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RESEARCH ARTICLE

CAN AN M-HEALTH APPLICATION IMPROVE THE BLOOD PRESSURE CONTROL IN NEWLY DIAGNOSED PATIENTS WITH ARTERIAL HYPERTENSION?

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Abstract

Introduction. Hypertension is a leading cause of overall morbidity and mortality worldwide. The use of telemonitoring opens new opportunities for close monitoring of patients with hypertension through self-monitoring of blood pressure at home and timely transfer of these to primary care physicians.

Objective. To assess the effect of using an mHealth application in improving blood pressure control in patients with newly diagnosed hypertension.

Methods and materials. Results from the first 6 months of a prospective randomized controlled multicenter trial with 12-months follow-up of newly diagnosed patients with hypertension. The intervention group received standard care + mHealth app, while the control group received standard care alone. The study monitored ambulatory blood pressure measurements at 0, 1, 3, 6 and 12 months.

Results. 95 participants in the intervention group and 97 in control group were recruited. In terms of systolic blood pressure values after 6 months, a decrease in the average systolic blood pressure was observed in both groups, with a decrease in the average by 22mmHg in the intervention, i.e. 20mmHg in the control group with a difference of 2mmHg in favor of the intervention group. A reduction in the average diastolic bood pressure of 13.4mmHg occurred in the intervention, i.e. 12.75mmHg in the standard care group, with a difference of 0.65mmHg in favor of the intervention group.

Conclusion. An mHealth application that enables two-way patient-physician communication is an auxiliary tool to standard care that may improve blood pressure control in newly diagnosed patients with hypertension.

Key Words: *Family doctor; hypertension; mHealth application; self-monitoring.*

Introduction

Hypertension (HTN) is a global public health problem and a leading cause of overall morbidity and mortality worldwide (1,2). In 2023, 1.28 billion of the world's population were diagnosed with HTN (1,2). and the prevalence is expected to reach 1.56 billion diagnosed patients in 2025 (3,4). According to the WHO report (5), in the Republic of North Macedonia (RNM) in 2019, the prevalence of diagnosed patients with HTN was 45%, of which 49% were male patients and 51% were female (6). Oot of these, 52% were patients prescribed with antihypertensive therapy, but only 23% of them managed to achieve good BP control (7).

Untimely diagnosed, untreated and/ or poorly managed hypertension is a direct cause of cardiovascular diseases (cerebrovascular stroke, myocardial infarction, heart failure, blindness, sexual dysfunction and chronic renal failure) (8). High blood pressure (BP) has a negative impact on the microcirculation and macrocirculation in organs with low resistance, such as the brain, kidneys, heart, eyes and blood vessels, which undergo corresponding anatomical and functional changes. Levingston et al., in a prospective study, showed that for every 20mmHg increase in ambulatory measured systolic blood pressure (SBP) or 10mmHg increase in diastolic blood pressure (DBP), the risk of fatal coronary arterial disease or stroke doubles (9). Reducing BP can significantly reduce overall premature morbidity and mortality (10). In a randomized study of intensive versus standard BP control (SPRINT study), it was shown that intensive BP control to target values for SBP<120mmHg compared to the standard target of SBP <140mmHg reduces the risk of cardiovascular diseases (CVD) by 25%, all-cause mortality by 27% and acute decompensation of heart failure by 36% (11,12). In contrast, Sobieraj et al., in a post-hoc analysis of the research data, showed that achieving low values for DBP had no significant effects on reducing CV risk (13). In the latest recommendations of the European Society of Cardiology (ESC) from 2024, the target values for blood pressure in patients with HTN are 120-129 for SBP and 70-79mmHg for DBP or, if this is not possible, the lowest value that can be reasonably achieved and is tolerable for the patient (14). According to these recommendations, the general practitioner/ family doctor, when diagnosing and also when managing patients with hypertension, needs to make an individualized plan for managing hypertension, which would lead to faster achievement of target values for BP and reduction of CVD risk. Proactive management of HTA also includes structured control examinations aimed at, through a holistic approach, the values obtained from the measured BP and appropriate investigations to promptly intensify therapy and achieve targeted treatment goals in a timely manner. Home BP monitoring for hypertension management is recommended as an intervention to achieve better BP control (Class 1, Level of Evidence B, ESC, 2024) (14). There are over 50 trials of different interventions based on self-monitoring (15). Self-monitoring of BP is associated with lower mean SBP at 12 months [-3.2 mmHg; 95% confidence interval (CI) -4.9 to -1.6 mmHg] (16).

In the past few years, there has been an increase in the use of mobile health (mHealth) applications within mobile technology, in the diagnosis and monitoring of many chronic non-communicable diseases (17,18) including hypertension (19). However, mHealth applications cannot provide independent monitoring of patients with HTN, i.e. they should be used as an auxiliary tool to standard care, regulated by the guidelines for managing HTN (20).
Purpose of this paper is to evaluate the effectiveness of an mHealth application in improving blood pressure control in patients with newly diagnosed hypertension.

Method and Materials

The study was designed as a prospective randomized controlled multicenter study with 12-months follow-up of newly diagnosed patients with HTN (2023/2024), followed by 19 family physicians on the territory of the RNM. This paper presents the initial results of a analysis of the BP control in the first 6 months from the beginning of the study.

