





Article

# Home Pulse Pressure Predicts Death and Cardiovascular Events in Peritoneal Dialysis Patients

Vincenzo Panuccio <sup>1,†</sup>, Pasquale Fabio Provenzano <sup>2,†</sup> , Rocco Tripepi <sup>2</sup>, Maria Carmela Versace <sup>2</sup>,  
Giovanna Parlongo <sup>1</sup>, Emma Politi <sup>1</sup>, Antonio Vilasi <sup>2</sup>, Sabrina Mezzatesta <sup>2</sup>, Domenico Abelardo <sup>2</sup>,  
Giovanni Luigi Tripepi <sup>2</sup> and Claudia Torino <sup>2,\*</sup> 

<sup>1</sup> Nephrology, Dialysis and Transplantation Unit—GOM “Bianchi-Melacrino-Morelli”, Via Vallone Petrara SNC, 89124 Reggio Calabria, Italy; enzopanuccio@gmail.com (V.P.); giovvy.parl@gmail.com (G.P.); emma.politi@gmail.com (E.P.)

<sup>2</sup> National Research Council—Institute of Clinical Physiology, Via Vallone Petrara SNC, 89124 Reggio Calabria, Italy; fprovenzano@ifc.cnr.it (P.F.P.); rtripepi@ifc.cnr.it (R.T.); mcversace@ifc.cnr.it (M.C.V.); avilasi@ifc.cnr.it (A.V.); smezzatesta@ifc.cnr.it (S.M.); dabelardo@ifc.cnr.it (D.A.); gtripepi@ifc.cnr.it (G.L.T.)

\* Correspondence: ctorino@ifc.cnr.it; Tel.: +39-0965-593252

† These authors contributed equally to this work.

**Abstract:** Increased arterial hypertension represents a prevalent condition in peritoneal dialysis patients that is often related to volume expansion. Pulse pressure is a robust predictor of mortality in dialysis patients, but its association with mortality is unknown in peritoneal patients. We investigated the relationship between home pulse pressure and survival in 140 PD patients. During a mean follow-up of 35 months, 62 patients died, and 66 experienced the combined event death/CV events. In a crude COX regression analysis, a five-unit increase in HPP was associated with a 17% increase in the hazard ratio of mortality (HR: 1.17, 95% CI 1.08–1.26  $p < 0.001$ ). This result was confirmed in a multiple Cox model adjusted for age, gender, diabetes, systolic arterial pressure, and dialysis adequacy (HR: 1.31, 95% CI 1.12–1.52,  $p = 0.001$ ). Similar results were obtained considering the combined event death–CV events as an outcome. Home pulse pressure represents, in part, arterial stiffness, and it is strongly related to all-cause mortality in peritoneal patients. In these high cardiovascular risk populations, it is important to maintain optimal blood pressure control, but it is fundamental to consider all the other cardiovascular risk indicators, such as pulse pressure. Home pulse pressure measurement is easy and feasible and can add important information for the identification and management of high-risk patients.

**Keywords:** home pulse pressure; peritoneal dialysis; ESKD



**Citation:** Panuccio, V.; Provenzano, P.F.; Tripepi, R.; Versace, M.C.; Parlongo, G.; Politi, E.; Vilasi, A.; Mezzatesta, S.; Abelardo, D.; Tripepi, G.L.; et al. Home Pulse Pressure Predicts Death and Cardiovascular Events in Peritoneal Dialysis Patients. *J. Clin. Med.* **2023**, *12*, 3904. <https://doi.org/10.3390/jcm12123904>

Academic Editor: Bernard Canaud

Received: 21 April 2023

Revised: 29 May 2023

Accepted: 6 June 2023

Published: 7 June 2023



**Copyright:** © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

## 1. Introduction

Chronic kidney disease (CKD) is a global health issue. The disease burden has noticeably risen in recent years, with an estimated increase in CKD-related years of life lost equal to 82% [1]. Among the comorbidities affecting these patients, hypertension has a prevalence twice higher than in the general population [2,3]. In addition, it is more frequently resistant to drug treatment [4], and it exhibits a circadian profile with an attenuated or abolished decline during night-time [5,6]. Different from the general population, in which blood pressure (BP) shows a linear, direct relationship with cardiovascular events [7–9], this association is more complex in these patients [10–13]. Data reported in the literature suggests that both low [14–18] and high peri-dialysis BP are associated with adverse outcomes [19–21], thus indicating a U-shaped association between BP, fatal and non-fatal CV events, and mortality [5,15,20,22–27]. Based on these observations, several research groups started pointing the finger against peri-dialytic blood pressure measurements, highlighting their high variability in the absence of standardized measurements [28], their poor agreement

with inter-dialytic measurements [29–31], and the lack of association with organ damage, such as left ventricular hypertrophy [32].

Different from peri-dialysis measurements, out-of-dialysis BP is more efficient in diagnosing hypertension [29] and in predicting organ damage [29,32,33] in hemodialysis (HD) patients. Most importantly, it shows a direct and linear association with mortality and cardiovascular outcomes [31,34,35] and a predictive power for death and cardiovascular outcomes, which overcomes that of pre- and post-dialysis measurements [31,34–37].

Among the out-of-dialysis measurements, 44 h ambulatory blood pressure measurement (ABPM) is the gold standard for the diagnosis of hypertension in dialysis patients; however, its applicability and tolerability are still a matter of debate [38,39]. For this reason, home BP monitoring is considered a more suitable option for the management of hypertension in hemodialysis patients [40,41].

Home BP monitoring represents the election choice for peritoneal dialysis (PD) patients who, due to the home-based treatment, routinely measure BP at home. However, information about the diagnostic accuracy of this measurement in these patients is scarce and in contrast with findings in HD patients. Among the studies published so far, most of them with limited sample size suggest an overestimation of daytime ambulatory BP and a worse performance in diagnosing hypertension compared with standardized BP [42,43]. More recently, a study performed on 81 PD patients showed a similar accuracy for 1-week averaged home BP and standardized clinic SBP in diagnosing hypertension [44]. To date, fewer studies have focused on the association between BP and clinical outcomes in PD patients [45–47]. However, as all these studies considered clinical, standardized BP measurements, to our knowledge, no evidence is currently available on the association between home BP and clinical outcomes in PD patients. Increased pulse pressure (PP), a component of blood pressure, is frequently observed in chronic renal failure patients [48,49], and it is associated with decreased arterial-wall compliance [50]. PP is a robust predictor of mortality in dialysis patients [51,52], but the association between home pulse pressure (HPP) and mortality is still unknown in dialysis patients. With this background in mind, we tested this hypothesis in a cohort of PD patients in a single unit in Calabria, Italy.

## 2. Materials and Methods

This study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethical Committee of our institution (Sezione Sud—Regione Calabria). Each participant provided written informed consent before enrolment.

