Received: 14 December 2021 | Revised: 18 January 2022 | Accepted: 19 January 2022

DOI: 10.1111/jch.14439

ORIGINAL ARTICLE

WILEY

# Global cognitive function correlates with P-wave dispersion in frail hypertensive older adults

Pasquale Mone MD[1,2,3] | Antonella Pansini MD[3] | Francesco Calabrò PhD[4] | Stefano De Gennaro MD[5] | Mafalda Esposito MD[5] | Paolo Rinaldi MD[5] | Antonio Colin MD[5] | Fabio Minicucci MD[5] | Antonio Coppola MD[5] | Salvatore Frullone MD[3] | Gaetano Santulli MD, PhD[1,4,6]

[1]Department of Medicine, Division of Cardiology, Wilf Family Cardiovascular Research Institute, Einstein Institute for Aging Research, Albert Einstein College of Medicine, New York City, NY, USA

[2]University Campania "Luigi Vanvitelli", Naples, Italy

[3]ASL Avellino, Avellino, Italy

[4]University of Naples "Federico II", Naples, Italy

[5]ASL Naples, Naples, Italy

[6]International Translational Research and Medical Education (ITME) Consortium, Naples, Italy

**Correspondence**
Pasquale Mone, MD and Gaetano Santulli, MD, PhD, Department of Medicine, Division of Cardiology, Wilf Family Cardiovascular Research Institute, Einstein Institute for Aging Research, Albert Einstein College of Medicine, New York City, NY, USA.
Email: pasquale.mone@einsteinmed.edu; gsantulli001@gmail.com

## Abstract

P-Wave Dispersion (PWD) is an ECG parameter defined as the difference between the longest and the shortest P-Wave duration. PWD has been associated with hypertension, a leading cause of age-related cognitive decline. Moreover, hypertension is associated with vascular dementia and Alzheimer's Disease. Based on these considerations, we evaluated PWD and global cognitive function in frail hypertensive older adults with a previous diagnosis of cognitive decline. We evaluated consecutive frail hypertensive patients ≥65-year-old with a Mini-Mental State Examination (MMSE) score <26. Patients with evidence of secondary hypertension, history of stroke, myocardial infarction, or therapy with beta-blockers or acetylcholinesterase inhibitors were excluded. Beta-blocker therapy causes a significant decrease in PWD; patients treated with acetylcholinesterase inhibitors were not included to avoid confounding effects on cognitive function. By examining 180 patients, we found that PWD significantly correlated with MMSE score. Strikingly, these effects were confirmed in a linear multivariate analysis with a regression model. To our knowledge, this is the first study showing that PWD correlates with global cognitive function in frail hypertensive older adults.

**KEYWORDS**
cognitive function, ECG, frailty, hypertension, older adults

## 1 | BACKGROUND

P-Wave Dispersion (PWD) is a non-invasive parameter defined as the difference between the longest and the shortest P-Wave duration on the surface electrocardiogram (ECG),[1,2] which has been investigated in atrial fibrillation (AF), hypertension, and stroke.[3–6]

Frailty is a worldwide increasing health problem in the elders and a biological syndrome of decreased physiological reserves with increased vulnerability to stressors.[7,8] Cognitive decline is one of the most serious social and economic problems.[9,10] Careful prevention seems to be the best way to reduce the incidence of dementia, identifying risk factors of dementia and mild cognitive impairment (MCI).[9,10] Cardiovascular diseases and their risk factors have been shown to have a strong impact on dementia and/or MCI,[9,11–13] also because the brain is very sensitive to hemodynamic alterations.[11,14] Hypertension is one of the most common diseases and its prevalence increases

with age.[15–17] Furthermore, it is a leading cause of age-related cognitive decline and is associated with vascular dementia and Alzheimer's disease.[18–24] Indeed, hypertension leads to chronic endothelial dysfunction contributing to atherosclerosis, inflammation, and oxidative stress.[25–32]

However, no study exploring the correlation between PWD and cognitive impairment in frail hypertensive older adults is currently available. Based on these considerations, we sought to evaluate PWD and global cognitive function in frail hypertensive older adults with cognitive impairment.

