Abstract

Background and objective: Frailty and disability are associated with cardiovascular risk factors, including hypertension, in older people; however, little is known about their association with ambulatory blood pressure (BP). Thus, we assessed the relationship of frailty and disability with ambulatory BP in older adults.

Design, setting, and participants: Cross-sectional study of 1047 community-living individuals aged ≥60 years in Spain.

Measurements: BP was determined with validated devices under standardized conditions during 24 hours. Frailty was defined as having 3 or more of the following criteria: weight loss, low grip strength, low energy, slow gait speed, and low physical activity. Disability was assessed with the Lawton-Brody questionnaire on instrumental activities of daily living. Associations with systolic BP (SBP) and dipping (nocturnal SBP decline) were modeled and adjusted for sociodemographic variables, body mass index, lifestyles, antihypertensive drug treatment, comorbidities, 24-hour heart rate, and conventional or ambulatory SBP as appropriate.

Results: Participants’ mean age was 71.7 years (50.8% men); 6% were frail and 8.1% had disability. Compared with nonfrail participants, those with frailty had 3.5 mm Hg lower daytime SBP (P = .001), 3.3% less SBP dipping (P = .003), and 3.6 mmHg higher nighttime SBP (P = .016). Compared with participants who are not disabled, those who are disabled had 2.5 mmHg lower daytime SBP (P = .002), 2.5% less SBP dipping (P = .003), and 2.7 mmHg higher nighttime SBP (P = .011).

Conclusions: In community-dwelling older adults, frailty and disability were independently associated with lower diurnal SBP, blunted nocturnal decline of SBP, and higher nocturnal SBP. These findings may help explain the higher mortality associated with low clinic SBP in frail older subjects observed in epidemiologic studies.

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associated with aging and chronic diseases, and also increase the risk of falls, hospitalizations, and mortality.14,15

A significant association of BP, hypertension, and other CVD risk factors with frailty and disability has been previously described.16–20 However, most studies on the relationship between BP and frailty/disability focused on conventional BP measurements,16–19 and only a few small, cross-sectional studies in older individuals have evaluated this relationship using ABPM.20–22 In addition, these latter studies were conducted in clinical settings or with voluntary patients, and adjusted for only a few covariates, not including important confounders (eg, physical activity, diet, or comorbidities).

A better characterization of the relationship between ABPM and frailty/disability could serve to identify the role of daytime and nighttime BP in these entities and to shed light on the complex and controversial relation between BP and mortality in older adults23,24; in particular, it remains poorly understood why in older adults with frailty or poor functional status, observational studies usually find higher mortality associated with lower BP while clinical trials show benefit from BP lowering even in the oldest old.25,26 Thus, this study examines the relationship of frailty and disability with conventional BP and daytime and nighttime ambulatory BP in a large sample of community-dwelling older adults in Spain.2

Methods

Study Design and Population

Data were taken from the Seniors-ENRICA cohort, whose methods have been previously reported.25,31 In brief, this cohort was established in 2008–2010 with 2614 individuals selected through stratified random sampling from the population aged ≥60 years in Spain.2 At baseline, information on sociodemographic variables, lifestyle, health status, and morbidity was collected by telephone interview; also a home visit was conducted to collect blood samples, and another home visit was performed in 2012–2013, when a second wave of data collection was performed with the surviving 2519 participants, of which 2037 provided updated information for the phone interview, the physical examination, diet, and medication. In this second wave, and because of logistic and cost reasons, ABPM was offered to 1698 individuals, and was performed in 1328 participants (response rate, 78.2%). Compared with participants without ABPM, those who underwent it had similar age and sex distribution, education levels, obesity, diabetes, current smoking, and previous history of CVD.

Personnel involved in data collection were trained and certified in the study procedures. Study participants gave written informed consent. The study was approved by the Clinical Research Ethics Committee of the “La Paz” University Hospital in Madrid.

Blood Pressure Measurement

BP was measured using standardized procedures and conditions, with validated automatic devices (Omron M6; Omron Healthcare, Lake Forest, IL) and appropriate-sized cuffs. BP was determined 3 times at 2-minute intervals, after resting 5 minutes in a seated position. In the analyses, BP was calculated as the mean of the last 2 of 3 readings. Thereafter, 24-hour ABPM was performed using a validated automated noninvasive oscillometric device (Microlife WatchBPO3 monitor; Microlife Corp, Widnau, Switzerland),28 programmed to register BP at 20-minute intervals during the day and at 30-minute during the nighttime for the 24-hour period. Appropriate cuff sizes were used. The patients were instructed to maintain their usual activities but keeping the arm extended and immobile at the time of cuff inflation. Valid ABPM registries had to fulfill several pre-established criteria, including 24-hour duration and at least 70% of systolic BP (SBP) and diastolic BP (DBP) successful recordings during the daytime and nighttime periods.24 Daytime and nighttime periods were defined individually according to the patient’s self-reported time of going-to-bed and getting-up.