The sample of family physicians was determined by fulfilling the following criteria. Inclusion criteria: ≥500 family patients aged 35-70 years, possessing ≥1 computer (with at least Windows 7), stable internet connection, desire and signed consent to participate in the study. Exclusion criteria: doctors who are mutual substitution in patients' care according to an agreement with the Health Insurance Fund of RNM (HIFRNM), (because a patient in RNM can receive healthcare from their primary care physician and their official replacement in the HIFRNM, and very often the doctors who are replacing each other work in the same clinic. For this reason, the doctors who are replacing each other cannot enter the study together, because it is impossible to follow the protocol, and it also challenges the protection of personal data), lack of readiness and desire to participate in the study. Since this was a multicenter study at the level of the entire territory, in order to achieve equal representation of patients, we invited 2 family doctors from each region (a total of 8 regions), with the exception of the city of Skopje, where we invited 6 family doctors. As a model for determining the number of doctors, we used the official division by statistical regions from the State Statistical Office of RNM (21).
Participants were required to meet the following criteria - Inclusion criteria: newly diagnosed patients with HTN (ambulatory measured SBP ≥140mmHg and/or DBP ≥90mmHg) age 35-70 years, possession of a smartphone, having a standardized semi-automatic or automatic sphygmomanometer, willingness and desire to participate in the study. Exclusion criteria: comorbidities (heart failure, chronic renal failure, hepatic failure, malignant diseases, secondary hypertension), pregnancy, cognitive diseases or problems with understanding instructions and patients who would not sign an informed consent.
For the included family physicians for each region, a 1:1 randomization was performed, through simple random selection, i.e., physicians who lead an intervention (IG) or control group (CG) from each region were included. Patients who met the criteria belonged to the IG, i.e. CG, according to the distribution by group of the family doctor who assigned the patient. Patients in

the IG received standard care & mHealth application, while those in the CG received standard care only. The blood pressure was measured with clinically validated upper arm blood pressure monitor - Omron M2, for the participants in the both groups at baseline, 1, 3, 6 and 12 months after inclusion in the study. The patients were informed of the entire protocol upon entry into the study by their primary care physicians and signed an informed consent. Upon entry into the study, the participants from both groups were educated by their physicians about: technique for correct blood pressure measurement with an upper arm sphygmomanometer and planned examinations as part of standard care. Additionally, the participants from IG were educated about self-monitoring of BP at home and entering BP and pulse values into the mHealth application and using SMS messages within the application itself.
The target values for good blood pressure control in the patients with hypertension were <130mmHg for SBP and <80mmHg for DBP, according to the latest recommendations of ESC, 2024 (14).

Intervention Description

The mHealth application was created with the support of the software company "Angor AG" Struga, RNM and consisted of 2 parts: a mobile application for patients and a program with a database for family doctors involved in the study.

The mobile application consisted of 3 parts: a part where the patient entered the measured values for BP and pulse, a part intended for two-way exchange of messages between the doctor and the patient in 2 forms: an info message, a message with an attached document and an informational part for the patient with access to a video link for the technique of correct BP measurement with a document for a hygiene-dietary regimen and appropriate physical activity. The mobile application was installed on the mobile smartphone of the patient included in the intervention group and it was activated by the family doctor with the patient's mobile phone number.

The program with the database for doctors consisted of 3 parts: a part with patients' data, a part for monitoring the measured values for BP and pulse that the patient entered in his application, and a part intended for two-way exchange of SMS messages between the doctor and the patient in 3 forms: info message, message with attached document and message with warning (for high BP, change of therapy or calling the patient to the outpatient clinic). Entry into the program was possible only with a special code and password provided for each doctor in order to protect patients' data. Participants from the intervention group on day zero received education on downloading and activating the application on the patients' mobile phone and training on its use for entering measured BP values at home. Patients also received a short leaflet on the frequency of entering measured BP values.

Statistical Analysis

The data obtained with the research were processed in the SPSS software package, version 26.0 for Windows. The analysis of the qualitative series was done by determining the coefficient of relationships, proportions and rates, and they were displayed as absolute and relative numbers. The numerical (quantitative) series were analyzed with the measures of central tendency (average, median, minimum values, maximum values, ranks), as well as measures of dispersion (standard deviation and standard error). Pearson Chi square test, Post Hoc Test, Wilcoxon Signed Ranks Test, Fischer exact test and Fisher Feeman Halton exact test were used to determine the association between certain attributive dichotomous traits. Difference test was used to compare proportions.

Results

According to the inclusion and exclusion criteria, the study included a total of 192 (100%) patients with HTN who were divided into intervention (n=95) and control group (n=97) using a simple random selection method. The recruitment period lasted approximately 9 months (February/ September 2023). The patients in the IG group received standard care + mHealth application, while those in the CG group received only standard care. The study assessed the effect of using the mHealth application in achieving targeted BP values. After 6 months of follow-up, 92 participants from the IG (2 patients from the Skopje region and 1 patient from the Polog region voluntarily left the study) and 96 participants (1 patient from the Polog region voluntarily left the study) from the CG remained included in the study and continued with follow-up until the completion of the entire 12-month protocol.

