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Relationship Between Estimated Pulse Wave Velocity and Mortality Risk in Patients with Atrial Fibrillation: A Retrospective Cohort Analysis of Medical Information Mart for Intensive Care-IV Database

ORIGINAL INVESTIGATION

ABSTRACT

Objective: Pulse wave velocity (PWV) serves as a reliable indicator of arterial stiffness and is correlated with the occurrence and prognosis of cardiovascular diseases. This analysis investigates the connection of estimated PWV (ePWV) with mortality risk among atrial fibrillation (AF) patients.

Methods: This retrospective cohort analysis incorporated data on critically ill AF patients derived from the Medical Information Mart for Intensive Care-IV (2008-2022). Estimated pulse wave velocity was computed by a validated formula. The connection of ePWV with mortality risk was examined using Cox regression analyses. Restricted cubic spline (RCS) curves were employed to evaluate the non-linear correlation and to determine the cutoff values for ePWV classification.

Results: Of these 14 659 AF patients enrolled, 30-day mortality occurred in 2587 (17.65%) patients, and 1-year mortality in 4765 (32.51%) patients. The RCS curves presented a non-linear correlation of ePWV with both 30-day and 1-year mortality risk ($P < .001$). Patients with ePWV levels ≥ 11.302 m/s had a higher risk of 30-day mortality (hazard ratio [HR] = 1.20 [95% CI: 1.06-1.19]) and 1-year mortality (HR = 1.11 [95% CI: 1.02-1.21]) versus those with ePWV < 11.302 m/s, and this correlation was also observed in subgroups according to age, gender, Sequential Organ Failure Assessment (SOFA) score, heart failure, vasoactive drugs, and AF types ($P < .05$). Moreover, ePWV levels combined with the SOFA score were a better predictor of 30-day/1-year mortality than the SOFA score alone.

Conclusion: Elevated ePWV levels were connected with a higher risk of short-term mortality among AF patients, and ePWV presented prognostic predictive ability.

Keywords: Atrial fibrillation, estimated pulse wave velocity, MIMIC-IV, non-linear correlation, short-term mortality

INTRODUCTION

Atrial fibrillation (AF), the predominant sustained arrhythmia, manifests as rapid and disorganized atrial activation, resulting in ineffective atrial contraction and an irregular ventricular response.[1] The prevalence and incidence of AF increase with age,[2] and AF-related mortality is also increasing globally.[3,4] AF also increases the risk of stroke, cognitive impairment, heart failure, and systemic thromboembolism.[5] Risk factors for AF encompass advanced age, smoking, male, alcohol consumption, obesity, hypertension, family history of AF, heart failure, intraoperative or postoperative atrial injury, and myocardial ischemia.[1,5] Hypertension merits particular attention, as it accounts for one-sixth of AF cases.[6,7] Hypertension can simultaneously promote the onset of AF, accelerate arteriosclerosis, and increase cardiovascular risk through common pathophysiological pathways.[8]

Arterial stiffness significantly contributes to the development and worsening of cardiovascular diseases.[9] Some studies have revealed that the development, symptom progression, and recurrence of AF are linked to arterial stiffness.[10,11]

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Carotid-femoral pulse wave velocity (PWV) stands as the gold standard in arterial stiffness evaluation and provides crucial information about cardiovascular health by quantifying the speed at which a pressure wave travels through arteries.[12] However, the practicality of PWV measurements is limited by their inconvenience.[13] Previous studies have proposed using estimated PWV (ePWV) levels, calculated from age and blood pressure, to reflect arterial stiffness and vascular aging.[14]Subsequent prospective studies have confirmed that ePWV is correlated with a raised risk of mortality[15] and stroke.[16] Several studies have also reported that elevated ePWV levels had a connection with an enhanced mortality risk among those with obesity[17] and heart failure.[18] The impact of PWV on mortality may be linked to increased pressure in the microvascular system of terminal organs and endothelial dysfunction caused by vascular dynamic changes.[18] However, the correlation of ePWV with mortality risk among AF patients remains unclear. Thus, this analysis intends to evaluate the connection of ePWV with mortality risk among AF patients, providing a reference for the prognostic management of AF.

METHODS

Study Design and Population

Data from the Medical Information Mart for Intensive Care-IV (MIMIC-IV) database (2008-2022) were employed in this retrospective cohort analysis. Medical Information Mart for Intensive Care-IV records real hospitalization data for inpatients at a medical center (Boston, MA, USA) from 2008 and beyond, and the data have been updated to 2022 (https://mimic.mit.edu/docs/iv/). Information about the patient's hospitalization, including laboratory data, medications, and vital signs, is recorded in the database. Medical Information Mart for Intensive database protocols were ethically sanctioned by the Institutional Review Boards of the Beth Israel Deaconess Medical Center and the Massachusetts Institute of Technology. Informed consent was not required due to the anonymity of patient information in the database. Patients with AF on their first intensive care unit (ICU) admission were enrolled in this analysis. Exclusion criteria were: (1) age < 18 years old; (2) ICU length < 24 hours; (3) missing information on systolic blood pressure (SBP); (4) missing data on diastolic blood pressure (DBP); and (5) missing information on survival status. Atrial fibrillation patients in the MIMIC-IV were determined using the International Classification of Diseases ninth/10th (ICD-9/10) codes (ICD-9: 42731; ICD-10: I480, I481, I4811, I4819, I482, I4820, I4821, I4891).[19]

HIGHLIGHTS

- Estimated pulse wave velocity (ePWV) is an effective estimate of arterial stiffness based on age and blood pressure.
- Estimated pulse wave velocity is nonlinearly correlated with 30-day/1-year mortality risk in atrial fibrillation (AF) patients.
- Estimated pulse wave velocity ≥ 11.302 m/s had a higher risk of 30-day and 1-year mortality in AF patients.

Ethics Approval and Consent to Participate

Given the use of fully anonymized and de-identified clinical data extracted from a publicly accessible database, ethical review and informed consent were not required for the present investigation.