Frailty Assessment

We used the operational definition of frailty developed by Fried et al.27 in the Cardiovascular Health Study. Specifically, frailty was defined as having at least 3 of the following 5 criteria: (1) exhaustion, based on a response of “≥3-4 days a week” to any of the following questions from the Center for Epidemiologic Studies Depression Scale: “I felt that anything I did was a big effort” or “I felt that I could not keep on doing things”; (2) low physical activity, defined as walking <2.5 h/wk in men and <2 h/wk in women; (3) slow walking speed, defined as the lowest quintile in our study sample for the 3-m walking speed test, adjusted for sex and height; (4) weight loss, defined as involuntary loss of ≥4.5 kg in the preceding year; and (5) weakness (low grip strength), defined as the lowest quintile in our study sample of maximum strength on the dominant hand, adjusted for sex and body mass index (BMI); strength was measured twice with a Jamar dynamometer on the dominant hand.

Disability Assessment

Disability was assessed according to instrumental activities of daily living (IADL) with the Lawton–Brody questionnaire.36 This scale evaluates the individual’s ability to use the telephone, go shopping, prepare meals, do housework, do laundry, use different means of transportation, take medication, and manage finances. Owing to cultural issues, meal preparation, housework, and laundry were excluded in men; thus, summary scores ranged from 0 to 5 in men, and from 0 to 8 in women. Disability was defined as <5 points in men and <8 in women.36

Other Variables

Study participants reported their sociodemographic characteristics: sex, age, educational level (primary; secondary; university), marital status (single/separated/widowed; married), cohabitation (living alone; living with the family, with flat mate, in an institution, or accompanied in any other situation); smoking status (no; yes); and alcohol consumption (no-drinker; drinker). Salt intake (g/d) was assessed with a validated computerized diet history developed from that used in the European Prospective Investigation into Cancer and Nutrition cohort study in Spain.37,38 Adherence to the Mediterranean diet was summarized with the Mediterranean diet adherence screener (MEDAS).39 MEDAS consists of 12 items with targets on food consumption and another 2 items with targets for food intake habits characteristic of the Mediterranean diet in Spain. One point is given for each target achieved. The total MEDAS score ranged from 0 to 14, with a higher score indicating better Mediterranean adherence. For the purpose of analysis, we excluded alcohol consumption from the MEDAS as this variable is considered separately in this study. Information on physical activity was also obtained with the validated European Prospective Investigation into Cancer and Nutrition study instrument, and individuals were classified as inactive or active.40 Participants also reported their usual sleep quality during the night (very good/good; or bad/very bad).41 Medication use was collected by a face-to-face interview and verified against drug packaging. Participants also reported if they suffered from any of the following physician-diagnosed diseases: cardiovascular diseases (myocardial infarction, stroke, and heart failure), diabetes mellitus, cancer at any site, asthma or chronic bronchitis, osteoarthritis, arthritis, hip fracture), or depression requiring drug treatment.
Beta is the change in the corresponding SBP parameter per 1 additional frailty category (non frail, prefrail, frail), was analyzed as a continuous variable but was classified into non-frailty, frailty (1–2 criteria), and frailty (≥3 criteria) for a later analysis; and disability was dichotomized (no/yes). The regression models were adjusted for sociodemographic variables (age, sex, educational level, marital status, and cohabitation), BMI, smoking, alcohol consumption, salt intake, Mediterranean diet score, physical activity, sleep quality, number of antihypertensive drugs, number of comorbidities, conventional SBP, nighttime SBP (for daytime SBP outcome), daytime SBP (for nighttime SBP outcome), 24-hour SBP (for dipping and night/day ratio outcomes), and 24-hour heart rate. These variables were coded as continuous/numerical (age, BMI, salt intake, MEDAS, number of BP medication, number of comorbidities, BPs, and heart rate) or categorical (the other variables) as defined above. Lastly, we examined the adjusted mean daytime SBP, nighttime SBP, dipping, and night/day ratio according to the frailty status (no/prefrail/frail) and disability status (no/yes), using general linear models adjusted for the same covariates as before.

Because we observed no significant interaction of the association between frailty or disability and BPs with sex, we presented results for all the study population. Statistical significance was set at \( P < 0.05 \), and the Bonferroni correction was used for post-hoc multiple comparisons. Finally, BMI was calculated as measured weight in kilogram divided by square height in meter.

