Home telemonitoring of arterial hypertension versus usual care: the HOROSCOPE study

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Abstract

Background: Control of hypertension has shown a decrease in blood pressure compared to usual care

Objective: The Horoscope trial aimed to assess the efficacy of home blood pressure (BP) telemonitoring (TLM) in controlling BP reduction in hypertensive patients compared with usual care.

Methods: This is a multi-center, prospective randomized, parallel-group trial comparing TLM with usual care during a period of 6 months in patients with hypertension.

Results: We included 525 patients randomly assigned in a 1-1 ratio to telemonitoring (TLM group ; n =260) or usual care (control group ; n=265). After 6 months of follow up, mean values of 24-hour systolic and diastolic blood pressure decreased in both TLM and control groups. The mean decrease was significantly greater in the TLM g roup vs control group (?3.29 mmHg Vs ?1.19; p=0.009) and (?2.9?mmHg Vs ,?0.07; p=0.002) for systolic and diastolic blood pressure, respectively.

Conclusions: This study shows that TLM results in significant BP reduction compared to usual care in a Tunisian population of patients with hypertension. Our findings highlight the importance of integrating telemedicine in the management of hypertensive patients ; it has the potential to improve the quality of the delivered care and to prevent cardiovascular consequences of uncontrolled BP. Clinical Trial: The study was approved by the Ethics committee of Monastir Medical University and is registered at Clinicaltrials.gov registry (NCT04607239).

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Abstract

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Conclusion

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Introduction

Hypertension is one of the main risk factors for cardiovascular disease and a leading cause for global morbidity and mortality (1-3), predominantly affecting individuals in low and middle-income

countries (4). The control of hypertension remains insufficient despite the availability of effective treatments, and blood pressure (BP) control rate was only about 32.5% worldwide among treated patients (5,6). A number of trials have demonstrated that patient self-monitoring has a small but statistically significant effect on improving BP control (7). However, telemonitoring, which involves clinicians reviewing patient-submitted blood pressure readings over the internet or via SMS, leads to significantly larger and clinically meaningful reductions in blood pressure (8). Despite conflicting evidence, two multicentre studies involving general practitioners reported a significant reduction in BP over a period of 6 months (9). A recent systematic review and meta-analysis of studies, based on modern information technology tools with automatic home BP monitoring transmission, demonstrated a significant improvement of BP treatment compared to classical methods of monitoring hypertensive patients (10). These results are worth-confirming, especially since the approach of this study can be economically interesting in the context of a resource-limited country (11,12). The aim of the HOROSCOPE (Home Telemonitoring of Arterial hypertension with Antihypertensive Treatment Titration: Randomised Controlled Prospective Trial) study is to demonstrate the impact of telemonitoring on BP control among patients with hypertension.

Methods

Study design and participants

This was a randomised Controlled unblinded trial. The detailed study protocol has previously been published (13). The recruitment for the trial started in April 2020. The data collection period lasted for approximately 2 years. The duration of the study per patient was 6 months. Data collection was completed by the end of 2022. Potentially eligible participants were identified based on records available in 15 centres located in the Sahel region of Tunisia. These centres included general practices, Primary Healthcare dispensaries, regional hospitals and university hospitals. The searches identified individuals potentially eligible in terms of age and hypertension diagnosis. The inclusion criteria specified individuals aged 35 years or older, diagnosed with hypertension, and having clinic

blood pressure readings not controlled below 140/90 mm Hg. They had to be on stable antihypertensive medication for at least 4 weeks before randomization and free from orthostatic hypotension, a cute coronary syndrome, coronary revascularisation, stroke within the past 3 months, chronic kidney disease of grade 4 or worse, New York Heart Association Class III or IV heart failure or left ventricular ejection fraction of <30% and dementia or any other cause that could prevent the implementation of remote monitoring (telemonitoring).