Outcomes

The endpoints assessed in this analysis were 30-day mortality and 1-year mortality, which referred to deaths from any cause within 30 days/1 year following the patient's ICU admission. The survival status of patients was monitored for a 1-year period following their ICU admission.

Calculation of Estimated Pulse Wave Velocity

The subsequent formula was applied to compute ePWV values [20]: $ePWV = (9.587 - [0.402 \times age] + [4.560 \times 0.001 \times age^2] - [2.621 \times 0.00001 \times age^2 \times MBP] + [3.176 \times 0.001 \times age \times MBP] - [1.832 \times 0.01 \times MBP])$. Where mean blood pressure (MBP) was computed as (DBP + 0.4× [SBP − DBP]). Blood pressure was measured at the time of initial ICU admission. In this analysis, ePWV was analyzed using continuous and categorical (<11.302, ≥11.302 m/s) values, respectively. The cutoff value for ePWV classification was derived from the inflection point (11.302) of the restricted cubic splines (RCS) curve.

Data Collection

Data on patients' first ICU admission were collected, covering age, gender, race, Sequential Organ Failure Assessment (SOFA), diabetes, heart failure, acute ischemic stroke (AIS), sepsis, acute kidney injury (AKI), Charlson Comorbidity Index (CCI), AF type, weight, heart rate, respiratory rate, international normalized ratio (INR), oxyhemoglobin saturation (SpO_2), red blood cell distribution width (RDW), temperature, white blood cell (WBC), anion gap, platelet, calcium, hemoglobin, hematocrit, glucose, blood urea nitrogen (BUN), ventilation, vasoactive drugs, antiarrhythmic, anticoagulant drugs, antiplatelet drugs, SBP, DBP, MBP, renal replacement therapy (RRT), length of ICU stay, and follow-up time. AF types include paroxysmal, persistent, chronic, and unspecified AF. The identification of AIS, heart failure, and diabetes used the ICD codes. The diagnosis of sepsis was established based on the Sepsis 3.0 criteria, which define the condition as a suspected infection and a SOFA score ≥ 2. The occurrence of AKI was determined using Kidney Disease Improving Global Outcomes (KDIGO) criteria.

Statistical Analysis

For continuous data, normality was checked via skewness and kurtosis, and variance homogeneity was determined using the Levene test. Continuous data are reported as mean and SD or median and quartiles (M [Q1, Q3]), and comparisons between groups via *t*-test, *t'*-test, or Wilcoxon rank-sum test as appropriate. Categorical data are shown as frequency and composition ratio (n [%]), and comparisons between groups using χ^2 or Fisher's exact test. Covariates featuring ≥20% missingness were excluded, whereas random forest interpolation was employed to impute those with <20% missing values. Comparative analyses were conducted to examine the differences in missing variables pre- and post-interpolation (Supplementary Table 1).

Potential confounders correlated with 30-day/1-year mortality were initially identified through univariable Cox regression, followed by bidirectional stepwise selection based on Akaike Information Criterion (AIC) minimization to screen variables demonstrating $P < .05$ in univariable analyses (Supplementary Tables 2 and 3). The correlation of ePWV with 30-day/1-year mortality risk was examined using uni- and multivariable Cox regression, and the correlation was presented as hazard ratio and 95% confidence interval (HR [95% CI]). Additional analyses were carried out according to age (<65, ≥65 years), gender, SOFA score (<4, ≥4), CCI (<6, ≥6), heart failure (presence vs. absence), vasoactive drug (used, not used), and AF type (paroxysmal, persistent, chronic, and unspecified) subgroups. Multivariable Cox regression adjusted for (1) age, gender, race, heart failure, AIS, AKI, AF type, SOFA, CCI, weight, heart rate, respiratory rate, SPO_2, platelet, INR, glucose, BUN, RDW, anion gap, ventilation, vasoactive drugs, RRT, antiarrhythmic, anticoagulant drugs, and antiplatelet drugs, when analyzed the risk of 30-day mortality; or (2) age, race, diabetes, heart failure, AIS, AKI, AF type, SOFA, CCI, weight, heart rate, respiratory rate, SPO_2, temperature, platelet, INR, hematocrit, glucose, BUN, RDW, anion gap, ventilation, RRT, antiarrhythmic, anticoagulant drugs, and antiplatelet drugs, when analyzed the risk of 1-year mortality. Potential multicollinearity among the variables included in the multivariable model was assessed using the variance inflation factor (VIF) (Supplementary Table 4). The non-linear correlation of ePWV with 30-day/1-year mortality risk was assessed through the RCS curve. The Kaplan–Meier (KM) curves were applied to examine the impact of ePWV on 30-day/1-year survival. Furthermore, the predictive value of ePWV (ePWV + SOFA vs. SOFA alone) for 30-day/1-year mortality was investigated by the area under the receiver operating characteristic (ROC) curve (AUC). R 4.4.3 software (Institute for Statistics and Mathematics, Vienna, Austria) was employed for all statistical analyses, where $P < .05$ indicated significant.

RESULTS

Patient Characteristics

The MIMIC-IV database contained records of 17 410 patients with AF prior to ICU admission. Application of exclusion criteria resulted in 14 659 eligible patients for analysis, after removing 2751 patients (Figure 1). The characteristics of AF patients are displayed in Table 1. Of these 14 659 AF patients, 30-day mortality occurred in 2587 (17.65%) patients, and 1-year mortality in 4765 (32.51%) patients. Patients had a mean age of 73.02 (±11.69) years, with males comprising 8792 (59.98%) patients. Patients demonstrated a mean SOFA score of 5.00 (±3.13), with a mean ePWV level of 11.39 (±2.61) m/s. Significant baseline characteristic differences existed between the ePWV <11.302 and ≥11.302 groups ($P < .05$), extending beyond ICU length, heart rate, and temperature.