### 2.1. Study Population

We included in this analysis all patients who started peritoneal dialysis at the Nephrology, Dialysis and Transplantation Unit of the Grande Ospedale Metropolitano “Bianchi-Melacrino-Morelli”, Italy, between August 1991 and December 2018 ( $n = 140$ ). All the enrolled subjects were of Caucasian descent and came from the same geographic area (Southern Italy). After the baseline visit, patients were followed up for a median time of 33 months (range: 20–58 months). One-hundred and six patients were treated with various anti-hypertensive drugs (33 on mono-therapy with ACE inhibitors, calcium channel blockers,  $\alpha$ - and  $\beta$ -blockers, vasodilators, diuretics or other drugs, 31 on double therapy, 26 on triple therapy, 10 on quadruple therapy, and 6 patients on quintuple or sextuple therapy, with various combinations of these drugs). The main demographic, somatometric, clinical, and biochemical characteristics of the study population are detailed in Table 1.

### 2.2. Clinical and Laboratory Measurements

Blood pressure was measured at home once a day, in the morning, before dialysis exchange, with an automatic blood pressure monitor. To perform the measurements, any monitor owned by the patients was allowed, provided it was an automatic upper-arm monitor that met the AHA standards. Detailed instructions on how to measure BP, with recommendations regarding the hydration status or the risk of infections, were provided

to the patients during the peritoneal training period. Briefly, patients were recommended to measure blood pressure seated, after 5 min of rest, only once, and to record this value in their diary. In case the measurement was markedly different from the blood pressure usually taken at home, they were advised to repeat the measurement a second time to confirm the value. Home pulse pressure (HPP) was calculated by subtracting diastolic BP from systolic BP. For this analysis, monthly average of all HPP values taken at home was considered. HPP variability was computed via the sample standard deviation (SD) of all HPP values. Dialysis adequacy was expressed by weekly Kt/V. Blood sampling was performed at baseline in the early morning after an overnight fast. Cholesterol, hemoglobin, PTH, calcium, phosphate, and C-reactive protein (CRP) were measured using standard methods in the routine clinical laboratory.

**Table 1.** Main demographic, somatometric, and clinical characteristics of the study population.

	Whole Group ( <i>n</i> = 140)
Age (years)	67 ± 14
BMI (kg/m <sup>2</sup> )	27 ± 4
Male sex <i>n.</i> (%)	83 (59.3)
Current smokers <i>n.</i> (%)	14 (10)
Past smokers <i>n.</i> (%)	35 (25)
Diabetics <i>n.</i> (%)	51 (36.4)
With cardiovascular comorbidities <sup>1</sup> <i>n.</i> (%)	66 (47.1)
On anti-hypertensive treatment <i>n.</i> (%)	106 (75.7)
Home Pulse Pressure (mmHg)	62 ± 16
Systolic Blood Pressure (mmHg)	139 ± 16
Diastolic Blood Pressure (mmHg)	77 ± 10
Cholesterol (mg/dL)	171 ± 40
Hemoglobin (g/dL)	11 ± 1.6
PTH (pg/mL)	202 ± 173
CRP (mg/L)	3.7 (3.2–10.3)
Calcium (mg/dL)	8.9 ± 1.3
Phosphate (mg/dL)	5.6 ± 1.6
Kt/V	1.9 ± 0.4

<sup>1</sup> Cardiovascular comorbidities: The presence, at baseline, of at least one of these comorbidities: angina, myocardial infarction, stroke, TIA, arrhythmia, peripheral arterial disease. Data are expressed as mean ± SD, median and inter-quartile range or as percent frequency, as appropriate.

### 2.3. Study End-Points

As HPP was measured in a month period, follow-up started the day of the last measurement. All-cause mortality and a combination of mortality and fatal and non-fatal cardiovascular events were the study end-points. Cardiovascular events were classified as follows: stroke (ischemic or hemorrhagic), documented by computed tomography, magnetic resonance imaging, and/or clinical and neurological evaluation; transient ischemic attacks (TIA); myocardial infarction confirmed by serial changes of ECG and cardiac biomarkers; ECG-documented angina episodes; heart failure, diagnosed on the basis of clinical and instrumental evidence, as reported before; ECG documented arrhythmia; peripheral ischemia or amputations; unexpected, sudden death highly suspected as of cardiac origin. Each cause of death was assessed by three independent physicians. In doubtful cases, diagnosis was attributed by consensus. During the review process, involved physician used all available medical information, including hospitalization forms and medical records. In case of death at home, family members and/or general practitioners were interviewed to better understand the circumstances which led to death.

## 2.4. Statistical Analysis

Data were expressed as mean  $\pm$  standard deviation (normally distributed data), median and inter-quartile range (non-normally distributed data), or as percent frequency (categorical data).

Pearson's correlation coefficient was used to evaluate the association between HPP and the main demographic, somatometric, and clinical variables (age, sex, cardiovascular events, laboratory data, and therapy). The relationship between blood pressure values (HPP, SBP, DBP, and PP variability) and cardiovascular comorbidities was tested by univariate and multivariate logistic regression analysis, adjusted for traditional and non-traditional confounding factors (age, gender, diabetes, dialysis adequacy, and systolic or diastolic arterial pressure). Univariate and multivariate Cox regression analyses, adjusted for age, gender, diabetes, systolic or diastolic arterial pressure, and dialysis adequacy, were used to assess the association between blood pressure values and mortality or the combined outcome. The effect of age and sex on the association between BP values and mortality/combined outcome was verified, including in the Cox model blood pressure values (HPP, SBP, DBP, BPP variability), age or sex, and their multiplicative term. Statistical analysis was performed via standard statistical packages (SPSS for Windows, Version 26, Chicago, IL, USA; STATA for Windows, Version 16, College Station, TX, USA).