Randomisation and masking

Potentially eligible patients are screened for eligibility 30 days prior to the study start date. Screening of potentially eligible patients started in April 2020, and lasted till the end of 2022. At the first visit, after obtaining informed consent, all included participants received therapeutic education. This included information on diet, sleep, physical activity, and other lifestyle advice prior to randomization. Baseline clinical data forms (BP, heart rate, NYHA, body mass index, electrocardiogram (ECG), renal function, blood glucose, etc.) and satisfaction questionnaires were completed. Measurements of baseline quality of life were assessed using the Medical Outcomes Study Short Form-12 (SF-12) questionnaire (14). A 24-hour BP Holter (CONTEC ABPM50, CONTEC Medical System, Qinhuangdao, Hebei Province, China) was applied to all included patients. Holter measurements were programmed to measure BP every 30 minutes from 6am to 10pm and every 60 minutes from 10pm to 6am. The cuff size is chosen according to the morphology of the participant and is placed on the non-dominant arm. The number of available BP measurements must be at least 32 (80%) of the 48 possible measurements. If not, the Holter monitor test will be re-taken. The device must not get wet (swimming pool, bath, shower) and normal activities must be maintained after installing the device. All included participants were invited to return 24 hours later to retrieve the device and were randomised in a 1-1 ratio to be assigned to telemonitoring (TLM group) or to usual care (Control group). Randomisation was performed by means of an interactive web responsive system, and patients were stratified by the investigation centre. Neither participants

nor investigators were masked to the group assignments. However, the cardiologist interpreting the results of the Holter parameters was kept unaware of the allocation list. Holter measurements were repeated for both groups at 6-month follow-up. Participants who were assigned to the TLM group were taught to use a validated BP monitor. They were asked to monitor their own BP in their non-dominant arm, twice daily, in the morning and evening, three times a week each month. Once a week, the research associate called the patients to check their treatment compliance and verbally collect the BP monitor measurements. Compliance evaluation was conducted by asking the patients whether they have been taking their medication correctly every day on time for the past week. Patients were asked to keep their empty treatment boxes. The remaining pills were counted, and patient compliance was reassessed. The research associate also reminded patients about the lifestyle and dietary measures they should adopt. Subsequently, the research assistant filled in the data entry fields in a specific electronic case report form. Patients were contacted every month via telephone by their attending physician for 6 months to titrate the antihypertensive treatment according to the data collected by the research associate. A "face-to-face" medical visit is scheduled after 3 months and at the end of the 6-month study; biological tests will be asked at the discretion of the physician. As for antihypertensive drug titration, the decision criteria is the percentage of home BP readings that reach the target. On day 90 and day 180, the medical visit was conducted face-to-face. The objective of titrating antihypertensive agents is to ensure that at least 75% of the blood pressure readings taken after the last visit fall within normal ranges. If less than 75% of the readings met the target, readjustment of the treatment was required. During the telephone follow-up calls, physicians encouraged participants to adhere to the treatment. Regardless of BP control, if patients experienced side effects, the involved antihypertensive drug was stopped or changed, or its dose was reduced.

Primary and secondary Outcomes

The primary outcome was Holter measured 24-hour SBP and DBP change from baseline to 6-months of follow-up. The secondary outcome includes BP load (BPL), defined as the percentage of

abnormally elevated BP readings; percentage of dipping, which is defined as the difference between the mean daytime and mean nighttime BP, normally ranging between 10% and 20% ; and quality of life (SF-12) (14) .

Statistical analysis

Categorical variables are expressed as frequencies and percentages, while continuous variables will be expressed as means with SDs. An analysis of variance was performed to compare the two study groups in terms of primary endpoint. The normality of continuous data was assessed by means of the Shapiro-Wilk test. Furthermore, a general linear model was used for repeated measures to compare the marginal means of Gaussian quantitative dependent variables before and after the intervention (a Bonferroni test was considered). A non-parametric test (the Friedman test) was used for the comparison of non-Gaussian quantitative variables before and after intervention. The Cochran Q test was performed to compare binary dependent variables before and after intervention. Differences between continuous variables were assessed using a 2-tailed Student t test or by its corrected version, as appropriate. The differences among the categorical variables were evaluated using the Pearson chi-square test. All tests were considered significant at the cutoff value of $P<0.05$.

Ethical considerations

The study was conducted in compliance with the Declaration of Helsinki, as well as national and institutional standards. The study was approved by the Ethics committee of Monastir Medical University and is registered at Clinicaltrials.gov registry (NCT04607239). Free and informed consent from all patients was obtained before their inclusion in the study.

Role of the funding source

The funders and sponsors of the study had no role in study design, data collection, data analysis, data interpretation, writing of the report, or in the decision to submit for publication.