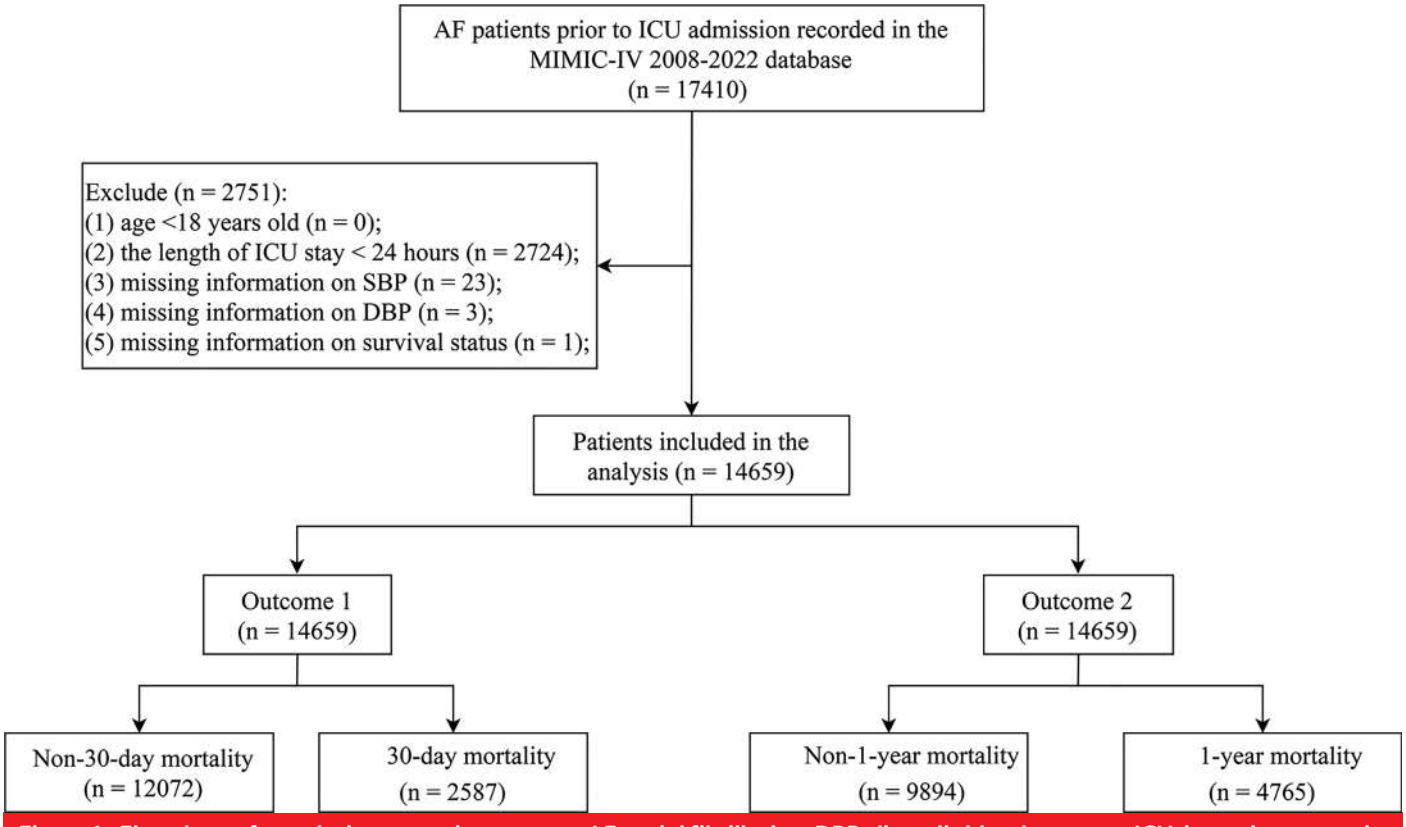

Figure 1. Flowchart of population screening process. AF, atrial fibrillation; DBP, diastolic blood pressure; ICU, intensive care unit; MIMIC-IV, the Medical Information Mart for Intensive Care-IV database; SBP, systolic blood pressure.