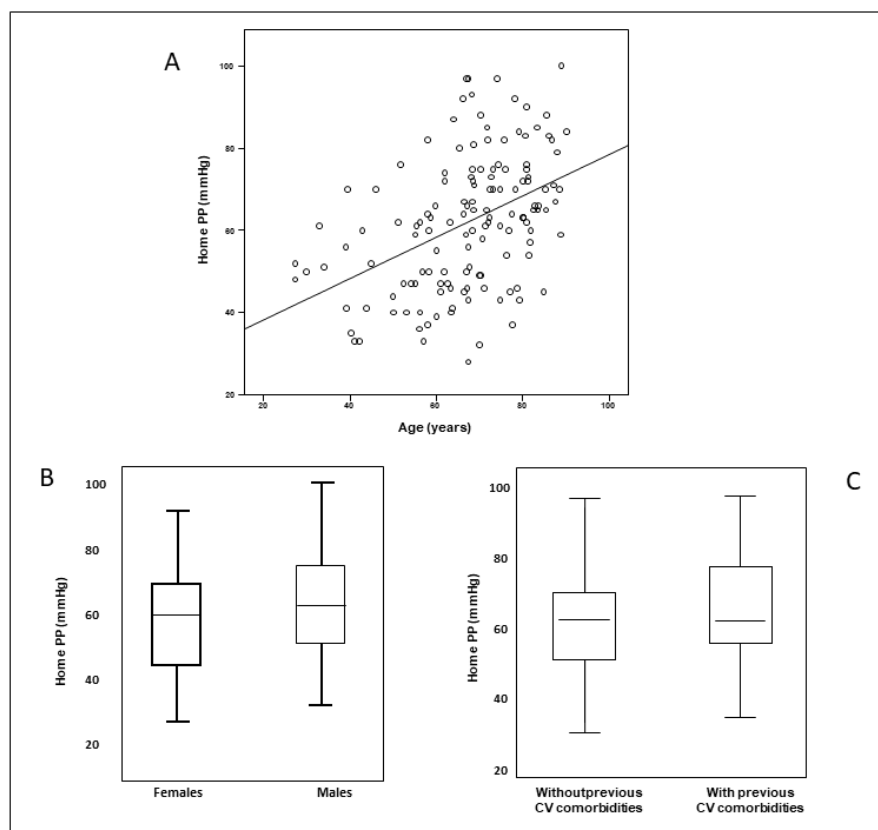
## 3. Results

The main clinical, demographic, and somatometric baseline characteristics of the study population are reported in Table 1. HPP was on average  $62 \pm 16$  mmHg, with systolic and diastolic BP of  $139 \pm 16$  mmHg and  $77 \pm 10$  mmHg, respectively. Eighty-three patients were males (59.3%), the mean age was  $67 \pm 14$  years, and BMI was  $27 \pm 4$  kg/m<sup>2</sup>. Overall, 10% of the patients were current smokers. Regarding the most important comorbidities, 36.4% of patients were diabetic, while 47.1% had previous cardiovascular events. The list of the main correlates of HPP is reported in Table 2. Correlation analysis showed a positive, significant association between HPP and age ( $r = 0.44$ ,  $p < 0.001$ ), male gender ( $r = 0.21$ ,  $p = 0.01$ ), and previous cardiovascular events ( $r = 0.28$ ,  $p = 0.001$ ) (Figure 1).

**Table 2.** Main demographic and clinical correlates of pulse pressure.

Variables	R	p
Age (years)	0.435	<0.001
Previous cardiovascular comorbidities	0.234	0.006
Diabetes	0.357	<0.001
NYHA Score	0.281	0.001
Kt/V	−0.147	0.083
Hemoglobin	−0.114	0.182
C-reactive protein	0.053	0.548
Phosphate	−0.162	0.057
PTHi	−0.066	0.449
VitD	0.057	0.501
Use of blood-pressure-lowering therapy	0.257	0.003
Use of erythropoiesis-stimulating agents	−0.105	0.218
Lipid-lowering therapy	−0.053	0.532

The association between HPP and previous cardiovascular comorbidities was confirmed at univariate logistic regression analysis, where for each 5-unit increase in HPP, a 4% increase in the odds of cardiovascular disease was observed (OR: 1.22, 95% CI: 1.08–1.38,  $p = 0.001$ ). This association was confirmed after adjustment for potential confounders such as age, gender, diabetes, and dialysis adequacy (OR: 1.21, 95% CI: 1.04–1.42,  $p = 0.02$ ). This association was no longer significant after introducing the same model systolic arterial pressure (OR: 1.22, 95% CI: 0.95–1.57,  $p = 0.13$ ).



**Figure 1.** Positive, significant association between HPP and age (A), male gender (B), and previous cardiovascular events (C).

Differently from HPP, pulse pressure variability was not associated with previous cardiovascular comorbidities, neither at univariate (OR for the 5-unit increase: 1.05, 95% CI: 0.98–1.05,  $p = 0.15$ ) or multivariate analysis (OR for the 5-unit increase: 1.05, 95% CI: 0.98–1.11,  $p = 0.15$ ).

The same analysis performed on the two components of HPP reported a positive, significant association between SBP and cardiovascular comorbidities (univariate: OR for the 5-unit increase: 1.14, 95% CI: 1.02–1.29,  $p = 0.03$ ; multivariate: OR for the 5-unit increase: 1.15, 95% CI: 1.00–1.33,  $p = 0.06$ ; multivariate + DBP: OR for the 5-unit increase: 1.21, 95% CI: 1.03–1.43,  $p = 0.02$ ). Conversely, the inverse relationship between DBP and cardiovascular comorbidities was not significant (univariate: OR for the 5-unit increase: 0.85, 95% CI 0.70–1.02,  $p = 0.08$ ; multivariate: OR for the 5-unit increase: 0.94, 95% CI 0.76–1.17,  $p = 0.60$ ; multivariate + SBP: OR for the 5-unit increase: 0.82, 95% CI: 0.64–1.06,  $p = 0.82$ ).

### 3.1. Survival Analysis

#### 3.1.1. All-Cause Mortality

During a mean follow-up of 35 months, 62 patients died. In a crude COX regression analysis, a five-unit increase in HPP was associated with a 17% increase in the hazard ratio of mortality (HR: 1.17, 95% CI 1.08–1.26,  $p < 0.001$ ) (Table 3). This result was confirmed in a multiple Cox model adjusted for age, gender, diabetes, systolic arterial pressure, and dialysis adequacy (HR: 1.31, 95% CI: 1.12–1.52,  $p = 0.001$ ) (Table 3). Forcing, in the model, previous CV events as potential confounders, the association remained statistically significant (HR: 1.30, 95% CI: 1.11–1.51,  $p = 0.001$ ).

**Table 3.** Univariate and multivariate survival analysis showing the association between pulse pressure and all-cause mortality.

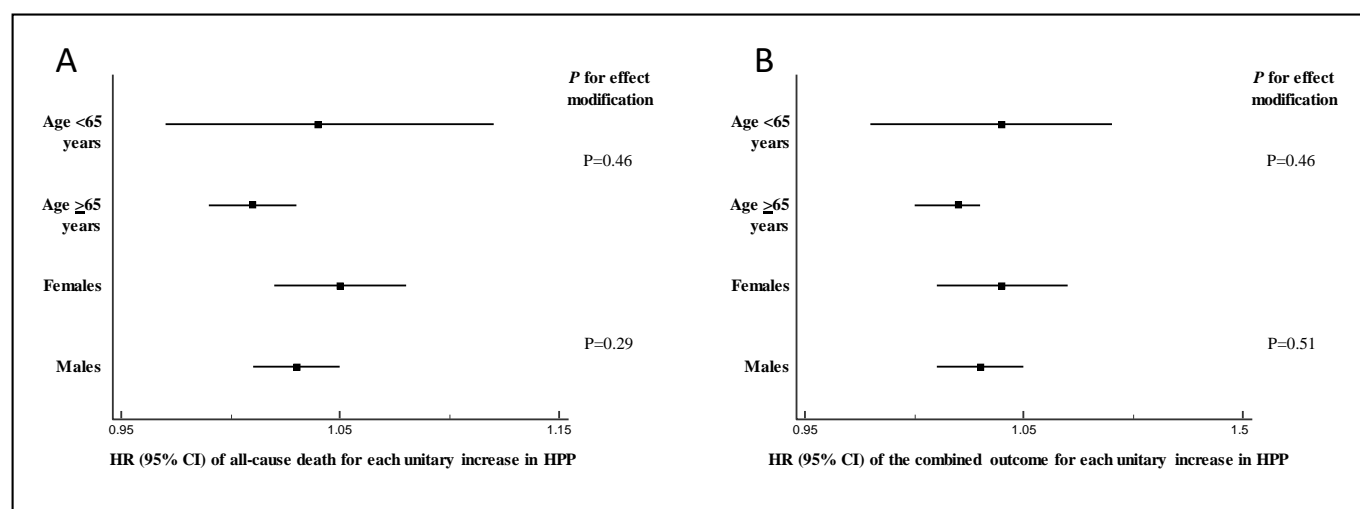
Variables (Units of Increase)	Crude Analysis	Fully Adjusted Analysis	Over-Adjusted Analysis
Pulse Pressure (5 mmHg)	1.17 (1.08–1.26), $p < 0.001$	1.31 (1.12–1.52), $p = 0.001$	1.30 (1.11–1.51), $p = 0.001$
Age (1 year)		1.05 (1.01–1.08), $p = 0.004$	1.04 (1.01–1.08), $p = 0.005$
Gender (0 = female; 1 = male)		0.82 (0.44–1.53), $p = 0.53$	0.79 (0.42–1.47), $p = 0.45$
Diabetes (0 = no; 1 = yes)		0.88 (0.51–1.51), $p = 0.63$	0.93 (0.93–1.62), $p = 0.80$
Kt/V (1 unit)		1.01 (0.51–2.01), $p = 0.97$	1.01 (0.51–1.99), $p = 0.98$
Systolic Blood Pressure (1 mmHg)		0.96 (0.93–0.99), $p = 0.009$	0.96 (0.93–0.99), $p = 0.01$
Cardiovascular comorbidities (0 = no; 1 = yes)			1.28 (0.72–2.28), $p = 0.40$