Regarding the gender distribution of 95 (100%) patients from the IG, it indicated the presence of 46 (48.42%) men and 49 (51.58%) women. In the CG out of a total of 97 (100%) patients, the presence of males and females was consistently 51 (52.58%) vs. 46 (47.42%). No significant association was found between the gender of the patients included in the study and the group to which they belonged (Pearson Chi-square test=0.332; df=1; p=0.5647). The mean age of the IG patients was 49.53±8.90 [95% CI (47.71–51.34)] years with an age range of 35/ 70 years. The CG patients had a mean age of 48.43±7.30 [95% CI 46.96–49.90)] years with an age range of 35/ 66 years. There was no significant difference between patients from the two groups (IG/KG) in terms of age (Mann-Whitney U Test: Z=(-0.619; p=0.5356). The proportion of participants from urban or rural areas in the entire research sample was consistently 126 (65.63%) vs 66 (34.38%). In both the IG and the CG, the majority of patients lived in urban areas, consistently 56 (58.95%) vs 70 (72.16%). 39 (41.05%) of the patients in the IG and 27 (27.84%) of those in the CG lived in rural areas. There was no significant association between the place of residence (village/ city) and the group to which the patients belonged for the Pearson Chi-square test: X2=3.717; df=1; p=0.0539.

In both groups of patients, IG and CG, an analysis was performed regarding the values of SBP and DBP (mmHg) at 4 follow-up times: zero time, 1, 3 and 6 months after the intervention.

The analysis of the distribution of the values obtained for SBP expressed in mmHg at each of the 4 follow-up times (zero, 1, 3 and 6 months after the intervention) indicated an irregular distribution of frequencies for: a) 0 time - Shapiro-Wilk W=0.8134; p=0.00001; b) 1 month - Shapiro-Wilk W=0.8832; p=0.00001; c) 3 months - Shapiro-Wilk W=0.9603; p=0.0057 and 6 months - Shapiro-Wilk W=0.9439; p=0.00062. According to the obtained distribution for SBP, appropriate tests were applied in the analysis. The values obtained for SBP were compared at each of the 4 measurement times, both intragroup and intergroup in IG and CG. Intragroup comparisons were made for SBP values in each of the two groups individually for the 4 follow-up times. In both groups, IG and CG, a significant decrease (Friedman Test: Chi-Square) in SBP was observed between the 4 follow-up times, with the highest value at time zero before the intervention and the lowest average value at 6 months after entering the study.

Table 1. Intragroup comparison of systolic blood pressure at four times.

Intragroup Analysis	**SBP (mmHg)**					**p**
	Number (N)	**Mean± SD**	**(Min/Max)**	**Median (IQR)**	**Mean Rank**	
Intervention group - IG						
"0" time	95	151±12.27	130/ 200	148 (144-157)	4.95	Chi-Square (92)=212.89; df=4; p=0,0001*
1 month	95	133±12.99	112/ 190	130 (125-140)	3.05	
3 months	95	129±9.49	110/ 160	130 (122-135)	2.47	
6 months	92	129±9.18	110/ 160	130 (120-137)	2.59	
Control group-CG						
"0" time	97	152±11.32	128/ 193	150 (145-160)	4.71	Chi-Square (96)=234,90; df=4; p=0,0001*
1 month	97	142±11.81	110/ 180	140 (135-150)	3.56	
3 months	97	137±9.24	110/ 160	135 (130-142)	2.84	
6 months	96	132±10.38	85/ 180	130 (130-140)	2.18	

IQR = 25th – 75th percentiles;

Friedman test; *significant p<0.05

To determine the reason for the significance of the differences between the SBP values, in each of the groups individually, Post Hoc Test analysis was applied. The differences in 6-time combinations were analyzed by testing with Wilcoxon signed rank test. In order to avoid Type 1 error, according to the Bonferroni correction, for the interpretation of the obtained results, a significant level of p<0.01 was accepted (Table 1-2).

In the IG, the average SBP was highest at the time 0 before the intervention and was 151±12.27mmHg with a min/max value of 130/200mmHg. In the post-intervention follow-up period, the average SBP value gradually decreased with the lowest average value after 6 months, namely 129±9.18mmHg with a min/max value of 110/160mmHg. A significant difference was found between the 4 measurement times in terms of the value for the SBP (Friedman Test: Chi-Square (92)=212.89; df=4; p=0.0001) (Table 1).

Table 2. Comparison of systolic blood pressure in six time combinations – IG/CG.