## 2 | METHODS

From March 2021 to September 2021, we evaluated 239 consecutive frail hypertensive older adults at the Local Health Authority (ASL) of Avellino and Naples ≥65-year-old with a Mini-Mental State Examination (MMSE) score <26.

Patients with evidence of secondary hypertension, history of stroke, myocardial infarction, AF, or therapy with beta-blockers or acetylcholinesterase inhibitors were excluded. Indeed, beta-blocker therapy has been shown to cause a significant decrease in PWD[33]; patients treated with acetylcholinesterase inhibitors were not included to avoid confounding effects on cognitive function.[34,35] PWD was assessed via a digital computerized system, confirmed by manual measurements on paper.

An informed consent was signed by each patient (or legal representative). Research has been performed according to the 1975 Declaration of Helsinki and its later amendments. The Campania Nord Institutional Review Board approved the protocol.

### 2.1 | Frailty assessment

Physical frailty assessment was performed following the Fried criteria[8,36]; a diagnosis of frailty status was made with at least three points out of the following five:

- Weight loss (unintentional loss ≥4.5 kg in the past year);
- Weakness (handgrip strength in the lowest 20% quintile at baseline, adjusted for sex and body mass index);
- Exhaustion (poor endurance and energy, self-reported);
- Slowness (walking speed under the lowest quintile adjusted for sex and height);
- Low physical activity level (lowest quintile of kilocalories of physical activity during the past week).

### 2.2 | Cognitive evaluation

Global cognitive function was assessed via the MMSE corrected for age and educational level of patients.[37] This cognitive test covers many cognitive skills, and scores range from 0 to 30.[37–40] MMSE is one of the most common and useful tests to evaluate global cognition and its score is influenced by demographic variables such as age and years of education.[37–41] Cognitive impairment was defined by a MMSE Score <26, as previously reported.[37,39]

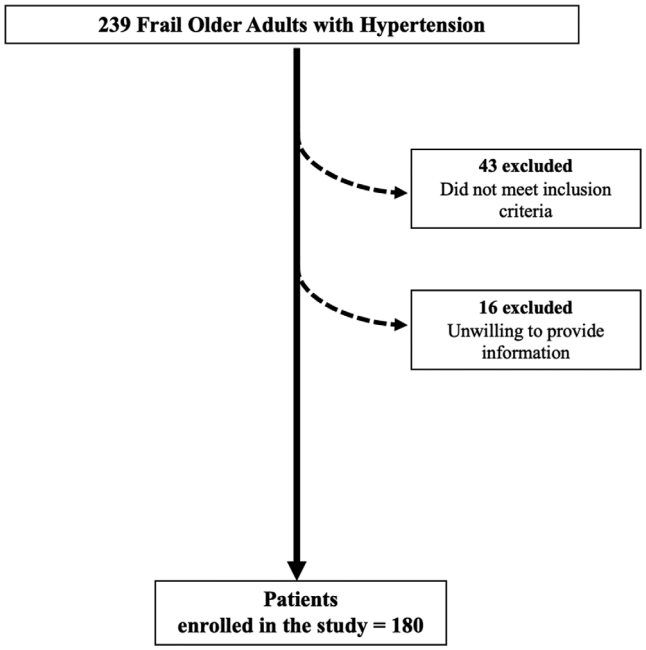


**FIGURE 1** Study flow chart

### 2.3 | Statistical analysis

All data are shown as mean ± SD. We calculated the number of patients required for the study to reject the null hypothesis 95% of the time (*i.e.*, with a one-tailed type II error rate of .05) with a two-tailed type I error at the .05 level of significance.

The sample size was calculated by G-POWER software. A linear multivariate analysis was performed with a regression model including age, blood pressure, heart rate, diabetes, dyslipidemia, and smoking status. A $p < .05$ was considered statistically significant. All calculations were performed using the software SPSS 26.

## 3 | RESULTS

One eighty patients entered the database (Figure 1). The study group had a mean of 74.9 ± 5.4 years. A slightly higher number of patients were women, with modest overweight. All patients were previously diagnosed with hypertension and, according to age, most of them were affected by comorbidity (no one had a history of previous acute myocardial infarction, heart failure, or stroke). All patients were treated with oral antihypertensive agents (Table 1).