The predictive power of HPP overcomes that of SBP and pulse pressure variability for all-cause mortality. As a result of our analysis, the association between these BP values and the considered outcome was not significant both at univariate (HR for 5-unit increase: 1.04, 95% CI: 0.96–1.14,  $p = 0.33$ ) and multivariate analysis (HR for 5-unit increase: 1.05, 95% CI: 0.94–1.17,  $p = 0.39$ ). Adding previous cardiovascular comorbidities in the model did not change the result (HR for the 5-unit increase: 1.04, 95% CI: 0.93–1.16,  $p = 0.47$ ).

As expected, DBP was protective for all-cause mortality (univariate analysis: HR for the 5-unit increase: 0.70, 95% CI: 0.62–0.80,  $p < 0.001$ ; multivariate analysis: HR for the 5-unit increase: 0.77, 95% CI: 0.66–0.89,  $p = 0.001$ ; multivariate analysis + previous cardiovascular comorbidities: HR for the 5-unit increase: 0.77, 95% CI: 0.66–0.90,  $p = 0.001$ ).

Finally, no association was found between pulse pressure variability and all-cause mortality (univariate analysis: HR for the 5-unit increase: 0.99, 95% CI: 0.97–1.03,  $p = 0.91$ ; multivariate analysis: HR for the 5-unit increase: 0.98, 95% CI: 0.92–1.03,  $p = 0.37$ ; multivariate analysis + previous cardiovascular comorbidities: HR for the 5-unit increase: 0.97, 95% CI: 0.92–1.03,  $p = 0.30$ ).

No effect modification by age or sex was found on the link between HPP and mortality ( $p$  for effect modification  $>0.22$ ) (Figure 2A) or on the association between the other BP measurements (SBP, DBP, and PP variability) and the same outcome (all  $p > 0.05$ ).

**Figure 2.** Forest plot showing the absence of effect modification by age and sex on the link HPP-mortality (A) and HPP and the combined event (B).

### 3.1.2. Combined Outcome—Death and Cardiovascular Events

During the follow-up of 35 months, 66 patients experienced the combined event of death/CV events. Survival analyses considering the combined event death-CV events as outcome showed similar results. In a crude Cox regression analysis, HPP was directly and strongly related to the combined outcome (HR: 1.17, 95% CI: 1.08–1.26,  $p < 0.001$ ) (Table 4). In strict parallelism with the results obtained with mortality, such an association remained significant also after adjustment for potential confounders such as age, gender, diabetes, systolic arterial pressure, and dialysis adequacy (HR: 1.28, 95% CI: 1.11–1.47,  $p = 0.001$ ) (Table 4). By also adding the previous CV events as potential confounders to the previous adjusted COX model, the association remained statistically significant (HR: 1.25, 95% CI: 1.08–1.44,  $p = 0.003$ ). DBP confirmed the protective role for the combined outcome both at univariate and multivariate analysis (univariate analysis: HR for the 5-unit increase: 0.74, 95% CI: 0.65–0.84,  $p < 0.001$ ; multivariate analysis: HR for the 5-unit increase: 0.78, 95% CI: 0.68–0.91,  $p = 0.001$ ; multivariate analysis + previous cardiovascular comorbidities: HR for the 5-unit increase: 0.78, 95% CI: 0.68–0.91,  $p = 0.001$ ).

**Table 4.** Univariate and multivariate survival analysis showing the association between pulse pressure and the combined event of death/cardiovascular events.

Variables (Units of Increase)	Crude Analysis	Fully Adjusted Analysis	Over-Adjusted Analysis
Pulse Pressure (1 mmHg)	1.17 (1.08–1.26), $p < 0.001$	1.28 (1.11–1.47), $p = 0.001$	1.25 (1.08–1.44), $p = 0.003$
Age (1 year)		1.04 (1.01–1.06), $p = 0.01$	1.04 (1.01–1.06), $p = 0.01$
Gender (0 = female; 1 = male)		0.98 (0.54–1.74), $p = 0.93$	0.87 (0.48–1.58), $p = 0.65$
Diabetes (0 = no; 1 = yes)		0.93 (0.55–1.56), $p = 0.77$	1.01 (0.60–1.70), $p = 0.98$
Kt/V (1 unit)		0.74 (0.37–1.49), $p = 0.40$	0.67 (0.33–1.35), $p = 0.26$
Systolic Blood Pressure (1 mmHg)		0.96 (0.94–0.99); $p = 0.01$	0.97 (0.94–0.99); $p = 0.02$
Cardiovascular comorbidities (0 = no; 1 = yes)			1.60 (0.92–2.81), $p = 0.10$

No association was found between SBP (univariate analysis: HR for the 5-unit increase: 1.05, 95% CI: 0.97–1.14,  $p = 0.19$ ; multivariate analysis: HR for the 5-unit increase: 1.06, 95% CI: 0.97–1.17,  $p = 0.22$ ; multivariate analysis + previous cardiovascular comorbidities: HR for the 5-unit increase: 1.05, 95% CI: 0.95–1.15,  $p = 0.34$ ) and pulse pressure variability and the combined outcome (univariate analysis: HR for the 5-unit increase: 0.99, 95% CI: 0.97–1.03,  $p = 0.84$ ; multivariate analysis: HR for the 5-unit increase: 0.98, 95% CI: 0.93–1.03,  $p = 0.49$ ; multivariate analysis + previous cardiovascular comorbidities: HR for the 5-unit increase: 0.98, 95% CI: 0.93–1.03,  $p = 0.44$ ).