Intervention group	**SBP (mmHg)**					
	1month/ 0 time	**3 months/ 0 time**	**6 months/ 0 time**	**3 months / 1 month**	**6 months / 1 month**	**6 months / 3 months**
Z	(-8.243)[c]	(-8.379)[c]	(-8.258)[c]	(-3.824)[c]	(-2.836)	(-0.238)[c]
Asymp. Sig. (2-tailed)	0.0001*	0.0001*	0.0001*	0.0001*	0.005*	0.812
Change confirmed	SBP1<SBP0 -90 SBP1>SBP0 -0 SBP1=SBP0-5	SBP3<SBP0 -93 SBP3>SBP0-0 SBP3=SBP0 -2	SBP6<SBP0-90 SBP6>SBP0-1 SBP6=SBP0 -1	SBP3<SBP1-55 SBP3>SBP1-27 SBP3=SBP1- 13	SBP6<SBP1-56 SBP6>SBP1-27 SBP6=SBP1-9	SBP6<SBP3 -31 SBP6>SBP3-39 SBP6=SBP3 -22
Control group	**1month/ 0 time**	**3 months/ 0 time**	**6 months/ 0 time**	**3 months / 1 month**	**6 months / 1 month**	**6 months / 3 months**
Z	(-7.116)[c]	(-7.994)[c]	(-8.094)[c]	(-4.668)[c]	(-6.102)	(-4.104)c

Asymp. Sig. (2-tailed)	0.0001*	0.0001*	0.0001*	0.0001*	0.0001*	0.001*
Change confirmed	SBP1<SBP0 -81 SBP1>SBP0 -9 SBP1=SBP0-7	SBP3<SBP0 -86 SBP3>SBP0-5 SBP3=SBP0 -6	SBP6<SBP0-88 SBP6>SBP0-2 SBP6=SBP0 -6	SBP3<SBP1-65 SBP3>SBP1-17 SBP3=SBP1- 15	SBP6<SBP1-72 SBP6>SBP1-11 SBP6=SBP1- 13	SBP6<SBP3 -58 SBP6>SBP3-18 SBP6=SBP3 -20
Wilcoxon Signed Ranks Test: according to Bonferroni correction significant at p<0.01 c. based on positive ranks;						

In the intervention group, for Bonferroni correction of p<0.01, a significant difference in the value of the SBP was determined by the Wilcoxon Signed Ranks Test in 5 out of 6 analyzed time combinations. In the IG a significantly lower SBP was registered at each subsequent measurement up to 6 months compared to zero time. In this group, the highest proportion of patients with reduced SBP compared to zero time was at 3 months – 93 (97.89%) from 95 followed by reduced BP at 1 and 6 months for 90 (97.82%) from 92 patients. After 6 months compared to zero, unchanged SBP was registered in only 1 (1.08%) patient at 6 months, and an increase in SBP was also registered in only 1 patient (1.08%) (Table 2).

Regarding the average SBP in the CG, the highest value was recorded at 0 time and was 152±11.32mmHg with a min/max value of 128/193mmHg. In the 6 months follow-up period, the average SBP value gradually decreased with the lowest average value of 132±11.32mmHg with a min/max value of 85/180mmHg after 6 months. In the CG, a significant difference was determined between the 4 measurement times in terms of SBP height (Friedman Test: Chi-Square (96)=234.90; df=4; p=0.0001) (Table 1). In the CG, for Bonferroni correction of p<0.01, a significant difference in the level of SBP was determined with the Wilcoxon Signed Ranks Test in all 6 analyzed time combinations. In the CG, a significantly lower SBP was registered at each subsequent measurement compared to the previous one in all 6-time combinations. We determined that 81 (83.50%) from 97 patients had a reduced SBP after 1 month compared to zero, and after 6 months compared to zero, a total of 88 (91.67%) from 96 patients. After 6 months compared to zero, an unchanged SBP was found in 6 (6.25%) patients, and an increase in SBP was determined in 2 patients (Table 2). After the results of the intergroup analysis, a comparison was made between the two groups - IG and CG, in terms of the obtained SBP values. The comparison was made before and at each of the four times after the intervention (Table 3).

Table 3. Intergroup comparison of SBP at four times.

Intergroup comparison	SBP (mmHg)				p
	(N)	Mean± SD	Min/Max	Median (IQR)	
„0" time					
IG	95	151±12.27	130/ 200	148 (144-157)	Z=(-1.112; p=0.266
CG	97	152±11.32	128/ 193	150 (145-160)	
1 month					
IG	95	133±12.99	112/ 190	130 (125-140)	Z=(-5.691; p=0.0001*
CG	97	142±11.81	110/ 180	140 (135-150)	
3 months					
IG	95	129±9.49	110/ 160	130 (122-135)	Z=(-5.587; p=0.0001*
CG	97	137±9.24	110/ 160	135 (130-142)	
6 months					
IG	92	129±9.18	110/ 160	130 (120-137)	Z=(-2.333; p=0.020*
CG	96	132±10.38	85/ 180	130 (130-140)	

IQR = 25^{th} – 75^{th} percentiles; IG = standard care & mHealth app.;

CG= standard care

Mann-Whitney U Test; *significant p<0.05

The comparison of IG and CG at each of the four follow-up times after the intervention indicated a significant difference in terms of SBP (Table 3 and Figure 1).