Results

Fifteen university and non-university medical centres participated in the study protocol including

Four EDs (Fattouma Bourguiba University Hospital, Sahloul University Hospital, Teboulba regional Hospital and Jammel regional Hospital, and two primary care centres and private outpatients clinics. Out of 598 patients assessed for eligibility, 56 patients were excluded for not-meeting inclusion criteria. 542 patients were enrolled and randomly assigned in a 1-1 ratio: 270 patients (49.8%) (were assigned to usual care control group) and 272 patients (50.1%) were assigned to telemonitoring (TLM group). Five patients from the control group and 12 patients from the TLM group were lost to follow-up because they had been withdrawn from the study before their final 6-month follow. Ultimately 525 patients were included in the final analysis, 265 patients (50.5%) in the control group and 260 patients (49.5%) in the TLM group (Figure 1). The characteristics of the patients at baseline were summarised in table 1. The mean age of study patients was 58.9 years ±9,8 with a sex ratio (M/F) of 0.96. Most patients 312 (59.4%) had no past medical history. The most common comorbidities were diabetes (18.2%), coronary artery disease (9.9%) and (10 %) were active smokers. Mean SBP at baseline was 140.9 mmHg ± 19.5 and mean DBP at baseline was 81.4 mmHg ±12.6. The groups were balanced in terms of demographic and clinical examination baseline findings (table 1). In both groups, mean 24-hour SBP and DBP at 6-month follow-up decreased compared to baseline. In the TLM group, mean 24-hour SBP decreased from 126.7 mmHg ±14 to 123.3 mmHg ±12 ($p<0.001$) and mean 24-hour DBP decreased from 74.6 mmHg ±9 to 71.6 mmHg ±9 ($p<0.001$). In the control group, mean 24-hour SBP decreased from 128.6 mmHg ±14 to 127.2 mmHg ±15 ($p=0.16$) and mean 24-hour DBP decreased from 74 ±10 to 73.9 mmHg ±11 ($p=0.80$). The mean decrease difference was significantly superior in TLM than in control groups [–3.29 (95% CI –5 to –1.5) vs –1.19 (95% CI –2.9 to –0.5); $p=0.009$ for SBP] and and [–2.9 (95% CI –4.2 to –1.7) vs –0.07 (95% CI –1.3 to 1.4); $p=0.002$ for DBP] respectively in the TLM group and the control group (Figure 2).

In both groups, mean 24-hour systolic and diastolic BP load at 6-month follow-up decreased compared to baseline. In the TLM group, mean 24-hour SBP load decreased from 45.2% to 38.1% ($p<0.001$) and mean 24-hour DBP load decreased from 37.5% to 30.4 % ($p<0.001$). In the control

group, mean 24-hour SBP load decreased from 47.1% to 44.5% (p=0.11) and mean 24-hour DBP load decreased from 35.9% to 34.2% (p=0.28). The mean decrease difference was significantly superior in TLM than in control groups [–7.2 (95% CI –10.3 to –4), to –2.5 (95% CI –5.8 to 0.3); p=0.04 for SBP] and –6.9 (95% CI –9.8 to –4) to −1.6 (95% CI – 4.7 to 1.2); p=0.01 for DBP] respectively in TLM group and Control groups (Figure 3). At baseline, results show a non-significant difference in systolic and diastolic dipper percentages at baseline in TLM vs control groups [37% vs 36% (p=0.28) and 53% vs 55% (p=0.72) respectively for systolic and diastolic dippers]. After 6 months of follow up results show a non-significant difference in systolic and diastolic dipper percentages at baseline in TLM vs control groups [33% vs 29% (p=0.86) and 50% vs 52% (p=0.65) respectively for systolic and diastolic dippers]. There was no significant difference in the SF-12 quality of life score between TLM and control groups at baseline (43.6 vs 43.7; p= 0.69) respectively. Similar results were shown after 6 months of follow up (43 VS 43.9; p =0.35).

Discussion

This study compared the effect of TLM on BP control with standard treatment in a Tunisian population. The use of TLM resulted in a statistically significant reduction in 24-hour SBP and DBP compared to standard treatment. Overall, the telemonitoring intervention resulted in lower 24-hour SBP and DBP. The mean difference between TLM and control groups was 4.7 mmHg and 5.3 mmHg respectively for the decrease of SBP and DBP at 6-month follow-up compared to baseline. Similarly, the study demonstrated that TLM led to a significant decrease in BPL compared to standard treatment.

