Is treated hypertension associated with a lower one-year mortality among older residents of long-term care facilities with multimorbidity?

Authors: Anna Kańtoch, Agnieszka Pac, Barbara Wizner, Jadwiga Wójkowska-Mach, Piotr Heczko, Tomasz Grodzicki, Barbara Gryglewska

Article type: Original article

Received: February 15, 2021.

Accepted: April 12, 2021.

Published online: April 20, 2021.

ISSN: 1897-9483
Is treated hypertension associated with a lower one-year mortality among older residents of long-term care facilities with multimorbidity?

Short title: Is treated hypertension related to lower mortality in LTCF residents?

Anna Kańtoch¹, Agnieszka Pac², Barbara Wizner¹, Jadwiga Wójkowska-Mach³, Piotr Heczko³, Tomasz Grodzicki¹, Barbara Gryglewska¹

1 Jagiellonian University Medical College, Faculty of Medicine, Department of Internal Medicine and Gerontology, University Hospital in Kraków, Kraków, Poland

2 Jagiellonian University Medical College, Faculty of Medicine, Department of Epidemiology and Preventive Medicine, Kraków, Poland

3 Jagiellonian University Medical College, Faculty of Medicine, Chair of Microbiology, Kraków, Poland

Correspondence to: Barbara Gryglewska, MD, PhD, Department of Internal Medicine and Gerontology, Faculty of Medicine, Jagiellonian University Medical College, University Hospital in Kraków, 2 Jakubowskiego Str., building I, 30-688 Kraków, Poland, phone: 0048 12 351 66 61, 12 400 29 00 Fax 12 400 29 17, e-mail: barbara.gryglewska@uj.edu.pl; bqrygle@su.krakow.pl

Conflicts of interest: none declared.

Key words: arterial hypertension, long-term care facility, multimorbidity, residents, survival
What is new?

Institutionalized populations are usually excluded from clinical trials because of multimorbidity, polypharmacy, cognitive impairment and frailty, so there is no precise evidence-based rules for treating hypertension in this population. That is why, it is recommended that pharmacotherapy of nursing home residents should be cautious and individualized. This is the first such large study in the Polish geriatric population with multimorbidity in long-term care facilities (LTCF), which enriches knowledge about the safety and benefits of antihypertensive treatment among the institutionalized frail older adults. The study showed that one-year survival was significantly higher in LTCF residents with treated hypertension compared to other multimorbid residents. In addition, the study showed that appropriate treatment of hypertension in older residents of nursing homes can be beneficial and should be introduced in the frail, institutionalized population, even in short period of time, as it may be a factor that protects the resident from premature death.
ABSTRACT

Introduction: Long-term care facility (LTCF) residents are typically excluded from clinical trials due to multimorbidity, dementia, and frailty, so there are no clear evidence-based rules for treating arterial hypertension in this population. Moreover, the role of hypertension as mortality risk factor in LTCFs has not yet been clearly established.

Objectives: The study aimed to investigate whether treated hypertension is associated with lower mortality among older LTCF residents with multimorbidity.

Patients and methods: The study was performed in a group of 168 residents aged ≥ 65 years in three LTCFs. Initial assessment included blood pressure (BP) measurements and selected geriatric scales: MNA-SF, AMTS and ADL. Hypertension, comorbidities, pharmacotherapy, antihypertensive drugs and mortality during one-year follow-up were extracted from the medical records. The data was compared in groups: Survivors and Deceased.

Results: Survivors and Deceased revealed similar age, DBP, number of diseases, medications, and antihypertensive drugs. However, Deceased had significantly lower SBP (P <0.05) and presented significantly worse functional, nutritional and cognitive status than Survivors (P <0.001). Hypertension (P <0.001) and antihypertensive therapy (P <0.05) were significantly more frequent among Survivors. Significantly more of the hypertensive-treated than other multimorbid residents survived the follow-up (P <0.001). Logistic regression analysis showed that treated hypertension had a protective effect on mortality [OR = 0.11 (95% CI, 0.03-0.39); P <0.001].

Conclusions: One-year survival of LTCF residents with treated hypertension was significantly higher than the others. Appropriate antihypertensive therapy may be a protective factor against death in frail nursing home residents, even in short period of time.
INTRODUCTION

The population is growing and aging, which is why more and more people may be placed in long-term care facilities (LTCFs) due to mental or physical disabilities. Residents of LTCFs could be characterized as disabled, frail, with cognitive impairment, malnutrition, and multimorbidity. These characteristics are the reason why this population is often excluded from randomized clinical trials and the literature on studies, algorithms or guidelines for treating the most common diseases in this population is still a gap. We only know that this population should be treated with caution, and therapy should be individualized [1].

Arterial hypertension is a well-known risk factor for many cardiovascular diseases, including coronary heart disease, chronic heart disease, stroke, and many other complications. Long-term antihypertensive therapy has been shown to reduce the incidence of cerebral, cardiovascular and mortality events, also in the older population. Recent randomized trials and meta-analysis revealed significant reductions in cardiovascular morbidity and mortality with antihypertensive treatment among community-living individuals [2-6].