**Statistical Analyses**

The analyses were conducted among 1047 individuals with at least 70% valid ABPM readings and complete information on study variables (78.8% of all with available ABPM). We used the relative percentage of systolic BP fall during the night [(daytime BP - nighttime BP)/daytime BP] and the night/day ratio as estimates of nocturnal BP dipping, such that the lower the ratio, the greater the dipping.\(^7\)\(^8\)

To compare means across groups, we used the Student t-test or analysis of variance, whereas for proportions we used the \( \chi^2 \) test. We examined the multivariable relationship of frailty and disability with daytime and nighttime SBP as well as with systolic dipping and night/day ratio, as only these BP variables were significantly associated with frailty/disability in bivariate analyses and given that the systolic BP component is predominant in older people.\(^6\)\(^9\) We ran multiple linear regressions with daytime SBP, nighttime SBP, systolic dipping and SBP night-to-day ratio modeled as continuous outcomes, and frailty and disability as the main independent variables. Frailty score was analyzed as a continuous variable but was classified into non-frailty, frailty (1–2 criteria), and frailty (≥3 criteria) for a later analysis; and disability was dichotomized (no/yes). The regression models were adjusted for sociodemographic variables (age, sex, educational level, marital status, and cohabitation), BMI, smoking, alcohol consumption, salt intake, Mediterranean diet score, physical activity, sleep quality, number of antihypertensive drugs, number of comorbidities, conventional SBP, nighttime SBP (for daytime SBP outcome), daytime SBP (for nighttime SBP outcome), 24-hour SBP (for dipping and night/day ratio outcomes), and 24-hour heart rate. These variables were coded as continuous/numerical (age, BMI, salt intake, MEDAS, number of BP medication, number of comorbidities, BPs, and heart rate) or categorical (the other variables) as defined above. Lastly, we examined the adjusted mean daytime SBP, nighttime SBP, dipping, and night/day ratio according to the frailty status (no/prefrail/frail) and disability status (no/yes), using general linear models adjusted for the same covariates as before.

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### Table 1

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<td>496 (47.4)</td>
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<td>962 (91.9)</td>
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<td>72.6 (6.7)</td>
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#### Table 2

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#### Table 3

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The relationships were modeled through multiple linear regressions adjusted for sociodemographic variables (age, sex, educational level, marital status, and cohabitation), BMI, smoking, alcohol, salt intake, MEDAS, physical activity, sleep quality, number of antihypertensive drugs, number of comorbidities, conventional SBP, nighttime SBP (for daytime SBP), daytime SBP (for nighttime SBP), 24-hour SBP (for dipping and night/day ratio), and 24-hour heart rate. Beta is the change in the corresponding SBP parameter per 1 additional frailty category (non frail, prefrail, frail).
Comparison: The analyses were performed with the SPSS v 21 (IBM, Armonk, New York).

Results

Among the 1047 participants, mean age was 71.7 years, 50.8% were men, 6% were frail, 47.4% prefrail, and 8.1% had disability. Mean conventional, 24-hour, daytime, and nighttime SBP were 137.8, 123.6, 126.6, and 117.1 mm Hg, respectively. Compared with individuals without frailty or disability, those with these conditions were older, more frequently women, less frequently married and alcohol drinkers, less adherent to the Mediterranean diet, more physically inactive, with worse sleep quality and higher BMI and comorbidity (Table 1).

Those with frailty (and prefrailty) or disability had not significantly different mean conventional and 24-hour SBP, but they had lower daytime SBP and less systolic dipping, and higher nighttime SBP, systolic night/day ratio, and 24-hour heart rate than their nonfrail counterparts who are not disabled (Table 1).

After full adjustment for potential confounders, 1 additional frailty category (nonfrail, prefrail, frail) was significantly associated with a 1.542-mm Hg lower daytime SBP (P = .001), a 1.334-mm Hg higher nighttime SBP (P = .006), a 1.334% less SBP dipping (P = .001), and a 0.012 higher systolic night/day ratio (P = .001) (Table 2). Compared with participants who are not disabled, those who are disabled had a 2.464-mm Hg lower daytime SBP (P = .002), 2.762-mm Hg higher nighttime SBP (P = .001), 2.599% less systolic dipping (P = .002), and 0.019 higher systolic night/day ratio (P = .008) (Table 3).

Lastly, adjusted mean daytime and nighttime systolic BPs, dipping, and night/day ratio according to frailty and disability status are shown in Figures 1 and 2. There was a statistical significant trend toward lower daytime SBP, higher nighttime SBP, lower nocturnal SBP decline, and higher night/day ratio values across the increasing frailty categories (Figure 1), and also in those with vs without disability (Figure 2). Specifically, daytime SBP was 3.5 mm Hg lower in frail patients (vs nonfrail) and 2.5 mm Hg lower in patients who are disabled (vs not disabled), and nighttime SBP was 3.6 mm Hg higher in frail patients and 2.7 mm Hg higher in those disabled.

