hyperalgesia, potentially influenced by opioid metabolites like morphine 3-glucuronide (M3G). The most common side effects of opioid usage are constipation (which has a very high incidence) and nausea. Constipation is a prevalent issue, affecting 40% to 95% of patients receiving opioid treatment, and can occur even after a single dose of morphine. The mechanisms underlying opioid-induced nausea and vomiting (OINV) are not completely understood, but they likely involve multiple complex factors. OINV may result from various opioid effects, including heightened sensitivity in the vestibular system (manifesting as symptoms like vertigo exacerbated by motion), direct actions on the chemoreceptor trigger zone, and delayed gastric emptying (leading to symptoms such as early satiety, bloating and worsening after meals). The side effects of opioid are sedation, dizziness, delayed gastric emptying, muscle rigidity, pruritus and dry mouth (8-14).

On the other hand, we have to mention side effects of placing an epidural catheter, which are typically transient. Decreased blood pressure, leading to feelings of dizziness or nausea, temporary urinary incontinence, pruritus (itchy skin), nausea, headaches and nerve injury are some of them, as documented in existing literature (2). It is evident that there is some similarity in the side effects of opioids and epidural anesthesia, which largely depends on the medications administered via the epidural catheter (2,15). The primary aim of this study was to mitigate these side effects by continuously delivering bupivacaine as a local anesthetic through the catheter. Considering both absolute contraindications (such as patients' refusal, sepsis and hypersensitivity to potential medications) and relative contraindications (including infection, coagulation disorders, prior spinal surgery, neurological conditions, thrombocytopenia and coagulopathies), we can mitigate risks to patients' health while maximizing the benefits of continuous epidural analgesia.

Conclusion

Continuous epidural analgesia intraoperatively effectively reduces the need for opioid medications and their associated side effects. Despite the proven effectiveness of opioids in treating various pain conditions, their use can result in significant side effects and complications. The study's evaluations highlight that epidural analgesia provides a viable alternative, minimizing the reliance on opioids and mitigating their negative impacts.

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ORIGINAL ARTICLE *UDK: 616-089.5-032:611.23]-06:616.24-008.4*

www.doi.org/10.55302/MJA2484093gb

EVALUATION OF THE EFFECTIVENESS OF ALVEOLAR RECRUITMENT MANEUVER TECHNIQUES

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Abstract

Introduction: The three primary causes of compression and absorption atelectasis after general endotracheal anesthesia are dyskinesia, dyspnea and elevation in FIO_2. General anesthesia eliminates the sigh reflex in all patients, resulting in atelectasis occurring rapidly. Alveolar recruitment maneuvers improve gas exchange, increase arterial oxygenation, and draw in collapsed alveoli. There is a wealth of literature supporting alveolar recruitment movements, and these days, mechanical ventilator settings include alveolar recruitment maneuvers. Our study's objective was to assess the effectiveness of alveolar recruitment techniques incorporated in the GE Healthcare Carestation 750.

Material and Methods: This evaluation covered all ASA I-III patients between the ages of 18 and 60 who were scheduled for general endotracheal anesthesia and did not have a history of cardiac or respiratory illness. Following tracheal intubation and the onset of general anesthesia, the patients were split into three groups: Group I - no intervention; Group II - single-step recruitment (pressure hold of 40mmHg for 20 seconds); Group III - multiple-step recruitment (Step I: Pinsp 30/PEEP 10; breathes 3; Step II: Pinsp 40/PEEP 10; breaths 3; Step III: Pinsp 50/PEEP 15; breaths 3). Changes in pulmonary compliance were the main result, and variations in PaO_2 and PaO_2/FIO_2 were the secondary result. Analyses of arterial blood gas were taken both prior to and during the recruitment maneuver. A 50% FiO_2 ratio was used.

Results: There were 75 patients in total for this evaluation. In contrast to the control groups, the alveolar recruitment maneuver groups exhibited greater pulmonary compliance (37% vs. 24% Group III vs. Group II). The groups that were also given alveolar recruitment strategies experienced an increase in intraoperative PaO_2 ($P<0.05$). Compared to the control groups, PaO_2/FIO_2 rose in the alveolar recruitment maneuver groups. During or after the alveolar recruitment operations, none of the patients experienced any problems.

Conclusion: The individuals undergoing the alveolar recruitment maneuver groups had improved oxygenation.

Keywords: *alveolar collapse; mechanical ventilation; multi-step recruitment; single step recruitment.*

**Parts of this text were published in: Gavrilovska Brzanov A., Petrusheva Panovska A., Jovanovski Srceva M., Brzanov N., Nastasovic T., Kuzmanovska B. Single-step, multi-step, or no alveolar recruitment maneuver? EJA 2024;41(62):533.*

Introduction

General endotracheal anesthesia, routine practice in various surgical procedures, can lead to significant respiratory complications, particularly concerning respiratory complications. Three primary causes of such complications are dyskinesia, the loss of sigh breath, and an increase in the fraction of inspired oxygen (FIO_2). These factors prominently contribute to the development of compression and absorption atelectasis during anesthesia (1,2). Atelectasis, characterized by the collapse of alveoli, poses a serious threat to respiratory function during and after surgical procedures. The elimination of the sigh reflex, which naturally occurs under general anesthesia, plays a pivotal role in this process. The sigh reflex is a protective mechanism that helps keep the alveoli open by periodically taking deeper breaths. When this reflex is suppressed by anesthesia, atelectasis can develop rapidly, affecting 100% of patients under general anesthesia as documented in numerous studies. This rapid alveolar collapse disrupts normal gas exchange, leading to decreased arterial oxygenation and increased risk of postoperative pulmonary complications (3,4). The impact of atelectasis on patients' outcomes cannot be overstated. It not only hampers gas exchange, but also predisposes patients to infections and longer recovery times. Therefore, addressing this issue is of paramount importance in anesthetic management. One of the promising approaches to mitigate this problem is the use of alveolar recruitment maneuver (ARM) (5).

ARM aims to reopen collapsed alveoli and to maintain their patency throughout the duration of anesthesia. These techniques involve the application of intermittent positive airway pressure or sustained inflation, which helps re-expand the collapsed alveoli, enhance gas exchange, and subsequently improve arterial oxygenation. The efficacy of these maneuvers is well-documented in the literature. For instance, research has shown that alveolar recruitment maneuvers can significantly reduce the incidence of postoperative pulmonary complications, improve oxygenation, and shorten the length of hospital stays (5-7).

The integration of ARM into mechanical ventilator settings represents a significant advancement in anesthetic practice. Modern mechanical ventilators are equipped with sophisticated settings that allow for the precise application of these maneuvers, tailored to the individual needs of the patient. This integration not only enhances the effectiveness of ventilation, but also simplifies the process for anesthesiologists, ensuring that optimal lung function is maintained throughout the procedure (5,6). In this context, the GE Healthcare Carestation 750 stands out as a state-of-the-art ventilator that incorporates advanced alveolar recruitment techniques. This study aims to evaluate the efficacy of these maneuvers as implemented in Carestation 750. By systematically analyzing its impact on gas exchange, alveolar recruitment and arterial oxygenation, we seek to determine the effectiveness of this technology in clinical practice.

Understanding the mechanics and benefits of these ARMs is crucial for anesthesiologists and healthcare professionals. As the use of general anesthesia continues to rise, the need for effective strategies to prevent and manage atelectasis becomes increasingly critical. The aim of our study was to evaluate the efficacy of different alveolar recruitment maneuvers incorporated in GE Healthcare Carestation 750.

Materials and Methods

Study Design and Setting

This study was conducted at the University Clinic for Anesthesiology, Reanimation and Intensive Care Medicine, Clinical Center "Mother Theresa", Faculty of Medicine, "Ss. Cyril and Methodius" University, Skopje, Republic of North Macedonia. The study protocol was reviewed and approved by the internal ethical review board of the institution. Informed consent was obtained from all participating patients prior to their inclusion in the study.

Participants

The study included patients aged 18 to 60 years, classified as American Society of Anesthesiologists (ASA) Physical Status I-III, who were scheduled for surgical interventions requiring general endotracheal anesthesia. Exclusion criteria included: pregnant woman, patients with any known history of cardiac or respiratory diseases to minimize confounding variables that could affect pulmonary function and the outcomes of the study.

Anesthesia and Intervention Protocol

After obtaining informed consent, the patients were prepared for surgery according to standard preoperative protocols. General anesthesia was induced using a standardized regimen, and tracheal intubation was performed. Upon successful induction of anesthesia and intubation, patients were randomly assigned to one of three groups:

Group I: Control Group (No Intervention) Patients in this group received no additional intervention beyond standard ventilation settings.

Group II: Single-Step Recruitment Maneuver Patients in this group underwent a single-step alveolar recruitment maneuver, which involved applying a sustained inspiratory pressure of 40 cmH2O for 20 seconds.

Group III: Multiple-Step Recruitment Maneuver Patients in this group underwent a multi-step alveolar recruitment maneuver, which was performed as follows:

Step I: Inspiratory pressure (Pinsp) of 30cmH_2O with positive end-expiratory pressure (PEEP) of 10cmH_2O for 3 breaths.

Step II: Inspiratory pressure (Pinsp) of 40cmH_2O with PEEP of 10cmH_2O for 3 breaths.

Step III: Inspiratory pressure (Pinsp) of 50cmH_2O with PEEP of 15cmH_2O for 3 breaths.

The FiO_2 was maintained at 50% for all groups throughout the procedure.

Outcome Measures

The primary outcome measure was the change in pulmonary compliance, which was assessed by measuring compliance before and after the recruitment maneuvers.

Secondary outcome measures included changes in arterial oxygen tension (PaO_2) and the PaO_2/FIO_2 ratio. Arterial blood gas (ABG) analyses were performed at two time-points: before the

induction of anesthesia and after the recruitment maneuvers. The ABG samples were analyzed to determine PaO_2 levels, which were then used to calculate the PaO_2/FIO_2 ratio where the FiO_2 was maintained at 50% for all groups throughout the procedure.

Data Collection and Analysis

All data were collected by trained anesthesia personnel who were blinded to the group assignments to minimize bias. The collected data included patients' demographics, baseline pulmonary function and outcome measures (pulmonary compliance, PaO_2, and PaO_2/FIO_2 ratios). Statistical analyses were performed using appropriate statistical software. Continuous variables were expressed as means ± standard deviations, and categorical variables were presented as frequencies and percentages. Differences between groups were analyzed using analysis of variance (ANOVA). A p-value of <0.05 was considered statistically significant.

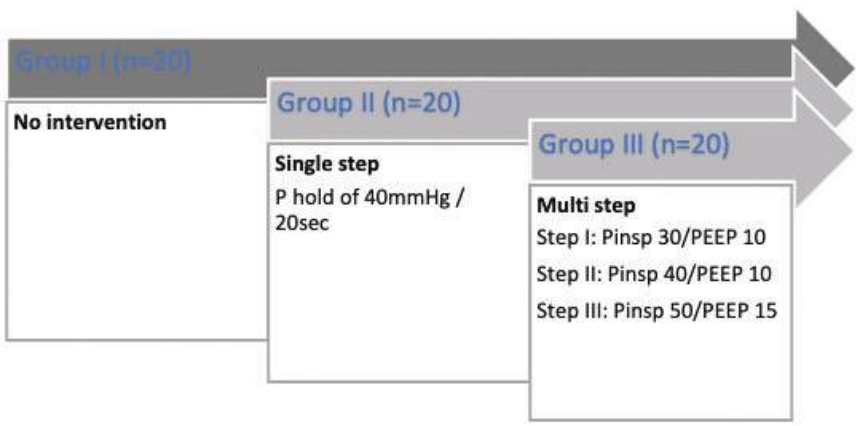

Figure 1. Recruitment Maneuver Intervention Protocol.

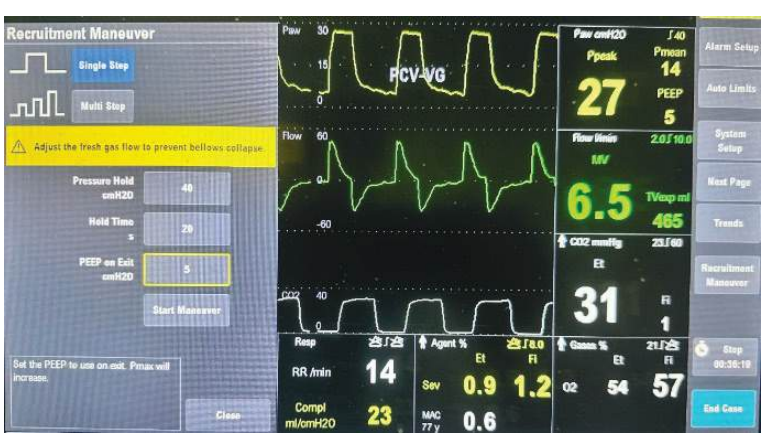

Figure 2. Single step alveolar recruitment maneuver.

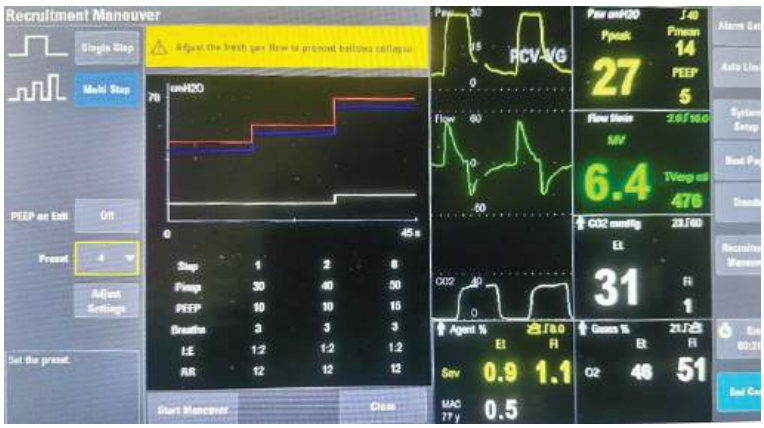

Figure 3. Multi step alveolar recruitment maneuver.

Results

A total of 75 patients were enrolled in this study, with 25 patients allocated to each of the three groups (Group I: Control, Group II: Single-Step Recruitment, Group III: Multiple-Step Recruitment). The demographic and baseline characteristics of the patients were comparable across the three groups, with no significant differences in age, gender, body mass index (BMI), or ASA physical status classification.

The primary outcome measure, pulmonary compliance, showed significant improvements in the groups that underwent alveolar recruitment maneuvers. Specifically, Group III (Multiple-Step Recruitment) exhibited a 37% increase in pulmonary compliance compared to baseline values, while Group II (Single-Step Recruitment) demonstrated a 24% increase. In contrast, the control group (Group I) showed no significant change in compliance (Table 1).

Table 1. Respiratory parameters in the Groups.

Group	Compliance mL/cmH_20		PaO_2 mmHg		PaO_2/FIO_2	
	Baseline	After intervention	Baseline	After intervention	Baseline	After intervention
I	53 ± 6.8	/	97 ± 23	/	421 ± 44	/
II	53 ± 6.7	65 ± 7.8	146 ± 27	177 ± 26	481 ± 31	584 ± 51
III	53 ± 5.0	72 ± 6.9	135 ± 27	172 ± 30	444 ± 34	567 ± 41

PaO_2 - partial pressure of oxygen; PaO_2/FIO_2 - the ratio of arterial oxygen partial pressure to fractional inspired oxygen

The data revealed a significant increase in PaO2 levels in both recruitment maneuver groups compared to the control group. The mean PaO2 increased markedly in Group II and Group III, indicating enhanced oxygenation due to the recruitment maneuvers. Statistical analysis confirmed that these increases were significant ($P<0.05$).

No adverse events or complications were reported during or following the alveolar recruitment maneuvers in any of the groups. All patients tolerated the procedures well, and there were no in-

stances of hemodynamic instability, barotrauma, or other respiratory complications associated to the recruitment maneuvers.

Discussion

These results collectively demonstrate that ARM significantly enhances pulmonary compliance and oxygenation without compromising patients' safety. The multi-step recruitment approach, in particular showed the most pronounced benefits, suggesting that a gradual and stepped increase in inspiratory pressures may be more effective in recruiting alveoli and improving respiratory mechanics. These results highlight the efficacy of ARM in improving lung mechanics during general anesthesia (6,7). This improvement underscores the effectiveness of ARM in enhancing gas exchange and maintaining adequate oxygenation during surgery. The observed improvements in pulmonary compliance and oxygenation suggest that incorporating ARM into standard anesthetic practice can enhance patients' outcomes by preventing and reversing atelectasis. Atelectasis, a common complication of general anesthesia, can lead to impaired gas exchange, hypoxemia and increased risk of postoperative pulmonary complications. By effectively recruiting collapsed alveoli, recruitment maneuvers help maintain optimal lung function, thereby reducing the risk of these complications (4,8).

Our findings align with previous studies that have reported the benefits of ARM. For instance, Hedenstierna demonstrated that recruitment maneuvers prevent atelectasis and improve oxygenation during general anesthesia. Similarly, Hartland et al. highlighted the efficacy of various recruitment strategies in enhancing pulmonary function. The consistency between our results and these earlier studies reinforces the robustness of ARM as an effective intervention for improving intraoperative respiratory outcomes (9,10).

In addition to these foundational studies, several other investigations have explored the benefits of ARM. Neumann et coauthors reported that systematic recruitment maneuvers significantly improved gas exchange and reduced the incidence of postoperative pulmonary complications in patients undergoing cardiac surgery (7). Similarly, an article of Fernandez-Bustamante demonstrated that a stepwise recruitment maneuver combined with individualized PEEP titration resulted in improved oxygenation and lung mechanics in patients with acute respiratory distress syndrome (ARDS) undergoing surgery (11). These studies further corroborate our findings and emphasize the utility of ARM across various surgical and clinical contexts. Moreover, in another study, the same authors showed that intraoperative ARM combined with high PEEP levels improved respiratory function and reduced atelectasis in obese patients undergoing laparoscopic surgery (12). Other studies also investigate the ARM in obese patients undergoing laparoscopic surgery and its benefits on respiratory effects after pneumo-peritoneum deterioration (13). Those study highlight the potential benefits of ARM in high-risk patient populations, supporting the broader applicability of our findings (7,11-15).

The study also confirms the safety and feasibility of performing ARM in an intraoperative setting. None of the patients experienced adverse events related to the recruitment procedures, indicating that both single-step and multiple-step maneuvers can be safely integrated into standard anesthetic protocols. This safety profile is critical for the widespread adoption of these techniques, as it reassures clinicians that recruitment maneuvers do not introduce additional risks to patient care (11-15).

The present plethora of literature provides an update on alveolar recruitment approaches taking into account the wide range of variations in their use, as well as the various parameters influencing the response to movement. Recruitment techniques could stop the reduction in oxygenation brought on by mechanical ventilation and lung de-recruitment (5,6,10-15). A panel of experts created consensus recommendations for the surgical patient's intraoperative protective ventilation. It is important to stress that two research topics fell short of the 70% consensus threshold. First, there is insufficient high-quality supporting evidence to support the routine recommendation of ARM for all patients following tracheal intubation, yet a majority of 57% agreed that it might be taken into consideration based on a unique risk-benefit analysis (16). Hartland and colleagues reviewed the literature and assessed the various alveolar recruitment techniques. With the exception of one study, various ARMs were identified (10). The researchers performed persistent manual inflations up to a PIP of 40cm H2O for their alveolar recruitment procedures. Pang et al. used ten sustained manual inflations over one minute, while Almarakbi et al. used a single sustained inflate for fifteen seconds. In both trials, the groups who underwent ARM had higher intraoperative PaO_2. On pulmonary compliance, however, only Almarakbi et al. published findings, which indicated a rise only in the groups that underwent ARM. Airway resistance and PaO_2/FIO_2 were not discussed in either study contrary to our investigations who take these variables into account (17,18). Three studies used stepwise PEEP increases as an ARM, beginning at 4cm H_2O and ending at 20cm H_2O. There was a statistically significant increase in the groups that underwent ARM in both studies that included intraoperative PaO_2. The pulmonary compliance of the ARM groups improved in all three trials. Findings were confirmed in our study as well. PaO_2/FIO_2 was only used as an outcome measure by Springer et al. and Whalen et al., and it was considerably higher in the ARM groups during the intraoperative phase (19,20).

Future research should also explore the long-term benefits of ARM, including their impact on postoperative recovery, length of hospital stay and overall patients' morbidity and mortality. Additionally, investigating the mechanistic aspects of recruitment maneuvers, such as their effects on lung tissue and inflammatory responses, could provide deeper insights into their therapeutic benefits. Comparative studies evaluating different recruitment strategies and their outcomes in various surgical and clinical contexts would also be valuable.

Conclusion

In conclusion, our study validates that in patients receiving general endotracheal anesthesia, alveolar recruitment maneuvers considerably improve arterial oxygenation and pulmonary compliance. To enhance patients' safety and respiratory outcomes, these methods ought to be included into routine anesthetic practice.