No effect modification by age or sex was found on the link between HPP and the combined outcome ( $p$  for effect modification  $> 0.51$ , Figure 2B) or on the association between the other BP measurements (SBP, DBP, and PP variability) and the same outcome (all  $p > 0.05$ ).

## 4. Discussion

In this study, we found a positive, significant association between HPP and clinical outcomes (all-cause mortality and the combined outcome mortality and fatal/non-fatal CV events), and these associations held true after adjustment for systolic blood pressure and previous cardiovascular comorbidities. HPP was also shown to be a better predictor of clinical outcomes than SBP and pulse pressure variability, whereas DBP confirmed its predictive role for the same outcomes.

Pulse pressure, an index of the pulsatile component of the cardiac cycle [53], has been associated with an increased risk of major cardiovascular events and all-cause and CV mortality in the general population [54–58]. Different from conventional blood pressure measurements, which present a U-shaped or reverse-J relationship with mortality in hemodialysis patients [11,14,27,59], pulse pressure has proven to have a strong and direct association with mortality in these patients [51,52], even after adjustment for systolic blood pressure [51]. In these patients, the capability of PP in predicting cardiovascular events such as ischemic heart disease seems superior to that of systolic pressure [58,60], even though, due to the high correlation between these two measurements, it is difficult to determine their effective contribution [61].

In PD patients, the increase in PP was significantly associated with all-cause mortality [45,47,52,62], cardiovascular mortality [45,52,62], and cardiovascular events [62], even after adjustment for SBP. Nevertheless, a large cohort study involving 2770 patients found an inverse association between PP short-term mortality and a direct one with long-term increased mortality [46]. In addition, in a large Chinese cohort (>7000 PD patients), higher PP (>60 mmHg) was associated with an increased risk of all-cause but not CV mortality [63]. However, all data shown so far refers to standardized pulse pressure measurements, i.e., blood pressure measurements taken at the dialysis unit via a standardized protocol.

In contrast with the other studies, we focused our analysis on BP measurements taken at home, thus without a standardized protocol, within the period of a month.

Unsurprisingly, we found a strong positive association between HPP and age, male gender, and previous cardiovascular events ( $r$  from 0.21 to 0.44,  $p < 0.01$ ). The association between HPP and previous cardiovascular comorbidities was independent of a list of potential confounders. This association was no longer significant after introducing the same model of systolic arterial pressure. In survival analysis, a five-unit increase in HPP was associated with a significant 17% (crude analysis) or 31% (adjusted analysis) increase in the hazard ratio of mortality. Similar results were obtained considering the combined death-CV events as an outcome. The predictive power of HPP overcame that of SBP or PP variability, as both failed to predict the considered outcomes. Different from the other BP measurements and in line with the literature, DBP was associated with a reduction of 30% of the risk of mortality and 26% of the risk of death and CV events in this population. Systolic, diastolic, and pulse pressure, though depending on vascular resistance and central artery stiffness, are variously affected by these components. DBP is raised by high peripheral vascular resistance and lowered by high arterial stiffness, so its values and, as a consequence, those of pulse pressure depend on the relative contribution of these factors. In contrast, pulse and systolic pressure are strongly interrelated because both rise with increases in vascular resistance and arterial stiffness [50].

The strong correlation between pulse pressure and arterial stiffness originates from age-related vascular calcification. This process translates into arterial stiffening, which in turn causes larger forward wave amplitude, earlier reflected wave arrival, and greater pulse pressure [64,65]. For this reason, although not a direct measure of arterial stiffness, pulse pressure is usually used as a surrogate marker of arterial compliance [66]. Taken together, this data suggests that the direct associations of HPP with clinical outcomes may be a direct consequence of arterial aging, a well-established cardiovascular risk predictor among people in dialysis patients [67,68].

The same dependence of SBP and PP from vascular resistance and arterial stiffness may explain why, when put together in our models, they remain both significantly associated with all-cause mortality and with the combined event mortality/CV events.

The main limitation of our study is the small sample size. However, with a follow up of about 3 years and almost half of the patients experiencing the event of interest, our cohort can be considered satisfactory. Secondly, enrolled patients were followed up in a single dialysis center, and this prevented our results from being generalized. Third, the overall number of the events collected was relatively small, thus limiting the number of potential confounders to be included in the models. Furthermore, smoking habits were

available only in a limited number of subjects. As a further limitation, data about aortic regurgitation was not available in our dataset, so we were not able to exclude from the analysis patients affected by this comorbidity.

In spite of these limitations, our study is the first to show that home blood pressure, measured within a period of a month, is linearly associated with death and cardiovascular events in clinical outcomes and that this association is independent of SBP.

## 5. Conclusions

In conclusion, home BP monitoring is considered a more suitable option for the management of hypertension in dialysis patients, and home pulse pressure represents, in part, arterial stiffness, and it is strongly related to all-cause mortality in peritoneal patients. In these high cardiovascular risk populations, multiple approaches, drug therapy associated with a better volume status control, lifestyle, and sodium and water intake are important to maintain optimal blood pressure control, but it is fundamental to consider all other cardiovascular risk indicators, such as pulse pressure. Home pulse pressure measurement is easy and feasible and can add important information to identify and manage high-risk patients.

**Author Contributions:** Conceptualization, V.P., R.T. and C.T.; methodology, G.L.T.; formal analysis, P.F.P., R.T., S.M., D.A. and G.L.T.; data curation, R.T., M.C.V., A.V., E.P. and G.P.; writing—original draft preparation, V.P., P.F.P. and C.T.; writing—review and editing, V.P., P.F.P., R.T., M.C.V., G.P., E.P., A.V., S.M., D.A., G.L.T. and C.T.; supervision, C.T. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Institutional Review Board Statement:** This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of our institution (Sezione Sud—Regione Calabria (n. 87, date 21 July 2021).

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in this study.

**Data Availability Statement:** The data presented in this study are available on request from the corresponding author. The data are not publicly available as related to sensitive data for which informed consent was needed.