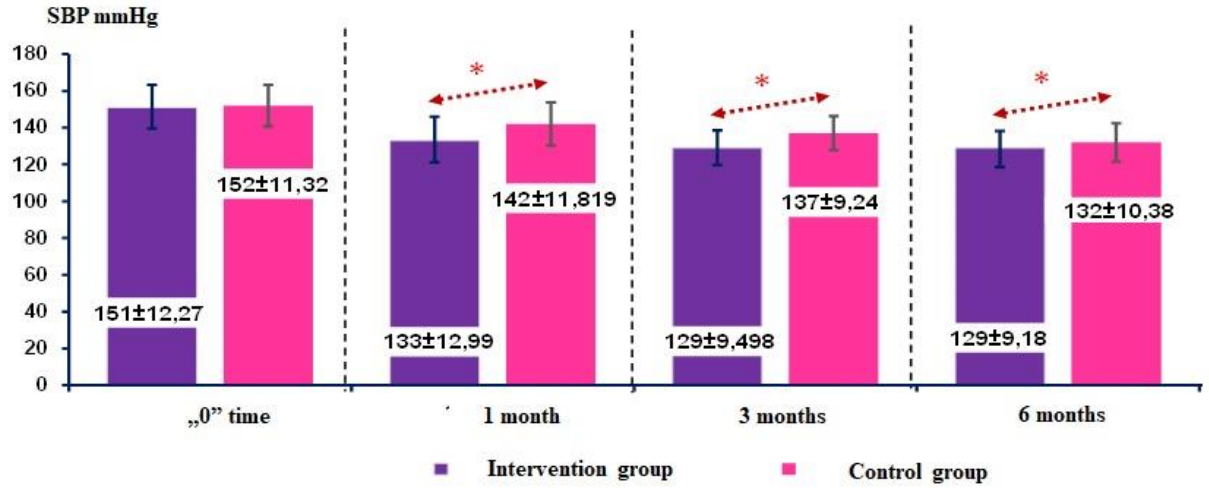

Figure 1. Intergroup comparison of systolic blood pressure at four times.

In both groups of participants, an analysis of DBP (mmHg) values was performed at four follow-up times: "0" time, 1, 3 and 6 months after the intervention. The analysis of the distribution of the values obtained for DBP expressed in mmHg at each of the 4 follow-up times indicated an irregular distribution of frequencies for: a) 0 time - Shapiro-Wilk W=0.9407; p=0.0003; b) 1 month - Shapiro-Wilk W=0.8832; p=0.00001; c) 3 months - Shapiro-Wilk W=0.6898; p=0.00001; d) 6 months - Shapiro-Wilk W=0.9470; p=0.0009. The values obtained for DBP were compared at each of the 4 measurement times, both intragroup and intergroup in the IG and CG (Table 4).

Table 4. Intragroup comparison of diastolic blood pressure at four times.

Intragroup analysis	**(mmHg)**					**p**
	(N)	**Mean± SD**	**(Min/Max)**	**Median (IQR)**	**Mean Rank**	
Intervention group						
""0"" time	95	94.40±7.65	80/ 120	93 (90-100)	4.66	Chi-Square (92)=169.81; df=4; p=0.0001*
1 month	95	83.88±7.42	70/ 110	84 (80-90)	3.14	
3 monthss	95	80.78±7.36	68/ 100	80 (74-88)	2.57	
6 monthss	92	81.00±6.25	68/ 92	80 (78-85)	2.54	
Control group						
""0" " time	97	94.43±7.04	80/ 110	90 (90-100)	4.54	Chi-Square

1 month	97	87.19±7.79	64/ 110	90 (82-90)	3.29	(96)=165.165
3 monthss	97	84.58±6.78	70/105	85 (80-90)	2.64	df=4; p=0.0001*
6 monthss	96	83.31±7.09	60/ 100	82 (80-90)	2.45	

IQR = 25th – 75th percentiles;

Friedman test; *sognficant p<0.05

In both groups, a significant decrease (Friedman Test) in DBP was observed between all follow-up times, with the highest value at time zero before the intervention and the lowest average value at 6 months after the intervention (Table 4). To determine the reason for the significance in the differences between DBP values, in each of the groups individually, Post Hoc Test analysis was applied. The differences in 6-time combinations were analyzed by testing with Wilcoxon signed rank test. In order to avoid Type 1 error, according to the Bonferroni correction, for the interpretation of the obtained results, a significance level of p<0.01 was accepted.

In the IG, the average DBP was the highest at time 0 before the intervention and was 94.40±7.65mmHg with a min/max value of 80/120mmHg. During the follow-up period, the mean DBP value gradually decreased with the lowest mean value after 3 months, 80.78±7.36mmHg with a min/max value of 68/100mmHg. In this group, for Bonferroni correction of p<0.01, a significant difference in DBP values was determined with the Wilcoxon Signed Ranks Test in 5 out of 6 analyzed time combinations for consecutive (Table 5). In IG, a significantly lower mean DBP was registered at each subsequent measurement up to 6 months compared to zero time. In this group, the highest proportion of patients with reduced DBP compared to zero time was after 6 months for 83 (89.58%). After 6 months compared to zero, unchanged DBP was registered in 4 (4.16%) patients, and an increase in DBP was in 5 (5.2%) patients (Table 5).

Table 5. Comparison of diastolic blood pressure in six-time combinations – IG/CG.