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CASE REPORT *UDK: 618.5-089.888.61-089.5:616.131-008.331.1*

www.doi.org/10.55302/MJA2484102k

ANESTHESIA FOR CAESAREAN SECTION IN A PATIENT WITH PULMONARY HYPERTENSION AFTER CORRECTED COMPLEX HEART DEFECT

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Abstract

Advances in medicine, especially in the treatment of congenital heart disease, are making it possible for many women with severe congenital heart disease to reach childbearing age and, of course, if they want to become pregnant and become mothers.

3-10% of those registered with congenital heart disease will develop pulmonary hypertension, which is always a poor prognostic sign and has particularly high mortality and morbidity, especially when undergoing operative treatment and anesthesia.

We present a case of successful anesthetic management for the caesarean section in a patient with pulmonary hypertension after a complex congenital heart defect corrected in childhood. The anesthesiology approach is always challenging and requires an individual and multidisciplinary approach to each individual patient.

Keywords*: anesthetic approach; caesarean section; pulmonary hypertension.*

Introduction

Nowadays, in obstetric's anesthesia, we meet more and more often patients who have cardiac diseases, patients who have undergone heart surgery, and who receive complex cardiac therapy.

Although in the developed world, the number of severe congenital heart diseases (CHD) is decreasing as a result of modern screening and consequent termination of pregnancy, the overall prevalence of patients with CHD is increasing, primarily as a result of modern surgical and technological development, so more than 90% of patients with CHD will now become adults, and many women will reach reproductive age and become pregnant[1].

But these conditions are associated tocomplications during pregnancy and childbirth and are one of the main causes of maternal morbidity and mortality.

Concomitant heart disease is the most common cause of non-obstetric morbidity and mortality in pregnant patients, accounting for 26.5% of all pregnancy deaths[2].

3-10% of patients with congenital heart disease develop pulmonary hypertension[3].

We present a case of successful anesthetic management for the cesarean section in a patient with pulmonary hypertension after congenital complex heart defect corrected in childhood.

Case Presenatation

A 34-years-old parturient, with first pregnancy, in 37thweek of gestation, cameatour clinic for labor and delivery.

The patient was born with dextrocardia, situs inversus and transposition of great blood vessels. At the age of 1, the patient underwent her first operation, the ASD and VSD were closed, and at the age of 24, the second RVOT-PA Conduit operation was performed. RVOT-PA Conduit is a surgical procedure in which the right heart is connected to the pulmonary artery through a conduit graft, while a different type of pulmonary valve is implanted. The second operation is the most frequent late operation in the treatment of congenital heart disease.

From the second operation until pregnancy, the patient subjectively feltwell, regularly wentfor check-ups, and didnot take any therapy.

During pregnancy, especially in the third trimester, the patient began to complain of shortness of breath and fatigue. Due to slightly elevated blood pressure, the patient received Methyl-Dopa 250mg every 8 hours and anticoagulant therapy every 12 hours. Before admission to the hospital, new cardiology and ultrasound examinationswereperformed.

To be able to assess the risk of cardiac complications in the mother during pregnancy, the best way is to use modified World Health Organization (mWHO) classification. This classification is currently the most accurate risk assessment system, and according to this scale, the patient was assessed as mWHO II/III.

Ultrasound examination showed a normal left ventricle, with orderly contractility and ejection fraction greater than 60%, normal left and right atrium; enlarged right ventricle; moderate mitral and tricuspid regurgitation. A conduit and a bioprostheticwere visualized on the pulmonary valve. A pulmonary arterial hypertension (PAH), that has not been registered before was registered, namely the mean pulmonary arterial pressure of (mPAP) 50mmHg.

Uponthe recommendation of a cardiologist, the patient was scheduled for an elective caesarean section.

On admission, the patient's blood pressure was 138/92, heart rate 98/min, saturation 98%. BMI is 26kg/m^2, Malampati 1. Antibiotic prophylaxis was given before entering the operating room. Gastroprotective and antiemetic prophylaxis werealso given. Anticoagulant therapy, therapeutic doses, was stopped 24 hours before. The patient was advised to drink clear liquids for up to 3 hours preoperatively.

Standard monitoring was set for the patient upon entering the operating room. Two large 16G cannulas were placed in a peripheral vein. In terms of hemodynamic parameters, shehad a normal heart rate of 84/min, mild hypertension of 146/92, normal saturation of 97% without an oxygen mask. 500ml of co-hydration was started with saline, and the phenylephrine solution was ready. For anesthesia, we decided on low dose spinal (low doses of Bupivacaine, with Fentanyl

and Morphine) in combination with general endotracheal anesthesia. 3mg isobaric Bupivacaine combined with 20mcg Fentanyl and 100mcg Morphine was applied at the L_3-L_4 level with a 27G Pencan needle. Our goal was to have good analgesia, but without the hemodynamic effect of spinal anesthesia. Before the induction of general anesthesia, Lidocaine 2% 1mg/kg and 50 micrograms of fentanyl were given. Preoxygenation with 100% O_2, slow induction with 2mg/kg Propofol, 20mg Ketamine, 1mg/kg Leptosuccinwas applied to the patient. Anesthesia was maintained with oxygen/air mixture at 50:50, sevoflurane and rocuronium 0.5mg/kg starting dose, with top-ups if needed.

The patient was stable during induction, and after induction low doses of phenylephrine were released continuously. A live newborn with Apgar 8/9 was delivered, 3mg Oxytocin was given as a bolus, 17mg was allowed to flow continuously at a rate of 5IU per hour. 10mg of furosemide was given immediately after extraction, delivery of the neonate (to prevent an increase in right atrial preload as a result of autotransfusion), and 10mg was given at the end of the intervention. The patient received a total of 1,000ml of crystalloids, had a total of 300ml of diuresis and 300ml of blood loss. Intraoperatively the patient received 100 micrograms of fentanyl, 50 micrograms before induction and 50 micrograms after the extraction of the baby. Postoperatively the patient received paracetamol and NSAIDs, double antibiotic therapy, anticoagulant therapy. The patient was cardiocirculatory stable all the time, with good diuresis, without pain. The mother and child were discharged home in stable general condition.

Discussion

Physiological changes that occur during pregnancy and childbirth are very specific and their understanding is very important to be able to predict all the complications that may occur in the peripartum period, as well as to determine the appropriate anesthetic technique, appropriate monitoring to minimize those complications and to provide the best care forthe patient.

Pulmonary hypertension (PH) is an important prognostic factor in patients with CHD, especially in pregnancy. It is defined as an increase in mean pulmonary arterial pressure PAP ≥20mmHg at rest[4]. It appears slightly more often in women and increases with biological age, as well as with the age when the defect is corrected. In terms of severity, it is divided into mild (20-40mmHg), moderate (40-55mmHg) and severe form (>55mmHg) of PH.

In pulmonary hypertension, the main component is elevated pulmonary vascular resistance. Because of this, the pressure in the right ventricle increases, and thus the work of the right ventricle. On the other hand, left ventricular output decreases. Therefore, it is very important to maintain the right ventricular filling, to maintain myocardial contractility, but also not to have excessive right ventricular preload because it can lead to right heart failure and arrhythmias. And thus, to maintain the output of the left ventricle. The goals of anesthesiologic management focus primarily on avoiding an increase in pulmonary vascular resistance, maintaining systemic vascular resistance, ensuring right ventricular preload and left ventricular afterload. Hypoxia, hypercarbia, acidosis, hypothermia and pain should be avoided and prevented.

The choice of anesthesia is a very important and delicate matter. Both general and regional anesthesia have been described in patients with pulmonary hypertension, each has its own disadvantages and advantages.

However, in relation to the little evidence we have from the literature, which are mostly case reports, no randomized controlled trials, epidural analgesia is recommended either alone gradually titrated with slow gradual administration of low doses or in combination with low-dose spinal anesthesia. The advantages of this type of anesthesia are reduced sympathetic activity and pain control, gradual onset of neuraxial block with the possibility of better maintenance of preload and afterload[6].

With respect to spinal anesthesia, neuraxial sympathetic blockade leads to a significant reduction in systemic vascular resistance, further preload can be reduced, and systemic hypotension, sometimes life-threatening can occur. That is why its use is debatable, in many recommendations it is even contraindicated[5,7].

And, of course, general anesthesia is occasionally required for cesarean delivery in patients with high-risk cardiovascular diseases. It is recommended in patients who require airway control, who require transesophageal echocardiography intraoperatively, who are on anticoagulant therapy and in whom the regional anesthesia is contraindicated. The advantage of ventilation control is primarily to prevent hypoxia and hypercarbia that precipitate an increase in pulmonary vascular resistance. On the other hand, the main disadvantages of general anesthesia are increased intrathoracic pressure and increased PVR. What is recommended during induction of general anesthesia is preoxygenation with 100% oxygen, slow, titrated induction, opioid or lidocaine to reduce the sympathetic response to intubation. It is important to note that during the induction of anesthesia, maintenance of hemodynamic stability is the most important and has priority over the risk of aspiration or neonatal sedation. During anesthesia, FIO_2>0.6, avoidance of NO_2 (increase PVR), hyperventilation, lung protective ventilation (Tv 6-8ml/kg) is recommended.

Comparedtoepidural anesthesia, general anesthesia is associated with increased mortality. Bedard et al. in their systematic review included all cases of pulmonary hypertension of various etiologies between 1997 and 2007 and compared them torelevant data published between 1978 and 1996. The review concluded that overall maternal mortality was significantly reduced and that the parturients who received general anesthesia were at greater risk of death, but the difference was not statistically significant.

We managed our parturient under low-dose spinal anesthesia with low doses of local anesthetic, but in combination with a short-acting and long-acting opioid. In this way, we obtained excellent analgesia, with an insignificant hemodynamic effect. Induction of general anesthesia was gradual and slow, with good preoxygenation. Fentanyl was given to reduce the stress response to intubation. General anesthesia remains a possible, even desirable, technique in many high-risk patients.

Conclusion

Patients with pulmonary hypertension have big morbidity and mortality risk. Anesthetic approach and management should be adapted individually to each patient. Slow titrated epidural analgesia or low dose combined spinal-epidural anesthesia is recommended. No conclusions can be drawn from this case report, but still it showed that cesarean sections can sometimes be performed under low dose single shot spinal combined with general anesthesia.

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CASE REPORT *UDK 618.14-056.7:615.256.3*

www.doi.org/10.55302/MJA2484107gjn

A CASE OF PREGNANCY AND SPONTANEOUS VAGINAL DELIVERY IN A PATIENT WITH UTERUS DIDELPHYS AND INTRAUTERINE DEVICE IN SITU

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Abstract

Uterus didelphys, a rare congenital Müllerian duct anomaly, presents unique challenges for reproductive management, especially when long-acting reversible contraceptives, such as intrauterine devices (IUDs), are used. Uterus didelphys is characterized by two separate uterine cavities, which may decrease IUD efficacy and elevate the risk of unintended pregnancy. This case report details a patient with a uterus didelphys and an IUD in situ who achieved a full-term, spontaneous vaginal delivery. The anomaly was discovered only after the patient presented with pregnancy, underscoring the importance of pre-insertion imaging for women with a clinical history suggestive of uterine anomalies. The advanced imaging modalities, such as ultrasound, saline infusion sonography (SIS) and three-dimensional ultrasound, are essential for accurately identifying Müllerian anomalies to guide appropriate contraceptive counseling and reproductive care. This case highlights the need for individualized approaches in the management of pregnancies with Müllerian duct anomalies and the potential for favorable outcomes. Given the scarcity of reports on pregnancies with uterus didelphys and concurrent IUD use, our findings contribute valuable insights into the effective management of reproductive anomalies and emphasize the critical role of comprehensive imaging before IUD placement.

Keywords: *pregnancy and IUD; Müllerian duct anomaly and pregnancy.*

Introduction

As women increasingly seek reliable birth control options, Long-Acting Reversible Contraception (LARC) has gained popularity due to its efficacy and minimal need for patients' intervention. People particularly favor the intrauterine device (IUD) due to its non-hormonal nature and cost-effectiveness. With an effectiveness rate exceeding 99%, fewer than two out of 100 women using an IUD over a five-years span will experience unintended pregnancy (1). Different models of IUDs, approved for use for 5 to 10 years, exhibit a toxic effect on sperm, reducing motility and inhibiting implantation due to the copper in the device (2).

The patient in this case was found to have uterus didelphys unicollis, which is a rare birth defect of the uterus also known as a Müllerian duct anomaly (MDA) (3). MDAs are a group of developmental problems in the female reproductive tract that happen when the Müllerian ducts don't form, fuse, or dissolve properly during embryonic development. We group MDAs into formation defects (agenesis), lateral fusion defects (e.g., arcuate, bicornuate, didelphys, septate, unicornuate), and vertical fusion defects (e.g., transverse vaginal septum) (4).

A lateral fusion defect can cause uterus didelphys, which is when the uterus, cervix and often the vagina, are all duplicated. It is a rare anomaly, occurring in about 1 in 3,000 women and in approximately 11% of women with MDAs (5). Uterus didelphys is less prevalent than other uterine anomalies, such as arcuate, septate or bicornuate uteri. It happens when the upper Müllerian ducts don't fuse completely, leaving two separate uterine cavities. These cavities usually have separate openings and may have two vaginas or a longitudinal vaginal septum. The underlying cause of this fusion failure remains unknown (6).

We can further classify uterine didelphys into two types:

- Uterus didelphys bicollis: each uterine cavity has its own cervix and vagina,
- Uterus didelphys unicollis: both uterine cavities join at a single cervix, leading to a single vagina (7).

Diagnosing MDAs, including uterus didelphys, can be challenging and often occurs during reproductive years. These anomalies are frequently associated to symptoms such as amenorrhea, dysmenorrhea, dyspareunia, pelvic pain, or obstetric complications such as recurrent pregnancy loss, preterm birth, malpresentation, intrauterine growth restriction, placental abruption and cervical insufficiency (8). A physical exam might show that the vagina and cervix are duplicates. Advanced imaging methods like transvaginal ultrasonography, sonohysterography, hysterosalpingography, MRI and hysteroscopy, help to look at the structure. In recent years, three-dimensional (3D) ultrasonography has emerged as a non-invasive, effective option for assessing uterine malformations (9).

Case Presentation

A 38-years-old patient, upon her family gynecologist's recommendation, presented to the perinatal unit at the University Clinic of Gynecology and Obstetrics for an evaluation of her current pregnancy and an assessment of the perinatological risk associated with her current intrauterine device, which was placed 10 years ago. The patient had a previously diagnosed congenital anomaly of the uterus of the Didelphys unicollis type.

Transvaginal ultrasonography clearly visualized two hemiuteria, each with completely separated individual cervical canals. A decidual changed endometrium and a linear hyperechogenic shadow, corresponding to the previously placed intrauterine device, were visible in the right hemiuterus. A gestational sac with a viable fetus with CRL-15.9mm (8w0d) was visualized in the left hemiuterus, with a properly configured yolk sac and normal fetal heart rate.

We explained to the patient the current obstetric findings, the impact of the present IUD on the further course and outcome of the pregnancy, and the risks associated with the congenital anomaly of the reproductive tract. Rest, and regular evaluations at the family gynecologist were advised. The first trimester screening was done in 12w4d, which showed fetus in the right size for the gestational age and no major fetal anomalies at the time of the ultrasound exam. A PRISCA 1 test was done, which showed a low combined trisomy 21 risk (1:3776) and a low risk for trisomy 13/18 (<1:10000).

The second trimester screening was done in 21st week, which showed a fetus in the right size for the gestational age and no major fetal anomalies at the time of the ultrasound exam. During the

entire pregnancy, the patient was prescribed gestational therapy.

The fetus was again the correct size for the gestational age during the next routine check-up in 27w6d, and the ultrasound exam revealed no major fetal anomalies. Corticosteroid therapy for fetal lung maturation (Amp. Flosteron, a 14mg No. II) was prescribed.

The perinatologist closely monitored the patient during the last trimester. She was admitted in the Department for Pathological Pregnancy at 38w4d with a diagnosis as a small-for-gestational-age (SGA) fetus, with an estimated fetal weight (EFW) of 2,343g +/- 342g (which corresponded to 33w6d). After close examination, the decision was made for labor induction, as third pregnancy, cephalic position of the fetus, and SGA diagnosis. The pregnancy ended with a spontaneous vaginal delivery of a single female newborn in a cephalic presentation with an orderly course. The weight and length of the newborn were 2,370g/ 48cm. She was discharged in a stable general condition on the fourth day postpartum.

Discussion

It is very rare for the Müllerian ducts to fail to fuse, which causes the uterus, cervix, and/ or vagina to be completely duplicated. This is called uterus didelphys. Estimates suggest that this anomaly makes up approximately 8% of congenital uterine anomalies and affects approximately 0.3% of the general population (10). The prevalence is somewhat higher among women with histories of infertility or pregnancy loss, where it has been observed at rates as high as 2.1% (11).

Research has shown that uterus didelphys is associated with certain reproductive complications, including increased risks for infertility, spontaneous miscarriage, intrauterine growth restriction (IUGR), preterm birth, breech presentation, low birth weight. Some reproductive problems are more likely to happen in women whose uterus didelphys is present. These include infertility, spontaneous miscarriage, intrauterine growth restriction (IUGR), preterm birth, breech presentation, low birth weight (<2500 g), postpartum hemorrhage, and perinatal death (12). While uterus didelphys does not generally affect the ability to conceive, pregnancies in patients with this condition frequently face complications. However, many patients with congenital uterine anomalies still achieve favorable reproductive outcomes, as highlighted by recent studies and meta-analyses (13).

The presence of an intrauterine device (IUD) in patients with uterus didelphys is rare in the literature, and limited data exist regarding its impact on pregnancy outcomes. Current medical guidelines say that women with major uterine abnormalities, like uterus didelphys, may not be able to use an IUD because it might not work well as a birth control method when there are two uterine cavities (14). Studies have indicated that pregnancies occurring with an IUD are most likely within the first-year post-insertion (15).

Updated IUD eligibility criteria now recommend imaging, particularly ultrasound, before or at the time of IUD insertion in patients with a significant clinical history or abnormal menstrual bleeding. In many cases, patients with uterus didelphys are asymptomatic with a normal pelvic examination, and the anomaly only becomes apparent incidentally. Additionally, cases of undiagnosed anomalies have reported IUD failures leading to pregnancies, highlighting the importance of comprehensive imaging to identify uterine anomalies before IUD placement (15).

Ultrasound remains the primary diagnostic tool for detecting uterus didelphys, with two-dimensional (2D) ultrasound frequently used in the initial evaluation. The secretory phase of the menstrual cycle, when the endometrium is the most visible, is the ideal time to perform the exam for optimal visualization. While 2D ultrasound may detect only around half of all uterine anomalies, combining it with saline infusion sonography (SIS) can improve visualization of intrauterine structures (16). In complex cases, three-dimensional (3D) ultrasound offers more detailed assessment, allowing accurate differentiation of uterus didelphys from other anomalies, like septate or bicornuate uterus, through coronal plane imaging (10).

For uterus didelphys, differential diagnosis includes other structural anomalies, such as septate or bicornuate uterus. Imaging findings of two separate endometrial cavities may suggest a septate uterus, which can be differentiated by the presence of a fundal indentation of at least 10 mm, commonly used to distinguish between bicornuate and septate configurations (17). Cervical duplication may also appear in cases of bicornuate, septate or didelphys uterus. An accurate evaluation of pelvic anatomy is therefore essential for appropriate diagnosis and management (11).

The use of IUDs has been associated with an increased risk of ectopic pregnancy, with some studies indicating up to a 16-fold increase compared to non-IUD users. It is essential that diagnosticians avoid misdiagnosing an intrauterine pregnancy in one cavity of a uterus didelphys as an ectopic pregnancy due to the presence of an IUD in the other cavity. Also, a thorough check of the adnexa is needed to rule out heterotopic pregnancy, which happens when an intrauterine pregnancy and an ectopic pregnancy happen at the same time (12).

Beyond ultrasound, hysterosalpingography (HSG) and magnetic resonance imaging (MRI) are valuable tools for diagnosing uterus dysplasia. HSG can reveal symmetrical uterine cavities and fallopian tubes, while MRI, although less accessible due to cost, provides high-resolution imaging and is the standard for complex cases. MRI's non-invasive nature, lack of ionizing radiation and excellent soft-tissue contrast, make it particularly useful in evaluating indeterminate cases (13).

The management approach for uterus didelphys depends on the clinical presentation. Generally, we advise intensified monitoring to mitigate the risk of complications when we diagnose the anomaly during routine prenatal care. For patients with recurrent pregnancy losses or preterm labor, surgical intervention, such as Strassman metroplasty, it may be considered. This uterine unification surgery aims to improve reproductive outcomes by resecting the septum to create a single, unified uterine cavity (16). Recent advancements in surgical techniques have improved the prognosis for patients undergoing such interventions (17).