Table 1. Characteristics of AF Patients

Variables	Total (n = 14 659)	ePWV < 11.302 (n = 7391)	ePWV ≥ 11.302 (n = 7268)	*P*
Age, years, mean (±SD)	73.02 (±11.69)	64.78 (±9.33)	81.41 (±6.90)	<.001
Gender, n (%)				<.001
Female	5867 (40.02)	2443 (33.05)	3424 (47.11)	
Male	8792 (59.98)	4948 (66.95)	3844 (52.89)	
Race, n (%)				<.001
White	10547 (71.95)	5263 (71.21)	5284 (72.70)	
Black	802 (5.47)	442 (5.98)	360 (4.95)	
Others	1655 (11.29)	907 (12.27)	748 (10.29)	
Unknown	1655 (11.29)	779 (10.54)	876 (12.05)	
Diabetes, n (%)				<.001
No	9932 (67.75)	4763 (64.44)	5169 (71.12)	
Yes	4727 (32.25)	2628 (35.56)	2099 (28.88)	
Heart failure, n (%)				<.001
No	8272 (56.43)	4465 (60.41)	3807 (52.38)	
Yes	6387 (43.57)	2926 (39.59)	3461 (47.62)	
AIS, n (%)				<.001
No	12930 (88.21)	6806 (92.08)	6124 (84.26)	
Yes	1729 (11.79)	585 (7.92)	1144 (15.74)	
Sepsis, n (%)				<.001
No	11340 (77.36)	5521 (74.70)	5819 (80.06)	
Yes	3319 (22.64)	1870 (25.30)	1449 (19.94)	
AKI, n (%)				<.001
No	6346 (43.29)	3022 (40.89)	3324 (45.73)	
Yes	8313 (56.71)	4369 (59.11)	3944 (54.27)	
AF type, n (%)				<.001
Paroxysmal	2376 (16.21)	1351 (18.28)	1025 (14.10)	
Persistent	383 (2.61)	224 (3.03)	159 (2.19)	
Chronic	843 (5.75)	324 (4.38)	519 (7.14)	
Unspecified	11057 (75.43)	5492 (74.31)	5565 (76.57)	
SOFA, score, mean (±SD)	5.00 (±3.13)	5.43 (±3.30)	4.56 (±2.89)	<.001
CCI, score, mean (±SD)	3.14 (±2.33)	3.00 (±2.36)	3.28 (±2.30)	<.001
Weight, kg, M (Q_1, Q_3)	80.66 (68.45, 94.60)	87.82 (75.00, 101.20)	74.84 (63.87, 86.08)	<.001
Heart rate, bpm, mean (±SD)	88.00 (±21.45)	87.95 (±21.33)	88.06 (±21.58)	.776
Respiratory rate, bpm, mean (±SD)	18.82 (±5.80)	18.36 (±5.68)	19.30 (±5.89)	<.001
SPO_2, %, mean (±SD)	97.15 (±3.26)	97.38 (±3.20)	96.92 (±3.30)	<.001
Temperature, °C, mean (±SD)	36.58 (±0.58)	36.58 (±0.58)	36.58 (±0.57)	.726
WBC, K/uL, M (Q_1, Q_3)	11.00 (8.10, 15.10)	11.70 (8.40, 15.90)	10.50 (7.70, 14.30)	<.001
Platelet, K/uL, mean (±SD)	192.47 (±96.60)	185.57 (±96.20)	199.49 (±96.52)	<.001
Calcium, mg/dL, mean (±SD)	8.37 (±0.67)	8.31 (±0.66)	8.43 (±0.67)	<.001
INR, ratio, mean (±SD)	1.52 (±0.40)	1.52 (±0.39)	1.51 (±0.41)	.031
Hematocrit, %, mean (±SD)	32.41 (±6.66)	32.13 (±6.80)	32.69 (±6.49)	<.001
Glucose, mg/dL, M (Q_1, Q_3)	132.00 (109.00, 165.00)	135.00 (111.00, 170.00)	130.00 (107.00, 160.00)	<.001
BUN, mg/dL, mean (±SD)	28.63 (±22.23)	27.28 (±22.54)	30.01 (±21.82)	<.001
RDW, %, mean (±SD)	14.99 (±2.24)	14.91 (±2.37)	15.07 (±2.09)	<.001
Anion gap, mEq/L, mean (±SD)	13.90 (±4.21)	13.57 (±4.47)	14.24 (±3.90)	<.001
Ventilation, n (%)				<.001
No	1667 (11.37)	693 (9.38)	974 (13.40)	
Yes	12992 (88.63)	6698 (90.62)	6294 (86.60)	

(*Continued*)

Table 1. Characteristics of AF Patients (*Continued*)

Variables	Total (n = 14 659)	ePWV < 11.302 (n = 7391)	ePWV ≥ 11.302 (n = 7268)	*P*
Vasoactive drugs, n (%)				<.001
No	8140 (55.53)	3516 (47.57)	4624 (63.62)	
Yes	6519 (44.47)	3875 (52.43)	2644 (36.38)	
RRT, n (%)				<.001
No	13501 (92.10)	6622 (89.60)	6879 (94.65)	
Yes	1158 (7.90)	769 (10.40)	389 (5.35)	
Antiarrhythmic, n (%)				<.001
No	3085 (21.05)	1455 (19.69)	1630 (22.43)	
Yes	11574 (78.95)	5936 (80.31)	5638 (77.57)	
Anticoagulant drugs, n (%)				<.001
No	8258 (56.33)	4036 (54.61)	4222 (58.09)	
Yes	6401 (43.67)	3355 (45.39)	3046 (41.91)	
Antiplatelet drugs, n (%)				<.001
No	6060 (41.34)	2624 (35.50)	3436 (47.28)	
Yes	8599 (58.66)	4767 (64.50)	3832 (52.72)	
Systolic, mm Hg, mean (±SD)	121.41 (±24.13)	112.24 (±19.53)	130.73 (±24.79)	<.001
Diastolic, mm Hg, mean (±SD)	66.74 (±17.99)	61.95 (±14.27)	71.60 (±19.96)	<.001
MBP, mm Hg, mean (±SD)	88.61 (±17.99)	82.07 (±14.30)	95.26 (±18.89)	<.001
ePWV, m/s, mean (±SD)	11.39 (±2.61)	9.25 (±1.39)	13.56 (±1.55)	<.001
Length of ICU stay, days, M (Q_1, Q_3)	2.78 (1.62, 5.07)	2.76 (1.51, 5.23)	2.79 (1.71, 4.91)	.453
30-days follow time, days, mean (±SD)	26.57 (±8.03)	27.54 (±6.95)	25.60 (±8.89)	<.001
30-day mortality, n (%)				<.001
No	12072 (82.35)	6435 (87.07)	5637 (77.56)	
Yes	2587 (17.65)	956 (12.93)	1631 (22.44)	
1-year follow time, days, mean (±SD)	269.04 (±147.75)	294.21 (±133.34)	243.46 (±157.01)	<.001
1-year mortality, n (%)				<.001
No	9894 (67.49)	5596 (75.71)	4298 (59.14)	
Yes	4765 (32.51)	1795 (24.29)	2970 (40.86)	

AF, atrial fibrillation; AIS, acute ischemic stroke; AKI, acute kidney injury; BUN, blood urea nitrogen; CCI, Charlson Comorbidity Index; ePWV, estimated pulse wave velocity; INR, international normalized ratio; MBP, mean blood pressure; RDW, red blood cell distribution width; RRT, renal replacement therapy; SOFA, Sequential Organ Failure Assessment; SPO_2, oxyhemoglobin saturation; WBC, white blood cell.

Correlation of Estimated Pulse Wave Velocity with 30-Day/1-Year Mortality Risk in Atrial Fibrillation Patients

The RCS curves demonstrated a non-linear correlation of ePWV with both 30-day mortality ($P < .001$) and 1-year mortality risk ($P < .001$) (Figure 2). The risk of 30-day and 1-year mortality tended to increase as ePWV levels elevated, with ePWV levels correlated with a decreased risk of 30-day/1-year mortality when ePWV < inflection point (11.302) and a raised risk of 30-day/1-year mortality when ePWV > inflection point.