We observed that PWD significantly correlated with MMSE ($r^2$: .390; $p < .001$, Figure 2). The independent effects on MMSE score were tested in a linear multivariate analysis with a regression model

**TABLE 1** Clinical characteristics of our population

| | |
|---|---|
| Number of patients | 180 |
| Age (years) | 74.9 ± 5.4 (66–90) |
| Sex (M/F) | 82/98 |
| BMI (kg/m$^2$) | 28.1 ± 2.9 (25–36) |
| SBP (mmHg) | 132.5 ± 10.3 (100–150) |
| DBP (mmHg) | 81.6 ± 9.5 (50–90) |
| HR (bpm) | 66.1 ± 8.7 (57–120) |
| PWD (sec) | .06 ± .02 (.03–.08) |
| **Comorbidities** | |
| Diabetes, *n* (%) | 74 (41.1) |
| Dyslipidemia, *n* (%) | 131 (72.8) |
| Smoking, *n* (%) | 73 (40.6) |
| **Active treatments** | |
| ACE inhibitors, *n* (%) | 106 (58.9) |
| Angiotensin receptor blockers, *n* (%) | 74 (41.1) |
| Calcium inhibitor, *n* (%) | 65 (36.1) |
| Statins, *n* (%) | 128 (71.3) |
| Diuretic, *n* (%) | 48 (26.7) |
| Aspirin, *n* (%) | 67 (37.6) |
| Clopidogrel, *n* (%) | 24 (13.3) |
| Oral antidiabetic drugs, *n* (%) | 45 (25.0) |
| Insulin, *n* (%) | 29 (16.0) |
| **Laboratory analyses** | |
| Fasting plasma glucose (mg/dl) | 119.2 ± 19.5 (84–191) |
| Creatinine (mg/dl) | .9 ± .2 (.7–1.4) |
| Total cholesterol (mg/dl) | 176.7 ± 32.7 (113–254) |
| HDL cholesterol (mg/dl) | 52.1 ± 16.2 (31–84) |
| LDL cholesterol (mg/dl) | 121.3 ± 23.3 (91–168) |
| **Global cognitive function** | |
| MMSE (range: 0–30) | 19.1 ± 3.4 (11–25) |

*Note*: Data are means ± SD (minimum, maximum values) for continuous variables or *n* (%) for categorical variables.
Abbreviations: ACE, angiotensin converting enzyme; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL: high-density lipoprotein; HR, heart rate; LDL: low-density lipoprotein; MMSE: Mini-Mental State Examination; PWD: P wave dispersion.

(Table 2), in which we found a significant effect of age ($p < .001$) and systolic blood pressure ($p$ : .031).

## 4 | DISCUSSION

To the best of our knowledge, this is the first study demonstrating a significant relationship between PWD and global cognitive function in frail hypertensive older adults.

Frailty leads to a high risk of death and adverse outcomes in cardiovascular diseases.[42–44]

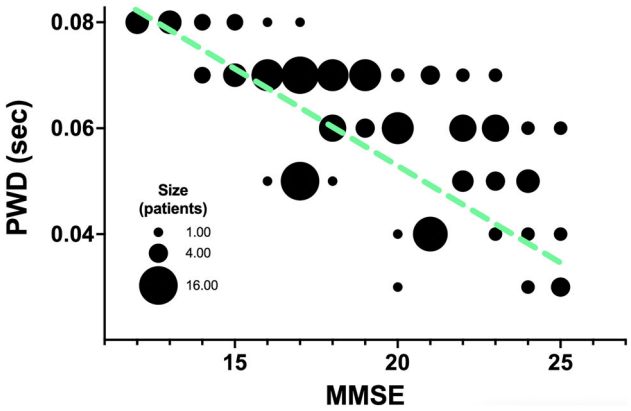


**FIGURE 2** Dispersion model depicting the relationship between P-Wave dispersion (PWD, expressed in seconds) and the Mini-Mental State Examination (MMSE) score ($r^2$: .390; $p < .001$)

A previous report demonstrated that QRS duration was significantly associated to frailty in chronic hemodialysis patients and frailty contributed to the observed cardiovascular risk in end-stage renal disease.[45] Similarly, another study evidenced that ECG abnormalities can predict a higher risk for later support/care-need certification in community-dwelling older adults with no prior history of cardiovascular disease.[46]

Our findings indicate that posing particular attention to a simple ECG parameter may help prevent or delay cognitive impairment, selecting patients to be screened via neuro-psychological tests or brain imaging, and identifying patients to be treated by pharmacological approaches. We confirmed our results with a linear regression multivariate analysis, showing the significant impact of age and systolic blood pressure; this result is very important in frailty because these subjects suffer from many diseases and a number of complications. Hence, a timely diagnosis of cognitive impairment should be very helpful to reduce the incidence of adverse outcomes and functional decline.