Conclusion

Congenital Müllerian anomalies present complex challenges in both diagnosis and management, requiring a tailored approach to address associated reproductive risks. Women with these anomalies face increased chances of adverse pregnancy outcomes, underscoring the importance of early, accurate diagnosis and individualized care strategies. For pregnant patients with MDAs, delivery planning should carefully consider maternal and fetal health, as well as patient's preferences. This case, involving a full-term pregnancy and successful spontaneous vaginal delivery in a patient with uterus didelphys and an intrauterine device in situ, highlights the possibility of favorable outcomes despite these complexities. This case also shows how important it is to be more aware of and check for Müllerian duct anomalies before putting in an IUD, since anom-

alies that aren't found can make contraception less effective. Given the rarity of such cases, our report contributes valuable insights into the effective, individualized management of patients with unique reproductive anatomy.

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CASE REPORT *UDK: 618.25-06:618.333*

www.doi.org/10.55302/MJA2484113l

TWO FETAL DEMISES IN TRIPLETS PREGNANCY IN SECOND TRIMESTER WITH IMPLICATIONS ON LIVE FETUS AND MOTHER'S HEALTHH

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Abstract

Triples pregnancies is when three fetuses are carried and delivered by mother at once. The overall incidence is 1of 7,300 pregnancies. As a result of the use of aided reproductive technology, the overall incidence of these pregnancies has increased. They are with increased perinatal risks because of intrauterine growth restriction, fetal discordance, intrauterine demise, congenital malformations, preterm birth, pre-eclampsia, gestational diabetes, anemia, risk for thrombosis, operative and anesthesiology complications.The main goal of this case report is presenting the implications of intrauterine dead of two fetuses in triplets conceived spontaneously at 25 gestational weeks. It was the second pregnancy after the earlier cesarean section. The ultrasound scan at our clinic revealed diamniotic, dichorionic pregnancy with fused placentas at 23 gestational weeks with three live discordant fetuses more than 20% between them with amount of amniotic fluid in normal range. At the next control scan two weeks later, one fetus was dead and after 4 days the other one died in the same amniotic sac. In 26th gestational week, iatrogenic premature delivery with second cesarean section in regional anesthesia was done. A vital male fetus with 1,050g and 31cmand two dead fetuses were delivered.The discordance between them was 9.2% and it was 40% with a live fetus. After 10 weeks the live newborn was discharged without serious sequels. It can be concluded that it is especially important to detect multi fetal pregnancy as soon as possible, especially number of fetuses, chorionicity and amnionicity, to prevent the above-mentioned complications.

Keywords: *demise; fetal; implication; maternal; triplets.*

Introduction

According to Helin's law for multiple pregnancies, the incidence of twins is 1of 86 pregnancies, triplets 1 of 862 and quadruplets 1 of 863 (1).The incidence of multiple gestations has increased in recent years due to aided reproductive technologies. Triplets and other multiple gestations are associated with increased risks of maternal and neonatal morbidity compared to singleton gestations. Premature deliveries before 34 gestational weeks (g.w.) are around 75% in triplet, 20% of twin pregnancies compared to 2 percent of singleton pregnancies (2). Diagnosis of multiple pregnancies is based on ultrasound examination, performed for confirming of fetal cardiac activity and gestational age. Generally recommended route of delivery is with the cesarean section avoiding the vaginal birth. Primary, determination of the number of placentas and amniotic sacs should be performed between 8 and 13 weeks of gestation. This is important for risk assessment,

antenatal counseling, further management and for screening for congenital anomalies, labeling the fetuses, the sites of placental implantation and sharing, the sites and types of placental cord insertion. The shared amniotic sacin monochorionic monoamniotic or dichorionic diamniotic tripletsis important risk factor for fetuses for cord entanglement and twisting with later death from cord compression. It is suggested to have hospital admission with this type of placentation at 26 weeks of gestation to help performance of one hour of continuous fetal heart rate watching every eight hours (3).Triplet pregnancies are also with the higher risk for gestational diabetes compared to singletons (12.8 versus 2.9 percent respectively) (4).

Case Presentation

The patient was 32 years old women with her second pregnancy conceived spontaneously. The first pregnancy was at-term with the cesarean section because of Fetal distress. An ultrasound was preformed, and surprisingly for her, the tree fetuses are detected. Till that scan, she knew that she was carrying two babies. The ultrasound scan at our clinic revealed diamniotic, dichorionic pregnancy with fused placentas at 23 gestational weeks (g.w.) with alive three fetuses. The discordance of more than 20% existed between two fetuses with sheared placenta and the fetus in another sac, with amount of amniotic fluid in normal range. The fetal dopplers were in normal range. Two weeks later, the first fetus died with biometry for 23 g.w., and after 4 days the other one in the same amniotic sac. She was admitted to hospital at 25.4 g.w. and administered with corticosteroid for fetal lung maturation. In 26th gestational week, iatrogenic premature delivery with second cesarean section in regional anesthesia was done. Before delivery proper preparations measure for delivery from anesthesiology aspects to prevent complication was done. A vital male fetus with 1,050g and 31cm with Apgar Score of 6 and 7(in first and fifth minute) was delivered. Both dead fetuses were male and weighted 650g and 590g with length 28cm and 27cm respectively (Picture 1).

Picture 1. Two intrauterine died fetuses, one hydropic with twisted umbilical cords.

The fetus who died first was hydropic with maceration, the second shown sign of recent dead. Postnatal discordance between them was 9.2% and it was 40 % with a live fetus. The placentas macroscopic was with obvious demarcation line at its maternal site andthe margins of both placentas could be distinguished (Picture 2).

Picture 2. Maternal site of placenta with with clear border of placentas.

Picture 3. Fetal site of placenta membrane and insertions of umbilicals cord.

On the fetal site of placenta, there was an interesting twisting of umbilical cords of both fetuses in the same amniotic sac with common insertion of umbilical cord of dead fetuses (Picture 3). After 10 weeks the newborn was discharged with neonatal weight of 1,900g and 46cm length, without serious sequels, but during hospitalization at NICUa large and various necessary interventions were done. During operation, there was a need for administration of uterotonic-20 i.e., Oxytocin and intramuscular application of prostaglandins due to uterine delay contraction to prevent blood loss. Postoperatively antibiotics, uterotonic and thromboprophylaxis were administered. The woman was discharged on the third postoperative day without early complication in stabile state.

Discussion

Almost 80 percent of triplet and order multiple pregnancies are result of aided reproductive technology (ART) (5). There is a risk for maternal health, especially for the heart because there is volume overload as pregnancy advance. So, in one study of triplet pregnancies, maternal me-

dian peak cardiac output was 8.44L/min and occurred at 32 to 36 weeks, while in singleton pregnancies was 6.1L/min at the same gestational age (6). There is the need for exact balance of liquid intake to prevent congestive heart failure and pulmonary edema. The risk for deep venous thrombosis and thromboembolic events is higher because of pelvic and leg veins compression of overdistended uterus. Neuraxial anesthesia is recommended for operative delivery or vaginal complicated delivery.

Gestational age of delivery for triplets is approximately 32 weeks versus 39 weeks in singletons. Because of pregnancy complications, there is common hospitalization before delivery. The most uneventful complication for fetuses is fetal demise. The rate of fetal demise after 22 weeks of gestation is related to chorioamnionitis. Fetal demise occurred in 0.8 percent of trichorionic triplet pregnancies versus 2.7 percent of monochorionic tri amniotic triplet pregnancies (7). None of the studies has exactly examined the outcomes of survivors of co-triplet demiseand this risk depends on whether they shared a chorionic sac with the demised triplet. In cases where there is demise of one or two triplets with monochorionic placentation, injury to the surviving fetus or fetuses occurs very soon. Because of this fact, the immediate delivery will not prevent adverse outcomes related to this event (8).

Perinatal mortality was approximately 2.5 percent (7,9) and monochorionic triplet pregnancies had a 2.6-fold greater risk of perinatal death than tri chorionic triplet pregnancies (7). In a study comparing dichorionic to trichorionic triplet gestations, the neonatal death rates were 22 and 7 percent, respectively, and the median gestational age at delivery was 31 and 33 weeks, respectively (10).

Conclusions

For monitoring triplet pregnancies, there is need for more ultrasound examination to recognize complications, congenital anomalies and twin-twin transfusion syndrome. Preterm birth is the most common cause of death and morbidity in triplet gestations. Iatrogenic preterm birth is usual in triplets. Compared to dichorionic survivors of a co-twin fetal demise, monochorionic survivors of a co-twin fetal demise have higher rates of later demise, preterm birth and neurodevelopmental impairment. Multiple gestations are at increased risk for uterine atony, postpartum hemorrhage and emergency hysterectomy, so preparation for these potential complications is important. There is no triplet pregnancy without implications for each one - fetus and for the mother.

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CASE REPORT *UDK: 616.711.6-009.7*

www.doi.org/10.55302/MJA2484118v

LIMBUS VERTEBRA MIMICKING AVULSION FRACTURE

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Abstract

A condition known as limbus vertebra occurs when the nucleus pulposus extends beneath the ring apophysis through a gap in the vertebral endplate. While involvement of the inferior and posterior margins is less common, it most frequently occurs at the anterosuperior corner of a single vertebral body, usually in the middle lumbar spine. Thenumber of differential diagnoses, such as tumors, infections or fractures, should be considered.

We discuss the case of a 29-years-old man who was sent to our emergency room following a height-related fall. He claimed palpable pain in his wrist, upper leg, chest and lower back, as well as a brief loss of consciousness. Anterior limbus vertebra (LV) was the diagnosis.

Keywords*: Interosseous herniation; fracture; limbus vertebra; low back pain.*

Introduction

A condition known as limbus vertebra occurs when the nucleus pulposus protrudes below the ring apophysis through a hole in the vertebra's endplate (1). While involvement of the inferior and posterior margins is less common, it most frequently occurs at the anterosuperior corner of a single vertebral body, usually in the middle lumbar spine (2).

A smooth, triangular piece of bone known as the ring apophysis may separate as a result of the anterior herniation of the nucleus pulposus. After that, this apophysis remains separated from the spinal body. The limbus vertebra is frequently misdiagnosed as a fracture, which results in needless intrusive operations. What distinguishes a limbus vertebra from a fracture on x-rays is the sclerotic edge surrounding the triangular piece. In contrast, sclerotic borders are absent from acute fractures. When a post-traumatic patient presents with back pain, it is a crucial differential diagnosis (3). In this case, we present a case of a 29-years-old male with LV who was misdiagnosed with a vertebral fracture after presenting with low back discomfort after trauma.

Case Presentation

We introduce a 29-years-old man who fell from a height at home and sustained a severe injury in our emergency room. He reported experiencing low back pain, wrist, upper leg and chest palpable discomfort, as well as a brief loss of consciousness. In addition to not being a heavy drinker or smoker, he had no prior pertinent medical history. At the time of the examination, he was hemodynamically stable, able to fully recite the event, aware, and had a soft abdomen that could

be palpated. The results of the neurological evaluation were normal. When the lumbar spine was extended and flexed, his range of motion was normal; however, the paravertebral muscles experienced pain and spasms. Mild soreness was felt when the proximal lumbar spine vertebrae were palpated. There were no obvious indications of inflammation. X-rays of the chest, left wrist, thigh and lumbosacral spine were taken; the results showed a fractured left wrist, which was referred for conservative care. A triangular fragment of bone that was corticated and connected to the front and top of the L3 vertebral body was visible on lateral x-rays of the lower back (Figure 1). A second CT scan showed a fractured, triangular piece of hard-edged bone that appeared to have come from a limbus vertebra, as well as rough edge on the cortical material in front of the L3 apophyseal plate with some depression (Figure 2).

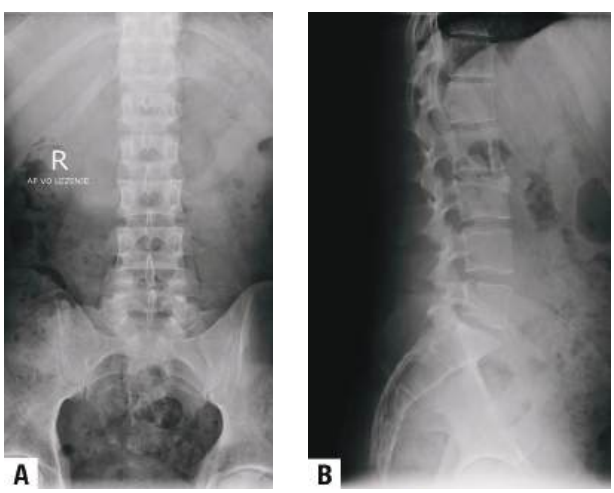

Figure 1. Anteroposterior view of the lumbar spine of the patient showing no acute abnormalities (A). Lateral views of the lumbar spine of the patient; white arrows indicate not well separated corticated triangular osseous focus at the anterosuperior aspect of the L3 vertebral body (B).This is the most consistent with a limbus vertebra at L3.

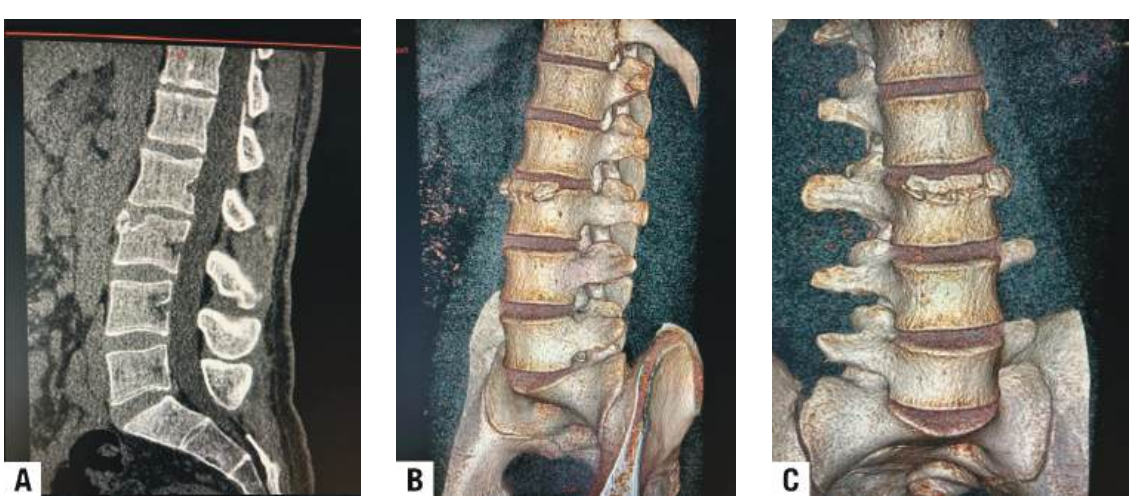

Figure 2. CT scan showed a cortical marginal irregularity of the L3 apophyseal plates with mild depression with an avulsiontriangular bony focus anteriorly with sclerotic edges compatible with a limbus vertebra(A), 3D volume rendering imaging (B,C).

Discussion

In 1927, Schmorl made the initial identification of the lumbus vertebra and suggested that it was caused by an intrabody disc material herniation that occurred during childhood or adolescence (4,5). Because of its appearance as a triangular bone fragment next to the margin of a vertebral body, plain radiographs frequently misread it as an infection, fracture or tumor. The existence of "disc material" was shown by pathological analyses of these fragments (6). Ghelman and Freiberger used discography in their 1976 work to demonstrate how contrast that was injected into the nucleus pulposus propagated throughout the limbus vertebra. Although reports also indicate the posteroinferior corner and other regional involvement, the anterosuperior edge of a single lumbar vertebral body is the most frequently reported location for the limbus vertebra (7). It is thought that traumas received during childhood and adolescence during the growth of the spine are the cause of limbus vertebrae (8).

The nucleus pulposus may herniate at the border between the ring apophysis and the subsequent vertebral body during this period due to chronic stress, trauma or birth abnormalities, potentially resulting in limbus vertebra (9). In reality, a portion of the ring apophysis ossifies independently after failing to fuse with the rest of the vertebra (10). The disorder is comparable to Schmorl's nodes, a syndrome in which nuclear material extrudes centrally in the lower thoracic spine and Scheurmann's illness (11). A simple radiograph may be enough to identify limbus vertebra in adults.

It usually appears as a tiny, triangular, bony mass with a sclerotic surface next to a vertebral body's edge on x-rays. Particularly for the confirmation of PVL, a condition in which pelvic tissues superimpose with L5 and S1 levels, CT and MRI are regarded as supplementary tests. However, because of its uneven appearance in children and adolescents, this bone segment could be mistaken for an infection or a tumor. Only in cases where imaging appearance is abnormal, additional tests are required for diagnosis. Increased uptake in the vertebral body is seen on a bone scan. By confirming that there is no bone edema, limbus vertebral MRI rules out fractures and suggests a developmental problem (13).

The anterior limbus vertebra (ALV) is frequently discovered by chance in asymptomatic individuals. However, a significant rate of intervertebral disc degeneration (IDD), which is comparable to Scheurmann's disease, has been observed in teen MRI investigations (13). On the other hand, low back pain was described by Henales et al. in pediatric AVL patients (14). Koyama et al. found a link between ALV and low back discomfort, pointing to risk variables such athletic experience and the COL11A1 genotype (15). Active young athletes are also more susceptible to ALV, according to Acosta et al. (16). ALV appears to develop during childhood and adolescence, according to Baranto et al.'s MRI follow-up on elite athletes, which showed no increase in apophyseal alterations with time (17).

Nerve compression in the posterior limbus vertebra (PVL) might mimic the symptoms of a disc herniation. Lumbus vertebrae frequently don't require treatment. Non-steroidal anti-inflammatory medicines (NSAIDs), muscle relaxants, and, if required, rehabilitation physical therapy are the usual conservative methods we use to treat symptomatic individuals. Surgical intervention may be required if conservative approaches are not successful. For the limbus fragment to be adequately excised, a total laminectomy is typically necessary (18). Various surgical procedures have also been used by other studies (19, 20). Although Akhaddar et al. suggested removing the

mobile fragment while leaving the stable fragment whole, some patients still feel pain following this course of treatment. The results of limbus vertebral surgery vary greatly (21).

Conclusion

Recognizing its characteristic imaging features aids clinicians in making an accurate diagnosis and providing timely treatment. In the differential diagnosis of mechanical lumbar pain, especially in young patients, one should consider the anterosuperior limbus vertebra.

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CASE REPORT *UDK: 616.831-006.484-089.87-089.5*

www.doi.org/10.55302/MJA2484123a

AWAKE BRAIN SURGERY IN A PATIENT WITH GLIOBLASTOMA

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Abstract

The awake craniotomy, as a surgical procedure, facilitates maximal resection of brain tumors with minimal or no damage to eloquent brain areas. Conscious sedation and asleep-awake-asleep techniques are two anesthetic techniques employed. During the awake phase, the patient should be alert and cooperative, with adequate analgesia as an essential component of the anesthetic management while neurological testing is performed. Ensuring airway patency, proper oxygenation and ventilation, avoidance of hypoxia and hypercarbia, and maintaining stable systemic and cerebral hemodynamics are crucial. We present a case of a right-handed 56-years-old man with speech difficulties manifested as fluent dysphasia and magnetic resonance findings of intra-axial supratentorial left-sided temporoparietal lesions. The patient was scheduled for awake brain surgery according to the affected eloquent language brain area of the dominant hemisphere. Asleep-awake-asleep anesthetic technique was utilized. Short-acting sedative agents propofol and dexmedetomidine were used, along with remifentanil and fentanyl as analgesics. After awakening, neurological testing of sensory, motor and cognitive functions was performed, revealing no new neurological deficits and achieving maximally safe microsurgical tumor resection with stable hemodynamics and no respiratory or intracranial adverse events. With histopathological findings of glioblastoma (WHO Grade IV), chemotherapy and radiotherapy followed the surgery. The available literature demonstrates the importance of the extent of tumor resection for improved outcomes and survival benefits in glioma surgery, with maximal resection without excising functional brain tissue, being the primary goal of awake brain surgery.

Key Words: *Asleep-awake-asleep technique; Awake brain surgery; glioblastoma.*

Introduction

In 1886, the first awake craniotomies were performed by Horsley under local anesthesia for epilepsy surgery (1). Surgical treatment for supratentorial tumors, vascular malformations and any other lesion located near eloquent areas of the brain, can be facilitated using awake craniotomy (2). The awake craniotomy is a neurosurgical procedure in which the patient is awake for neurological testing during a whole procedure or a part of it. The brain cortex responsible for all functions we can examine is the eloquent cortex, like the motor and language cortex, so any supratentorial intra-axial lesion under the eloquent cortex could be considered (3). The awake

craniotomy as a procedure is frequently considered in the surgical treatment of different types of gliomas, so maximal reduction of the tumor can be done while minimizing damage to the eloquent areas of the brain. Providing adequate analgesia and anxiolysis, systemic and cerebral hemodynamic stability, establishing airway patency and proper ventilation, as well as patient's cooperation are challenges for the anesthesiologist. In general, there are two anesthetic techniques for this procedure: conscious sedation and asleep–awake–asleep technique.