Table 2 lists the Cox regression results of ePWV with 30-day/1-year mortality risk. Elevated ePWV levels presented a higher risk of 30-day and 1-year mortality in both unadjusted (30-day: HR = 1.42 [95% CI: 1.37-1.48]; 1-year: HR = 1.44 [95% CI: 1.40-1.49]) and adjusted models (30-day: HR = 1.23 [95% CI: 1.13-1.33]; 1-year: HR = 1.12 [95% CI: 1.06-1.19]). Compared with ePWV < 11.302 m/s, AF patients with ePWV ≥ 11.302 m/s still had a higher risk of 30-day mortality (HR = 1.20 [95% CI: 1.06-1.19]) and 1-year mortality (HR = 1.11 [95% CI: 1.02-1.21]) in adjusted models.

The comparison between AF patients and non-AF patients demonstrated that the ePWV levels of AF patients (11.39 [±2.61] vs. 9.70 [±2.65]), as well as the 30-day (17.65% vs. 11.90%) and 1-year mortality (32.51% vs. 22.36%) rates, were significantly higher than those of non-AF patients (Supplementary Table 5). High ePWV levels remained associated with a higher risk of 30-day (HR = 1.20 [95% CI: 1.14-1.27]) and 1-year mortality (HR = 1.09 [95% CI: 1.05-1.14])among non-AF patients (Supplementary Table 6). The likelihood ratio test suggested that there may be a multiplicative interaction between ePWV and AF on the risk of 1-year mortality ($P = .031$).

The KM curves revealed lower 30-day ($P_{log\text{-}rank} < .0001$) and 1-year ($P_{log\text{-}rank} < .0001$) survival probabilities for ePWV ≥ 11.302 m/s versus ePWV < 11.302 m/s (Figure 3). Furthermore, when the ePWV levels were used to predict the mortality risk of AF patients (Figure 4), the AUC of the ePWV level combined with the SOFA score in predicting the 30-day mortality risk ($AUC_{ePWV+SOFA}$: 0.698 [95% CI: 0.687-0.709] vs. AUC_{SOFA}: 0.631 [95% CI: 0.619-0.643]; $P_{Delong} < .001$) and 1-year mortality risk ($AUC_{ePWV+SOFA}$: 0.668 [95% CI: 0.659-0.678]

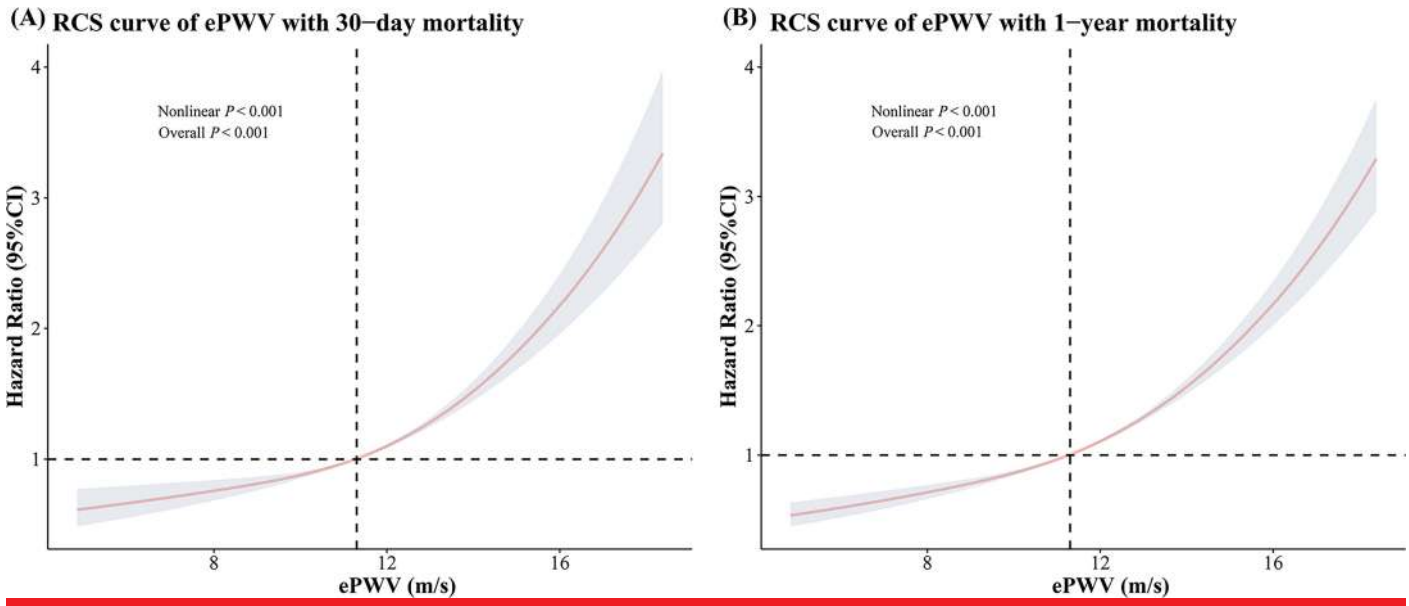

Figure 2. The RCS curve of the relationship between ePWV and 30-day/1-year mortality risk in critically ill AF patients. The solid line represents the hazard ratio, and the dashed lines represent the 95% confidence interval. The reference value is the median ePWV. AF, atrial fibrillation; ePWV, estimated pulse wave velocity; RCS, restricted cubic splines.