Furthermore, frail older adults with a diagnosis of hypertension should be carefully screened with ECG, echocardiography, 24- or 48-h ECG Holter, stress tests, and 24-h blood ambulatory blood pressure monitoring.[47,48] We speculate that this kind of approach would bring to an early diagnosis and to a prompt therapeutical approach that could counteract cognitive dysfunction and/or delay the onset of cognitive impairment and dementia.

The exact mechanisms linking PWD and hypertension need to be investigated. Indeed, hypertension is known to lead to endothelial alterations and microvascular dysfunction, increasing inflammation and oxidative stress,[49–58] which may underlie structural and electromechanical alterations in the heart.

Our study is not exempt from limitations. PWD can be influenced by a wide range of parameters, not only cardiovascular (for instance atrial size), but also endocrine, renal, and respiratory conditions[59,60]; unfortunately, we did not have these pieces of information available for all patients; additionally, we did not adjust our data by the severity of hypertension, the degree of left ventricular hypertrophy, or the control of diabetes. Evidently, our findings cannot be extended to younger pop-

**TABLE 2** Linear multivariate analysis, performed with MMSE as dependent variable

| | | | | | | 95.0% CI | |
|---|---|---|---|---|---|---|---|
| | B | Standard error | Beta | *t* | *p* | Lower bound | Upper bound |
| Age | −.331 | .033 | −.619 | −9.988 | <.001 | −.396 | −.265 |
| SBP | .071 | .033 | .223 | 2.170 | .031 | .006 | .136 |
| DBP | −.065 | .041 | −.179 | −1.603 | .111 | −.145 | .015 |
| HR | .034 | .030 | .081 | 1.126 | .262 | −.026 | .094 |
| Diabetes | .033 | .428 | .005 | .076 | .939 | −.812 | .877 |
| Dyslipidemia | −.179 | .526 | −.023 | −.339 | .735 | −1.218 | .861 |
| Smoking | .618 | .467 | .088 | 1.322 | .188 | −.305 | 1.540 |

ulations. Further studies with longer follow-up and a larger population are warranted to confirm our findings.

## 5 | CONCLUSION

Taken together, our data indicate that PWD on the ECG correlates with global cognitive function in frail hypertensive older patients. The results of our study are significant because they have evidenced a strong association between MMSE and PWD in the above-mentioned group.

### ACKNOWLEDGMENT

The Santulli's Laboratory is supported in part by the National Institutes of Health (NIH): National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK: R01-DK123259, R01-DK033823), National Heart, Lung, and Blood Institute (NHLBI: R01-HL146691, T32-HL144456), National Institute on Aging (NIA: R56-AG066431) to G.S. and by the American Heart Association (AHA-20POST35211151 to J.G.).

### DISCLOSURE STATEMENT

The authors have nothing to disclose.

### CONFLICT OF INTEREST

The authors declare no conflicts of interest.

### AUTHOR CONTRIBUTIONS

Coordination of the study was performed by Pasquale Mone and Gaetano Santulli. Data collection and analysis were performed by Pasquale Mone, Antonella Pansini, Stefano De Gennaro, Mafalda Esposito, Paolo Rinaldi, Antonio Colin, Fabio Minicucci, Antonio Coppola, and Salvatore Frullone. Statistical analysis was performed by Pasquale Mone, Francesco Calabrò, and Gaetano Santulli. Data interpretation was performed by all authors. Pasquale Mone and Gaetano Santulli prepared the manuscript. All authors reviewed and approved the final draft.