**Acknowledgments:** We thank Demetrio Cutrupi for his administrative support in the submission phase.

**Conflicts of Interest:** The authors declare no conflict of interest.

## References

1. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet* **2015**, *385*, 117–171. [[CrossRef](#)] [[PubMed](#)]
2. De Nicola, L.; Chiodini, P.; Zoccali, C.; Borrelli, S.; Cianciaruso, B.; Di Iorio, B.; Santoro, D.; Giancaspro, V.; Abaterusso, C.; Gallo, C.; et al. Prognosis of CKD patients receiving outpatient nephrology care in Italy. *Clin. J. Am. Soc. Nephrol.* **2011**, *6*, 2421–2428. [[CrossRef](#)]
3. Agarwal, R.; Nissenson, A.R.; Batlle, D.; Coyne, D.W.; Trout, J.R.; Warnock, D.G. Prevalence, treatment, and control of hypertension in chronic hemodialysis patients in the United States. *Am. J. Med.* **2003**, *115*, 291–297. [[CrossRef](#)]
4. Rossignol, P.; Massy, Z.A.; Azizi, M.; Bakris, G.; Ritz, E.; Covic, A.; Goldsmith, D.; Heine, G.H.; Jager, K.J.; Kanbay, M.; et al. The double challenge of resistant hypertension and chronic kidney disease. *Lancet* **2015**, *386*, 1588–1598. [[CrossRef](#)] [[PubMed](#)]
5. Minutolo, R.; Agarwal, R.; Borrelli, S.; Chiodini, P.; Bellizzi, V.; Nappi, F.; Cianciaruso, B.; Zamboli, P.; Conte, G.; Gabbai, F.B.; et al. Prognostic role of ambulatory blood pressure measurement in patients with nondialysis chronic kidney disease. *Arch. Intern. Med.* **2011**, *171*, 1090–1098. [[CrossRef](#)] [[PubMed](#)]
6. Tripepi, G.; Fagugli, R.M.; Dattolo, P.; Parlongo, G.; Mallamaci, F.; Buon cristiani, U.; Zoccali, C. Prognostic value of 24-hour ambulatory blood pressure monitoring and of night/day ratio in nondiabetic, cardiovascular events-free hemodialysis patients. *Kidney Int.* **2005**, *68*, 1294–1302. [[CrossRef](#)] [[PubMed](#)]
7. Sytkowski, P.A.; D’Agostino, R.B.; Belanger, A.J.; Kannel, W.B. Secular trends in long-term sustained hypertension, long-term treatment, and cardiovascular mortality. The Framingham Heart Study 1950 to 1990. *Circulation* **1996**, *93*, 697–703. [[CrossRef](#)] [[PubMed](#)]
8. Page, M.R. The JNC 8 hypertension guidelines: An in-depth guide. *Am. J. Manag. Care* **2014**, *20*, E8.

9. Lewington, S.; Clarke, R.; Qizilbash, N.; Peto, R.; Collins, R. Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* **2002**, *360*, 1903–1913.
10. Charra, B.; Calémard, E.; Ruffet, M.; Chazot, C.; Terrat, J.C.; Vanel, T.; Laurent, G. Survival as an index of adequacy of dialysis. *Kidney Int.* **1992**, *41*, 1286–1291. [[CrossRef](#)] [[PubMed](#)]
11. Salem, M.M.; Bower, J. Hypertension in the hemodialysis population: Any relation to one-year survival? *Am. J. Kidney Dis.* **1996**, *28*, 737–740. [[CrossRef](#)]
12. Mazzuchi, N.; Carbonell, E.; Fernández-Cean, J. Importance of blood pressure control in hemodialysis patient survival. *Kidney Int.* **2000**, *58*, 2147–2154. [[CrossRef](#)]
13. Duranti, E.; Imperiali, P.; Sasdelli, M. Is hypertension a mortality risk factor in dialysis? *Kidney Int. Suppl.* **1996**, *55*, S173–S174.
14. Salem, M.M. Hypertension in the haemodialysis population: Any relationship to 2-years survival? *Nephrol. Dial. Transplant* **1999**, *14*, 125–128. [[CrossRef](#)]
15. Kalantar-Zadeh, K.; Kilpatrick, R.D.; McAllister, C.J.; Greenland, S.; Kopple, J.D. Reverse epidemiology of hypertension and cardiovascular death in the hemodialysis population: The 58th annual fall conference and scientific sessions. *Hypertension* **2005**, *45*, 811–817. [[CrossRef](#)]
16. Port, F.K.; Robinson, B.M.; McCullough, K.P.; Morgenstern, H. Predialysis blood pressure on survival in hemodialysis patients. *Kidney Int.* **2017**, *91*, 755–756. [[CrossRef](#)] [[PubMed](#)]
17. Robinson, B.M.; Tong, L.; Zhang, J.; Wolfe, R.A.; Goodkin, D.A.; Greenwood, R.N.; Kerr, P.G.; Morgenstern, H.; Li, Y.; Pisoni, R.L.; et al. Blood pressure levels and mortality risk among hemodialysis patients in the Dialysis Outcomes and Practice Patterns Study. *Kidney Int.* **2012**, *82*, 570–580. [[CrossRef](#)] [[PubMed](#)]
18. Torino, C.; Tripepi, R.; Versace, M.C.; Vilasi, A.; Tripepi, G.; Panuccio, V. Clinical Epidemiology of Systolic and Diastolic Orthostatic Hypotension in Patients on Peritoneal Dialysis. *J. Clin. Med.* **2021**, *10*, 3075. [[CrossRef](#)] [[PubMed](#)]
19. Inrig, J.K.; Patel, U.D.; Toto, R.D.; Szczech, L.A. Association of blood pressure increases during hemodialysis with 2-year mortality in incident hemodialysis patients: A secondary analysis of the Dialysis Morbidity and Mortality Wave 2 Study. *Am. J. Kidney Dis.* **2009**, *54*, 881–890. [[CrossRef](#)]
20. Inrig, J.K.; Oddone, E.Z.; Hasselblad, V.; Gillespie, B.; Patel, U.D.; Reddan, D.; Toto, R.; Himmelfarb, J.; Winchester, J.F.; Stivelman, J.; et al. Association of intradialytic blood pressure changes with hospitalization and mortality rates in prevalent ESRD patients. *Kidney Int.* **2007**, *71*, 454–461. [[CrossRef](#)]
21. Chen, J.; Gul, A.; Sarnak, M.J. Management of intradialytic hypertension: The ongoing challenge. *Semin. Dial.* **2006**, *19*, 141–145. [[CrossRef](#)] [[PubMed](#)]
22. Agarwal, R. Hypertension and survival in chronic hemodialysis patients—past lessons and future opportunities. *Kidney Int.* **2005**, *67*, 1–13. [[CrossRef](#)] [[PubMed](#)]
23. Li, Z.; Lacson, E.; Lowrie, E.G.; Ofsthun, N.J.; Kuhlmann, M.K.; Lazarus, J.M.; Levin, N.W. The epidemiology of systolic blood pressure and death risk in hemodialysis patients. *Am. J. Kidney Dis.* **2006**, *48*, 606–615. [[CrossRef](#)] [[PubMed](#)]
24. Amar, J.; Vernier, I.; Rossignol, E.; Bongard, V.; Arnaud, C.; Conte, J.J.; Salvador, M.; Chamontin, B. Nocturnal blood pressure and 24-hour pulse pressure are potent indicators of mortality in hemodialysis patients. *Kidney Int.* **2000**, *57*, 2485–2491. [[CrossRef](#)]
25. Foley, R.N.; Herzog, C.A.; Collins, A.J. Blood pressure and long-term mortality in United States hemodialysis patients: USRDS Waves 3 and 4 Study. *Kidney Int.* **2002**, *62*, 1784–1790. [[CrossRef](#)]
26. Park, J.; Rhee, C.M.; Sim, J.J.; Kim, Y.L.; Ricks, J.; Streja, E.; Vashistha, T.; Tolouian, R.; Kovesdy, C.P.; Kalantar-Zadeh, K. A comparative effectiveness research study of the change in blood pressure during hemodialysis treatment and survival. *Kidney Int.* **2013**, *84*, 795–802. [[CrossRef](#)]
27. Zager, P.G.; Nikolic, J.; Brown, R.H.; Campbell, M.A.; Hunt, W.C.; Peterson, D.; Van Stone, J.; Levey, A.; Meyer, K.B.; Klag, M.J.; et al. “U” curve association of blood pressure and mortality in hemodialysis patients. *Kidney Int.* **1998**, *54*, 561–569. [[CrossRef](#)] [[PubMed](#)]
28. Rahman, M.; Griffin, V.; Kumar, A.; Manzoor, F.; Wright, J.T.; Smith, M.C. A comparison of standardized versus “usual” blood pressure measurements in hemodialysis patients. *Am. J. Kidney Dis.* **2002**, *39*, 1226–1230. [[CrossRef](#)] [[PubMed](#)]
29. Agarwal, R.; Andersen, M.J.; Bishu, K.; Saha, C. Home blood pressure monitoring improves the diagnosis of hypertension in hemodialysis patients. *Kidney Int.* **2006**, *69*, 900–906. [[CrossRef](#)] [[PubMed](#)]
30. Agarwal, R.; Lewis, R.R. Prediction of hypertension in chronic hemodialysis patients. *Kidney Int.* **2001**, *60*, 1982–1989. [[CrossRef](#)] [[PubMed](#)]
31. Agarwal, R.; Peixoto, A.J.; Santos, S.F.F.; Zoccali, C. Pre- and postdialysis blood pressures are imprecise estimates of interdialytic ambulatory blood pressure. *Clin. J. Am. Soc. Nephrol.* **2006**, *1*, 389–398. [[CrossRef](#)] [[PubMed](#)]
32. Agarwal, R.; Brim, N.J.; Mahenthiran, J.; Andersen, M.J.; Sana, C. Out-of-hemodialysis-unit blood pressure is a superior determinant of left ventricular hypertrophy. *Hypertension* **2006**, *47*, 62–68. [[CrossRef](#)]
33. Thompson, A.M.; Pickering, T.G. The role of ambulatory blood pressure monitoring in chronic and end-stage renal disease. *Kidney Int.* **2006**, *70*, 1000–1007. [[CrossRef](#)] [[PubMed](#)]
34. Bansal, N.; McCulloch, C.E.; Rahman, M.; Kusek, J.W.; Anderson, A.H.; Xie, D.; Townsend, R.R.; Lora, C.M.; Wright, J.; Go, A.S.; et al. Blood pressure and risk of all-cause mortality in advanced chronic kidney disease and hemodialysis: The chronic renal insufficiency cohort study. *Hypertension* **2015**, *65*, 93–100. [[CrossRef](#)]