Hypertension is considered a main risk factor for stroke, ischemic heart disease and chronic renal disease. It is a global health problem due to its increasing prevalence alongside with high morbimortality (15) It is estimated that the number of hypertensive people will increase by 15-20% by 2025, reaching close to 1.5 billion (16), especially in low- and middle-income countries (17,18). Despite effective treatment options for some individuals, control of blood pressure remains

inadequate in a substantial portion of the hypertensive population. BP telemonitoring is proposed as a promising and efficient method to deliver more integrated healthcare services directly at the patients' home (19). Several studies have indeed reported improvements in BP control, medication adherence, and patient satisfaction with telemonitoring compared to traditional care methods (20). The results of this study were similar to those shown in a recent study conducted in China including 190 patients randomised to either the home BP telemonitoring or the usual care for 12 weeks (21). Results from this study showed that TLM results in greater BP reduction, better BP control, and higher medication adherence than usual care. In patients with poorly controlled hypertension, using digital tools has significantly decreased SBP and DBP mean compared to the usual care group (−3.4 mmHg vs −0.5 mmHg) (22). One meta-analysis of 32 randomised controlled studies including patients with hypertension living in urban areas demonstrated higher BP control rate among the remote BP monitoring group (relative ratio 1.226; $p < 0.001$) compared to the usual care group (23). The more recent Meta-Analysis of Katz et al including randomised clinical trials or cohort studies that investigated digital health interventions for managing hypertension showed that BP reductions were greater in the intervention groups compared with the standard care groups. This study reinforced these findings and broadened the scope of positive outcomes to include patients in low-income countries. Importantly, it is also essential to consider the magnitude of the effect and its relevance, as a reduction of 5 mmHg in systolic blood pressure (SBP) could reduce the risk of cardiovascular events by 10% (24). Moreover, the use of 24-hour ambulatory BP monitoring to demonstrate BP-lowering effect in this study is particularly important and strengthens the clinical relevance of its findings because 24-hour systolic ambulatory BP has a stronger predictor value of cardiovascular complications than office SBP (25). Interestingly, it was observed that patients in the TLM group displayed a higher decrease of BP load than those in the control group. This is an additional indicator of the positive effect of TLM on BP status (26). This study compared quality of life using SF-12 between control and TLM groups and it showed no significant difference between

them. These results can be attributed to the duration of the study, which was not long enough to detect a significant change in satisfaction rates. Also, results regarding dipper percentages could stem from several factors, including limited sample size, limited duration and potential measurement inaccuracies. The limitations of the trial include the relatively short duration of the intervention, which may have obscured pathophysiological changes that require more time to manifest. This study did not measure or discuss potential variations in diet or physical activity levels among participants, thus preventing determination of the independent effects of these factors. Individuals with advanced underlying conditions were not included in this study. In addition, barriers to TLM including affordability, acceptability, long-term adherence, and cost of the technology, could limit the widespread adoption of TLM approach (27). Therefore, the results of this study could not be generalised to the entire hypertensive population.

Conclusion

This study shows that TLM can be a beneficial tool to control BP compared to usual practice. However, further studies involving a larger number of patients and extended durations are needed to confirm these results. Additionally, the cost and the feasibility of applying this approach to a broad range of patients, especially in low-income countries, need to be specifically studied.