Case Presentation

A 56-years-old right-handed male patient presented to the neurosurgery department with a three-weeks history of speech difficulties manifested as fluent dysphasia. While working as an elementary school teacher, the patient initially noted the speech disturbances manifested as word-retrieval difficulties (e.g., he wants to say a word/ phrase but can't recall it). Afterward, his spouse noticed the speech difficulties, described as problems with counting, basic arithmetic skills and word retrieval difficulties. The complaints mentioned above gradually worsened over the past three weeks. The neurological assessment indicated fluent dysphasia,- mainly anomic, with no other neurological deficits. A contrast-enhanced brain MRI revealed ring-enhancing intra-axial supratentorial temporoparietal left-sided lesions (Figure 1). Two of the five above-mentioned lesions were of greater diameter, with peritumoral vasogenic edema, thick walls, and a core area with a reduced signal (Figure 1), proposing multifocal glioblastoma as the most probable diagnosis.

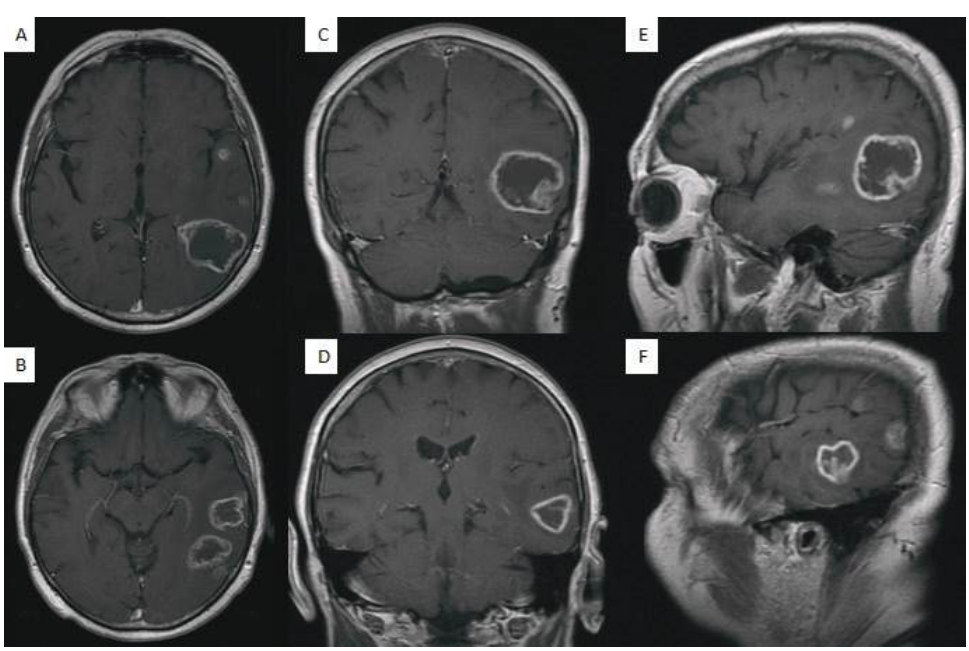

Figure 1. Contrast-enhanced brain MRI.
A, B – axial T1 sequences - two greater diameter ring-enhancing lesions of surgical interest (greatest diameters of 25.3mm - temporal and 41mm - temporoparietal, respectively).
C, D – coronal T1 sequences. E, F – sagittal T1 sequences.

Surgical treatment was initially planned to achieve maximum safe tumor resection and histopathological verification. Subsequently, after further in-depth evaluation, the patient was

scheduled for awake brain surgery according to the affected eloquent language brain area of the dominant hemisphere, neurological examination findings, the need for intracranial decompression and maximal safe resection, and histopathological verification for further treatment planning. A preoperative assessment by an anesthesiologist was done, and consent was taken from the patient after giving information about the procedure. The patient was without significant medical history. Anticonvulsive therapy with carbamazepine was initiated after the diagnosis of the tumor, along with intravenous dexamethasone and mannitol, before the surgery. The asleep-awake-asleep anesthesia technique was utilized (Figure 2). After standard non-invasive and invasive blood pressure monitoring, the patient was induced in general anesthesia with midazolam and propofol, fentanyl as opioid analgetic, and muscle relaxation with rocuronium. Mechanical ventilation was initiated after the insertion of the endotracheal tube. The patient was positioned in a semi-lateral position (left shoulder elevated) with the head rotated around 45 degrees to the right and placed on a horseshoe headrest, with protection of all bony prominences and nerves. After sterile skin preparation and draping of the surgical field, the scalp was infiltrated along with the planned incision with local anesthetic lidocaine. He underwent a left-sided temporoparietal craniotomy, and microsurgical maximally safe resection of the two (out of five) larger diameter lesions (Figure 1) was performed (Figure 2 – C). General anesthesia was maintained with propofol in continuous infusion (50–70μg/ kg/min), and analgesia was provided with boluses of fentanyl and remifentanil infusion (0.075 – 0.15μg/kg/min). Later, dexmedetomidine infusion was added in doses of 0.5-0.7μg/kg/h after a bolus dose of 0.5μg/kg over 10 minutes. Fifteen minutes before the patient's planned awakening, propofol infusion was discontinued. Dexmedetomidine infusion in lower doses (0.2μg/kg/h) and remifentanil (0.01 – 0.02μg/kg/min) remained for maintaining proper analgesia and anxiolysis through an awake phase.

Shortly after, the patient was awakened when his name was called loudly. He was cooperative, without pain, and had stable systemic hemodynamics. The endotracheal tube was removed, with good oxygen saturation and airway patency. Continuous intraoperative assessments of language, sensory, cognitive and motor functions were performed, and all the examined functions were preserved entirely (identical to preoperative assessments) while achieving maximal safe tumor resection (Figure 2-B). Again, general anesthesia was induced for hemostasis and closure of the skull. The endotracheal tube was reinserted with video laryngoscopy, and ventilation was controlled. No adverse events occurred, such as airway obstruction, hemodynamic instability, raised intracranial pressure, intracranial hemorrhage, or seizures. He was discharged on the ninth postoperative day with fluent dysphasia, which was present at admission, without any new neurological deficits.

The histopathology findings revealed tumor proliferation built by atypical glial cells (protoplasmic and fibrillary astrocytes with gemistocytes), cellular and nuclear atypia, bizarre giant cells and bizarre nuclei. Furthermore, newly formed blood vessels with marked endothelial proliferation, coagulative palisade tumor necrosis, and intratumoral hemorrhage fields were noted. The described morphology was consistent with glioblastoma (WHO Grade IV). Further treatment continued at the oncology clinic, where he underwent postoperative chemotherapy and radiotherapy, and regular follow-ups were scheduled and performed.

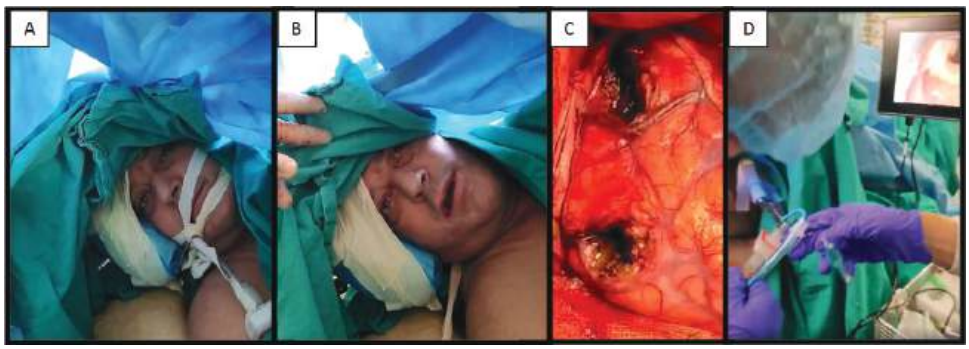

Figure 2. Awake brain surgery (asleep-awake-asleep technique) - Intraoperative photographs (approved with patient's consent).
A – view of the initial part of the asleep-awake anesthesia technique.
B – intraoperative assessment of language/ motor functions (awake part).
C – Microsurgical maximal safe tumor resection of two larger-diameter lesions via temporoparietal craniotomy.
D – reintubation utilizing video laryngoscopy (asleep part).

Discussion

The available literature demonstrates the importance of the extent of tumor resection for improved outcomes and survival benefits in glioma surgery, with maximal resection without excising functional brain tissue being the primary goal of awake brain surgery (4-10). An extensive literature review shows that the indications for awake surgery for glioma patients include assessment of language functions, sensorimotor pathways, visuospatial pathways and executive functions (11). Generally, the main indications for awake brain surgery include resection of tumors in eloquent brain areas such as Brodmann areas 1,2,3,4, language cortex (Broca's and Wernicke's area), and motor eloquent area (8).The current standard of care for glioblastoma encompasses maximally safe microsurgical resection and following chemotherapy and radiotherapy (12). Awake craniotomy for glioblastoma removal in eloquent areas leads to fewer neurological deficits, improved overall survival, and longer progression-free survival while maintaining quality of life. This highlights the safety and feasibility of the procedure, along with its positive outcomes (13, 14).

Choosing suitable patients is crucial for this procedure's success and prevents perioperative complications. Because of the necessity for patient cooperation, individuals with somnolence, drowsiness, confusion, altered mental status, psychiatric disorders and severe dysphasia, should be considered carefully (3). Ensuring adequate oxygenation and ventilation during all phases of awake surgery may be difficult for patients with morbid obesity, especially those with obstructive sleep apnea. Along with the anticipated difficult airway, these factors present relative contraindications (15). In patients with uncontrolled coughing, increased intracranial pressure and uncontrolled seizures, there is also a relative contraindication for awake craniotomy (16). Patient cooperation is essential; therefore, declining the procedure after a full explanation is an absolute contraindication.

The awake craniotomy, a procedure used in supratentorial brain tumor surgery, allows for neurological testing and facilitates maximal tumor excision with minimal damage to functional brain tissue. A literature review from PubMed and Medline databases showed shorter hospital

stays, slightly less mean extent of resection, and slightly less surgery time in awake craniotomy compared to craniotomy under general anesthesia (17). Postoperative neurological deficits were less frequent with awake craniotomy, and the neurological outcome and quality of resection were better in awake craniotomy groups compared to general anesthesia groups with lesions in eloquent areas (18).

Some surgical factors preclude awake brain surgery, like the risk of massive bleeding in highly vascular tumors, uncomfortable surgical positions like prone or park bench for infratentorial tumors, or tumors where resection can cause severe pain, like those with dural involvement (19).

The preoperative assessment, beyond medical comorbidities and medications, such as antiepileptic medications and ongoing antiedematous therapy with dexamethasone, which should be continued until the surgery, also includes explaining the procedure, its reasons and its benefits to the patient. Beyond standard intraoperative monitoring, additional assessments are tailored to patient's needs and may involve invasive blood pressure, central venous catheter, urinary catheter, BIS and entropy monitoring. Providing good analgesia on the scalp during an awake phase is facilitated by infiltrating local anesthesia on the surgical incision. Generally, two anesthetic techniques can be used for awake craniotomy: conscious sedation or monitored anesthesia care and the asleep-awake-asleep technique. Spontaneous ventilation is maintained through the procedure, with oxygen supplementation in patients with conscious sedation. Sedative drugs used for conscious sedation are midazolam, propofol (continuous infusion 50–150μg/kg/min), and dexmedetomidine (a bolus dose of 0.5–1μg/kg administered over 10 minutes, followed by a continuous infusion rate of 0.2–0.7μg/kg/h). Dexmedetomidine can be continued as an anxiolytic and analgesic in doses of 0.2μg/kg/h) during neurological testing. Analgesia is provided with fentanyl (boluses of 0.5–1μg/kg) and remifentanil (continuous infusion in doses from 0.01–0.05μg/kg/min) and continued in low doses during testing (0.01–0.02μg/kg/min) (2). Dexmedetomidine, a sedative and analgesic that acts as an α2-adrenoceptor agonist without causing respiratory depression, is commonly used for awake craniotomies (20). With conscious sedation as a technique and avoidance of manipulation of the airway, fluctuations of the hemodynamic and intracranial pressure are avoided. Anyway, with excessive sedation, there is a risk of airway obstruction, respiratory depression and apnea, all leading to hypoxia and hypercarbia.

The asleep-awake-asleep technique generally has an advantage over conscious sedation: It is more comfortable for the patient during painful parts of the procedure and reduces the risk of respiratory complications with controlled partial pressures of oxygen and carbon dioxide. Repeated airway manipulation during transitions from one phase to another can trigger laryngospasm or uncontrolled coughing, leading to increased intracranial pressure or intracranial bleeding. General anesthesia is induced with propofol, and ventilation usually is controlled by inserting a laryngeal mask or cuffed endotracheal tube. Anesthesia is maintained with continuous propofol, dexmedetomidine or volatile agent infusion. Analgesia is provided with boluses of fentanyl or continuous infusion of remifentanil. Propofol infusion is discontinued 15-20 minutes before neurological testing. Depending on the surgery, after the dural opening, the patient can be awakened for neurological testing and continuation of the surgery in the awake phase. Dexmedetomidine and remifentanil infusion may continue in low doses to ensure adequate analgesia and anxiolysis in alert but cooperative patients. When neurological testing and tumor surgery are completed, the patient is again induced into general anesthesia, usually with endotracheal intubation and mechanical ventilation. Techniques like video laryngoscopy and fiber-optic laryngoscopy are used for endotracheal reintubation.

Intraoperative seizures, respiratory adverse events, and loss of patient cooperation are the most common complications. Seizures occur in 2.2% to 21.5% of the patients, more often in younger patients with a history of seizures and receiving multiple antiepileptic medications. Frequently, there are seizures intraoperatively in low-grade glioma and frontal lobe tumor surgery (16). Ice-cold lactated Ringer (10-20mL) irrigation of the brain surface after opening the dura is usually an effective treatment (21) (22). Respiratory adverse events include airway obstruction, respiratory depression, apnea, hypoxia, hypercarbia and coughing. Hypoxia and hypercarbia potentially lead to surgical complications, increased intracranial pressure and open brain herniation. With adequate doses of sedative drugs, anesthesiologists should avoid oversedation and respiratory depression, and dexmedetomidine is advantageous for the lack of respiratory depression (23). The patient's head should be adequately positioned for proper emergency reaction for airway access and ensuring ventilation. If complications occur and the patient is unresponsive or uncooperative because of an intracranial event, the anesthesiologist should secure the airway after preoxygenation and induce the patient in general anesthesia. Intracranial events, somnolence, hypoxia, hypercarbia, full bladder, hypotension, agitation, oversedation and inadequate analgesia, are causes of loss of patient cooperation.

Conclusion

The development of anesthetic techniques, including short-acting agents such as propofol, dexmedetomidine and remifentanil, has facilitated the performance of awake brain surgery. Careful planning and early recognition of intraoperative complications, if any, as well as ensuring proper oxygenation, ventilation, systemic and cerebral perfusion, and adequate analgesia during both the asleep and awake phases of the procedure, along with sedation for asleep patients, are the mainstays of anesthetic management for awake craniotomy. The maximal safe microsurgical resection of brain tumors can be achieved using this procedure, thereby minimizing damage to functional brain tissue in eloquent areas.

* Informed consent for the publication of the photograph with open eyes was obtain from the patient.

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CASE REPORT *UDK: 616.833-056.7:616-089.5*

www.doi.org/10.55302/MJA2484131ts

REGIONAL ANESTHETIC MANAGEMENT OF A PATIENT WITH CHARCOT MARIE TOOTH DISEASE WITH HIP FRACTURE

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Abstract

Introduction: Charcot-Marie-Tooth disease (CMT) is a hereditary peripheral neuropathy characterized by progressive peripheral muscular atrophy and muscle-sensitive disorders, especially in extremities. The choice of anesthesia in these patients is a great challenge, as the neurological symptoms may worsen.

Case presentation: Female S.G., 53 years old, with a previously diagnosed Charcot Marie Tooth disease, was admitted to the Clinic for Orthopedic Diseases in Skopje for the treatment of a basicervical fracture of the femur. Apart from the existing neurological disease, the patient had no other comorbidities. An indication for surgery was set, and regional, i.e. spinal anesthesia was the choice for the surgical management of the patient. In the postoperative period, the patient was treated with analgesic therapy. After 9 days of treatment at the Clinic for Orthopedic Diseases, the patient was discharged in good general condition, without worsening of the neurological symptoms.

Conclusion: Regional anesthesia has been shown to be a safe type of anesthesia in surgical treatment of the lower limb.

Keywords: *anesthetic treatment; Charcot-Marie-Tooth disease; postoperative complications; regional anesthesia; sedation.*

Introduction

Charcot-Marie-Tooth disease (CMT) is a hereditary peripheral neuropathy characterized by progressive peripheral muscle atrophy and muscle-sensory impairment, especially in the extremities (1). Pathophysiological, it is characterized by genetic changes that cause a defect in the myelin sheath (demyelination) of peripheral nerves (CMT1, CMT3 and CMT4), or damage to axons (CMT2) (1-3). As a result of this myelin or axonal degradation, the conduction of nerve impulses in motor and sensory neurons is reduced, leading to progressive distal muscle weakness, wasting and atrophy, and loss of sensation, often accompanied by neuropathic pain. Clinical symptoms are similar in the different types of CMT, their severity, and progression (2-4).

In most cases, the disease begins with weakness in the lower extremities, followed by weakness in the hands and forearms. Due to muscle weakness and atrophy, deformities of the feet and

lower legs, upper extremities, and in rare cases scoliosis may occur. In axonal degeneration, the phrenic nerve may be affected, accompanied by deterioration of respiratory function due to diaphragmatic weakness (6-8). Cardiac problems such as mitral valve prolapse, QT prolongation, AV block and dysrhythmias may also occur (4).

Diagnosis of CMT is made through history and physical exam, and can be confirmed with electromyography (EMG), nerve conduction studies (NCS), nerve biopsies and/or genetic testing (9,10).

However, in resource poor settings diagnosis and treatment are often delayed. This can lead to the need for surgical correction of soft-tissue contractures and bony deformities (9-11).

The choice of anesthesia in these patients is a major challenge, as each type of anesthesia has risks and can lead to a worsening of neurological symptoms and the patient's general condition (9-13).

Case Presentation

Female S.G., 53 years old, with previously diagnosed Charcot Marie Tooth disease, was admitted on August 12th, 2024, to the Clinic for Orthopedic Diseases in Skopje for treatment of a basicervical fracture of the femur. The patient was injured 10 days before admission to our clinic and was hospitalized in another hospital, where a contraindication for surgical treatment was set, due to high anesthetic risk and resource poor settings for the treatment of critical patients. An indication for surgical treatment was set at the Clinic for Orthopedic Diseases in Skopje. From the anamnestic data, it was determined that the patient's CMT was diagnosed in the early period of puberty. The patient reported weakness in the legs and difficulty walking, but the medical history was normal, with no respiratory or cardiovascular problems. She was not receiving any chronic therapy and was allergic to Penicillin.

The initial assessment upon admission revealed stable respiratory status without recent coughing episodes, absence of wheezing or dyspnea, and no edema, hemodynamic or cardiac disorders were found. Chest X-ray was normal, SpO2 - 97%, which is why spirometer analysis was not performed. The ECG was normal and without changes. A complete laboratory analysis and hemostasis were performed, which were also without significant changes. She denied previous surgical interventions. She was not smoker. She is classified in ASA II status. After 2 days, the patient was scheduled for implantation a subtotal prosthesis. The choice of anesthesia was regional (spinal) anesthesia. After explaining the risks associated with spinal anesthesia and the growing evidence about the safety of this form of anesthesia in relation to the underlying condition, the patient accepted the technique and signed the informed consent.

The patient had a normal constitution (height 163cm, weight 65kg) and we expected an easy performance of the intrathecal block. Of course, we considered that with regional anesthesia there was a lower risk of worsening of the neurological deficit compared to general anesthesia.

Preoperatively, the patient was sedated with tbl diazepam 5mg. Before performing spinal anesthesia, basic monitoring such as ECG, non-invasive blood pressure, pulse oximetry and diuresis was performed. Initial parameters were: NIBP 100/60, HR 65b/min and SpO2 96%. Before the introduction to anesthesia, midazolam 1mg and ketamine 10mg were applied. Spinal anesthesia was performed under sterile conditions in the left lateral position, L3-L4 space, with a 25G needle. Clear cerebrospinal fluid was obtained and 1.5mg isobaric 0.5% bupivacaine was applied.

The patient was managed on an oxygen mask with a flow rate of 4L/min, 1500ml saline 0.9% and one unit of erythrocytes at the end of the intervention. The surgical intervention lasted 2 hours and the patient was stable throughout the entire period with normal vital parameters. The block lasted 5 hours and after its discharge there were no changes from baseline in the motor and sensory status of the lower limb.

In the postoperative period the patient was treated with antibiotics, anticoagulant therapy and pain relief with paracetamol, NSAIDS and tramadol only on the first postoperative day. On the second postoperative day, physical therapy started. She was discharged from the surgical clinic after 9 days in good general condition.