The prevalence of hypertension among nursing home residents’ ranges from 16% to 71%, and over 70% of them are treated with antihypertensive drugs [7], but the role of hypertension as a risk factor for mortality in LTCFs has not yet been clearly established, particularly in a short period of time. Moreover, there is some controversy regarding the relationship between blood pressure (BP) level and mortality in older hypertensive residents of LTCFs. A Predictive Values of Blood Pressure and Arterial Stiffness in Institutionalized very aged (≥ 80 years) population (PARTAGE) study revealed that elevated BP was not associated with a higher risk of mortality or major cardiovascular events among nursing home residents during 2-year follow-up [8]. However, they also showed a significant interaction between low systolic BP (SBP) and a higher risk of mortality in patients with low SBP who received multiple BP medications compared to other participants [9]. The mortality risk is particularly high among
nursing home residents aged above 80 years old, as exhibited by Rådholm et al. (2016) in a Swedish population, during a 30-month follow-up period [10].

The study aimed to investigate whether the diagnosis and treatment of hypertension is associated with a lower one-year all-cause mortality among older LTCF residents with multimorbidity and geriatric problems.

PATIENTS AND METHODS

Study design

The presented analysis was a substudy of continuous surveillance of infections in long-term care facilities, carried out among 193 residents [11]. In short, the processes of LTCFs selection and recruitment of patients were as follows. Based on the list of LTCFs in Kraków (Poland), we selected facilities for old and chronically ill patients, in which the number of residents over 65 years old was over 50%. The study was performed in three LTCFs: two residential homes and one nursing home. Subjects recruited into the study had to be able to give written informed consent before inclusion. The exclusion criterion was age under 65.

An initial assessment of sociodemographic and medical data, estimation of functional capacity, and clinical evaluation results were collected in each setting at the beginning of the study. All-cause mortality was recorded after one year of follow-up on the basis of medical records. During the observation period, there were no cases of transfer, dismissal or discharge of the study participants from the facility. The study protocol was approved by the Jagiellonian University's local ethics committee and conformed to the guidelines set forth by the Declaration of Helsinki. The study protocol was also approved and implemented voluntarily by the management of chosen institutions.
Terminology

A resident was defined as someone who had been at the LTCF for more than 48 hours during the initial assessment. A residential home was defined as a place where people who are incapable of independent living, require assistance and/or supervision in performing daily activities. A nursing home was defined as a place of residence of people requiring 24-hour medical care or a qualified nurse.

Throughout the text, the authors use the following terms: Survivors to denote those residents who survived the entire follow-up period and Deceased to denote those residents who died before the end of the follow-up period.

Tests and Measures

Prepared questionnaire forms were completed, and study measurements were carried out by trained, qualified nursing staff from each facility. Data from the medical records of residents included information on hypertension, comorbidities, pharmacotherapy, antihypertensive medication use, and follow-up mortality. An initial clinical evaluation included blood pressure, weight and height measurements, and assessment of nutritional, functional and cognitive status on the basis of geriatric scales.

Definition of hypertension

Blood pressure measurements were carried out twice at the upper arm in a sitting position using oscillometric devices. The average of two measurements was taken for further analysis. Hypertension was defined as a history of hypertension or antihypertensive treatment (information extracted from medical records); or hypertension was diagnosed based on baseline measurements using oscillometric devices based on the following definition of hypertension: systolic blood pressure (SBP) of 140 mm Hg or greater and/or diastolic blood
pressure (DBP) 90 mm Hg or more [12]. Uncontrolled hypertension was defined as SBP of 140 mm Hg or greater and/or DBP 90 mm Hg or more in patients taking antihypertensive medications that were identified by investigators from baseline BP measurements [13].

**Nutritional status**

Weight and height were used to calculate the Body Mass Index (BMI) according to the following formula: the body mass in kilograms was divided by the square of the body height in meters. These measurements were carried out in standard procedures by researchers. BMI was not calculated among bedridden residents. The risk of malnutrition was estimated using a validated nutrition screening tool- Mini Nutritional Assessment Short-Form (MNA-SF) [14]. The scores range of MNA-SF was 0 to 14. Normal nutritional status was defined when a person reached 12 - 14 points; the risk of malnutrition was at 8 - 11 points, malnutrition was diagnosed at 0 - 7 points.

**Functional and cognitive status**

Functional and cognitive capacity was estimated using the following tools: basic Activity of Daily Living and Abbreviated Mental Test Score. Activities of Daily Living (ADL- scores range from 0 to 6) consisted of self-care tasks that included but were not limited to functional mobility, bathing, and showering, dressing, self-feeding, personal hygiene/ grooming, and toilet hygiene [15]. Abbreviated Mental Test Score (AMTS- scores range from 0 to 10), a rapid screening, was conducted to assess aged patients for the possibility of dementia [16]. A score of 0 - 3 points was interpreted as severe cognitive impairment, 4 - 6- moderate cognitive impairment, and more than 6 points- normal mental status.
Statistical analysis