Discussion

This study shows that nocturnal systolic BP was greater and dipping and daytime systolic BP were smaller in older adults with frailty or disability. These findings may be important because both higher nocturnal BP and blunted SBP decline have been associated with a worse CVD risk profile and an increased risk of CVD and all-cause mortality; also, the coexistence of these 2 BP conditions is associated with the worst risk profile. 

Interestingly, moderate reductions of nocturnal BP can be achieved with simple lifestyle measures. There is great variability in the prevalence of frailty depending on the measurement tool used but, as an average, 10% of people aged ≥65 years have frailty. The frequency of frailty in our study (6%) is similar to the 7% reported in community-dwelling participants aged ≥65 years in the Cardiovascular Health Study. Further, in the general US population, 10.3% of individuals with hypertension and 6.6% of nonhypertensive participants reported IADL disability. However, the direct cross-country
comparisons of disability prevalence could be difficult due to methodological differences among studies.46,47 Our results are in agreement with those reported by Yano et al20 in a smaller, cross-sectional study of 148 treated elderly hypertensive patients, where slower walking speed was associated with high nocturnal SBP level and with diminished nocturnal SBP dipping independently of the 24-hour BP levels. This association has also been reported in a small sample of 77 elderly individuals in Brazil where the frail group showed higher 24-hour and sleep SBP and DBP values than the nonfrail group.21 Our results are also consistent with those by Hajjar et al22 on 80 older adults with and without stroke, where less dipping magnitude in SBP was associated with slower gait speed and worse IADL.

Regarding potential mechanisms of the associations found, poor physical (and cognitive) function have been associated with brain lesions that could influence the BP dipping pattern.22 Also, reduced mobility during the day in patients who are frail or disabled may lower physical activity, which may alter the daytime BP profile and diminish nocturnal BP dipping.48 Moreover, functional disabilities could result from high BP (including less nocturnal dipping), possibly through the development of coronary disease, stroke, or white matter lesions.22

Our results have clinical implications. Observational epidemiologic studies,16,24,25 contrary to clinical trials,26–29 support the caution that frail older adults may not benefit from, and may even be harmed, by intensive BP lowering, which requires several medications.49 One recent study has suggested that the association of low SBP with higher mortality in the oldest individuals, even if frail, may be explained by reverse causation because of the decline of SBP close to death.50 Although exploratory analyses in some major trials have found benefit from lowering BP across frailty categories,29,31 frail older adults may be underrepresented in trial samples, and the results of clinical trials might not be generalizable to wider community-dwelling populations. Further, the lower mortality with low BP found in clinical trials in the short term is compatible with the higher mortality observed in epidemiologic studies in the medium or long term. Moreover, data interpretation should be cautious because most previous studies used BP only measured in the office, and not ABPM data that includes nighttime BP and dipping values, which could be associated with poor functional outcomes as our study shows. Interestingly, the circadian BP alterations in older adults who are frail and disabled remained after adjustment of comorbidities, BP levels, and other covariates, suggesting that low daytime SBP and blunted dipping might be a real marker of increased vascular frailty and disability. Suggestively, our findings that, besides lower daytime SBP, a blunted dipping and higher nighttime SBP occur in older adults who are frail and disabled, might help explain why in observational studies, low clinic BP was associated with higher mortality in older adults, especially with frailty or poor functional status.16,24,25

Compared with previous research on this subject, the main strengths of this study are its large sample size, adjustment for a wide range of important confounders (including sleep quality and antihypertensive treatment), and its focus on a community-living older population rather than on clinical setting. Given that this study was not strictly representative of the general older population of Spain, extrapolations should be interpreted with caution. Nevertheless, the baseline sociodemographic and clinical characteristics of the participants were similar to those who did not participate. Also, antihypertensive therapy was based on the participant’s declaration and, therefore, may be imprecise; nevertheless, medication was checked against prescription containers. Lastly, our study’s cross-sectional design does not allow for drawing conclusions on the timing sequence and causality of the relationship of frailty and disability with ambulatory BP.
Conclusions

In conclusion, in this relatively large sample of community-living older individuals in Spain, frailty and disability were associated with blunted systolic dipping, higher nocturnal SBP, and lower daytime SBP regardless of conventional BP and a number of confounders. ABPM may provide additional information over usual conventional BP measurements in the clinical evaluation of older individuals with frailty or disability, and may help explain the higher mortality risk with lower clinic BP among frail older adults observed in nonrandomized studies. However, longitudinal studies on the association between frailty, disability, and ABPM are required to verify and extend our results.

References