Acknowledgments

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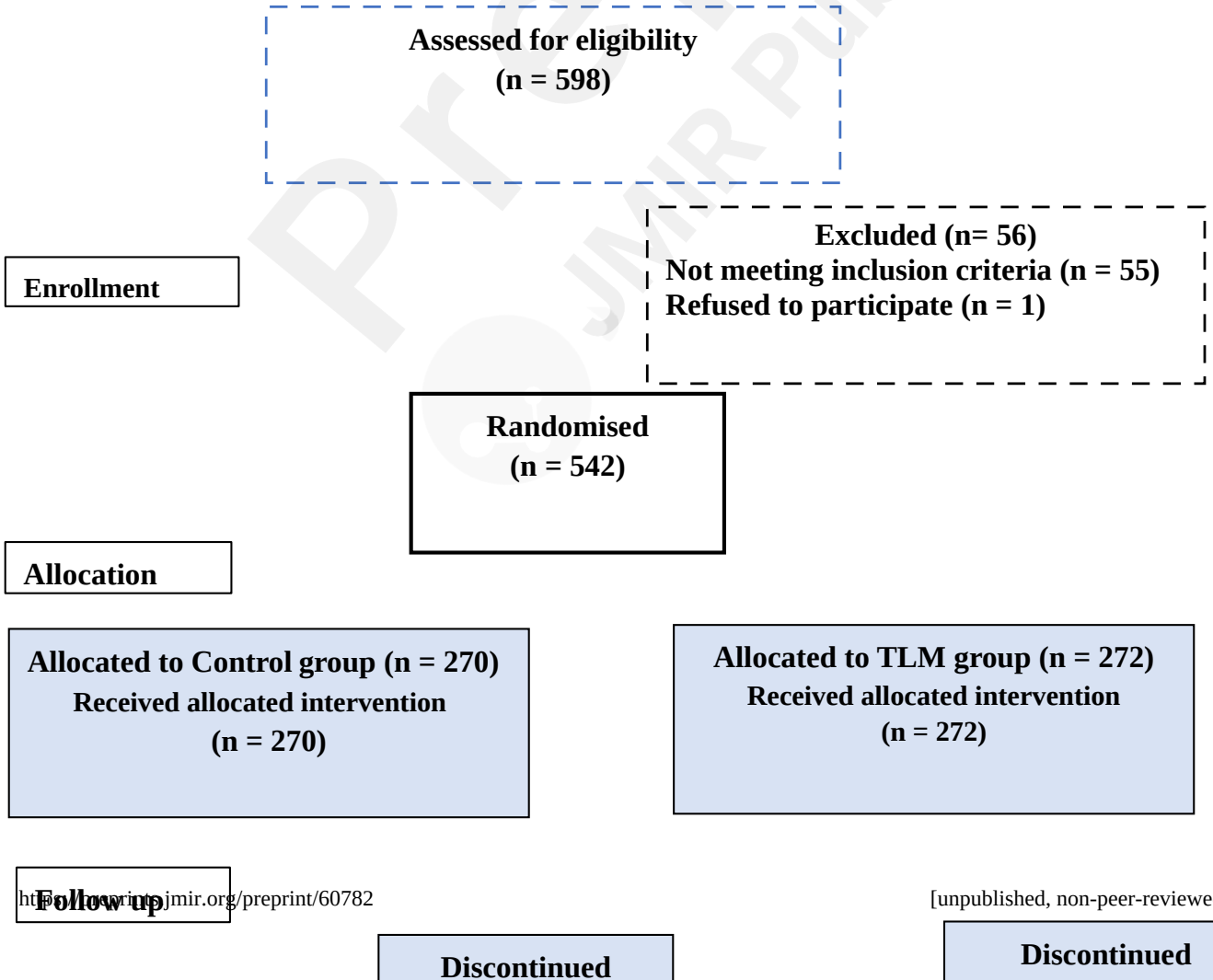

Analysis

Analysed (n = 265)

Analysed (n = 260)

Figure 1.

Figure 2.