(mmHg)						
Intervetion group	**1 month/ 0 time**	**3 months/ 0 time**	**6 months/ 0 time**	**3 months / 1 month**	**6 months / 1 month**	**6 months / 3 months**
Z	(-7.602)[c]	(-7.964)[c]	(-7.885)[c]	(-3.916)[c]	(-8,.47)	(-0.353)[c]
Asymp. Sig. (2-tailed)	0.0001*	0.0001*	0.0001*	0.0001*	0.005*	0.724

Changed confirmed	DBP1<DBP0 -78 DBP1>DBP0 -3 DBP1=DBP0-14	DBP3<DBP0 -81 DBP3>DBP0-6 DBP3=DBP0 -8	DBP6<DBP0-83 DBP6>DBP0-4 DBP6=DBP0 -5	DBP3<DBP1-49 DBP3>DBP1-17 DBP3=DBP1- 29	DBP6<DBP1-0 DBP6>DBP1-92 DBP6=DBP1-0	DBP6<DBP3 -33 DBP6>DBP3-31 DBP6=DBP3 -28
Control group	**1 month/ 0 time**	**3 months/ 0 time**	**6 months/ 0 time**	**3 months / 1 month**	**6 months / 1 month**	**6 months / 3 months**
Z	(-6.697)[c]	(-7.726)[c]	(-7.747)[c]	(-3.410)[c]	(-8.525)	(-2.010)c
Asymp. Sig. (2-tailed)	0.0001*	0.0001*	0.0001*	0.0001*	0.0001*	0.044
Changed confirmed	DBP1<DBP0 -72 DBP1>DBP0 -8 DBP1=DBP0-17	DBP3<DBP0 -83 DBP3>DBP0-7 DBP3=DBP0 -7	DBP6<DBP0-81 DBP6>DBP0-6 DBP6=DBP0 -9	DBP3<DBP1-56 DBP3>DBP1-19 DBP3=DBP1- 22	DBP6<DBP1-0 DBP6>DBP1-96 DBP6=DBP1- 0	DBP6<DBP3 -39 DBP6>DBP3-26 DBP6=DBP3 -31
Wilcoxon Signed Ranks Test: according to Bonferroni correction significant at p<0.01 c. based on positive ranks;						

In the CG, the average DBP in this group was the highest at time „0" before the intervention and was 94.43±7.04mmHg with a min/max value of 80/110mmHg. During the follow-up period, the average DBP value gradually decreased with the lowest average value of 83.31±7.09mmHg with a min/max value of 60/100mmHg after 6 months. In the CG, a significant difference was determined between the 4 measurement times in terms of DBP height (Friedman Test: Chi-Square (96)=165.165; df=4; p=0.0001). In this group, for Bonferroni correction of p<0.01, a significant difference in the height of the DBP was determined with the Wilcoxon Signed Ranks Test in all 6 analyzed time combinations for consecutive. In this group, significantly lower DBP was registered at each subsequent measurement compared to the previous one in 5 out of 6 time combinations. We determined that 86 (85.66%) from 97 patients had reduced DBP after 3 months compared to zero, and after 6 months compared to zero, a total of 81 (84.38%) from 96

patients. After 6 months compared to zero, unchanged DBP was in 9 (9.38%) patients, and in 6 (6.25%) an increase in DBP was determined (Table 6).

Table 6. Intergroup comparison of DBP at five times.

Intergroup comparison	**(mmHg)**				**p**
	(N)	**Mean± SD**	**(Min/Max)**	**Median (IQR)**	
„0" time					
IG	92	94.40±7.65	80/ 120	93 (90-100)	Z=(-0.418; p=0.676
CG	96	94.43±7.04	80/ 110	90 (90-100)	
1 month					
IG	92	83.88±7.42	70/ 110	84 (80-90)	Z=(-3.240; p=0.001*
CG	96	87.19±7.79	64/ 110	90 (82-90)	
3 months					
IG	92	80.78±7.36	68/ 100	80 (74-88)	Z=(-3.199; p=0.001*
CG	96	84.58±6.78	70/105	85 (80-90)	
6 months					
IG	92	81.00±6.25	68/ 92	80 (78-85)	Z=(-2.645; p=0.008*
CG	96	83.31±7.09	60/ 100	82 (80-90)	
IQR = 25^{th} – 75^{th} percentiles; Mann-Whitney U Test; *significant p<0.05					

A comparison was made between the two groups in terms of the obtained DBP values. The values obtained from the individual analysis of the comparison of the two groups (Mann-Whitney U Test) in terms of the height of the DBP for each of the 4 follow-up times indicated a significant difference for all times, except for the "0" time (Table 6 and Figure 2).

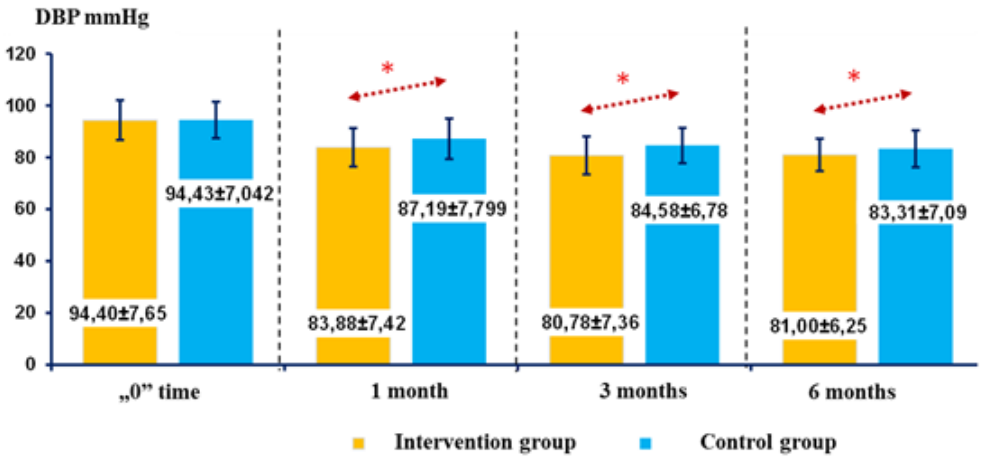

Figure 2. Intergroup comparison of dyastolic blood pressure at four times.