vs. AUC_{SOFA}: 0.578 [95% CI: 0.568-0.587]; P_{Delong} < .001) was marked greater than the AUC of the SOFA score alone. The net reclassification improvement (NRI) and integrated discrimination improvement (IDI) values of the models also indicated that the ePWV + SOFA model had a better predictive performance for predicting 30-day mortality (NRI: 0.425 [95% CI: 0.383-0.466]; IDI: 0.038 [95% CI: 0.034-0.041]) and 1-year mortality (NRI: 0.427 [95% CI: 0.393-0.461]; IDI: 0.057 [95% CI: 0.053-0.061]) than the SOFA model (Supplementary Table 7). Decision curve analysis further demonstrated that the ePWV + SOFA model yielded a higher net benefit than the SOFA-only model (Supplementary Figure 1). Compared with the age and MBP of the components, ePWV showed a better predictive performance for 30-day mortality (AUC_{ePWV}: 0.610 [95% CI: 0.598-0.622]; AUC_{age}: 0.547 [95% CI: 0.539-0.555]; AUC_{MBP}: 0.511 [95% CI: 0.498-0.523]) and 1-year mortality (AUC_{ePWV}: 0.627 [95% CI: 0.617-0.637]; AUC_{age}: 0.556 [95% CI: 0.549-0.562]; AUC_{MBP}: 0.514 [95% CI: 0.504-0.525]) (Supplementary Figure 2).

The correlations of ePWV with 30-day/1-year mortality risk in different subgroups are performed. The findings indicated that ePWV ≥ 11.302 m/s was linked to a higher risk of 30-day (Figure 5) and 1-year mortality (Figure 6) in age (<65, ≥65 years), gender (male, female), SOFA (<4, ≥4), CCI (<6, ≥6), heart failure (presence, absence), vasoactive drug (used, not used), and AF type (paroxysmal, persistent, and unspecified) subgroups (all $P < .05$).

Table 2. The Results of Cox Regression Between ePWV and 30-day/1-year Mortality Risk in AF Patients

		Unadjusted Model		Adjusted Model	
Outcomes	**Variables**	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
30-day mortality	ePWV	1.42 (1.37-1.48)	<.001	1.23 (1.13-1.33)	<.001
	ePWV				
	<11.302	Ref		Ref	
	≥11.302	1.84 (1.70-1.99)	<.001	1.20 (1.07-1.35)	.002
1-year mortality	ePWV	1.44 (1.40-1.49)	<.001	1.12 (1.06-1.19)	<.001
	ePWV				
	<11.302	Ref		Ref	
	≥11.302	1.89 (1.78-2.00)	<.001	1.11 (1.02-1.21)	.016

Multivariable Cox regression model adjusted for (1) 30-day mortality: age, gender, race, heart failure, AIS, AKI, AF type, SOFA, CCI, weight, heart rate, respiratory rate, SPO_2, platelet, INR, glucose, BUN, RDW, anion gap, ventilation, vasoactive drugs, RRT, antiarrhythmic, anticoagulant drugs, and antiplatelet drugs; (2) 1-year mortality: age, race, diabetes, heart failure, AIS, AKI, AF type, SOFA, CCI, weight, heart rate, respiratory rate, SPO_2, temperature, platelet, INR, hematocrit, glucose, BUN, RDW, anion gap, ventilation, RRT, antiarrhythmic, anticoagulant drugs, and antiplatelet drugs.

AF, atrial fibrillation; AIS, acute ischemic stroke; AKI, acute kidney injury; BUN, blood urea nitrogen; CCI, Charlson Comorbidity Index; ePWV, estimated pulse wave velocity; HR, hazard ratio; Ref, reference; INR, international normalized ratio; RDW, red blood cell distribution width; RRT, renal replacement therapy; SOFA, Sequential Organ Failure Assessment; SPO_2, oxyhemoglobin saturation temperature.