Descriptive and comparative statistics as well as logistic regression were used for statistical analysis. Descriptive statistics were based on the mean, standard deviation (SD), median, and quartile distribution. Study participants' data were compared between two groups: Survivors (group I) and Deceased (group II) during a one-year of follow-up. Comparisons between two groups were performed using the t-student test and the U-Mann Whitney test for normally distributed continuous variables and those for which normality was not confirmed, respectively. Chi-Square test was used to compare categorical variables between groups. A multivariable logistic regression model was used to determine independent mortality risk factors among older residents of long-term care facilities with multimorbidity. First, the Chi-square test was used to perform the univariate analysis of categorical variables. A multivariable analysis was then performed using logistic regression for risk factors considered significant in the univariate analysis. All logistic regression results were presented as Odds Ratios (OR) and 95% Confidence Intervals (CI). *P values of < 0.05* were considered statistically significant. Statistical analysis was performed using Statistica 13.

Compliance with ethical standards: All procedures performed in study involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments, or comparable ethical standards.

Consent to participate: Informed consent was obtained from all individual participants included in the study.
RESULTS

General characteristics

The total study group consisted of 193 residents from three LTCFs: 107 people were selected from a nursing home and 86 from two residential homes. However, we did not obtain blood pressure measurements for 4 residents, and in 21 cases the residents were under the age of 65, so these study participants were excluded from the analysis and ultimately the study sample consisted of 168 people (Figure 1).

The analyzed population

The general characteristics of the analyzed population are as follows: the mean (SD) age was 78.7 (8.5) years, mostly women (62%), most of study participants were at risk of malnutrition based on the median MNA-SF score 11 (range 0 - 14), in a normal mental state based on median AMTS score 7 (range 0 - 10) and showed moderate impairment based on median ADL score 3 (range 0 - 6). The majority of study participants were diagnosed with four or more diseases and were taking six or more medications. The mean (SD) systolic and diastolic blood pressures were 128 (18.6) and 72 (11.0) mm Hg, respectively. Twenty-one residents (12.5%) died during the one-year follow-up, of which only five (3%) were residents with hypertension.

Study groups

Survivors (n = 147) and Deceased (n = 21) revealed similar age, diastolic BP, number of diseases, number of medications, and antihypertensive drugs. Deceased presented a significantly worse functional, nutritional and cognitive status than Survivors (Table 1). The mean value of systolic blood pressure (SBP) was significantly lower among Deceased than Survivors ($P < 0.05$). What is more, Deceased lived more often in a nursing home and
suffered from dementia, diabetes and urinary incontinence. Hypertension ($P < 0.001$) and antihypertensive therapy ($P < 0.05$) were significantly more frequent among Survivors than Deceased. All hypertensive residents were treated with antihypertensive drugs throughout the follow-up period. Oral antidiabetic were significantly more common among Deceased than Survivors ($P = 0.009$).

**Hypertension**

Figure 2 shows that 95% of the hypertensive-treated population (n = 94) and 78% of the other multimorbid population (n = 74) survived one-year follow-up ($P < 0.001$). Survival in the older LTCF population was higher by 17% in residents with treated hypertension compared to other multimorbid residents.

In logistic regression analysis (Table 2), the presence of hypertension, diabetes and dementia were significantly related to mortality, while urinary incontinence was not significantly associated with mortality. The analysis revealed that treated hypertension had a protective effect on mortality of residents of long-term care facilities [OR = 0.11 (95% CI, 0.03 to 0.39); $P < 0.001$].

**DISCUSSION**

Our study showed that treated hypertension had a protective effect on mortality in the LTCF population, and the survival was 17% higher in residents with treated hypertension. In addition, in our study, we characterized the population of Deceased residents of LTCFs who were more likely to die in short-term follow-up. Deceased can be characterized as follows: they live in a nursing home more often, have much lower SBP, and significantly worse nutritional, functional and cognitive status than Survivors. Moreover, the diagnosis of hypertension was significantly less common in the population of Deceased. Our findings suggest that the lower SBP could have had an impact on the deterioration of cognitive,
functional and even nutritional status, and next on the earlier death of the Deceased group. This observation is a novelty as the literature only shows an association between low SBP and cognitive function in the older population. A prospective cohort study with a 1-year follow-up conducted among older adults aged ≥ 75 years undergoing antihypertensive therapy showed that SBP < 130 mm Hg is associated with additional cognitive decline [17]. The impact of low SBP on the nutritional and functional status in the population of nursing home residents has not been clearly defined. Further research will focus on these correlations. However, it is probable that degenerative changes in the central nervous system may affect hunger regulation and physical fitness.

Hypertension is a well-recognized risk factor for cardiovascular morbidity and mortality, even in the geriatric population [1, 18]. Optimal control of blood pressure is necessary to reduce the risks of cardiovascular, cerebrovascular, and renal diseases [12, 19]. The definition of hypertension in very old patients (≥ 80 years) is still under discussion, but according to the ESC/ESH 2018, pharmacotherapy should be initiated at a BP threshold of ≥ 160/90 mm Hg [20].