35. Alborzi, P.; Patel, N.; Agarwal, R. Home blood pressures are of greater prognostic value than hemodialysis unit recordings. *Clin. J. Am. Soc. Nephrol.* **2007**, *2*, 1228–1234. [\[CrossRef\]](#) [\[PubMed\]](#)
36. Agarwal, R. Blood pressure and mortality among hemodialysis patients. *Hypertension* **2010**, *55*, 762–768. [\[CrossRef\]](#)
37. Bansal, N.; McCulloch, C.E.; Lin, F.; Alper, A.; Anderson, A.H.; Cuevas, M.; Go, A.S.; Kallem, R.; Kusek, J.W.; Lora, C.M.; et al. Blood Pressure and Risk of Cardiovascular Events in Patients on Chronic Hemodialysis: The CRIC Study (Chronic Renal Insufficiency Cohort). *Hypertension* **2017**, *70*, 435–443. [\[CrossRef\]](#)
38. Jardine, A.G. Con: Ambulatory blood pressure measurement in patients receiving haemodialysis: A sore arm and a waste of time? *Nephrol. Dial. Transpl.* **2015**, *30*, 1438–1441. [\[CrossRef\]](#)
39. Zoccali, C.; Tripepi, R.; Torino, C.; Tripepi, G.; Mallamaci, F. Moderator's view: Ambulatory blood pressure monitoring and home blood pressure for the prognosis, diagnosis and treatment of hypertension in dialysis patients. *Nephrol. Dial. Transpl.* **2015**, *30*, 1443–1448. [\[CrossRef\]](#)
40. Shimbo, D.; Abdalla, M.; Falzon, L.; Townsend, R.R.; Muntner, P. Studies comparing ambulatory blood pressure and home blood pressure on cardiovascular disease and mortality outcomes: A systematic review. *J. Am. Soc. Hypertens.* **2016**, *10*, 224–234.e17. [\[CrossRef\]](#) [\[PubMed\]](#)
41. Shimbo, D.; Artinian, N.T.; Basile, J.N.; Krakoff, L.R.; Margolis, K.L.; Rakotz, M.K.; Wozniak, G. Self-Measured Blood Pressure Monitoring at Home: A Joint Policy Statement from the American Heart Association and American Medical Association. *Circulation* **2020**, *142*, E42–E63. [\[CrossRef\]](#) [\[PubMed\]](#)
42. O'Shaughnessy, M.M.; Durcan, M.; Kinsella, S.M.; Griffin, M.D.; Reddan, D.N.; Lappin, D.W. Blood pressure measurement in peritoneal dialysis: Which method is best? *Perit. Dial. Int.* **2013**, *33*, 544–551. [\[CrossRef\]](#) [\[PubMed\]](#)
43. Wang, M.C.; Tseng, C.C.; Tsai, W.C.; Huang, J.J. Blood pressure and left ventricular hypertrophy in patients on different peritoneal dialysis regimens. *Perit. Dial. Int.* **2001**, *21*, 36–42. [\[CrossRef\]](#)
44. Vaios, V.; Georgianos, P.I.; Vareta, G.; Dounousi, E.; Dimitriadis, C.; Eleftheriadis, T.; Papagianni, A.; Zebekakis, P.E.; Liakopoulos, V. Clinic and Home Blood Pressure Monitoring for the Detection of Ambulatory Hypertension Among Patients on Peritoneal Dialysis. *Hypertension* **2019**, *74*, 998–1004. [\[CrossRef\]](#)
45. Fang, W.; Yang, X.; Bargman, J.M.; Oreopoulos, D.G. Association between pulse pressure and mortality in patients undergoing peritoneal dialysis. *Perit. Dial. Int.* **2009**, *29*, 163–170. [\[CrossRef\]](#) [\[PubMed\]](#)
46. Udayaraj, U.P.; Steenkamp, R.; Caskey, F.J.; Rogers, C.; Nitsch, D.; Ansell, D.; Tomson, C.R.V. Blood pressure and mortality risk on peritoneal dialysis. *Am. J. Kidney Dis.* **2009**, *53*, 70–78. [\[CrossRef\]](#) [\[PubMed\]](#)
47. Liu, J.H.; Chen, C.C.; Wang, S.M.; Chou, C.Y.; Liu, Y.L.; Kuo, H.L.; Lin, H.H.; Wang, I.K.; Yang, Y.F.; Huang, C.C. Association between pulse pressure and 30-month all-cause mortality in peritoneal dialysis patients. *Am. J. Hypertens.* **2008**, *21*, 1318–1323. [\[CrossRef\]](#)
48. London, G.M.; Marchais, S.J.; Safar, M.E.; Genest, A.F.; Guerin, A.P.; Metivier, F.; Chedid, K.; London, A.M. Aortic and large artery compliance in end-stage renal failure. *Kidney Int.* **1990**, *37*, 137–142. [\[CrossRef\]](#)
49. Barenbrock, M.; Spieker, C.; Laske, V.; Heidenreich, S.; Hohage, H.; Bachmann, J.; Hoeks, A.P.G.; Rahn, K.H. Studies of the vessel wall properties in hemodialysis patients. *Kidney Int.* **1994**, *45*, 1397–1400. [\[CrossRef\]](#)
50. Kannel, W.B.; Dawber, T.R.; McGee, D.L. Perspectives on systolic hypertension. The Framingham study. *Circulation* **1980**, *61*, 1179–1182. [\[CrossRef\]](#)
51. Klassen, P.S.; Lowrie, E.G.; Reddan, D.N.; DeLong, E.R.; Coladonato, J.A.; Szczech, L.A.; Michael Lazarus, J.; Owen, W.F. Association between pulse pressure and mortality in patients undergoing maintenance hemodialysis. *JAMA* **2002**, *287*, 1548–1555. [\[CrossRef\]](#)
52. Tozawa, M.; Iseki, K.; Iseki, C.; Takishita, S. Pulse pressure and risk of total mortality and cardiovascular events in patients on chronic hemodialysis. *Kidney Int.* **2002**, *61*, 717–726. [\[CrossRef\]](#)
53. Da Nichols, W.W.; O'Rourke, M.F. *McDonald's Blood Flow in Arteries: Theoretic, Experimental and Clinical Principles*; Anybook Ltd.: London, UK, 1998.
54. Benetos, A.; Rudnichi, A.; Safar, M.; Guize, L. Pulse pressure and cardiovascular mortality in normotensive and hypertensive subjects. *Hypertension* **1998**, *32*, 560–564. [\[CrossRef\]](#) [\[PubMed\]](#)
55. Domanski, M.J.; Mitchell, G.F.; Norman, J.E.; Exner, D.V.; Pitt, B.; Pfeffer, M.A. Independent prognostic information provided by sphygmomanometrically determined pulse pressure and mean arterial pressure in patients with left ventricular dysfunction. *J. Am. Coll. Cardiol.* **1999**, *33*, 951–958. [\[CrossRef\]](#)
56. Chae, C.U.; Pfeffer, M.A.; Glynn, R.J.; Mitchell, G.F.; Taylor, J.O.; Hennekens, C.H. Increased pulse pressure and risk of heart failure in the elderly. *JAMA* **1999**, *281*, 634–639. [\[CrossRef\]](#) [\[PubMed\]](#)
57. Domanski, M.J.; Davis, B.R.; Pfeffer, M.A.; Kastantin, M.; Mitchell, G.F. Isolated systolic hypertension: Prognostic information provided by pulse pressure. *Hypertension* **1999**, *34*, 427–433. [\[CrossRef\]](#)
58. Franklin, S.S.; Khan, S.A.; Wong, N.D.; Larson, M.G.; Levy, D. Is pulse pressure useful in predicting risk for coronary heart Disease? The Framingham heart study. *Circulation* **1999**, *100*, 354–360. [\[CrossRef\]](#)
59. Port, F.K.; Hulbert-Shearon, T.E.; Wolfe, R.A.; Bloembergen, W.E.; Golper, T.A.; Agodoa, L.Y.C.; Young, E.W.; Salem, M. Predialysis blood pressure and mortality risk in a national sample of maintenance hemodialysis patients. *Am. J. Kidney Dis.* **1999**, *33*, 507–517. [\[CrossRef\]](#) [\[PubMed\]](#)
60. Safar, M.E. Pulse pressure, arterial stiffness, and cardiovascular risk. *Curr. Opin. Cardiol.* **2000**, *15*, 258–263. [\[CrossRef\]](#)