### ORCID

*Francesco Calabrò PhD* https://orcid.org/0000-0002-1484-0217
*Gaetano Santulli MD, PhD* https://orcid.org/0000-0001-7231-375X

### REFERENCES

1. Carmona Puerta R, Lorenzo Martinez E, Rabassa Lopez-Calleja M, et al. Vectorial theory surpasses the local theory in explaining the origin of P-wave dispersion. *J Electrocardiol*. 2021;66:152-160.
2. Marks D, Ho R, Then R, et al. Real-world experience with implantable loop recorder monitoring to detect subclinical atrial fibrillation in patients with cryptogenic stroke: the value of p wave dispersion in predicting arrhythmia occurrence. *Int J Cardiol*. 2021;327:86-92.
3. Li TYW, Yeo LLL, Ho JSY, et al. Association of electrocardiographic P-wave markers and atrial fibrillation in embolic stroke of undetermined source. *Cerebrovasc Dis*. 2021;50(1):46-53.
4. Tosun V, Korucuk N, Kilinc AY, et al. Evaluation of atrial electromechanical functions in dipper and nondipper hypertension patients using left atrial strain P-wave dispersion and P terminal force. *Echocardiography*. 2018;35(9):1318-1325.
5. Lazzeroni D, Parati G, Bini M, et al. P-wave dispersion predicts atrial fibrillation following cardiac surgery. *Int J Cardiol*. 2016;203:131-133.
6. Gaisl T, Wons AM, Rossi V, et al. Simulated obstructive sleep apnea increases P-wave duration and P-wave dispersion. *PLoS One*. 2016;11(4):e0152994.
7. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *Lancet*. 2013;381(9868):752-762.
8. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001;56(3):M146–M156.
9. Petersen RC, Lopez O, Armstrong MJ, et al. Practice guideline update summary: mild cognitive impairment: report of the guideline development, dissemination, and implementation subcommittee of the American Academy of Neurology. *Neurology*. 2018;90(3):126-135.
10. McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement*. 2011;7(3):263-269.
11. Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W, Ferri CP. The global prevalence of dementia: a systematic review and metaanalysis. *Alzheimers Dement*. 2013;9(1):63-75. e62.
12. Agrimi J, Spalletti C, Baroni C, et al. Obese mice exposed to psychosocial stress display cardiac and hippocampal dysfunction associated with local brain-derived neurotrophic factor depletion. *EBioMedicine*. 2019;47:384-401.
13. Frankish H, Horton R. Prevention and management of dementia: a priority for public health. *Lancet*. 2017;390(10113):2614-2615.
14. Qiu C, Winblad B, Fratiglioni L. The age-dependent relation of blood pressure to cognitive function and dementia. *Lancet Neurol*. 2005;4(8):487-499.
15. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the

prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71(6):e13-e115.
16. Wu CY, Hu HY, Chou YJ, Huang N, Chou YC, Li CP. High blood pressure and all-cause and cardiovascular disease mortalities in community-dwelling older adults. *Medicine (Baltimore)*. 2015;94(47):e2160.
17. Zhou B, Perel P, Mensah GA, Ezzati M. Global epidemiology, health burden and effective interventions for elevated blood pressure and hypertension. *Nat Rev Cardiol*. 2021;18(11):785-802.
18. Mone P, Gambardella J, Pansini A, et al. Cognitive impairment in frail hypertensive elderly patients: role of hyperglycemia. *Cells*. 2021;10(8):2115.
19. de Menezes ST, Giatti L, Brant LCC, et al. Hypertension, prehypertension, and hypertension control: association with decline in cognitive performance in the ELSA-Brasil cohort. *Hypertension*. 2021;77(2):672-681.
20. Iulita MF, Girouard H. Treating hypertension to prevent cognitive decline and dementia: re-opening the debate. *Adv Exp Med Biol*. 2017;956:447-473.
21. Turana Y, Tengkawan J, Chia YC, et al. Hypertension and dementia: a comprehensive review from the HOPE Asia Network. *J Clin Hypertens (Greenwich)*. 2019;21(8):1091-1098.
22. Vicario A, Martinez CD, Baretto D, Diaz Casale A, Nicolosi L. Hypertension and cognitive decline: impact on executive function. *J Clin Hypertens (Greenwich)*. 2005;7(10):598-604.
23. Cherubini A, Lowenthal DT, Paran E, Mecocci P, Williams LS, Senin U. Hypertension and cognitive function in the elderly. *Am J Ther*. 2007;14(6):533-554.
24. Yaffe K, Bahorik AL, Hoang TD, et al. Cardiovascular risk factors and accelerated cognitive decline in midlife: the CARDIA study. *Neurology*. 2020;95(7):e839-e846.
25. Daiber A, Steven S, Weber A, et al. Targeting vascular (endothelial) dysfunction. *Br J Pharmacol*. 2017;174(12):1591-1619.
26. Ito F, Sono Y, Ito T. Measurement and clinical significance of lipid peroxidation as a biomarker of oxidative stress: oxidative stress in diabetes, atherosclerosis, and chronic inflammation. *Antioxidants (Basel)*. 2019;8(3):72.
27. Toya T, Ahmad A, Attia Z, et al. Vascular aging detected by peripheral endothelial dysfunction is associated with ECG-derived physiological aging. *J Am Heart Assoc*. 2021;10(3):e018656.
28. Kinzenbaw DA, Chu Y, Pena Silva RA, Didion SP, Faraci FM. Interleukin-10 protects against aging-induced endothelial dysfunction. *Physiol Rep*. 2013;1(6):e00149.
29. Santulli G, Trimarco B, Iaccarino G. G-protein-coupled receptor kinase 2 and hypertension: molecular insights and pathophysiological mechanisms. *High Blood Press Cardiovasc Prev*. 2013;20(1):5-12.
30. Sepulveda C, Palomo I, Fuentes E. Mechanisms of endothelial dysfunction during aging: predisposition to thrombosis. *Mech Ageing Dev*. 2017;164:91-99.
31. Alonso-Bouzon C, Carcaillon L, Garcia-Garcia FJ, Amor-Andres MS, El Assar M, Rodriguez-Manas L. Association between endothelial dysfunction and frailty: the Toledo Study for Healthy Aging. *Age (Dordr)*. 2014;36(1):495-505.
32. Higashi Y, Kihara Y, Noma K. Endothelial dysfunction and hypertension in aging. *Hypertens Res*. 2012;35(11):1039-1047.
33. Camsari A, Pekdemir H, Akkus MN, Yenihan S, Doven O, Cin VG. Long-term effects of beta blocker therapy on P-wave duration and dispersion in congestive heart failure patients: a new effect? *J Electrocardiol*. 2003;36(2):111-116.
34. Xu H, Garcia-Ptacek S, Jonsson L, Wimo A, Nordstrom P, Eriksdotter M. Long-term effects of cholinesterase inhibitors on cognitive decline and mortality. *Neurology*. 2021;96(17):e2220-e2230.
35. Hu Z, Wang L, Ma S, et al. Synergism of antihypertensives and cholinesterase inhibitors in Alzheimer's disease. *Alzheimers Dement (N Y)*. 2018;4:542-555.
36. Mone P, Gambardella J, Lombardi A, et al. Correlation of physical and cognitive impairment in diabetic and hypertensive frail older adults. *Cardiovasc Diabetol*. 2022:In press.
37. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12(3):189-198.
38. Sands LP, Yaffe K, Covinsky K, et al. Cognitive screening predicts magnitude of functional recovery from admission to 3 months after discharge in hospitalized elders. *J Gerontol A Biol Sci Med Sci*. 2003;58(1):37-45.
39. Carpinelli Mazzi M, Iavarone A, Russo G, et al. Mini-Mental State Examination: new normative values on subjects in Southern Italy. *Aging Clin Exp Res*. 2020;32(4):699-702.
40. Carlesimo GA, Caltagirone C, Gainotti G. The Mental Deterioration Battery: normative data, diagnostic reliability and qualitative analyses of cognitive impairment. The Group for the Standardization of the Mental Deterioration Battery. *Eur Neurol* 1996;36(6):378-384.
41. Limongi F, Noale M, Bianchetti A, et al. The instruments used by the Italian centres for cognitive disorders and dementia to diagnose mild cognitive impairment (MCI). *Aging Clin Exp Res*. 2019;31(1):101-107.
42. Ekerstad N, Swahn E, Janzon M, et al. Frailty is independently associated with short-term outcomes for elderly patients with non-ST-segment elevation myocardial infarction. *Circulation*. 2011;124(22):2397-2404.
43. Ida S, Kaneko R, Imataka K, Murata K. Relationship between frailty and mortality, hospitalization, and cardiovascular diseases in diabetes: a systematic review and meta-analysis. *Cardiovasc Diabetol*. 2019;18(1):81.
44. Uchmanowicz I. Oxidative stress, frailty and cardiovascular diseases: current evidence. *Adv Exp Med Biol*. 2020;1216:65-77.
45. Chao CT, Huang JW. Frailty severity is significantly associated with electrocardiographic QRS duration in chronic dialysis patients. *PeerJ*. 2015;3:e1354.
46. Okuno T, Watanabe K, Nakajima K, et al. Major electrocardiographic abnormality predicts support/care-need certification and/or death in community-dwelling older adults with no history of cardiovascular disease. *Geriatr Gerontol Int*. 2017;17(11):1967-1976.
47. Zhao Y, Liu Y, Sun Q, et al. Effects of blood pressure and heart rate circadian rhythms on left atrial function. *J Hypertens*. 2021;39(11):2318-2324.
48. Cavefors O, Holmqvist J, Bech-Hanssen O, et al. Regional left ventricular systolic dysfunction associated with critical illness: incidence and effect on outcome. *ESC Heart Fail*. 2021.
49. Weng LC, Hall AW, Choi SH, et al. Genetic determinants of electrocardiographic P-wave duration and relation to atrial fibrillation. *Circ Genom Precis Med*. 2020;13(5):387-395.
50. Auricchio A, Ozkartal T, Salghetti F, et al. Short P-wave duration is a marker of higher rate of atrial fibrillation recurrences after pulmonary vein isolation: new insights into the pathophysiological mechanisms through computer simulations. *J Am Heart Assoc*. 2021;10(2):e018572.
51. Ungvari Z, Toth P, Tarantini S, et al. Hypertension-induced cognitive impairment: from pathophysiology to public health. *Nat Rev Nephrol*. 2021;17(10):639–654.
52. Mone P, Gambardella J, Wang X, Jankauskas SS, Matarese A, Santulli G. miR-24 targets the transmembrane glycoprotein neuropilin-1 in human brain microvascular endothelial cells. *Noncoding RNA*. 2021;7(1):9.
53. Marfella R, Paolisso G. Increased arterial stiffness trumps on blood pressure in predicting cognitive decline in low-risk populations. *Hypertension*. 2016;67(1):30-31.