Discussion

In this randomized controlled trial, we aimed to assess the impact of a smartphone-based mHealth application + standard care on blood pressure control in newly diagnosed hypertensive patients. To obtain baseline data on the impact of this intervention, an analysis of blood pressure measurements obtained during planned outpatient check-ups at primary care physicians at 0, 1, 3 and 6 months after study entry, was performed in the intervention and control groups. At study entry, no statistically significant difference was observed in SBP and DBP values, gender, age, place of residence (urban/ rural) between subjects in the two groups. Regarding SBP values, a decrease in mean SBP was observed at all 4 follow-up times in both groups, with a decrease in mean SBP of 22mmHg in the intervention group, i.e., 20mmHg in the control group, i.e., 14.56%, i.e., 13.15% respectively, with a difference of 2mmHg in favor of the intervention group. Better SBP control was also shown in the intragroup analysis with a significantly higher number of patients with reduced SBP compared to the control group. These reduced SBP values were also sustainable after 6 months of the study with 97.8% of the subjects in the intervention group, i.e., 91.5% of the control group with reduced SBP values. Regarding DBP values, a significantly lower DBP was registered at each subsequent measurement up to 6 months compared to zero time with reduced DBP after 6 months, 89.58% in the intervention group, i.e. 84.38% in the control group. In the study, in both groups after 6 months of follow-up, a reduction in the average DBP of 13.4mmHg occurred in the group receiving standard care + mHealth application, i.e., 12.75mmHg in the standard care group, with a difference of 0.65mmHg in favor of the intervention group. The data obtained support the idea that the m-health application can help as an additional intervention to standard healthcare to achieve a slightly higher percentage of good BP control.

The available literature has been rapidly investigating the effect of telemonitoring on hypertension control over the past 2 decades. In the TASMINH4 (22) study (2018), the effect of telemonitoring on blood pressure control was investigated, compared to self-monitoring and standard care. After 12 months of follow-up, systolic blood pressure values were lower in both intervention groups than in the standard care group (self-monitoring: 137.0 [SD 16.7]mmHg, telemonitoring: 136.0 [SD 16.1]mmHg, standard care: 140.4 [SD 16.5]mmHg). This study is significant in its contribution due to results indicating that self-monitoring of CP has an exceptional role in good control of CP, while telemonitoring is a tool that timely informs the patient and involves the doctor in monitoring the patient's condition, which is consistent with the goals set in our study.

In a randomized controlled trial by McManus et al. (2021), 622 patients with hypertension were followed by 76 primary care physicians. Patients in the intervention group transferred their home blood pressure measurements to a secure online platform, where the patient and primary care physician had access to the data. This platform offered a feedback system for BP measurements, optional lifestyle counseling and motivational support. After 12 months, data were available from 552 participants with imputation for the remaining 70 participants (11.4%). The mean SBP decreased from 151.7/86.4 to 138.4/80.2mmHg in the intervention group and from 151.6/85.3 to 141.8/79.8mmHg in the standard care group, yielding a mean difference in SBP of -3.4mmHg (95% confidence interval -6.1 to -0.8mmHg) and a mean difference in DBP of -0.5mmHg (-1.9 to 0.9mmHg). The results of this study, due to the similarity of the study design, can be easily compared to the results of our study, which point towards slightly improved BP control with the use of an mHealth application.

In a similar randomized controlled trial by McKinstry et al (23) in a six-months intervention with self-monitoring and transmission of blood pressure values to a secure website for review by a nurse or physician from the primary care clinic, showed that the intervention led to significant improvement in SBP (4.3mmHg; 95% CI, 2.0 to 6.5; p= 0.0002) and non significant improvement in DBP (0.9mmHg; 95% CI, 0.9 to 3.6; p=0.001) with standard care. The results of our study are in line with those of McKinstry's study, as in a relatively short period of hypertension management by general practitioners through self-measurement at home by patients with telemonitoring, more effective results were obtained in reducing BP values than usual care.

In a meta-analysis by Paula, Maldonado and Gadelha (24) including 76 studies, where the aim was to assess the effectiveness of telehealth-based interventions on disease control rates and clinical parameters in patients with chronic non-communicable diseases, including systolic and diastolic blood pressure, telehealth technologies were shown to significantly improve blood pressure and could be a valuable additional tool for comprehensive hypertension management. In a randomized study by Chavami et al. (25) with 6-months follow-up, patients in the intervention group were more likely to have successfully controlled their blood pressure (88.6% vs. 78.5%; P < 0.001) and had a higher chance of successfully controlling their blood pressure (odds ratio [OR]: 2.13; 95% CI: 1.51 - 3.03). Also in the study by Gong et al. (26) after 6 months of

monitoring the effect of the mHealth application, participants in the intervention group at the end of the study showed a significantly greater reduction in SBP and DBP than the control group ($P < 0.05$) and the percentage of participants with controlled blood pressure was higher in the intervention group ($P < 0.05$).