However, the aggressive lowering of blood pressure is still controversial in very old or frail patients, especially nursing homes. Recent randomized trials and meta-analysis which revealed the benefits of intensive blood pressure control among the older hypertensives did not include very frail patients, those with multiple morbidities, significant cognitive impairment, loss of autonomy, and residents of nursing homes [2-6].

Frailty status is probably the most important factor modifying the relationship between blood pressure and outcomes of both observational studies among the community and institutionalized geriatric populations [8-10, 21-23]. Longitudinal analysis of primary care electronic health record data for a large cohort of community-dwelling octogenarians in the United Kingdom found that mortality rates increased with frailty category [24]. At each level
of frailty, mortality rates were lowest among participants with SBP from 140 to 159 mm Hg, and highest at SBP < 110 mm Hg. The results were similar in those treated with antihypertensive medications and those who were not on treatment. Similarly, Dregan et al. (2016) showed that all-cause mortality was higher in the lower extremes of SBP values (< 110 mm Hg) and the lowest risk of cardiovascular disease and all-cause mortality among treated octogenarians was observed in the SBP range of 140 to 149 mm Hg and of 160 to 169 mm Hg in the community-dwelling octogenarians [25]. In the Milan Geriatrics study, higher SBP was related to lower mortality among functionally and cognitively impaired aged subjects [23].

In the nursing home cohort, Rådholm et al. (2016) revealed that very old participants with SBP < 120 mm Hg had higher mortality compared to those with SBP 120–139 mm Hg, and this association was independent of changes in the use of antihypertensive medications [10]. However, Benetos et al. (2015) presented that residents with SBP below 130 mm Hg who received combination antihypertensive therapy had a higher risk of death compared to the rest of the participants [9]. Similarly, Kerry et al. (2020) found that the use of multiple antihypertensive medications among hypertensive residents in residential care services in Australia was associated with an increased risk of death, particularly in residents with dementia and frailty [26]. In our study, we also observed lower values of SBP among the Deceased, although they took antihypertensive medications less frequently than Survivors. However, the presence of diabetes and geriatric syndromes (dementia, urinary incontinence) also had a negative impact on the probability of survival.

The association of frailty and hypertension has not yet been precisely determined. The latest meta-analysis published by Vetrano et al. (2018) revealed that the pooled prevalence of hypertension in frail individuals was 72%, and the pooled prevalence of frailty in individuals with hypertension was only 14% [27]. Frailty may induce to increase BP values by chronic
inflammation which directly stimulates the renin-angiotensin-aldosterone system [28].

Moreover, frailty has been shown to reduce the ability to use adenosine triphosphate, which may impair vascular smooth muscle relaxation [29].

In addition, according to the analysis of data from the UK Biobank, the probability of frailty in hypertensive subjects after adjustment to age, gender, socioeconomic status, smoking and BMI was significantly higher compared to people without hypertension [30]. The influence of arterial hypertension on the occurrence of frailty is probably related to the increased incidence of cardiovascular and cerebrovascular diseases.

On the other hand, the diagnosis of hypertension and its optimal treatment may be a protective factor against death, as demonstrated in our institutional geriatric population. As in our study, data from the Veterans Health Administration showed that the diagnosis of hypertension was one factor protecting the survival of community-dwelling veterans aged 80–99 [31]. Lately, Meng et al. (2018) documented the association of preexisting hypertension with reduced cardiovascular mortality in patients with systolic heart failure, even after adjustment for all potential risk factors [32]. Probably, appropriate constant care and protection of patients through antihypertensive treatment may have prognostic significance even for older inhabitants of long-term care facilities. This assumption was confirmed by the results of extended follow-up in older populations of randomized, placebo-controlled trials for hypertension treatment [33-35]. The Syst-Eur extension results showed that immediate treatment compared to delayed treatment reduced the incidence of stroke and cardiovascular complications in younger elderly with hypertension [33]. In the SHEP trial, over four years of the more extended treatment period for isolated systolic hypertension was associated with a longer life expectancy after 22 years of follow-up in the initially active treatment group than in the previous placebo group [34]. The results of the extension of the HYVET trial showed that the benefits of blood pressure control increased within 12 months, even in octogenarians.
In the Polish multicenter WOBASZ II study, it was shown that the highest control of arterial hypertension (37.7%) was observed among patients aged 80 years and older [36].

Although lowering blood pressure is a necessary goal to reduce cardiovascular events in hypertensive patients, reducing inflammation in hypertension may also be significant. Antihypertensive drugs such as angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEIs/ARBs) present anti-inflammatory activity, but also beta-blockers and calcium channel blockers may modify inflammatory markers [37]. Probably, antihypertensive treatment may also reduce inflammation among frailty and pre-frailty subjects and affect survival. In our study, Survivors took antihypertensive drugs more frequently than Deceased ($P < 0.05$). This observation may be supported by the results of a study conducted among 52,727 hospitalized patients with sepsis, which showed that short-term mortality from sepsis was lower among those who were already treated with ACEIs/ARBs when sepsis occurred [38].