54. Hajjar I, Goldstein FC, Martin GS, Quyyumi AA. Roles of arterial stiffness and blood pressure in hypertension-associated cognitive decline in healthy adults. *Hypertension*. 2016;67(1):171-175.
55. Mone P, Gambardella J, Pansini A, et al. Cognitive dysfunction correlates with physical impairment in frail patients with acute myocardial infarction. *Aging Clin Exp Res*. 2021.
56. Peng M, Chen G, Tang KL, et al. Blood pressure at age 60–65 versus age 70–75 and vascular dementia: a population based observational study. *BMC geriatrics*. 2017;17(1):252.
57. Mone P, Pansini A. Gait speed test and cognitive decline in frail women with acute myocardial infarction. *Am J Med Sci*. 2020;360(5):484-488.
58. Santisteban MM, Ahn SJ, Lane D, et al. Endothelium-macrophage crosstalk mediates blood-brain barrier dysfunction in hypertension. *Hypertension*. 2020;76(3):795-807.
59. Unver S, Ozmen N, Aparci M, Atasoyu EM, Evrenkaya TR. The influence of the amount of ultrafiltration in chronic hemodialysis on P wave dispersion. *Ren Fail*. 2007;29(2):207-212.
60. Perez-Riera AR, de Abreu LC, Barbosa-Barros R, Grindler J, Fernandes-Cardoso A, Baranchuk A. P-wave dispersion: an update. *Indian Pacing Electrophysiol J*. 2016;16(4):126-133.

**How to cite this article:** Mone P, Pansini A, Calabrò F, et al. Global cognitive function correlates with P-wave dispersion in frail hypertensive older adults. *J Clin Hypertens*. 2022;24:638–643. https://doi.org/10.1111/jch.14439