Discussion

This type of disease is rare in anesthesiology practice, and as a result it is difficult to obtain relevant information on the type of anesthesia (6). Most of the published studies include a small number of patients and represent case reports. Regarding the anesthetic management of patients with CMT, there is controversial information regarding general versus regional techniques.

In the presented case, spinal anesthesia and preoperative sedation and analgesia with midazolam and ketamine were performed. The patient was stable perioperatively, without any disturbance of vital parameters (respiratory function and ECG changes) and without worsening of pre-existing preoperative neurological findings.

General anesthesia in patients with CMT carries risks when using certain anesthetics. Chronic denervation of peripheral nerves is a predisposing factor for hyperkalemia. However, in practice, significantly elevated potassium levels are rarely observed, probably because denervation occurs slowly. However, potassium levels should be checked preoperatively. For this reason, the use of succinylcholine for induction of anesthesia is not recommended (1-3). On the other hand, non-depolarizing muscle relaxants have a prolonged effect caused by muscle atrophy, which in turn leads to an increase in the number of acetylcholine receptors in the neuromuscular junction. Their careless use can worsen the weakness of the intercostal muscles and diaphragm, and thus respiratory function. Therefore, they should be dosed carefully (3). Regarding the use of inhalation anesthetics, there are data on triggering malignant hyperthermia (MH) (3), although there is no report of a case of MH so far. Considering that CMT is a peripheral neuropathy and not a myopathy, it is considered that the occurrence of malignant hyperthermia triggered by inhalation anesthetics is unfounded (4).

In a case report from 2021, a 24-years-old male with a previous diagnosis of CMT at the age of 14, was presented for the removal of a renal calculus. General anesthesia was performed, with induction with midazolam, fentanyl and propofol, and maintenance of anesthesia with dexmedetomidine infusion 0.5μg/kg/h. Atracurium was used as a muscle relaxant. Capnography was used as an indicator for repeating the dose of the muscle relaxant. At the end of the intervention reversal of the neuromuscular block was performed with neostigmine. The patient demonstrated all clinical signs of adequate reversal and satisfactory recovery (4).

Vinci P., Lapi G. in a study from 2011, presented a case of a 73-years-old woman with two surgical interventions at an interval of 22 months (umbilical hernioplasty; transvaginal hysteroannexiectomy (5). The patient has previously been diagnosed with CMT2 (axonal degeneration),

and reported severe sensory impairment in the lower extremities, particularly worsened after an epidural anesthesia performed several years ago for osteosynthesis of a hip fracture. Total intravenous anesthesia was performed for both interventions. Fentanyl and propofol were used for induction and maintenance of anesthesia, and atracurium was used as a muscle relaxant. The reversal of the block was performed with atropine and prostigmin. The patient was successfully extubated, but during both interventions in the immediate postoperative period she developed respiratory failure, which is why she was re-intubated and mechanically ventilated for 2½ hours after the first and 10 hours after the second surgical intervention (5). This study confirms the findings that patients with CMT2 have a higher risk of developing intercostal and diaphragmatic muscle weakness and are at higher anesthetic risk.

For minor surgical interventions in patients with CMT disease, light sedation can be safely used, as referenced in a study in 2016, in which midazolam and propofol were used for tooth extraction and implant placement in a 51-years-old man. After sedation, the patient was administered the local anesthetic lidocaine 2% (6).

Of course, there is also concern about the application of regional anesthesia, which is associated with peripheral nerve denervation. It has been thought that neuraxial blocks can worsen pre-existing nerve deficits. In the study by Rodrigez et al., a single subarachnoid (epidural) block was successfully performed in a 63-years-old male with diabetes mellitus and pulmonary comorbidity for fixation of a hip fracture. The choice for regional anesthesia was made in order to avoid respiratory deterioration with the use of general anesthesia and intubation (7). Roriz et al. also reported the safe performing of spinal anesthesia in a patient undergoing lower extremity orthopedic surgery (8), while Brock et al. demonstrated the successful use of combined spinal-epidural anesthesia for labor and cesarean section in patients with CMT (10).

Several studies have demonstrated safe and successfully performed peripheral nerve blocks (11-13). Localization of the nerve using ultrasound has been shown to be simpler and more reliable, demonstrated in a small group of 3 patients (11), compared to the use of a neurostimulator (12,13). Regardless of the technique used to perform the block, successful anesthesia and postoperative analgesia were achieved in patients with CMT in all three studies. Schmitt et al. used a catheter to achieve a continuous distal sciatic nerve block for foot surgery in a group of 27 patients with CMT. Localization of the sciatic nerve was guided by a nerve stimulator (13). In this study, it was determined that patients with the highest pain threshold required the least analgesia during the block. The authors believe that this phenomenon is due to demyelination of sensory and peripheral nerves. Patients with CMT, due to demyelination, have different pain sensitivity and therefore an individual approach to each patient is required. Local anesthetic was successfully applied through the placed catheter in the patients during three postoperative days, without complications and worsening of the previously determined neurological deficit (13).

Ritter and colleagues used a combined neuraxial block and ultrasound-guided peripheral nerve block for surgery for a foot deformity, in a patient with pronounced muscle atrophy, limb deformities and facial indicators for difficult intubation. With this combination of two regional anesthetic techniques, the authors report successful management of anesthesia in the patient, with minimal perioperative sedation and avoidance of the risk of difficult or impossible intubation.

The choice of the type of anesthesia in patients with CMT remains a dilemma. An individual approach to each patient is required, depending on the severity of symptoms and the type of trauma or disease to be treated surgically.

Conclusion

In this presented case, spinal anesthesia was performed without worsening neurological or sensory symptoms in the immediate and later postoperative period and proved safe type of anesthesia for lower extremity surgery.

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CASE REPORT *UDK: 616-089.5-056.3*

www.doi.org/10.55302/MJA2484136k

ANESTHESIA MANAGEMENT IN A PATIENT WITH ROCURONIUM ALLERGY

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Abstract

Neuromuscular blocking agents (NMBAs) are commonly used in anesthesia but are also leading causes of perioperative anaphylaxis, posing a significant challenge for anesthesiologists.

This case report describes the anesthetic management of a 63-years-old male with a documented allergy to rocuronium undergoing femoro-femoral crossover bypass surgery. Despite negative allergy testing prior to surgery, the procedure was conducted without the use of NMBAs to avoid potential anaphylaxis. Induction and maintenance of the anesthesia were achieved with propofol and remifentanil, ensuring excellent intubation conditions and hemodynamic stability throughout the whole surgery. The patient had an uneventful recovery and was discharged on the third postoperative day. This report highlights the feasibility and safety of an NMBA-free anesthetic approach, particularly for patients with contraindications. It underscores the importance of individualized anesthetic planning and the effective use of alternative techniques to ensure patient's safety and optimal surgical outcomes.

Keywords: *avoiding muscle relaxants; general anesthesia; neuromuscular blocking agent free anesthesia; rocuronium allergy.*

Introduction

During general anesthesia, muscle relaxants are frequently employed to help with intubation, enhance surgical conditions, lessen shivering, guarantee patient's immobility throughout procedures, and consume less oxygen. For many surgical procedures, adequate muscular relaxation is essential because it facilitates the execution of certain operations by surgeons and the management of the patient's airway by anesthesiologists (1,2). Any medication can potentially lead to perioperative anaphylaxis, but neuro muscular blocking agents (NMBAs), antibiotics, latex and chlorhexidine are the most common causes. Allergic reactions to NMBAs continue to be a significant concern for anesthesiologists, as death can still occur even when the reactions are promptly and effectively managed (3). Muscle relaxants are the primary agents causing intraoperative anaphylaxis. NMBAs account for 50-70% of the allergic reactions during anesthesia. The predominant mechanism for hypersensitivity to NMBs is acute type I allergic reactions, with anaphylaxis being the most severe form (4). After diagnosing anaphylaxis due to NMBAs,

it is essential to find safe alternatives for future anesthesia. A patient who has experienced anaphylaxis from one NMBA may also react to other NMBAs due to cross-reactivity. Although drug provocation testing is the standard method for confirming or ruling out allergies, it carries considerable risk (5).

Case Presentation

In this report, we present the medical management of a 63-years-old patient, male, smoker, with a BMI of 22.5 and ASA 3, with a documented allergy to rocuronium happened due to vascular surgery vascular prothesis pp bypass right iliac-femoral, 18 years before. The patient was experiencing pain and numbness in the right leg over the past few weeks, had absent pulses bilaterally in the groin area and was diagnosed with occlusion of the bypass. He underwent vascular surgery crossover femoro-femoral bypass. Despite negative allergy testing before the surgery, the decision was made to proceed without the use of neuromuscular blocking agents, providing excellent conditions for tracheal intubation via intravenously given propofol and remifentanil, and the operation was completed uneventfully and without the need for the use of a muscle relaxant.

The patient was admitted to the Clinic of Thoracic and Vascular Surgery. Because of a documented allergy to rocuronium and "Cafetine", in order to avoid anaphylaxis, anesthesia management was indicated in accordance with the patient. At first a cardiologist was consulted. The electrocardiogram was normal and showed sinus rhythm, the echocardiogram showed ejection fraction of 65%, compensated for heart valves of the heart with mild changes and arterial doppler showed occlusion of the bypass. With the history of hypertension and thrombosis he was receiving antihypertensive and antiplatelet agent therapy prescribed by cardiologists. The antiplatelet therapy was switched to Low-Molecular-Weight Heparin, 5 days before surgery. Laboratory data and coagulation tests were unremarkable with exception of slightly elevated D-dimers at 1118ng/mL (0-500). Our patient is a smoker (10 cigarettes per day), auscultation revealed bilateral diminished vesicular breath sounds, spirometry showed mild restriction.

During the pre-op visit, on the day of surgery, preoperative standard investigations were performed, and all were within normal ranges. The patient was assigned to ASA 3 and Mallampati 1. Informed consent for high-risk surgery was obtained, and the patient continued taking his antihypertensive medications until the morning of surgery. Premedication with Diazepam 5mg was administered the night before and in the morning of the surgery, and the patient fasted overnight. An intravenous saline solution of 1000mL was infused over 8 hours overnight. He received standard measurement for prophylaxis with corticosteroids and antihistamine according to protocol. Preoperative antibiotic prophylaxis was made with Vancomycin when he started coughing and had difficulty in breathing shortly after antibiotic administration. With a possible diagnosis of allergy reaction, we administered corticosteroids additionally. The planned surgery was not suspended.

In the operating room standard non-invasive monitoring was established, automated non-invasive blood pressure, pulse oximeters, electrocardiograms. and the patient's vital signs remained stable throughout, with baseline pulse rate being 53 beats per minute, blood pressure was 120/80mmHg, and oxygen saturation was 96%. An 18-gauge intravenous needle was inserted, and a 0.9% NaCl solution was initiated. After preoxygenation with 100% oxygen and premedication using 2mg midazolam, induction into general anesthesia for orotracheal intubation (OETT) was achieved with 100mcg fentanyl and 200mg propofol.

After induction, tracheal intubation was performed uneventfully, an 8.0-mm endotracheal tube (ETT) was successfully placed without needing muscle relaxants. After intubation the patient was with 100% saturation on pulls-oximetry and airway pressure up to 18cm H2O. Mechanical ventilation was set on pressure controlled volume guaranteed mode (PCV-VG), tidal volume of 7ml/kg and respiratory rate of 12 per minute, fresh flow rate 2l/min, positive end-expiratory pressure (PEEP) of 5cm H20, inspired oxygen fraction 50%, partial pressure of end tidal Carbone dioxide: 35mm Hg, I:E ratio of 1:2. A 20-gauge needle over the right radial artery for invasive blood pressure monitoring and a central venous catheter into the right internal jugular vein after induction of anesthesia were placed.

Anesthesia was maintained using propofol 7mg/kg/min and remifentanil at 0.3mcg/kg/min. During anesthesia, the antibiotic prophylaxis and antiemetics were administered. Intraoperative fluid management was maintained with adequate intravascular volume status and diuresis, and throughout the surgery the patient remained hemodynamically stable with normal vital signs.

At the conclusion of the procedure, without any complication occurred during 5 hours of anesthesia, the patient was awake and successfully extubated in the operating room with saturation 97%. Early postoperative recovery in the Post Anesthesia Care Unit (PACU) was uneventful. Surgery resulted in a significant improvement in recirculation. The patient was discharged home in stable and good condition after a few days and he didn't admit any problems during a follow-up visit within 1 week of the surgery.

Discussion

Neuromuscular blocking drugs, both depolarizing and nondepolarizing are among the most frequently used medications in anesthesia. However, their use can sometimes result in serious complications. Incomplete recovery from neuromuscular blockers is linked to negative outcomes, including upper airway obstruction, reintubation, atelectasis, pneumonia, extended stays in the post anesthesia care unit (PACU), and reduced patient's satisfaction (6).

On one hand, the use of rocuronium has been on the rise, so it's unsurprising that reports of side effects like anaphylaxis are also increasing. Some authors suspect a high rate of "rocuronium-mediated anaphylaxis" and have recommended careful monitoring of these adverse reactions. On the other hand, many studies have demonstrated successful intubation without neuromuscular blockers. Baillard C. et al. announced that in their institution, the use of muscle relaxants for intubation decreased from 100% to 25% between 1995 and 2000, without any associated complications. Additionally, they want to highlight that neuromuscular blocking agents are the primary drugs responsible for life-threatening events during anesthesia and their use is not always surgically required. We embrace this recommendation, and we believe comprehensive reporting is crucial to better understand the potential risks of rocuronium-related anaphylaxis (7). In one study, administering propofol alone at a dose of 2.5mg/kg for tracheal intubation allowed successful intubation in 19 out of 20 patients and created ideal intubation conditions in 14 out of 20 patients. All these studies demonstrate that intubation can be achieved without the use of neuromuscular blockers when these drugs are contraindicated or when their use is preferable to avoid (8).

Different techniques are available, which can be applied based on the clinical scenario and the anesthetist's expertise. Fentanyl has been shown to reduce the pressor response to laryngosco-

py within 5 minutes of administration. Streibel and colleagues designed a double-blind, randomized controlled trial comparing intubation conditions between two groups: one receiving thiopentone, fentanyl and suxamethonium, and the other receiving propofol and fentanyl. The study, involving 25 patients, found no significant difference in intubation conditions between the two groups (9). In one study retrospectively 81 cases of adenotonsillectomy were reviewed. The objective of the study was to investigate what happens when general anesthesia is given without the use of neuromuscular blocking medication. Their findings revealed that using general anesthesia without a neuromuscular blocking agent significantly reduces both the operation time and intraoperative bleeding (10). In one randomized, double-blind study, the intubating conditions after anesthesia induction with propofol, midazolam and fentanyl were compared to those after using propofol, lignocaine and fentanyl. The study concluded that the combination of fentanyl, midazolam and propofol, more consistently provides favorable conditions for intubation compared to the fentanyl, lignocaine and propofol combination. Intubation was successfully achieved in our case in accordance with this study where all patients received the fentanyl, midazolam and propofol combination (11).

NMBAs are among the most frequent triggers of perioperative anaphylaxis. While a positive skin test can aid in identifying NMBAs that may cause a reaction, it remains uncertain whether a negative skin test can reliably ensure the safety of NMBAs when administered systemically. A retrospective cohort study of patients with suspected NMBA-induced anaphylaxis was gathered at Seoul National University Hospital between June 2009 and May 2021. The chemical similarities among NMBAs may play a role in their cross-reactivity in skin tests. Although skin tests have a high negative predictive value for NMBA-induced anaphylaxis, the possibility of recurrent anaphylaxis remains a concern (12). In the current issue of Anesthesiology, from Reddy et al. a retrospective, observational cohort study conducted across two hospitals, has confirmed that the incidence of anaphylaxis is higher with the use of rocuronium and succinylcholine, compared to atracurium. Our patient was documented with allergy to rocuronium (13). It is crucial to develop and maintain the ability to perform intubation without neuromuscular blocking agents (NMBAs) for certain, though uncommon, clinical scenarios. These include patients with NMBA allergies, those with myotonias or other neuromuscular/ muscular disorders, as well as individuals at high risk for malignant hyperthermia. Additionally, there are surgical situations were avoiding NMBAs is necessary, such as preserving nerve function for intraoperative neuromonitoring (14).

Conclusion

This case highlights the effectiveness and safety of a neuromuscular-blocking agent-free anesthetic approach in managing patients with specific contraindications, such as allergies to rocuronium. The combination of propofol and remifentanil, delivered as continuous infusions, provided sufficient anesthesia depth, hemodynamic stability and optimal conditions for intubation. Importantly, the strategy ensured a smooth postoperative recovery, devoid of complications such as discomfort, hoarseness, or vocal cord sequelae. This case underscores the importance of individualized anesthetic planning and the need for vigilance in balancing patient's safety with procedural requirements because success is not solely dependent on "what we give" but rather on "how effectively we administer it".

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PERSPECTIVE *UDK: 616.12-008.313-073.432.19-032:611.329*

www.doi.org/10.55302/MJA2484142z

THE FIRST USE OF A MODIFIED LARYNGEAL MASK GASTRO® IN THE WATCHMAN PROCEDURE

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Case Presentation

A 76-years-old woman, 165cm, 53kg, ASA 2, was scheduled for a Watchman procedure, i.e. closure of the left atrial appendage (LAA) in patients with chronic atrial fibrillation, particularly in patients who cannot be treated with anticoagulants (1). The procedure was performed by advancing and deploying a device with a spring or umbrella-like structure into the right atrium under transesophageal echocardiography (TEE) guidance through the interatrial septum (1).

The patient recently experienced a hemorrhagic transient ischemic attack, while on apixaban. Although she recovered without complications, anticoagulation was discontinued due to risks causing another hemorrhagic event with potentially unpredictable outcomes.

As an alternative to anticoagulation, the patient agreed to a Watchman procedure.

The interventional scenario was complicated by the patient's history of pneumonectomy for lung cancer, which had resulted in paralysis of the ipsilateral vocal cord. The patient refused endotracheal intubation, fearing damage to her remaining functional vocal cord. As an alternative, the LMA-Gastro® (Teleflex®, Athlone, Ireland) (Figure 1A+B) was selected, allowing for both airway management (ventilation/ respiration) and insertion of the TEE probe (2). All LMA-Gastro sizes can accommodate endoscopes that fit in a 14mm diameter channel and a 2D-TEE trial (GE6VT-D, 14mm) passed through the endoscopic port (Figure 1C+D), but the LMA shape created friction that impeded free manipulation. As a result, the first modification was made as previously described (3). On the procedure day, the use of a 3D-TEE probe (17mm transverse dimension) was necessary, but it could not pass through the endoscopic port, and an additional modification was necessary. The breathing port and endoscopic port were built together, but the latter extends by 4cm into the body of the LMA to create a bite bock. The two ports were separated, leaving only the breathing port (Figure 1C) connected to the body of the LMA-Gastro®, and allowing the 3D-TEE probe to easily pass through the now-empty gastric entry channel (Figure 1E-1F-1G).

After Intravenous induction of GA modified LMA-Gastro® (size 3) was inserted, ventilation was assessed. A reliable $ETCO_2$ trace was observed on the monitor and mechanical ventilation was initiated with volume-controlled ventilation and a positive end-expiratory pressure of 5cm H_2O under oxygen and sevoflurane. The procedure went uneventful.