A pooled analysis by Lippi et al. (2020) suggested that hypertension may be associated with up to 2.5 times higher risk of severe and fatal COVID-19, especially in older adults [39]. On the other hand, Meng et al. (2020) showed that ACEIs/ARBs improve the clinical outcomes of COVID-19 patients with hypertension by regulating the immune function and suppressing inflammatory responses [40]. Several recently published studies have confirmed that ACEIs/ARBs are not associated with increased mortality in hypertensive patients with COVID-19 and should not be discontinued [41-44]. A systematic review and meta-analysis by Wang et al. (2021) supported this observation and added that the use of ACEIs/ARBs is associated with a lower risk of ventilator support [45].

Our study had some limitations. The study only provided the results of all-cause mortality. What is more, the study population was not very large, and the follow-up period was only a year, but even in such a relatively short time, healthcare providers need more information to
consider making the proper care decisions. Another weak point could be the inclusion of study participants from both nursing and residential homes. However, this study's main aim was to investigate the geriatric population of LTCFs in general rather than under specific conditions, which can be considered the strength of the study. In addition, we did not assess the frailty syndrome among the study participants, which may be a weakness of our study as it may be an important modifying factor in the relationship between BP values and outcomes. Also, we could not obtain information from institutions about the presence of complications, cardiovascular events, and exacerbations of chronic diseases in the studied population during the follow-up period.

CONCLUSIONS

Our study showed that one-year survival in the older LTCF population was higher in residents with treated hypertension. Appropriate treatment of hypertension may be a factor that protects from death in the frail nursing home residents, even in a short period of time.

The results of the study may suggest that healthcare professionals in any long-term care facility should periodically screen older LTCF residents to detect and evaluate the effectiveness of treatment for hypertension in this particular population. The follow-up care and antihypertensive treatment of hypertensive residents in LTCFs may be prognostic as it may reduce the incidence of many cardiovascular side effects. Treating hypertension in this population may also provide systematic medical visits, which may give a chance to find other health problems. What is more, systematic medication review, screening for malnutrition and dementia for every LTCF resident are also very important to implement not only on admission to the facility, but also periodically during the stay in the facility. This minor intervention may reduce the risk of hospitalization, for example due to drug-drug interactions, which is a very common cause of hospitalization in the geriatric population.
Contribution statement

AK conceived the concept and design of the study, performed analysis and interpretation of data, wrote the article and gave final approval of the version to be submitted. AP contributed to interpretation of data, revised the article critically for important intellectual content and gave final approval of the version to be submitted. BW contributed to interpretation of data, revised the article critically for important intellectual content and gave final approval of the version to be submitted. JWM contributed to acquisition of data, coordinated funding for the project, revised the article critically for important intellectual content and gave final approval of the version to be submitted. PH contributed to acquisition of data, revised the article critically for important intellectual content and gave final approval of the version to be submitted. TG conceived the concept and design of the study, contributed to acquisition of data, performed interpretation of data, revised the article critically for important intellectual content and gave final approval of the version to be submitted. BG conceived the concept and design of the study, contributed to acquisition of data, performed interpretation of data, contributed to writing the article and revised it critically for important intellectual content and gave final approval of the version to be submitted.

Acknowledgements:

The Ministry of Science and Higher Education, No. N N404 047236; to JWM.
References:

1. Kańtoch A, Gryglewska B, Wójkowska-Mach J, et al. Treatment of Cardiovascular Diseases Among Elderly Residents of Long-term Care Facilities. JAMDA. 2018; 19: 428-432.

2. Warwick J, Falaschetti E, Rockwood K, et al. No evidence that frailty modifies the positive impact of antihypertensive treatment in very elderly people: an investigation of the impact of frailty upon treatment effect in the HYpertension in the Very Elderly Trial (HYVET) study, a double-blind, placebo-controlled study of antihypertensives in people with hypertension aged 80 and over. BMC Med. 2015; 13: 78.

3. Williamson JD, Supiano MA, Applegate WB, et al. Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged ≥75 Years: A Randomized Clinical Trial. JAMA. 2016; 315: 2673-2682.

4. Ettehad D, Emdin CA, Kiran A, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. Lancet. 2016; 387: 957-967.

5. Bundy JD, Li C, Stuchlik P, et al. Systolic Blood Pressure Reduction and Risk of Cardiovascular Disease and Mortality: A Systematic Review and Network Meta-analysis. JAMA Cardiol. 2017; 2: 775-781.

6. Weiss J, Freeman M, Low A, et al. Benefits and Harms of Intensive Blood Pressure Treatment in Adults Aged 60 Years or Older: A Systematic Review and Meta-analysis. Ann Intern Med. 2017; 166: 419-429.

7. Welsh T, Gladman J, Gordon AL. The treatment of hypertension in care home residents: a systematic review of observational studies. JAMDA. 2014; 15: 8-16.

8. Benetos A, Gautier S, Labat C, et al. Mortality and cardiovascular events are best predicted by low central/peripheral pulse pressure amplification but not by high blood
pressure levels in elderly nursing home subjects: the PARTAGE (Predictive Values of Blood Pressure and Arterial Stiffness in Institutionalized Very Aged Population) study. J Am Coll Cardiol. 2012; 60: 1503-1511.