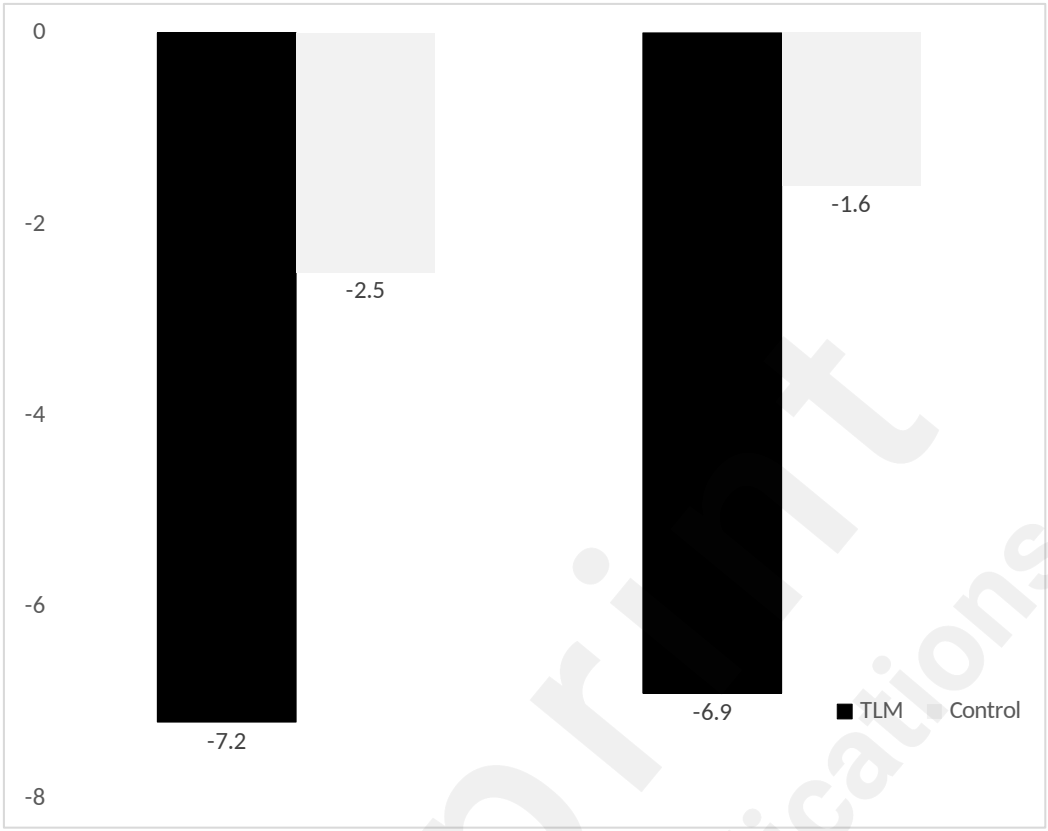

Figure 3.

Figure legends

Figure 1. Study Flowchart

Figure 2. Mean decrease of 24-hour systolic (SBP) and diastolic (DBP) blood pressure at 6-month follow-up compared to baseline in TLM and Control groups.

Figure 3. Mean decrease of 24-hour systolic (SBP) and diastolic (DBP) blood pressure load at 6-month follow-up compared to baseline in TLM and Control groups.

Table 1. The characteristics of the patients at baseline

	Control N= 265	TLM N=260	P
Age, years, mean (SD)	59 (10.5)	58.7 (9.1)	0.6
Sex-ratio (M/F)	1	0.9	0.2
BMI, kg/m^2, mean (SD)	32 (19.1)	30.3 (6)	0.62
Comorbidities, n (%)			
Diabetes	88(33.2)	74 (28.1)	0.2
Coronary artery disease	20 (7.5)	32(12.3)	0.07
Congestive Heart Failure	1 (0. 4)	0	0.31
COPD	2 (0.8)	0	0.15
Obstructive Sleep Apnoea	4 (1 .5)	2 (0.8)	0.43
Active smoker	24 (9)	29 (11)	0.45
Stroke	1(0.4)	2 (0.8)	0.55
Antihypertensive medications, n (%)			
Number 1	186(78.5)	176(77.2)	0.85
2	46(19.4)	40(17.5)	
3	5(2.1)	9(3.9)	
≥4	0(0)	2(0.9)	
ACE inhibitors	91 (35.4)	90 (35.7)	0.94
Calcium antagonists	84(32.7)	94(37.3)	0.27
Angiotensin II blockers	136(52.9)	128(50.8)	0.63
Diuretics	114(44.4)	100(39.7)	0.28
Beta-blockers	31(12.1)	41(16.3)	0.17
Alpha 1 blocker	4(1.6)	1(0.4)	0.18
Physical exam			
SBP, mmHg, mean (SD)	141.7(16.3)	138.6(20.9)	0.16
DBP, mmHg mean (SD)	82 (11,1)	80.2(13.7)	0.30
HR, b/min median, IQR	77(11.3)	77(10)	0.43
Biological serum analysis			
Glucose, g/l, median IQR	1.28(1.2)	1.18(1.2)	0.74
HDL, g/l , mean(SD)	1 .1(0.4)	0 .9(0.4)	0.18
Triglyceride, g/l , mean(SD)	1.6(0.8)	1.5(0.6)	0.52
Cholesterol, g/l, mean (SD)	4.4	3.4	0.22
Creatinine, µl/l ,mean(SD)	77(18.5)	77(18.6)	0.96

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Abbreviations: **BMI** Body Mass Index; **COPD** Chronic Obstructive Pulmonary Disease; **SBP** Systolic Blood Pressure; **DBP** Diastolic Blood Pressure;

HR Heart Rate