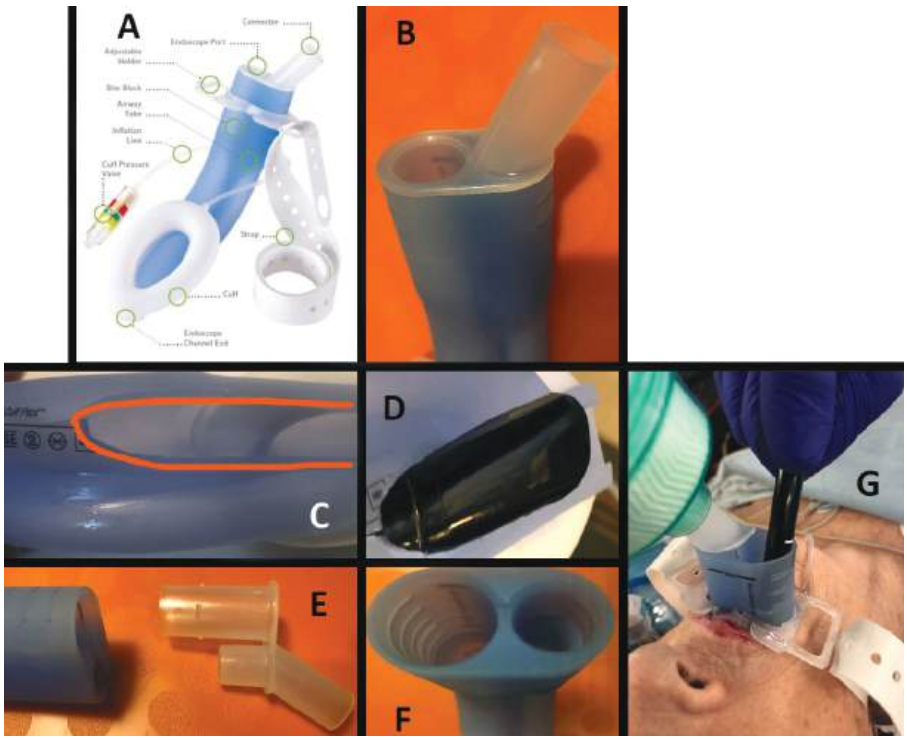

Figure 1. LMA-Gastro® Teleflex
A. Picture from the official Teleflex website showing the commercially available LMA-Gastro®. Image courtesy of Teleflex Incorporated 2024. All rights reserved.
B. Picture centered on the proximal part of the mask, showing the two-port connector (ventilation connector and endoscope port).
C. Top view of device, showing the modified LMA-Gastro® with manual removal of the distal part and back part allowing to accommodate up to a 14mm tube.
D. Endoscopic 2D TEE probe passing through the 14mm endoscope channel exit in the dry test.
E. Proximal part of the LMA-Gastro® with the proximal two-port connector removed.
F. Proximal part of the LMA-Gastro® after the removal of the connector. The large diameter channel is the endoscopic one.
G. The LMA Gastro® in a ventilated patient after withdrawing the endoscope connector

Discussion

The procedure was elective but with a sense of urgency because no anticoagulants were given. At the time this patient was cared for, no valuable alternative method was available. The new airway device (Jcerity Endoscoper Airway® - JEA, Zhejiang Jcerity Medical Technology, Huzhou, China) is now available and its 20mm endoscopic opening would have easily accommodated the 3D-TEE probe (4). It also has an open built-in back opening which is similar to modification previously made manually (3). This device was not available to us and may still be restricted to use only in China. Although the Gastro-Laryngeal Tube® was also available and presents with a port dedicated for inserting a gastro-duodenal endoscope, the internal diameter of its endoscopic port is 13.8mm and would not have allowed to pass the large 3D-TEE tube. The modified LMA-Gastro® was our only option.

Aminian et al. recently described applying smaller 2D TEE probes (external diameter 8mm), allowing LAA closure to be performed under sedation. However, only the standard large TEE probe

allows 3D imaging. If the 3D-TEE is required, GA may be necessary and the diameter of the endoscopic port of the airway device should be large enough to accommodate such a probe (5).

Managing this case required quick adaptation of an existing device to meet an unforeseen challenge. This situation demonstrates how flexible, "out-of-the-box" thinking can lead to successful outcomes and potentially inspire new applications for the LMA-Gastro®.

Acknowledgements

We acknowledge the dedicated colleagues from The Hadassah Medical Centre, both Campuses, whose expertise ensured the success of this procedure: Dr. Boaz Kalush (Anesthesia), Prof. David Leibovitz (Cardiology), Dr. Elhanan Fried (ICU), Prof. Ronen Durst (Cardiology), Dr. Yitzhak Biton (Cardiology).

We thank Teleflex for allowing the use of picture of the LMA-Gastro® (Figure 1A).

Image courtesy of Teleflex Incorporated 2024. Teleflex Incorporated. All rights reserved.

The patient gave consent to the publication of her clinical history.

Key Words: *endoscopy; laryngeal mask airway; left atrial appendage closure; transesophageal echocardiography.*

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www.doi.org/10.55302/MJA2484145s/

BRAIN DEATH DETECTION

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Abstract

This article will elaborate the definition of brain death as well as the initial diagnostic assessment of patients suspected of brain death. We will explain the protocol for brain death detection as simple as possible, elaborating all diagnostic approaches available for proving brain death presence. Since, early recognition of symptoms that indicate potential brain death in the patient is of vital importance, the clinical assessment of patients suspected of brain death will be explained step by step in order to provide a simple but comprehensive guide for nurses, resident doctors and specialists that work in an Intensive Care Units where brain death is most commonly diagnosed and deceased donor are treated further on. Diagnosing brain death must be carried out according to all rules and protocols, to avoid any omission or error in making a very important and serious diagnosis. Close and frequent monitoring by the nurse and physicians is the most important toll beyond any others when we speak about early and on time brain death detection.

Keywords: *brain death; clinical assessment; diagnosis.*

Introduction

Brain death (BD) is a condition in which there is a complete and irreversible failure of the central nervous system - CNS. The most often encountered causes that lead to the occurrence of irreversible brain damage are severe neurotrauma, spontaneous brain hemorrhage, traumatic brain hemorrhage and anoxic hypoxic encephalopathy. In percentage terms, brain death the most often occurs due to cerebrovascular lesions (48%), craniocerebral injuries (32%), anoxic ischemic brain lesion (13%), brain tumors (4%) and other remaining causes in total of 3%. These patients are the most often treated in intensive care units, where the total number of deaths diagnosed with BD is 10-16%, and the total in all hospital institutions is 1-5% (1). Regarding the timely diagnosis and early detection of BD, a very important tool is the observation of patients with the above-mentioned diagnoses upon admission to intensive care units. Every intensive care unit should have a transplant coordinator who would organize and manage the entire process together with the intensive care unit team, as well as the team that will perform the transplantation. Early recognition of symptoms that indicate potential brain death in the patient is of vital importance. In such cases, measures are immediately taken, primarily to save the injured person, and if, despite all efforts, brain death occurs, then the entire medical team should be focused on maintaining the vitality of the potential donor's organs until their successful explanations. Patients who have suffered massive brain injuries, most often during hospital-

ization, show symptoms that indicate extremely severe brain damage, which are the most often irreversible (1). Usually, at the first examination, these patients have a Glasgow Coma Scale of less than seven, which indicates a poor prognosis.

The Glasgow Coma Scale is used for neurological assessment of patients and is a sum of points from three components: ocular, vestibular and motor response. The total sum of these points is a very important diagnostic parameter. The minimum sum of these points is three, and the maximum is fifteen. A score of 0-12 points indicates moderate neurological impairment, while anything below 8 is considered a comatose state of the patient (2,3).

Scoring using the Glasgow Coma Scale:

1) Opening eyes

- Spontaneous (4 points)
- On command (3 points)
- With painful jaw (2 points)
- No response (0 points)

2) Speech function

- Spontaneous speech (5 points)
- Confused speech (4 points)
- Unintelligible words (3 points)
- Unintelligible voices (2 points)
- Inability to speak (1 point)

3) Motor function

- Follows command (6 points)
- Performs emphasized movement (5 points)
- Indicates pain (4 points)
- Flexion (3 points)
- Extension (2 points)
- No response (1 point)

During the examination, there may be asymmetry between the two sides of the body, and then the side that reacts more painfully is assessed (2).

Dilated and non-reactive pupils, absence of spontaneous respirations, as well as absence of reactions even in the most painful state, are the first symptoms that indicate brain death (2,3). They are the most often first noticed by the nurse who participates in the treatment of the patient. When the first symptoms characteristic for brain death are observed, medical examinations should be immediately started to prove existence of brain death. In the meantime, emphasis is placed on hemodynamic maintenance and perfusion of organs and tissues in the potential donor.

The process itself from undertaking investigative methods to prove brain death to organ explantation should last from 12-24 hours. After proving the presence of brain death in the patient, according to the legal rules of the country, the doctor who is responsible for treating the patient should inform the family about the patient's health condition and explain the possibility of organ donation, and thus the possibility of saving another human life. Attention must be paid to legal and medical regulations, and everything must take place without any legal or ethical lapses.

Brain Death Detection Methods

According to the World Brain Death Project, every patient that will be treated as a possible organ donor because of BD should have a previously established neurologic diagnosis that can lead to an irreversible and complete loss of all brain functions. All clinical conditions and diseases that can confound the clinical examination and may mimic BD should be excluded prior to establishing the final diagnosis (4). There are generally three steps used for the successful and on-time detection of potential organ donors. They are:

1) Administrative method - involves monitoring of all patients that are admitted in the intensive care units.

2) Presence of a coordinator for assessing a potential donor - Every brain-dead patient is a potential donor. The coordinator is always guided by the answers to the following questions:

- Who is a potential donor?
  (Severe brain injuries: brain hemorrhages, neurotraumas, cerebrovascular stroke, anoxic ischemic brain lesion);
- What pathological changes are there?
  (Severe brain injuries, Glasgow coma < 7);
- Where is it the most often found?
  (Emergency centers, intensive care units, neurosurgical centers).

3) Connection with other centers - Ensuring more successful mutual communication and cooperation, to timely prove brain death in the patient, maintain hemodynamic stability of the donor and evaluate the donor. For on-time recognition of potential donors and proof of brain death in the patient, there must be a perfect protocol. The protocol should consist of: a team, a member of which is directly responsible for recognizing and monitoring the health condition of the potential donor; protocol for facilitating recognition and identification of a potential donor and mutual cooperation of the entire medical team. The existence of a professional and educated team, responsible for identification, maintaining hemodynamic stability and good perfusion of the organs of the potential donor, as well as the existence of an organized and trained team for explantation and implantation of the transplant, are key factors for successful transplantation.

The need for organ transplantation is increasing significantly, and the largest number of donated organs are obtained from deceased organ donors who were diagnosed with brain death. Therefore, timely recognition and diagnosis of brain death in a potential organ donor is of immense importance. The success of transplantation as the entire process depends on the early recognition of the potential donor, whose clinical picture is most often recognized in the first 24 hours of admission to the ICU (Intensive Care Center), and 25% of them are recognized in the

first 48 hours or more. A qualified team of intensivists, neurosurgeons and neurologists perform the first clinical examination of the potential donor, while the neurologist and nephrologist are responsible for conducting instrumental tests to prove brain death. There are two basic concepts of brain death: whole brain death and brainstem death. Whole brain death - In this case, there is an irreversible cessation of the functions of the cerebellum and cerebellum, as well as the brainstem. In the case of whole brain death, a clinical examination and instrumental tests are required to establish an accurate diagnosis. In case of Brainstem death there is an irreversible loss of consciousness and spontaneous breathing. Only a clinical examination can prove the absence of the brainstem activity.

Diagnosing Brain Death

Brain death is a condition in which there is an irreversible loss of all brain functions, including brainstem functions. The function of other organs, due to their possible explantation, can be preserved for a short time with the help of various medications and mechanical support. Brain death occurs because of an increase in intracranial volume, which the most often occurs due to brain edema or due to the presence of a collection or obstruction that impedes the circulation of cerebrospinal fluid. With the increase in intracranial pressure, blood circulation to the brain gradually slows down until it stops completely. When brain death occurs, the condition is irreversible and circulatory death occurs quickly. The most common causes that lead to brain death are stroke, brain hemorrhage, or severe traumatic injuries to the head and brain. The diagnosis of brain death takes place in four stages:

I. Existence of prerequisites for establishing a diagnosis of brain death. Prerequisites that must exist in order to make a decision to approach procedures for diagnosing brain death are:

- the patient is in a comatose state,
- the patient does not have spontaneous breathing,
- knowledge of the exact cause of brain damage,
- brain damage is irreversible.

II. Exclusion of reversible causes - Conditions that may give a clinical picture like brain death or challenge the diagnosis of the same are:

- a state of hypothermia < 35 degrees Celsius,
- intoxication with drugs: benzodiazepines, antiepileptics, anesthetics, barbiturates or alcohol,
- hypotension with systolic pressure <80mm Hg,
- metabolic and endocrinological conditions: myasthenia gravis, hepatic encephalopathy.

First, in these situations, the first step is to correct the current condition, then proceed to conduct instrumental tests that prove circulatory arrest of the brain (3).

III. Clinical examination

1. Pupil status - In order the pupils to be defined as non-reactive, all diseases and medications that would cause the pupils to be in such state must be excluded. A condition in which the pupils

are moderately or completely dilated, in a neutral position, where there is an absence of photo motor reflex, as well as ocular movement, is considered a positive test for brain death.

2. Corneal reflex - absence of spontaneous blinking, where the stimulus is stronger than in conscious patients.

3. Trigeminal nerve - with strong stimulation in the area of innervation of the trigeminal nerve, the reaction is absent.

4. Oculocephalic reflex - This test is not performed in patients with cervical injuries. Method of performance - by holding the eyelids open, the patient's head is abruptly rotated to one side, the head is held in that position for 3-4 seconds and then the head is abruptly rotated to the other side. In a deceased patient, the eyes follow the movement of the head. In patients with brain death, there is an absence of the oculocephalic reflex.

5. Oculovestibular test - Method of performance - the patient's head is raised by 30 degrees and 50ml of cold water is introduced into the ear canal with a plastic catheter. In patients with brain death, there is an absence of any eye movement. For an accurate result, attention must be paid to the possible existence of an ear injury, the presence of blood or cerumen in the ear canal. Also, during treatment with sedatives, anticonvulsants, in the presence of previous ear diseases, as well as in the case of a fracture of the temporal bone, the result may be false.

6. Pharyngeal reflex - Method of performance - with a spatula, the root of the tongue and the back of the throat are stimulated. In patients with brain death, the pharyngeal reflex is absent.

7. Tracheal reflex - This is the last reflex to disappear in patients with brain death. Method of performance - with a suction catheter, through the endotracheal tube, the trachea is stimulated. In patients with brain death, the tracheal reflex is absent.

8. Muscle atony.

9. Atropine test - Method of performance - atropine is administered intravenously at a dose of 0.04mg/kg body weight. A positive test is considered when the acceleration of the heart rate is not greater than 10% of the initial heart rate.

10. Apnea test - This test is performed last. It proves the absence of spontaneous respirations during the disconnection from the respirator. The patient should be disconnected from the respirator for a time interval that would result in a sufficient increase in CO_2 in the atrial blood, which would provoke the neurons of the respiratory center. The apnea test can be performed with and without the help of a respirator.

o Without the help of a respirator - The patient is ventilated for 10-20 minutes with 100% oxygen. $PaCO_2$ should be 5.3kPa (40mmHg) or higher before disconnecting from the respirator. After disconnecting the patient from the respirator, oxygen is introduced at 6 l/minute through a catheter in the endotracheal tube. Wait until $PaCO_2$ reaches 8.0kPa (60mmHg).

o Without a respirator - The ventilation mode should be CPAP, PEEP 10-12cmH_2O, FiO_2

- monitoring oxygenation and capnography,
- monitoring the arterial blood pressure through invasive monitoring,

- with each apnea, the module should be returned to CPAP,
- depending on the initial values, after 5-10 minutes, a reading of CO_2 is taken on the capnography at the end of expiration,
- when CO_2 reaches a value of 50mmHg, arterial blood is taken for analysis of $PaCO_2$ and PaO_2,
- every 2 minutes, arterial blood is taken for analysis until $PaCO_2$ reaches a value of 60mmHg,
- upon detection of spontaneous respirations, saturation lower than 85%, PaO_2 <65mmHg, systolic pressure lower than 65mmHg or cardiac arrhythmia, the test is stopped.

The clinical examination is performed in two stages (2). The first examination includes: examination of the pupils, corneal reflex, trigeminal reflex, oculocephalic reflex, oculovestibular reflex, pharyngeal reflex, tracheal reflex, muscle atony and atropine test. After 24 hours, the clinical examination is repeated, including the apnea test. After obtaining a positive clinical examination for brain death, instrumental tests are performed on the potential donor (2,3.7).

IV. Instrumental tests

Instrumental tests are used to examine the bioelectric activity and blood circulation in the brain. These tests should be non-invasive, reliable, precise, fast and economical, be performed without transporting the patient and be easily interpreted by the doctor working in the intensive care unit (5-9).

1. Selective brain panangiography - This examination can detect several findings that are compatible with brain death: complete cessation of arterial contrast and absence of venous filling, cessation of cerebral circulation in the Circle of Willis and significantly slow arterial-venous time. A delay greater than 15 seconds is not compatible with brain function. The biggest disadvantage of this procedure is the transportation of the patient to the X-ray machine intended for angiography.

2. Radionuclide scintigraphy - A highly sensitive technique, independent of previous drug administration and the current clinical condition of the patient, performed using 123 and Tc99m.

3. Transcranial Doppler sonography - This technique examines blood circulation through the brain and monitors possible circulatory arrest. It is suitable for repeated performance due to the possibility of performing it at the patient's bedside.

4. Evoked Somatosensory Potentials - This test examines the visual, auditory, and somatosensory pathways using light, auditory and electrical stimulus at different frequencies. Hypothermia can give false results with visual stimulus. Chronic deafness, temporal bone fractures, and eardrum or middle ear injuries can give false results with auditory testing. When examining sensory pathways, false results can be obtained if there is peripheral nerve damage.

5. EEG - With this recording, which lasts about 30 minutes, no brain-generated bioelectrical activities are detected in the event of brain death. In some cases, due to the presence of cardiac activity, it is possible to record electrical activity. All conditions that compromise the clinical examination also compromise the EEG examination.

At the Clinic for Anesthesia, Resuscitation and Intensive Care (CARIC), in the period from 2021-2023, there were a total of 12 cadaveric donors. In the intensive care unit at CARIC, in

2021, a total of nine cadaveric donors were recorded. In 2022, there was only one cadaveric donor. In 2023, a total of two cadaveric donors were recorded. The cause of brain death in seven of them was intracerebral hemorrhage and subarachnoid hemorrhage in severe polytrauma, while in the remaining five, the cause was spontaneous brain bleeding. At the Clinic for Neurosurgery, in the period from 2021-2023, a total of seven cadaveric donors were recorded. In the intensive care unit of the Clinic of Neurosurgery, a total of 318 patients died from spontaneous intracerebral hemorrhage and subarachnoid hemorrhage in the period from 2021 to 2023. Seven of these patients were processed as potential donors. A ruptured aneurysm was the cause of the cerebral hemorrhage in 71.4%, and in the remaining 28.6% the cause was a hypertensive crisis. As previously was noted in the literature, cerebrovascular events and neurotrauma were the most frequent cause of death according to our experience as well. Diagnosis of brain death was established in the ICU from an anesthesiologist, following the above-described protocol step by step in a multidisciplinary collaboration with nurses, ICU stuff and interventional radiologist.

Conclusion

Diagnosing brain death must be carried out according to all rules and protocols, to avoid any omission or error in making a very important and serious diagnosis. Regarding the fact that most of the cases of BD diagnosis are met in the ICU, systematic approach of clinical and instrumental examination is needed in order to establish clear diagnosis of BD. Close and frequent monitoring by the nurse and physicians is the most important tool beyond any others when we speak for early and on time brain death detection.

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www.doi.org/10.55302/MJA2484153j

THE MOST COMMON HYPERTENSIVE DISORDERS IN PREGNANCY

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Abstract

Hypertensive disorders are the most common medical complications that can occur during pregnancy, with an incidence ranging between 5–10%. These disorders are the leading cause of maternal mortality worldwide.

Objective: The aim of this retrospective study is to analyze the two-years archives data of the University Clinic of Gynecology and Obstetrics (UC OF G&OB) at the Clinical Center "Mother Teresa" – Skopje, concerning the hypertensive disorders during pregnancy, and to determine the main causes for its development, as well as the potential for their prevention.

Materials and Methods: The methodology used for the development of this specialist paper is primarily research-based and analytical. The analytical approach is based on data obtained from the Archives of the UC OF G&OB. The research approach included survey interviews designed for gynecologists, which were conducted with 4 gynecologists. The survey consisted of several open-ended questions.

Results: The research concluded that gestational hypertension the most often appears in, or after the 37th gestational week. Severe forms of hypertensive diseases during pregnancy include preeclampsia, eclampsia and HELLP syndrome. Preeclampsia occurs in 2-7% of the cases, and it is the most common disorder in women pregnant for the first time. Obesity is a definitive risk factor for preeclampsia, and the risk increases as the body mass index rises, especially in pregnant women who gained 1kg per week during the third trimester.

Conclusions: The doctor or nurse who refers to the patient should consult with the physician at the perinatal center regarding the referral and appropriate treatment. All data regarding the severity of the case, including prenatal information and a detailed medical record, should be sent along with the patient. Blood pressure should be stabilized, and convulsions should be controlled.

Keywords: *hypertension; pregnancy; gestational week.*

Introduction

Hypertension complicates approximately 7-10% of all pregnancies (1). It is much more common in the first-time mothers than in multiparas. The term hypertension in pregnancy is used to describe a broad spectrum of conditions, ranging from mild increases in blood pressure to severe forms of hypertension with various types of organ damage and dysfunction (2). The manifestations in these patients may be presented with similar clinical features, such as hypertension and proteinuria. However, they may stem from different causes, including chronic hypertension, kidney insufficiency or pure preeclampsia. The three most common forms of hypertension in pregnancy are acute gestational hypertension, preeclampsia and chronic essential hypertension (3).

Hypertension may preexist before pregnancy or may be diagnosed for the first time during pregnancy. Chronic hypertension is defined as hypertension that exists before pregnancy or is diagnosed for the first time before the 20th gestational week. Hypertension that persists 42 days after delivery is also classified as chronic hypertension.