9. Benetos A, Labat C, Rossignol P, et al. Treatment With Multiple Blood Pressure Medications, Achieved Blood Pressure, and Mortality in Older Nursing Home Residents: The PARTAGE Study. JAMA Intern Med. 2015; 175: 989-995.

10. Rådholm K, Festin K, Falk M, et al. Blood pressure and all-cause mortality: a prospective study of nursing home residents. Age Ageing. 2016; 45: 826-832.

11. Wójkowska-Mach J, Gryglewska B, Czekaj J, et al. Infection control: point prevalence study versus incidence study in Polish long-term care facilities in 2009-2010 in the Małopolska Region. Infection. 2013; 41:1-8.

12. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens. 2013; 31: 1281-1357.

13. Gebremichael GB, Berhe KK, Zemichael TM. Uncontrolled hypertension and associated factors among adult hypertensive patients in Ayder comprehensive specialized hospital, Tigray, Ethiopia, 2018. BMC Cardiovasc Disord. 2019; 19: 121.

14. Kaiser MJ, Bauer JM, Ramsch C, et al. Validation of the Mini Nutritional Assessment short-form (MNA-SF): a practical tool for identification of nutritional status. J Nutr Health Aging. 2009; 13: 782-788.

15. Katz S, Ford AB, Moskowitz RW, et al. Studies of illness in the aged. The Index Of ADL: A Standardized Measure Of Biological And Psychosocial Function. JAMA. 1963; 185: 914-919.
16. Hodkinson HM. Evaluation of a mental test score for assessment of mental impairment in the elderly. Age Ageing. 1972; 1: 233-238.

17. Streit S, Poortvliet RKE, Elzen WPJD, et al. Systolic Blood Pressure and Cognitive Decline in Older Adults With Hypertension. Ann Fam Med. 2019; 17: 100-107.

18. Forouzanfar MH, Liu P, Roth GA, et al. Global Burden of Hypertension and Systolic Blood Pressure of at Least 110 to 115 mm Hg, 1990-2015. JAMA. 2017; 317: 165-182.

19. Qaseem A, Wilt TJ, Rich R, et al. Pharmacologic Treatment of Hypertension in Adults Aged 60 Years or Older to Higher Versus Lower Blood Pressure Targets: A Clinical Practice Guideline From the American College of Physicians and the American Academy of Family Physicians. Ann Intern Med. 2017; 166: 430-437.

20. Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018; 39: 3021-3104.

21. Odden MC, Covinsky KE, Neuhaus JM, et al. The association of blood pressure and mortality differs by self-reported walking speed in older Latinos. J Gerontol A Biol Sci Med Sci. 2012; 67: 977-983.

22. Gutiérrez-Misis A, Sánchez-Santos MT, Banegas JR, et al. Walking speed and high blood pressure mortality risk in a Spanish elderly population. J Hum Hypertens. 2015; 29: 566-572.

23. Ogliari G, Westendorp RG, Muller M, et al. Blood pressure and 10-year mortality risk in the Milan Geriatrics 75+ Cohort Study: role of functional and cognitive status. Age Ageing. 2015; 44: 932-937.

24. Ravindrarajah R, Hazra NC, Hamada S, et al. Systolic Blood Pressure Trajectory, Frailty, and All-Cause Mortality >80 Years of Age: Cohort Study Using Electronic Health Records. Circulation. 2017; 135: 2357-2368.
25. Dregan A, Ravindrarajah R, Hazra N, et al. Longitudinal Trends in Hypertension Management and Mortality Among Octogenarians: Prospective Cohort Study. Hypertension. 2016; 68: 97-105.

26. Kerry M, Bell JS, Keen C, et al. Multiple antihypertensive use and risk of mortality in residents of aged care services: a prospective cohort study. Aging Clin Exp Res. 2020; 32: 1541-1549.

27. Vetrano DL, Palmer KM, Galluzzo L on behalf of the Joint Action ADVANTAGE WP4 group, et al. Hypertension and frailty: a systematic review and meta-analysis. BMJ Open. 2018; 8: e024406.

28. Muñoz-Durango N, Fuentes CA, Castillo AE, et al. Role of the Renin-Angiotensin-Aldosterone System beyond Blood Pressure Regulation: Molecular and Cellular Mechanisms Involved in End-Organ Damage during Arterial Hypertension. Int J Mol Sci. 2016; 17: 797.

29. Akki A, Yang H, Gupta A, et al. Skeletal muscle ATP kinetics are impaired in frail mice. Age (Dordr). 2014; 36: 21-30.

30. Hanlon P, Nicholl BI, Jani BD, et al. Frailty and pre-frailty in middle-aged and older adults and its association with multimorbidity and mortality: a prospective analysis of 493 737 UK Biobank participants. Lancet Public Health. 2018; 3: e323-e332.

31. Cho J, Copeland LA, Stock EM, et al. Protective and Risk Factors for 5-Year Survival in the Oldest Veterans: Data from the Veterans Health Administration. J Am Geriatr Soc. 2016; 64: 1250-1257.