The mHealth application used in our study enabled two-way doctor-patient communication via SMS messages through the application, which enabled smooth and fast communication, the possibility of timely intensification of therapy and monitoring of the patient's condition. In the randomized study by Leopold et al. (27) which monitored the impact of a complex mHealth application, with two-way doctor-patient communication, on blood pressure, the results have shown that the intervention increased the BP control rate significantly by 23.1% points (95% CI: 5.4-40.8%): intervention 59.8% (95% CI: 47.4-71.0%) compared to 36.7% (95% CI: 24.9-50.3%) in the control group. Systolic BP decreased by 21.1mmHg in the intervention and 15.5mmHg in the control group, which indicated a relevantly better control of BP with the help of the application.

Some studies have not shown a positive effect of telemonitoring on BP control. One such study is the randomized controlled trial by Mehta et al. (28) that included patients aged 18–75 years treated in family medicine outpatient clinics in Philadelphia. Patients had been seen at least twice in the previous 24 months and had at least 2 elevated blood pressure measurements (>150/90mmHg or >140/90mmHg for patients aged 18–59 years or with diabetes or chronic kidney disease) during the visits. Patients were randomized 2:2:1 to telemonitoring of blood pressure and medication adherence (RM), telemonitoring of blood pressure and medication adherence with feedback provided to a social support partner (SP) and usual care (UC). Patients were followed for 4 months. 246 patients were included in the analysis: 100 patients in the RM group, 97 in the SP group and 49 in the UC group. Compared to the control group, there was no significant difference in SBP or DBP at the 4-month visit in the RG group (mean difference adjusted for SBP, -5.25 [95% CI, -10.65 to 0.15]mmHg; mean difference adjusted for DBP, -1.94 [95% CI, -5.14 to 1.27]mmHg) or the SP group (mean difference adjusted for SBP, -0.91 [95% CI, -6.37 to 4.55]mmHg; mean difference adjusted for DBP, -0.63 [95% CI, -3.77 to 2.51]mmHg). Out of the 206 patients at 4 months, blood pressure was controlled in 49% of patients in the RG group, 31% of patients in the SS group, and 40% of patients in the control group; these rates did not differ significantly between the intervention and control groups.

The mHealth application in our study, in addition to enabling the transfer of BP values in real time to the family doctor, also had a section in its structure intended for educating the patient on the correct BP measurement technique and a section with data on the hygiene and dietary regimen, in order to improve the patient's education about the disease and his active involvement in the treatment itself. An educated patient is an equal ally of the doctor who actively invests, especially in the part of adhering to an appropriate hygiene and dietary regimen. In the study by Liu et al., (29) after 6 months of follow-up, in addition to a statistically significant improvement in BP in the intervention group versus the control group, the same group also improved in

knowledge about hypertension, lifestyle, healthy diet, adherence, salt intake and physical activity. In our research, risk factors associated with HTN were determined, but monitoring of the impact of the mHealth application on them was not planned.

In the available literature, no study could be found that investigated the effect of an mHealth application on blood pressure control in patients with newly diagnosed hypertension, which is of exceptional importance because the rapid reduction in blood pressure values and their maintenance, especially in newly diagnosed patients, significantly delays target organ damage.

To confirm the effect of this type of application and sustainability over a longer period of time, it is necessary to complete our research by fulfilling the entire protocol and following up with the participants within 12 months. In order to define the applicability of mHealth applications in different regions of the world, future research is recommended in which the effect on blood pressure control will be monitored in different settings.

Limitations of the Study

The study had several limitations. First, all participants in the intervention group owned mobile phones and were likely to have higher socioeconomic status. In addition, not having a smartphone makes it difficult to recruit individuals for clinical trials and to collect accurate and complete data for trials, especially when relying on mobile technologies for data collection and monitoring progress in self-management. Second, patients' blood pressure was monitored based on their self-reported blood pressure readings, rather than accurate measurements by healthcare professionals. Although participants were educated to measure their blood pressure more accurately according to a given schedule and were shown a video on the app showing proper blood pressure measurement technique, it was not guaranteed that everyone followed the instructions, which could introduce bias into the measurement results. Strategies for assessing the accuracy of patient-reported data and how to involve family members to facilitate self-monitoring in patients who are unable to manage their condition themselves also need further investigation. Third, there is a lack of previous research studies investigating the impact of an mHealth application in patients with newly diagnosed HTN that would allow for comparison of results, as self-monitoring of BP in these patients is of utmost importance for the purpose of timely titration of antihypertensive therapy to achieve targeted values.

Conclusion

An mHealth application that enables two-way patient-physician communication is an intervention that, as an auxiliary tool to standard care, can improve blood pressure control in newly diagnosed patients with hypertension. In order to confirm the complete effect of the

mHealth application on blood pressure control and the benefit for family physicians when using it in managing patients with hypertension, it is necessary to complete the planned protocol.

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