61. Celentano, A.; Palmieri, V.; Di Palma Esposito, N.; Pietropaolo, I.; Arezzi, E.; Mureddu, G.F.; De Simone, G. Relations of pulse pressure and other components of blood pressure to preclinical echocardiographic abnormalities. *J. Hypertens.* **2002**, *20*, 531–537. [[CrossRef](#)]
62. Dai, S.; Chen, Y.; Shang, D.; Ge, X.; Xie, Q.; Hao, C.M.; Zhu, T. Association of Ambulatory Blood Pressure with All-Cause Mortality and Cardiovascular Outcomes in Peritoneal Dialysis Patients. *Kidney Blood Press. Res.* **2020**, *45*, 890–899. [[CrossRef](#)] [[PubMed](#)]
63. Xie, X.; Lv, D.; Zheng, H.; Zhang, X.; Han, F.; Chen, J. The associations of blood pressure parameters with all-cause and cardiovascular mortality in peritoneal dialysis patients: A cohort study in China. *J. Hypertens.* **2020**, *38*, 2252–2260. [[CrossRef](#)] [[PubMed](#)]
64. Mitchell, G.F.; Parise, H.; Benjamin, E.J.; Larson, M.G.; Keyes, M.J.; Vita, J.A.; Vasan, R.S.; Levy, D. Changes in arterial stiffness and wave reflection with advancing age in healthy men and women: The Framingham Heart Study. *Hypertension* **2004**, *43*, 1239–1245. [[CrossRef](#)] [[PubMed](#)]
65. Mitchell, G.F.; Wang, N.; Palmisano, J.N.; Larson, M.; Hamburg, N.M.; Vita, J.A.; Levy, D.; Benjamin, E.J.; Vasan, R.S. Hemodynamic correlates of blood pressure across the adult age spectrum: Noninvasive evaluation in the Framingham Heart Study. *Circulation* **2010**, *122*, 1379–1386. [[CrossRef](#)] [[PubMed](#)]
66. Mackenzie, I.S.; Wilkinson, I.B.; Cockcroft, J.R. Assessment of arterial stiffness in clinical practice. *QJM* **2002**, *95*, 67–74. [[CrossRef](#)] [[PubMed](#)]
67. Georgianos, P.I.; Sarafidis, P.A.; Lasaridis, A.N. Arterial stiffness: A novel cardiovascular risk factor in kidney disease patients. *Curr. Vasc. Pharmacol.* **2015**, *13*, 229–238. [[CrossRef](#)] [[PubMed](#)]
68. London, G.M.; Safar, M.E.; Pannier, B. Aortic Aging in ESRD: Structural; Hemodynamic; and Mortality Implications. *J. Am. Soc. Nephrol.* **2016**, *27*, 1837–1846. [[CrossRef](#)]

**Disclaimer/Publisher's Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.