Gestational hypertension is the most common cause of hypertension during pregnancy, with an incidence ranging from 6 to 17%, and it significantly increases in multiple pregnancies (4).

Preeclampsia accounts for about 70% of all cases of hypertensive complications during pregnancy.

Hypertensive complications during pregnancy represent a broad spectrum and can have either minimal consequences for the mother and fetus or pose life-threatening conditions for both. Mild or moderate preeclampsia that occurs toward the end of pregnancy carries a low risk of hypertension in the next pregnancy. Severe preeclampsia, which occurs in the early stages of pregnancy, around the 28th week of gestation, presents a high risk for the woman to develop serious hypertensive complications in the next pregnancy.

There are many terms and phrases used to describe hypertensive complications during pregnancy, to the point that specialists from different regions of the world may not fully understand each other during conversations. These differences complicate the interpretation of results from various studies. These disorders were once referred to as "toxemia of pregnancy" or "pregnancy toxemia," as it was believed to be caused by a circulating toxin. However, no such toxin has been discovered to date, so this term has been abandoned and lacks scientific foundation for its use. J. Roberts (1989, Book No. 20, p. 777) defines the term "pregnancy toxemia" as archaic, stating that it neither describes the disease nor clarifies its etiology and should reasonably be discarded (4).

The American College of Obstetricians and Gynecologists (ACOG) classifies hypertensive complications (HC) of pregnancy as follows (Table 1). (5)

Table 1. Hypertensive disorders of pregnancy.

• Chronic hypertension
• Gestational hypertension
• Preeclampsia/eclampsia
• Chronic hypertension with superimposed preeclampsia/eclampsia

The age of the pregnant women is the key factor of risk for development preeclampsia, the age under 15, is 2.5 times greater than in women aged 30-34 years. The risk also increases after the age of 35. A history of preeclampsia in a previous pregnancy significantly increases the risk of developing preeclampsia in the next pregnancy (odds ratio +10.8), i.e., it is 10 times more likely. Women with increased body weight (odds ratio +2.7), women who work during pregnancy, and women with a family history of hypertensive diseases are also at increased risk. When a woman has a spontaneous abortion, the chances of developing preeclampsia in the subsequent pregnancy decrease (6,7).

The second reason for high blood pressure during pregnancy is mostly caused by an unhealthy lifestyle and diet during pregnancy, particularly a diet high in salt, physical inactivity and many other factors. Untreated preeclampsia can lead to eclampsia, which is one of the most severe pregnancy disorders that can result in death for both the baby and the mother. The global mortality rate for eclampsia is 3% (8).

The diagnosis of eclampsia is confirmed when the following criteria are met - general edema, proteinuria, hypertension and convulsions. Hypertension is considered a hallmark in the diagnosis of eclampsia. It can be severe (systolic blood pressure of at least 160mmHg and diastolic blood pressure of at least 110mmHg), which occurs in 20 to 54% of cases, or mild (systolic blood pressure between 140 and 160mmHg, diastolic blood pressure between 90 and 110mmHg), which occurs in 30 to 60% of cases. Several clinical symptoms can help in the diagnosis of eclampsia, including persistent occipital and frontal headaches, blurred vision, photophobia, epigastric pain, or pain in the upper right quadrant, as well as altered mental status (9).

The motivation for this research and writing this specialist paper is primarily personal, arising from the still-high rate of pregnant women with preeclampsia, and more rarely with eclampsia and HELLP syndrome.

We have formulated a hypothesis: "The majority of preeclampsia cases are associated with hypertension, obesity and older pregnant women.".

Objectives of the Study

The aim of this retrospective study is to analyze the two years archives data of the University Clinic of Gynecology and Obstetrics (UC OF G&OB) at the Clinical Center "Mother Teresa" – Skopje, concerning the hypertensive disorders during pregnancy, and to determine the frequencies of the HC, main causes for development of HC, and to discuss the potential for their prevention.

Material and Method

This is a retrospective analytical study conducted at the University Clinic of Gynecology and Obstetrics at the Clinical Center – Skopje, where the archive materials for two-years period from 01.01.2022 to 31.12.2023 were studied. The study was a survey interview with gynecologists (involving 4 gynecologists). The survey consisted of several open-ended questions.

The obtained data will be presented in tabular and graphical form, followed by an analysis of the data to draw conclusions.

Results

The data presented in this specialist paper were obtained under archive number (04 – 1463/1 from 21.10.2024).

During this period, a total of 64 patients with developed preeclampsia were hospitalized at the Department of Gynecology and Obstetrics. The patients were from all over the country. All patients had hypertension >140/90 mm/Hg, some had proteinuria and facial edema.

A statistical analysis was conducted, covering 71 patients. Out of these patients, 48 were primigravids (first-time pregnancies), making up 68% of the total number of hospitalized patients; 3 were pregnant with multiple fetuses (4%), and 20 patients were in their second pregnancy (28%).

The distribution of the type of hypertensive complication is presented in Figure 1.

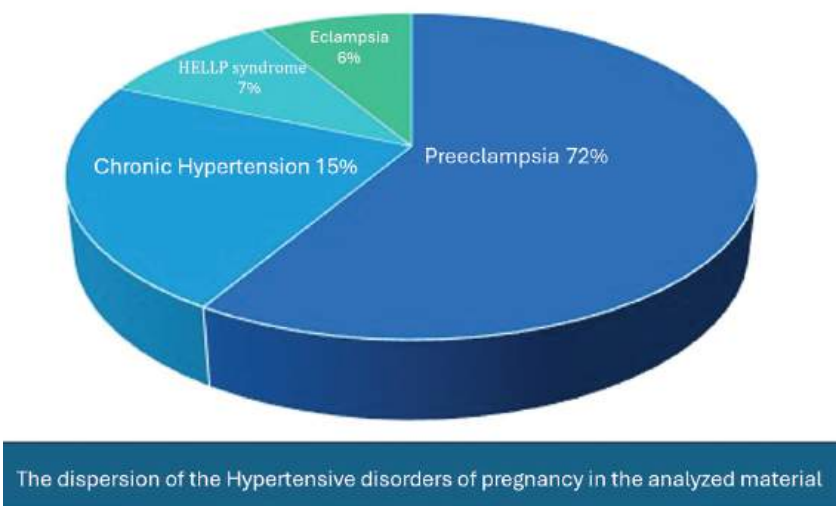

Figure 1. A graphical presentation of patients with preeclampsia who were hospitalized at University G&OB Clinic Skopje is provided (Figure 2).

Figure 2. Percentage of the pregnant women with preeclampsia in the gestation weeks.

The data were processed according to the age of the patients, the number of pregnancies, and a survey about how many of them had a family history of hypertension during pregnancy (Fig. 3).

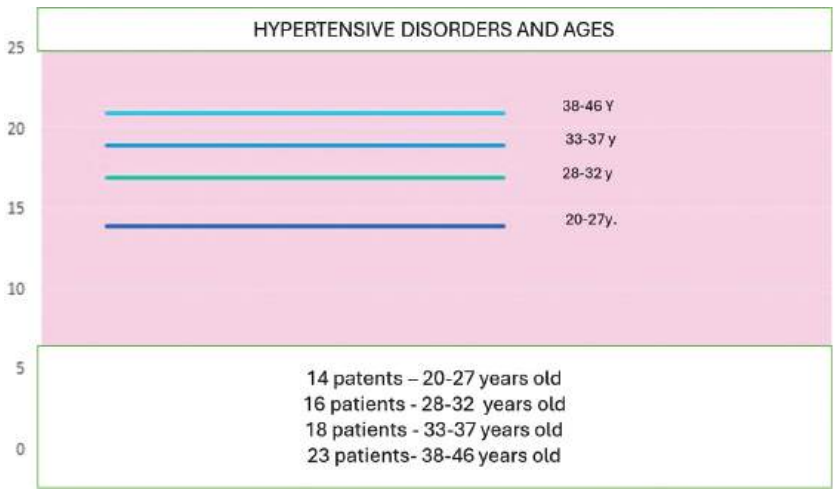

Figure 3. Hypertensive complications in analyzed materials.

Discussion

The treatment of such patients involves hospitalization for the remainder of the pregnancy due to the knowledge that hospital care reduces the possibility and frequency of progression to severe disease and allows for quick intervention in cases of sudden worsening, such as the development of abruptio placentae, eclampsia or hypertensive crises (10,11,12). However, these complications are becoming increasingly rare, as we live in a time when women's awareness of the importance of regular gynecological checks during pregnancy is rising. Therefore, even if there is some disturbance, it would be detected in time and treated accordingly. Moreover, results from studies on women with gestational hypertension, selected randomly, and several studies observing women with mild hypertension and mild preeclampsia, suggest that most of these women can be safely treated at home or in a day-care center, provided they undergo frequent checks of their condition and their fetus's condition (13,14,15,16). It must be noted that many of the women included in this study had only gestational hypertension before developing any serious condition. Continuous rest for the remainder of the pregnancy is often recommended for pregnant women with mild hypertension. However, no concrete evidence has been found that such a practice improves pregnancy outcomes. Furthermore, no published studies of randomly selected women compare continuous bed rest with physical activity limitation in treating mild preeclampsia. On the other hand, prolonged bed rest during the remainder of pregnancy increases the risk of thromboembolism.

The social and scientific justification for this thesis is based on the methodology used, which ensures that recommendations from specialists (gynecologists) for easier prevention and control of eclampsia during pregnancy are provided. The social and professional justification for this topic arises from the importance of raising awareness among pregnant women, especially those with previous risk factors for developing a pathological condition related to pregnancy, such as preeclampsia, eclampsia and HELLP syndrome. The goal is timely intervention and symptom recognition to minimize the incidence of these diseases and, in the worst cases, reduce mortality (17).

Conclusion

The hypertensive disorders during pregnancy still stays an actual topic in our country. The prevention of the hypertension and primary care of the pregnant women is the main moto to decrease the incidences of complications. The doctor or nurse who refers to the patient should consult with the physician at the perinatal center regarding the referral and appropriate treatment. All data regarding the severity of the case, including prenatal information and a detailed medical record, should be sent along with the patient. Blood pressure should be stabilized, and convulsions should be controlled.

Acknowledgements:
The author of this paper would like to thank Professor Dr. Biljana Eftimova for her help and guidance in the preparation of this paper.

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www.doi.org/10.55302/MJA2484160k

CHALLENGES WITH COVID-19 PATIENTS IN INTENSIVE CARE UNITS

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Abstract

Airway management in patients with COVID-19 presents significant challenges due to the highly infectious nature of the virus and the potential for respiratory failure in severe cases. Effective management strategies are essential, not only to optimize patients' outcomes, but also to protect healthcare providers. This article examines the clinical considerations, procedural adaptations and protective measures required for managing airways in COVID-19 patients, particularly in critical care settings. The collaborative role of the anesthesiologist and nurse practitioner is emphasized, as teamwork enhances efficiency and safety in these high-risk procedures. Nurse practitioners support anesthesiologists through rapid response, preparation of necessary equipment, and ensuring compliance with infection control protocols, allowing anesthesiologists to focus on complex airway interventions.

Techniques like early intubation, high-flow nasal cannula (HFNC) and non-invasive ventilation (NIV) are balanced with the risks of aerosol generation. Additionally, the use of personal protective equipment (PPE) and modified intubation techniques, such as video laryngoscopy, reduce exposure risk. Rapid sequence intubation (RSI) is preferred to limit aerosolization, while prone positioning and lung-protective ventilation strategies manage severe hypoxemia. This structured, team-based approach underscores the vital role of interdisciplinary collaboration in optimizing airway management for COVID-19 patients while safeguarding healthcare personnel.

The COVID-19 pandemic has fundamentally transformed airway management practices, emphasizing stricter infection control protocols and adaptations to reduce aerosol generation. Increased reliance on techniques like video laryngoscopy, rapid sequence intubation, and enhanced teamwork among healthcare providers has become essential to minimize exposure and ensure patients' safety in high-risk settings.

Keywords: *airway management; acute respiratory distress syndrome; Sars-CoV-2; covid19.*

Introduction

Securing and managing the airways in patients with COVID-19 posed significant challenge for the entire medical team. On one hand, this was due to the infectious nature of the virus and the severe respiratory complications often associated with the infection. On the other hand, the methods for securing and maintaining the airway had to be carefully considered to minimize the potential transmission of the infectious agent to healthcare workers and other hospitalized patients. Managing airway hygiene and oral cavity care was one of the challenges during the pandemic.

Nurses working in intensive care units possess specialized skills that separate them apart from other healthcare professionals, such as airway management, the use and maintenance of life support equipment including ventilators, and the use of high-flow oxygen therapy devices.

COVID-19, caused by the SARS-CoV-2 virus, primarily affects the respiratory system, which can be manifested in a range from mild upper respiratory infections to pneumonia, and can lead to the development of acute respiratory distress syndrome (ARDS) and respiratory failure. In severe cases, patients may require advanced airway management, including oxygen therapy, non-invasive ventilation (NIV) or intubation with mechanical ventilation. These interventions require careful planning and execution to ensure patients' safety and protect healthcare workers.

One of the main concerns when managing airways in COVID-19 patients is the high risk of aerosol generation, which increases the likelihood of virus transmission to healthcare workers. Procedures such as intubation, extubating, and bag-mask ventilation generate aerosols containing viral particles. This necessitates the use of personal protective equipment (PPE), such as N95 respirators, face shields, gowns and gloves during these high-risk interventions and airway manipulations. Additionally, reducing the number of personnel involved in the procedure and using rapid sequence induction (RSI) can help minimize exposure time and risk.

Regarding airway management techniques, pre-oxygenation, careful planning and skilled intubation are critical to avoid complications. Video laryngoscopy is often preferred over direct laryngoscopy due to the ability to intubate from a greater distance from the patient's airway. The use of mechanical ventilation strategies that align with lung-protective principles, including low tidal volumes and appropriate positive end-expiratory pressure (PEEP), is essential to prevent further lung damage.

Effective airway management in COVID-19 patients, not only provides optimal respiratory support, but also prioritizes infection control measures to protect healthcare workers, making it a key aspect of managing critically ill patients during the pandemic.

Materials and Methods

Oxygen therapy is a key aspect of the treatment of patients with COVID-19, especially those with moderate to severe hypoxia. For the purposes of this study, different types of oxygen therapy used in COVID-19 patients were reviewed to ensure proper oxygenation and to monitor blood oxygen levels.

Nasal Cannula

Materials: Sterile nasal cannulas are used, which are placed into the patient's nostrils. The cannulas are secured with elastic straps behind the ears and under the chin.

Method: The oxygen flow is adjusted to 1-6 liters per minute, depending on the patient's needs. Oxygen saturation (SpO2) is regularly monitored to ensure adequate oxygenation.

Simple Oxygen Face Mask

Materials: Simple face masks are used, covering the patient's nose and mouth. The masks are secured with elastic straps or ties behind the ears or around the head.

Method: The oxygen flow is adjusted to 5-10 liters per minute, and oxygen saturation is monitored to ensure sufficient oxygenation.

Non-Rebreather Mask (NRM)

Materials: The non-rebreather mask is used to deliver high concentrations of oxygen. It contains one-way valves that prevent re-inhalation of exhaled air. It has a reservoir bag that fills with oxygen before use.

Method: The oxygen flow is set to 10-15 liters per minute. This method is used for patients with moderate to severe hypoxia, and blood oxygen levels are regularly monitored.

In all cases, for each type of oxygen therapy, standard procedures are followed for equipment preparation, patient's assessment, and monitoring of the patient's response to the therapy. All patients are monitored for signs of discomfort, skin irritation or respiratory distress. Each treatment is documented in the patient's medical chart, noting the oxygen saturation level and any issues encountered during therapy.

Results

The results from the analysis of airway management and therapy for patients with COVID-19 highlight key aspects and challenges faced by nurses and healthcare workers in intensive care units. Key results include:

High Risk of Aerosolization and Virus Transmission: The generation of aerosols during procedures such as intubation, extubating and bag-mask ventilation, increases the risk of virus transmission to the medical team. These procedures require the use of appropriate personal protective equipment (PPE) such as N95 respirators, face shields, gloves and protective gowns to reduce the risk of infection.

Safe Intubation and Ventilation Techniques: Proper execution of pre-oxygenation and intubation, using video laryngoscopy, has proven to be an effective method for safer airway management, with a lower risk of complications in COVID-19 patients. The use of mechanical ventilation with low tidal volumes and appropriate positive end-expiratory pressure (PEEP) helps minimize lung damage.

Non-Invasive Respiratory Support (NIV): Non-invasive ventilation with CPAP and BiPAP was used as the initial respiratory support option for some COVID-19 patients. These methods help

reduce the need for invasive intubation and are effective in improving oxygenation. However, they require careful control and monitoring, as they may increase risks such as hypoxemia or inadvertent virus transmission.

Dangers of Severe COVID-19 Patients: Patients with severe COVID-19 often experience impaired breathing and significant lung damage. They require continuous intensive care with mechanical ventilators, while healthcare staff must be trained and prepared to perform complex interventions, such as extubating and the administration of respiratory stimulant medications.

Risk of Hypoxemia and Over-Deep Breathing: Excessive use of high oxygen levels can lead to hypoxemia and organ damage, particularly to the brain and heart. Monitoring oxygen levels and optimizing ventilation parameters is crucial in preventing these complications.

Protocols for Respiratory Support Management: Developing protocols that include clear guidelines for respiratory support and therapy in COVID-19 patients is essential for improving outcomes. Healthcare professionals must be continuously trained on new protocols while working as a team to ensure rapid and accurate diagnosis and treatment.

Need for Continuous Monitoring: Continuous monitoring of vital parameters, such as oxygen saturation, pulmonary function and arterial pressure, is key to preventing complications and detecting deteriorations early. Monitoring and the use of advanced technologies (such as invasive and non-invasive methods for respiratory function monitoring) can be particularly important for healthcare workers.

Overall, the results emphasize the need for thorough preparation and strict adherence to respiratory support protocols during the COVID-19 pandemic, as well as the importance of using innovations and modern methods in medical care to improve patients' outcomes.

Statistics

During the COVID-19 pandemic, data were collected from 160 tested patients in the COVID center of the Intensive Care Unit, all of whom required hospitalization, indicating a hospitalization rate of 100%. This means that all patients had sufficiently severe conditions that required urgent medical intervention. However, out of these 160 patients, 42 died, resulting in a mortality rate of 26.25%. This high mortality rate highlights the seriousness of the disease and the challenges faced by medical teams in treating critical cases.

Table 1. Patients in the COVID Center.

Tested	Hospitalized	Survived	Deceased
160 (100%)	160 (100%)	118 (73.75%)	42 (26.25%0

During hospitalization, 109 patients (68.12% of the total) required oxygen support, indicating that most of the patients faced moderate to severe respiratory distress that required additional oxygen. Oxygen therapy is often the first line of intervention for patients with respiratory failure, highlighting the seriousness of their condition. Of the 109 patients who required oxygen support, 58 patients (36.25%) progressed to the point where mechanical ventilation was neces-

sary, indicating the severity of their respiratory weakness.

Table 2. Types of Support in the COVID Center.

Hospitalized	Oxygen Support	Ventilator Support
160 (100%)	109 (68.12%)	58 (36.25%)

Respiratory Support:

Non-invasive Mechanical Ventilation (NIV): 52 patients were treated with non-invasive mechanical ventilation (NIV), out of which 42 patients survived, and 10 died. NIV was most used as the first line of therapy for patients with respiratory weakness, as it helps avoid complications that can arise from invasive ventilation, such as infections or airway injuries.

Mechanical Ventilation (MV): 18 patients required mechanical ventilation (MV), indicating the severity of their condition. Only two of these patients survived, while 16 died. This difference in outcomes emphasizes the severity and risks associated with mechanical ventilation.

Table 3. Outcome of Respiratory Support:

Type of Ventilation n/%	Deceased	Survived
NIV (Non-invasive Mechanical Ventilation) 52 (100%)	10 (19.23%)	42| (80.76%)
MV (Mechanical Ventilation) 18 (100%)	16 (88.8%)	2 (11.11%)

The data from the COVID Center show a high percentage of hospitalization and mortality among patients with COVID-19, highlighting the severity of the disease and the need for intensive respiratory support. However, non-invasive mechanical ventilation (NIV) demonstrated significant effectiveness in treating patients with respiratory weakness, while mechanical ventilation (MV) carries greater risk and a higher mortality rate. These statistics emphasize the importance of early detection and treatment of respiratory issues, as well as the need for continued efforts to optimize respiratory interventions.

Conclusion

The COVID-19 pandemic significantly impacted airway management in healthcare settings, primarily due to the risk of virus transmission through aerosol-generating procedures. Healthcare workers implemented enhanced protective measures, such as wearing full personal protective equipment (PPE), including N95 masks, face shields, and gowns, particularly during intubation and extubating.