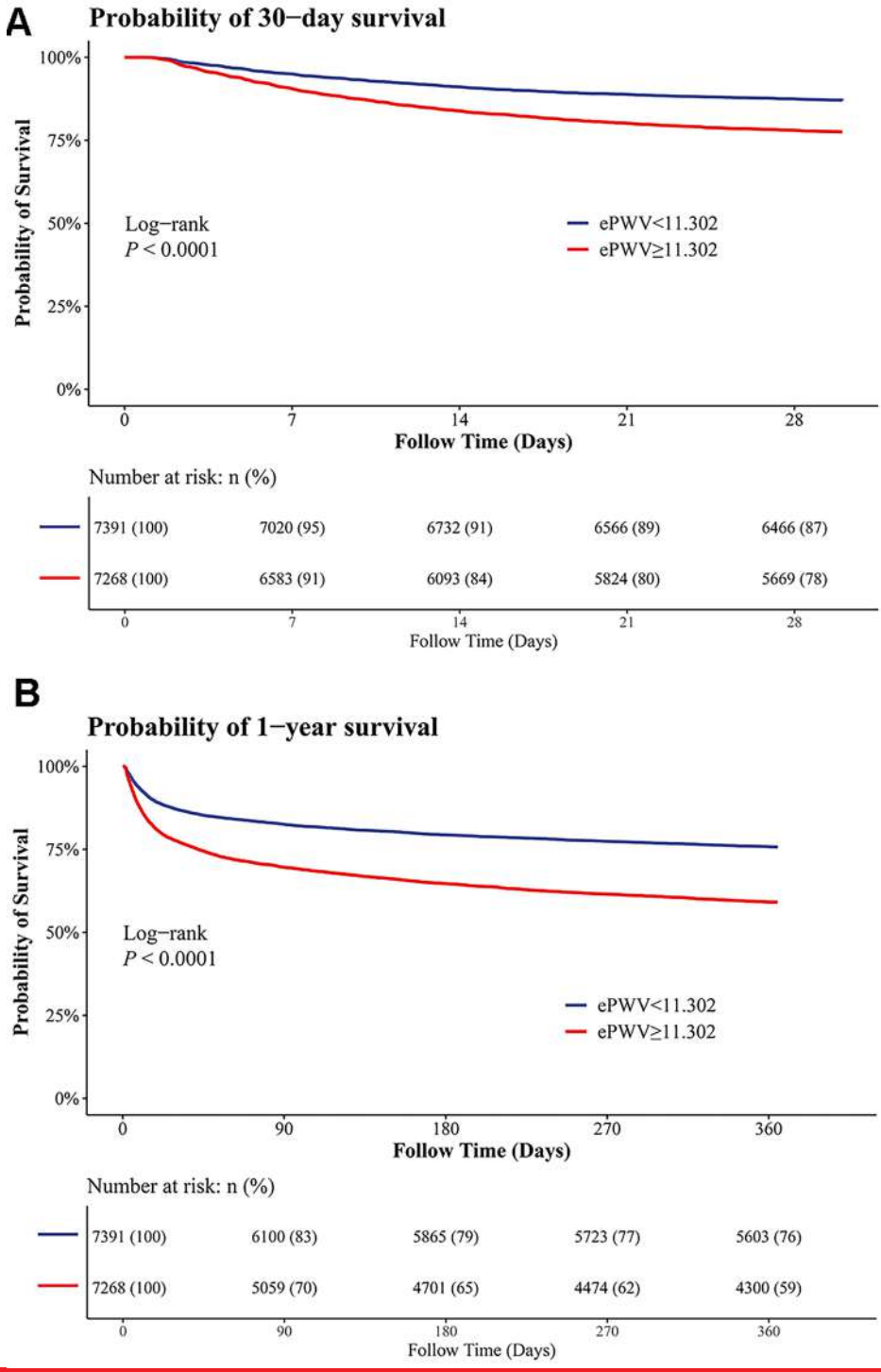

Figure 3. The KM curves for 30-day (A) and 1-year (B) survival according to ePWV categories (<11.302 vs. ≥11.302 m/s) in critically ill AF patients. AF, atrial fibrillation; ePWV, estimated pulse wave velocity; KM, Kaplan–Meier.

DISCUSSION

This analysis investigated the connection of ePWV with mortality risk among critically ill AF patients. The primary findings indicated that elevated ePWV was independently correlated with a higher risk of 30-day and 1-year mortality, with the association persisting across various subgroups. The RCS curve found a non-linear connection, with an inflection point at 11.302 m/s, beyond which the risk of mortality rose sharply. Furthermore, the combination of ePWV with the SOFA score enhanced the predictive value for mortality versus the SOFA score alone.

As the gold standard for evaluating aortic stiffness, carotid-femoral PWV captures the speed of pressure wave propagation through the arterial tree,[12] reflecting the intrinsic

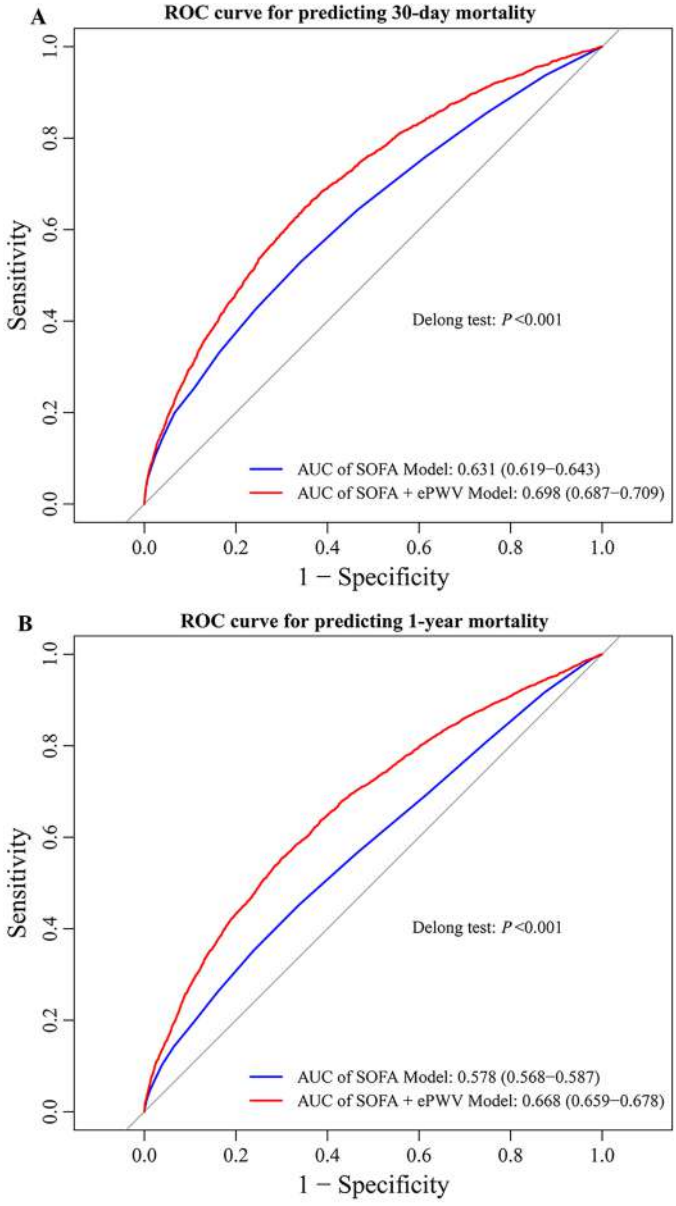

Figure 4. The receiver operating characteristic (ROC) curve of the predictive effect of ePWV on 30-day/1-year mortality in AF patients. (A) predicting 30-day mortality risk; (B) predicting 1-year mortality risk. AF, atrial fibrillation; AUC, the area under the curve; ePWV, estimated pulse wave velocity; ROC, receiver operating characteristic; SOFA, Sequential Organ Failure Assessment.