32. Meng FC, Li YH, Lin GM, et al. Association of preexisting hypertension with the morality in patients with systolic heart failure in Taiwan: The TSOC-HFrEF registry. Indian Heart J. 2018; 70: 604-607.
33. Staessen JA, Thijssen L, Fagard R, et al. Effects of immediate versus delayed antihypertensive therapy on outcome in the Systolic Hypertension in Europe Trial. J Hypertens. 2004; 22: 847-857.

34. Kostis JB, Cabrera J, Cheng JQ, et al. Association between chlorthalidone treatment of systolic hypertension and long-term survival. JAMA. 2011; 306: 2588-2593.

35. Beckett N, Peters R, Tuomilehto J, et al. Immediate and late benefits of treating very elderly people with hypertension: results from active treatment extension to Hypertension in the Very Elderly randomised controlled trial. BMJ. 2011; 344: d7541.

36. Niklas A, Marcinkowska J, Kozela M, et al. Blood pressure and cholesterol control in patients with hypertension and hypercholesterolemia: the results from the Polish multicenter national health survey WOBASZ II. Pol Arch Intern Med. 2019; 129: 864-873.

37. Silva IVG, de Figueiredo RC, Rios DRA. Effect of Different Classes of Antihypertensive Drugs on Endothelial Function and Inflammation. Int J Mol Sci. 2019; 20: 3458.

38. Hsu WT, Galm BP, Schrank G, et al. Effect of Renin-Angiotensin-Aldosterone System Inhibitors on Short-Term Mortality After Sepsis: A Population-Based Cohort Study. Hypertension. 2020; 75: 483-491.

39. Lippi G, Wong J, Henry BM. Hypertension in patients with coronavirus disease 2019 (COVID-19): a pooled analysis. Pol Arch Intern Med. 2020; 130: 304-309.

40. Meng J, Xiao G, Zhang J, et al. Renin-angiotensin system inhibitors improve the clinical outcomes of COVID-19 patients with hypertension. Emerg Microbes Infect. 2020; 9: 757-760.
41. Pranata R, Permana H, Huang I, et al. The use of renin angiotensin system inhibitor on mortality in patients with coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis. Diabetes Metab Syndr. 2020; 14: 983-990.

42. COVID-19 RISk and Treatments (CORIST) Collaboration. RAAS inhibitors are not associated with mortality in COVID-19 patients: Findings from an observational multicenter study in Italy and a meta-analysis of 19 studies. Vascul Pharmacol. 2020; 135: 106805.

43. Baral R, White M, Vassiliou VS. Effect of Renin-Angiotensin-Aldosterone System Inhibitors in Patients with COVID-19: a Systematic Review and Meta-analysis of 28,872 Patients. Curr Atheroscler Rep. 2020; 22: 61.

44. Barochiner J, Martínez R. Use of inhibitors of the renin-angiotensin system in hypertensive patients and COVID-19 severity: A systematic review and meta-analysis. J Clin Pharm Ther. 2020; 45: 1244-1252.

45. Wang Y, Chen B, Li Y, et al. The use of renin-angiotensin-aldosterone system (RAAS) inhibitors is associated with a lower risk of mortality in hypertensive COVID-19 patients: A systematic review and meta-analysis. J Med Virol. 2021; 93: 1370-1377.
Table 1. The general characteristics of Survivors and Deceased residents.