Airway management protocols shifted towards methods that minimize aerosol spread. For example, non-invasive ventilation methods like CPAP and HFNC were used cautiously, often in negative pressure rooms, when possible, to reduce exposure. Additionally, intubation became a priority over manual ventilation whenever feasible, and rapid sequential intubation (RSI) became more common to limit the duration of close contact with patients. Video laryngoscopy

also gained importance as it allowed maintaining a greater distance during intubation.

These changes improved healthcare worker safety but added complexity and required more resources in airway management practices.

Acknowledgments

The author would like to express gratitude to Prof. D-r Maja Mojosova-Mijovska for her selfless assistance and support in the development of this research and paper.

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www.doi.org/10.55302/MJA2484166v

CRITICAL CARE CHALLENGES IN MANAGING POLYTRAUMA: INSIGHTS FROM INTENSIVE CARE UNIT ADMISSIONS

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Abstract

Background: When a patient experiences more than two serious injuries that endanger their life or the function of essential organs, it is known as polytrauma. To lower the danger of death or long-term sequelae, this complicated medical issue necessitates immediate interdisciplinary treatment. Rapid evaluation of vital functions, patient's stabilization, and provision of the required diagnostics for additional intervention, form the cornerstone of treatment.

Aim: The study aims to analyze the processes involved in caring for patients with polytrauma, from initial assessment and stabilization to secondary resuscitation, treatment and rehabilitation. It emphasizes the importance of an organized medical approach in reducing mortality, morbidity and disability among these patients.

Materials and methods: The study is a retrospective analysis of the total number of patients with polytrauma admitted and treated at University Clinic for Traumatology, Orthopedics, Anesthesia, Reanimation, Intensive Care and Emergency Center (UCTOARICEC), Clinical Center "Mother Theresa" at the Intensive Care Unit in Skopje. We included patients aged between 2 and 96 years, spanning a three-year period (2021–2023). We collected and processed data from patients' admission records, age, gender, place of residence, diagnosis and outcomes, using documentation and statistics maintained at Clinic for Anesthesia, Reanimation, Intensive Care. We processed and analyzed the data using appropriate statistical methods, which included measures of central tendency, such as mean, median, and mode.

Results: According to the research conducted over the past three years, most of the polytraumatized patients were male, with the highest number of such patients admitted in 2021. We presented statistical analysis and data collection in tables and graphs, based on gender, place of residence, type and origin of injury and age.

Conclusion: Over the past few decades, there has been a significant increase in the number of polytrauma cases and multiple injuries. Today, polytrauma ranks third after malignancies and heart diseases. Modern approaches to treating polytrauma greatly benefit from algorithms, which help achieve better outcomes by minimizing omissions and errors and elevating the quality of healthcare to the highest level.

KeyWords: *management; multiple injured patients; polytrauma.*

Introduction

Traumatic injury is a preventable disease that has existed since the beginning of civilization. Humans have never been immune to injuries. There is substantial evidence showing that even the most primitive ancestors of modern humans were familiar with many fracture treatment techniques (1). About 150 years ago, primary amputation was the treatment for open fractures, which were synonymous with death due to hemorrhage or sepsis. The mortality rate for open fractures remained high (>50%) even in the 19thcentury, despite conditions that were considered ideal at the time. The prognosis of patients with fractures significantly improved with advances in understanding of bacterial contamination and infection transmission, thanks to Pasteur, Koch, Lister and Semmelweis. Additionally, the use of the Thomas splint with fixed traction prior to hospital transportation and proper wound management, as advocated by Pare and Larrey (surgeon of Napoleon), significantly improved patients' outcomes. Greek medicine was the first to use the term "trauma". Hippocrates and the medical schools of that time developed a symptomatic approach to trauma. An external force can inflict an injury on the human body, ranging in intensity from minor to severe, as defined by the medical term trauma. Over time, the causes of trauma have changed, but its importance and impact on individuals and society remain significant (2).

Trauma occurs suddenly and without warning, most often affecting the young and productive population. The three most common mechanisms of major trauma are motor vehicle accidents, firearms and falls. Trauma is a leading cause of mortality and disability worldwide, representing a significant public health issue. Trauma mortality has a trimodal distribution: immediate death, early death and late death (3). Immediate deaths occur due to massive injuries like ruptured organs, while early deaths often result from conditions such as hemorrhagic shock. Late deaths, often from sepsis or multiple organ failure, can happen days or weeks after the injury. The "classic" trimodal distribution is associated with blunt trauma, while a bimodal distribution (early or immediate deaths) is characteristic of penetrating injuries (4).

More than half of all traffic-related deaths occur among vulnerable road users: pedestrians, cyclists and motorcyclists. Injuries sustained in traffic accidents are among the most severe, with high mortality rates on the site or later due to the injuries. However, 50% of fatalities occur at the site of the accident or within minutes. This is known as immediate death (immediate killing trauma), caused by factors such as rupture of the heart, aorta or major blood vessels, brain stem laceration, or severe cerebral hemorrhage. Of polytraumas, 30% can be classified as early deaths, occurring within hours due to tension pneumothorax, hemorrhagic shock, rupture of the liver or spleen, hypoxemia, compromised airways or brain injuries. During this period, surgical interventions are lifesaving, referred to as "damage control" in the "golden hour." Effective resuscitation is crucial for the outcome. Out of all polytraumas, 20% can be classified as late death, occurring in the following days or weeks due to sepsis, respiratory issues, heart failure or acute multiple organ failure (MOF) (5,6).

The mechanisms of injury are classified into blunt, penetrating and thermal injuries. The severity of penetrating trauma is directly linked to the kinetic energy of the projectile at impact and the elasticity of the injured tissue. Projectiles cause a primary cavity due to crushing injury and a

temporary cavity resulting from the blast effect on surrounding tissues. Blunt injuries distribute energy across a larger area compared to typical penetrating injuries, often resulting in multiple simultaneous injuries across different body parts. These injuries are more complex and challenging to treat. Thermal or inhalation injuries account for over 75,000 cases requiring hospital care annually, with a morbidity rate of 10% (7).

Patients with severe burns may initially appear stable upon admission, but within 24 hours can become critically endangered due to respiratory and circulatory failure. Treatment depends on the severity of the burns and the extent of inhalation injury (8).

The principles of care for patients with multiple traumas include simultaneous assessment and resuscitation, a thorough physical examination, diagnostic evaluations, and clear prioritization of life-saving surgical interventions. A well-organized trauma service can significantly reduce trauma-related mortality and morbidity by integrating pre-hospital care systems with trauma centers for definitive patient's treatment (9).

Polytrauma is a medical term describing the condition of a person who has suffered multiple traumatic injuries affecting different parts of the body and organ systems. It is defined by the severity, location of injuries and the patient's physiological parameters. Polytrauma typically involves at least two body systems, where one injury is life-threatening, such as damage to two body cavities alongside fractures of long bones.

According to classification in practical medicine, polytrauma is generally divided into three degrees:

- Grade I – Relatively mild injury without traumatic or hemorrhagic shock (with timely treatment, the outcome is favorable).
- Grade II – Moderate injuries with the development of traumatic shock (requiring long-term rehabilitation focused on stabilizing negative outcomes).
- Grade III – Fatal, extremely severe injuries leading to irreversible and rapid changes in life-supporting systems, with the possibility of saving life measured in minutes.

Clinical manifestations depend on the location, severity and systemic response to the traumatic factor (1).

The aim of our evaluation was to analyze and evaluate the critical care challenges associated with managing polytrauma patients in the intensive care unit (ICU), focusing on early assessment, stabilization, secondary resuscitation and rehabilitation to reduce mortality, morbidity and long-term disability rates.

Material and Methods

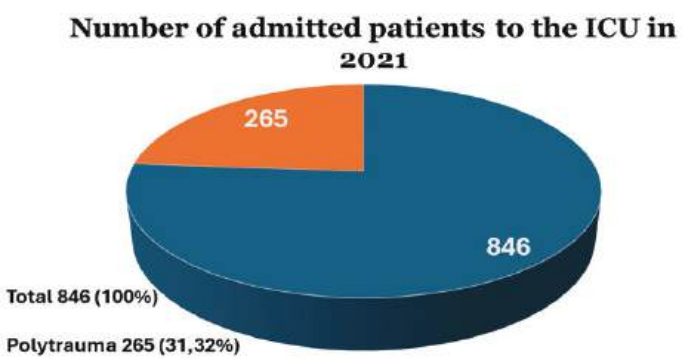
The study is a retrospective analysis of polytrauma patients admitted and treated at the University Clinic for Traumatology, Orthopedics, Anesthesia and Intensive Care and Emergency Center, Clinical Center "Mother Theresa", at "Ss. Cyril and Methodius" University, Skopje, Republic of North Macedonia, in the Intensive Care Unit (ICU). The analysis spans a three-year period (2021–2023) and includes patients with injuries caused by unknown trauma, traffic accidents, gunshot wounds and sharp objects.

Inclusion Criteria: patients aged between 2 and 96 years, patients admitted to the Intensive Care Unit with documented polytrauma and patients with complete patients' admission records with demographic data (age, gender, place of residence), diagnosis and outcomes.

The data were collected from the patient admission records and analyzed using documentation and statistics maintained at the Clinic for Anesthesia, Reanimation and Intensive Care. The data processing involved appropriate statistical methods, including measures of central tendency such as mean, median and mode.

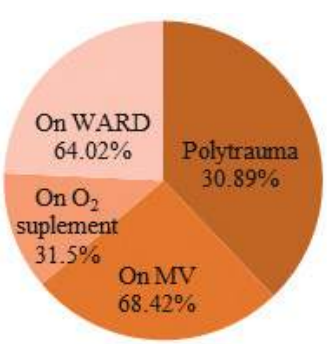
Results

In 2021, the ICU of UCTOARICEC, Skopje, 846 patients were admitted during the study period, out of which 265 (31.32%) were polytrauma cases from unknown causes, traffic accidents, gunshot wounds and sharp object injuries (Graphic 1). Out of these, 151 (56.98%) required mechanical ventilation, while 114 (43.02%) were placed on oxygen masks. A total of 173 (65.28%) patients were discharged, 79 (29.81%) died, and 13 (4.91%) were transferred to other cities or countries. Among the deceased, 27 (34.18%) were victims of traffic accidents (Table 1).



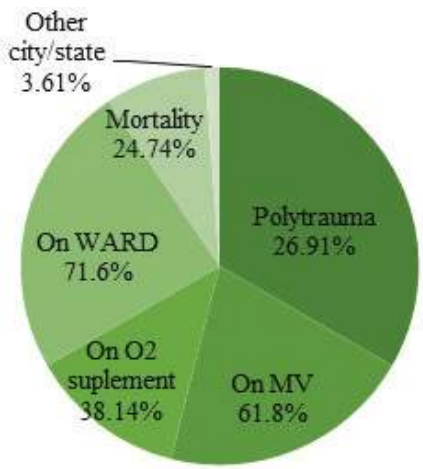
Graphic 1. Graphical presentation of patients admitted to ICU in 2021.

Out of the 738 patients hospitalized to the intensive care unit in 2022, 228 (30.89%) had polytrauma. Out of these, 72 (31.58%) were on oxygen masks, and 156 (68.42%) were on mechanical ventilation. Thirteen (5.70%) patients were sent to different cities or countries, 69 (30.26%) patients died, and 146 (64.04%) patients were discharged. 24 (34.78%) of the dead were involved in road accidents.



Graphic 2. Graphical representation of patients admitted to ICU in 2022.

Out of the 721 patients hospitalized to the ICU in 2023, 194 (26.91%) had polytrauma. 120 (61.86%) of these were on mechanical ventilation, while 74 (38.14%) were using oxygen masks. Out of the patients, 139 (71.65%) were sent home, 48 (24.74%) passed away, and 7 (3.61%) were moved to another city or country. Twenty of the dead (41.67%) were involved in automobile accidents.



Graphic 3. Graphical representation of patients admitted to ICU in 2023.

ICU admissions declined over the three years (846 in 2021, 738 in 2022, 721 in 2023), reflecting either improved prevention or reduced trauma incidence. Polytrauma cases showed a downward trend (31.32% in 2021, 30.89% in 2022, and 26.91% in 2023). The percentage of polytrauma patients requiring mechanical ventilation increased slightly in 2022 (68.42%) compared to 2021 (56.98%) but decreased to 61.86% in 2023. Conversely, the use of oxygen masks decreased slightly over the three years, suggesting either a shift in treatment practices or case severity trends. Discharge rates improved significantly in 2023 (71.65%) compared to 2021 (65.28%) and 2022 (64.04%). Mortality rates declined notably from 29.81% in 2021 to 24.74% in 2023. Among deceased patients, the percentage of deaths due to traffic accidents fluctuated: 34.18% in 2021, 34.78% in 2022, 41.67% in 2023.

Table 1. Summarized a three-year comparison of ICU admissions.

Year	Total ICU Admissions	Polytrauma Cases	Mechanical Ventilation	Oxygen Mask	Discharged	Mortality	Transfers
2021	846	265 (31.32%)	151 (56.98%)	114 (43.02%)	173 (65.28%)	79 (29.81%)	13 (4.91%)
2022	738	228 (30.89%)	156 (68.42%)	72 (31.58%)	146 (64.04%)	69 (30.26%)	13 (5.70%)
2023	721	194 (26.91%)	120 (61.86%)	74 (38.14%)	139 (71.65%)	48 (24.74%)	7 (3.61%)

Discussion

This retrospective study analyzed polytrauma patients admitted to the ICU at UCTOARICEC, Clinical Center "Mother Teresa," Skopje, from 2021 to 2023. A total of 265 (31.32%) polytrauma

patients were admitted in 2021, 228 (30.89%) in 2022, and 194 (26.91%) in 2023, representing a significant portion of the ICU admissions during these years. These patients primarily sustained injuries resulting from traffic accidents, firearm injuries and sharp object injuries, with a smaller percentage having undetermined or unknown mechanisms of injury. This reflects the varied nature of polytrauma cases in our region and the diverse etiologies contributing to the burden of severe injuries.

The demographic breakdown revealed that most of the polytrauma patients were male (62%), consistent with global trends that show a higher incidence of trauma in males. The most affected age groups were individuals over 60 years and young adults aged 20-40 years, both of whom are at higher risk for severe injury due to factors such as reduced physical resilience in the elderly and risky behavior in younger adults (11,12). Notably, many patients were from regions outside the capital, Skopje, suggesting potential disparities in trauma care access and transport time, particularly for patients residing in rural areas. This highlights the need for strengthening pre-hospital and regional trauma care systems to reduce delays in care for patients in more distant locations (13).

Regarding clinical outcomes, mechanical ventilation was required for 151 (56.98%) patients in 2021, 156 (68.42%) in 2022, and 120 (61.86%) in 2023. The increased reliance on mechanical ventilation over the years reflects the growing severity and complexity of the polytrauma cases admitted to the ICU, underscoring the crucial role of advanced respiratory support in trauma management. The use of oxygen masks also remained significant, with 114 (43.02%) patients in 2021, 72 (31.58%) in 2022, and 74 (38.14%) in 2023 requiring supplemental oxygen. This highlights the varied clinical presentation and the necessity for tailored respiratory interventions depending on the patient's condition (14,15).

Mortality rates in our study were notably high, with 79 (29.81%) deaths in 2021, 69 (30.26%) in 2022, and 48 (24.74%) in 2023. These figures are in line with global trauma mortality rates, though the proportion of trauma-related fatalities remained a significant concern [6]. Traffic accidents were the leading cause of death, accounting for 34.18% of the deaths in 2021, 34.78% in 2022, and 41.67% in 2023. This trend mirrors the broader global context where road traffic injuries remain the leading cause of trauma-related death, particularly in low- and middle-income countries (LMICs) like Republic of North Macedonia. In 2023, Republic of North Macedonia reported 127 fatalities due to traffic accidents, marking a 2.41% increase from the previous year. This reinforces the critical need for public health interventions aimed at improving road safety and reducing the burden of road traffic accidents. The findings align with broader regional and global trends in trauma care. Worldwide, approximately 1.35 million people die annually due to road traffic accidents, with Europe accounting for over 20,000 fatalities each year. In some countries, like Germany and Sweden, road safety measures have led to significantly lower fatalities, with Germany reporting 34 deaths per million people and Sweden - 22 per million. However, in Southern and Eastern Europe, including Republic of North Macedonia, the rates are higher, indicating a persistent gap in road safety compared to Western and Northern Europe. These disparities underscore the need for urgent interventions to improve road infrastructure and safety standards across the region (9,10,16).

Furthermore, raising public awareness regarding the dangers of alcohol consumption, distracted driving (e.g., mobile phone use), and speeding is crucial for improving road safety. Education campaigns targeting young drivers, stricter enforcement of traffic laws, and the implementation of advanced vehicle technologies such as collision avoidance systems can significantly reduce

the risk of accidents (17).

The high incidence of polytrauma in our study highlights the need for continuous improvements in trauma care systems, from pre-hospital care through rehabilitation. Polytrauma patients often are presented with complex, multi-system injuries that require multidisciplinary management, including surgery, intensive monitoring and respiratory support. The role of ICU staff in managing these cases is critical, and ongoing training for healthcare professionals is essential to maintaining high standards of care. Furthermore, the development of robust rehabilitation systems is vital for improving long-term outcomes for trauma survivors (18-21).

Beyond the direct medical costs, non-fatal injuries impose a substantial economic burden on society due to lost productivity, long-term care needs and rehabilitation expenses. Developing more efficient trauma systems, improving patients' outcomes through early intervention and investing in long-term rehabilitation services are crucial steps toward reducing both the human and economic costs of trauma (22,23).

Trauma management, particularly for polytrauma patients, requires a well-coordinated and multidisciplinary approach to effectively address the various aspects of patients' care. A timely and accurate assessment, using tools such as the Rapid Trauma Assessment (RTA) or the Advanced Trauma Life Support (ATLS) guidelines, is crucial for identifying life-threatening injuries and stabilizing patients. Prompt intervention in pre-hospital setting and timely transport to specialized trauma centers have been shown to reduce mortality rates in polytrauma patients (20-23).

Once in the hospital, trauma care should follow established protocols to address airway management, hemorrhage control and prevention of shock, with close monitoring for signs of organ failure or complications such as infections. The use of modern technology, such as point-of-care ultrasound (POCUS) and CT imaging, helps in the rapid assessment and decision-making process, ensuring patients receive the most appropriate treatment quickly (24). In the ICU setting, adequate respiratory support and fluid management are critical components of trauma care, particularly in polytrauma cases that require mechanical ventilation and intensive monitoring (20).

Moreover, improving rehabilitation and long-term trauma care is essential to reducing the long-term disability burden. Early rehabilitation, multidisciplinary care, and addressing both the physical and psychological aspects of recovery can significantly enhance outcomes for patients, reduce the societal burden and improve quality of life post-trauma (25).

Conclusion

In conclusion, the findings of this study highlight the urgent need for a comprehensive, multi-sectoral approach to trauma care in the Republic of North Macedonia. Addressing the challenges of trauma care requires systemic improvements, including the development of infrastructure, better training for healthcare professionals, and enhanced public awareness on road safety and safe driving practices. These efforts should be coupled with strengthening healthcare systems to manage the growing burden of polytrauma. Strengthening trauma care protocols, from pre-hospital to rehabilitation, is essential for managing polytrauma cases effectively and ensuring that patients receive the necessary intensive care. Furthermore, addressing road safety, increasing public education will be crucial steps in reducing traffic-related injuries. The combined efforts of healthcare systems, governmental bodies, and society as a whole can lead to bet-

ter survival rates and improved recovery for polytrauma patients, making a substantial impact on public health.

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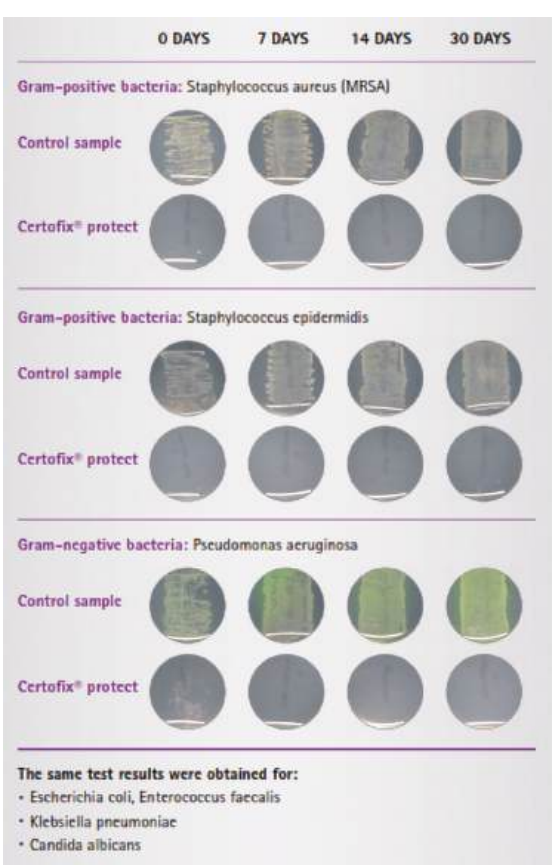

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