|                               | N valid | Survivors (n = 147) | Deceased (n = 21) | P value |
|-------------------------------|---------|---------------------|-------------------|---------|
| Age, years, mean (SD)         | 168     | 78 (8.4)            | 79.5 (9.0)        | 0.792   |
| Female sex, number (%)        | 168     | 91 (62%)            | 13 (62%)          | 1.000   |
| Place of residence, number (%)|         |                     |                   |         |
| Nursing home                  | 168     | 73 (50%)            | 16 (76%)          | <0.05   |
| Residential home              |         | 74 (50%)            | 5 (24%)           |         |
| Measurement, mean (SD)        |         |                     |                   |         |
| Systolic BP, mm Hg            | 168     | 129 (19.2)          | 122 (12.4)        | <0.05   |
| Diastolic BP, mm Hg           | 168     | 72 (11.2)           | 71 (9.5)          | 0.176   |
| BP level* , number (%)        |         |                     |                   |         |
| BP ≤ 120/60 mm Hg             | 168     | 35 (24%)            | 5 (24%)           | 0.127   |
| BP: 120-139/60-89 mm Hg       |         | 69 (47%)            | 14 (67%)          |         |
| BP: ≥ 140/90 mm Hg            |         | 43 (29%)            | 2 (9%)            |         |
| Functional and nutritional status, median [quartile 1, quartile 3] |         |                     |                   |         |
| ADL, score                    | 165     | 3 [1 , 6 ]          | 0 [0 , 3 ]        | <0.001  |
| MNA-SF, score                 | 164     | 12 [9 , 13]         | 8 [6 , 10 ]       | <0.001  |
| Nutritional status based on the MNA-SF, number (%) |  |
|---------------------------------------------|---|
| normal                                      | 165 |
| number (%)                                  |    |
| normal                                      | 78 (54%) |
| risk of malnutrition                        | 46 (32%) |
| malnutrition                                | 20 (14%) |
| BMI, kg/m², mean (SD)                       | 119 |
| number (%)                                  |    |
| normal                                      | 25 (5.3) |
| risk of malnutrition                        | 22 (5.9) |
| 0.737                                       |    |
| Cognitive status, median [quartile 1, quartile 3] |  |
| AMTS, score                                 | 165 |
| number (%)                                  |    |
| AMTS, score                                 | 8 [6, 9] |
| risk of malnutrition                        | 4 [1.5, 7.5] |
| 0.001                                       |    |
| Number of diseases, median [quartile 1, quartile 3] | 166 |    |
| number (%)                                  |    |
| Number of diseases, median [quartile 1, quartile 3] | 4 [3, 5] |
| risk of malnutrition                        | 4 [2, 5] |
| 0.586                                       |    |
| Number of medications in general, median [quartile 1, quartile 3] | 162 |    |
| number (%)                                  |    |
| Number of medications in general, median [quartile 1, quartile 3] | 6 [4, 9] |
| risk of malnutrition                        | 7 [5, 10] |
| 0.074                                       |    |
| Number of antihypertensive drugs, median [quartile 1, quartile 3] | 168 |    |
| number (%)                                  |    |
| Number of antihypertensive drugs, median [quartile 1, quartile 3] | 2 [1, 3] |
| risk of malnutrition                        | 1 [0, 2] |
| 0.226                                       |    |
| Comorbidities, number (%)                   |  |
| Congestive heart failure                    | 168 |
| number (%)                                  |    |
| Congestive heart failure                    | 59 (40%) |
| risk of malnutrition                        | 11 (52%) |
| 0.287                                       |    |
| Coronary heart disease                      | 168 |
| number (%)                                  |    |
| Coronary heart disease                      | 99 (67%) |
| risk of malnutrition                        | 10 (48%) |
| 0.076                                       |    |
| Hypertension                                | 168 |
| number (%)                                  |    |
| Hypertension                                | 89 (61%) |
| risk of malnutrition                        | 5 (24%) |
| 0.001                                       |    |
| Uncontrolled hypertension                   | 168 |
| number (%)                                  |    |
| Uncontrolled hypertension                   | 48 (33%) |
| risk of malnutrition                        | 3 (14%) |
| 0.086                                       |    |
| Condition                        | Number (N) | Diagnosed (%) | Not Diagnosed (%) | p-value |
|---------------------------------|------------|---------------|-------------------|---------|
| Diabetes                        | 168        | 39 (27%)      | 13 (62%)          | <0.001  |
| Dementia                        | 168        | 47 (32%)      | 12 (57%)          | <0.05   |
| Urinary incontinence            | 168        | 51 (35%)      | 15 (71%)          | <0.001  |

Pharmacotherapy, number (%)

| Category                             | Number (N) | Diagnosed (%) | Not Diagnosed (%) | p-value |
|--------------------------------------|------------|---------------|-------------------|---------|
| Antihypertensive drugs in general    | 168        | 121 (82%)     | 13 (62%)          | <0.05   |
| Angiotensin-converting enzyme (ACE) inhibitors | 168 | 84 (57%) | 8 (38%) | 0.100 |
| Beta-blockers                        | 168        | 57 (39%)      | 7 (33%)           | 0.630   |
| Diuretics in general                 | 168        | 57 (39%)      | 8 (38%)           | 0.952   |
| Calcium channel blockers             | 168        | 26 (18%)      | 3 (14%)           | 0.699   |
| Mineralocorticoid receptor antagonist, MRA | 168 | 17 (12%) | 3 (14%) | 0.718 |
| Oral antidiabetic                    | 168        | 22 (15%)      | 8 (38%)           | 0.009   |

*Cut-off points based on the BP distribution (tertiles)*

Data are presented as means (SD), numbers (percentages) or median [quartile 1, quartile 3].

**Abbreviations:**

ADL, Activities of Daily Living (scores range from 0 to 6; the normal functional status: 5 - 6 points);

AMTS, Abbreviated Mental Test Score (scores range from 0 to 10; the normal mental status > 6 points);

BMI, Body Mass Index;

BP, Blood pressure;
MNA-SF, Mini Nutritional Assessment Short-Form (scores range from 0 to 14; the normal nutritional status: 12 - 14 points);

**Table 2.** Risk factors for mortality among older residents of long-term care facilities with multimorbidity.

| Risk factor         | Adjusted Odds Ratio\(^a\) | -95% CI | +95% CI | P value |
|---------------------|----------------------------|---------|---------|---------|
| Hypertension        | 0.11                       | 0.03    | 0.39    | <0.001  |
| Diabetes            | 8.14                       | 2.52    | 26.33   | <0.001  |
| Dementia            | 3.82                       | 1.17    | 12.48   | <0.05   |
| Urinary incontinence| 2.50                       | 0.79    | 7.92    | 0.117   |

\(^a\)The odds of death adjusted for hypertension, diabetes, dementia and urinary incontinence.

**Abbreviations:** CI, Confidence Intervals
Figure 1. Study flow chart

Figure 2. Survivors and Deceased due to the presence of hypertension.