elastic and compliant properties of arterial walls. Pulse wave velocity has been definitively linked to cardiovascular endpoints and mortality risk across both hypertensive cohorts and the general population.[21] The difficulty in clinical measurement of carotid-femoral PWV has limited its wide application. Greve et al[20] proposed a formula to estimate carotid-femoral PWV levels based on age and blood pressure. They revealed that ePWV and measured carotid-femoral PWV had similar predictive value for major cardiovascular events.[20] Therefore, this analysis examined the correlation of ePWV with mortality among AF patients. In different ePWV level groups (<11.302, ≥11.302 m/s), the 30-day mortality and 1-year mortality were higher in the group with higher ePWV levels. This may be related to the greater severity of AF in patients with high ePWV levels. The results also found that elevated ePWV was connected to a higher risk of 30-day and 1-year mortality. Prior research has identified the connection of high ePWV with raised mortality risk in individuals with obesity[17] and AKI combined with congestive heart failure.[18] A prospective analysis also indicated that elevated ePWV is correlated with a higher stroke risk in middle-aged men. Elevated PWV levels reflect reduced compliance in elastic arteries. Elevated PWV may result from various causes, such as vascular endothelial damage, increased hemodynamic load, inflammatory stress, oxidative stress, degeneration of elastic fibers in the vascular wall, underlying atherosclerosis, and impaired microcirculatory perfusion.[22,23] Several studies indicated that elevated PWV is correlated with increased left atrial inner diameter, left ventricular diastolic dysfunction, and a higher risk of AF.[24,25] Moreover, the results found that ePWV combined with the SOFA score was a better predictor of 30-day/1-year mortality than the SOFA score alone. This suggests that ePWV may be able to be merged into a tool for prognostic prediction among AF patients to enhance the predictive effect of the tool. Although PWV provides more comprehensive prognostic information than conventional cardiovascular risk factors,[26] clinicians rarely implement targeted interventions solely based on elevated PWV in routine critical care settings. This is partially attributed to insufficient high-quality evidence supporting PWV-guided fluid resuscitation, vasoactive agent titration, or anti-stiffness therapy among critically ill patients.

The exact mechanism by which carotid-femoral PWV affects the mortality of AF patients remains unclear. Several studies indicated that arterial remodeling and functional alterations could significantly contribute to AF development.[24,27] Elevated PWV measurements reflect progressive arterial stiffening. Atherosclerosis is linked to the structure and remodeling of the atria, which is an important process leading to the onset and progression of AF.[28] Physiological investigations revealed that arterial stiffening may induce both diastolic and systolic impairments in left ventricular function through elevated cardiac preload and afterload.[29] Progressive arterial stiffening promotes left ventricular hypertrophy, diastolic dysfunction, and left atrial dilation, thereby elevating AF risk.[30] Arterial stiffness increases cardiac afterload and causes premature pulse wave reflections during systole,[31] and these increases in afterload result in reduced strain and increased dilation of the left ventricle.[32] Elevated arterial stiffness correlates with heightened coronary vascular resistance and reduced diastolic blood supply, potentially compromising ventricular performance.[12] Sudden elevations in pulsatile load can elevate left atrial filling pressures, trigger neurohormonal stimulation, and induce systemic cardiovascular inflammation, potentially promoting AF pathogenesis.[21,33] Elevated pressure pulsatility resulting from arterial stiffness can induce hemodynamic stress changes, potentially causing aneurysms and cerebrovascular rupture.[34] Additionally, it may promote transient cerebral

Subgroups	Outcome/Total	N(%)	HR (95% CI)	P
Age<65	**386/3316**			
ePWV Continuous	386/3316	3316 (100)	1.09 (1.02–1.17)	0.008
ePWV ≥ 11.302	22/117	117 (3.53)	1.93 (1.25–2.99)	0.003
Age≥65	**2201/11343**			
ePWV Continuous	2201/11343	11343 (100)	1.11 (1.09–1.13)	<0.001
ePWV ≥ 11.302	1609/7151	7151 (63.04)	1.41 (1.28–1.56)	<0.001
Gender=Female	**1200/5867**			
ePWV Continuous	1200/5867	5867 (100)	1.10 (1.07–1.14)	<0.001
ePWV ≥ 11.302	840/3424	3424 (58.36)	1.42 (1.22–1.65)	<0.001
Gender=Male	**1387/8792**			
ePWV Continuous	1387/8792	8792 (100)	1.12 (1.09–1.15)	<0.001
ePWV ≥ 11.302	791/3844	3844 (43.72)	1.48 (1.31–1.69)	<0.001
SOFA<4	**622/5275**			
ePWV Continuous	622/5275	5275 (100)	1.13 (1.09–1.18)	<0.001
ePWV ≥ 11.302	465/3034	3034 (57.52)	1.47 (1.18–1.83)	0.001
SOFA=4	**1965/9384**			
ePWV Continuous	1965/9384	9384 (100)	1.10 (1.08–1.13)	<0.001
ePWV ≥ 11.302	1166/4234	4234 (45.12)	1.46 (1.31–1.63)	<0.001
CCI<6	**643/6674**			
ePWV Continuous	643/6674	6674 (100)	1.18 (1.13–1.23)	<0.001
ePWV ≥ 11.302	316/2236	2236 (33.50)	1.91 (1.56–2.33)	<0.001
CCI≥ 6	**1944/7985**			
ePWV Continuous	1944/7985	7985 (100)	1.09 (1.06–1.11)	<0.001
ePWV ≥ 11.302	1315/5032	5032 (63.02)	1.31 (1.17–1.46)	<0.001
Heart failure=No	**1301/8272**			
ePWV Continuous	1301/8272	8272 (100)	1.12 (1.08–1.15)	<0.001
ePWV ≥ 11.302	772/3807	3807 (46.02)	1.47 (1.28–1.69)	<0.001
Heart failure=Yes	**1286/6387**			
ePWV Continuous	1286/6387	6387 (100)	1.11 (1.08–1.14)	<0.001
ePWV ≥ 11.302	859/3461	3461 (54.19)	1.50 (1.30–1.71)	<0.001
Vasoactive drug use=No	**1280/8140**			
ePWV Continuous	1280/8140	8140 (100)	1.09 (1.06–1.12)	<0.001
ePWV ≥ 11.302	928/4624	4624 (56.81)	1.49 (1.28–1.73)	<0.001
Vasoactive drug use=Yes	**1307/6519**			
ePWV Continuous	1307/6519	6519 (100)	1.12 (1.09–1.15)	<0.001
ePWV ≥ 11.302	703/2644	2644 (40.56)	1.44 (1.27–1.64)	<0.001
AF type=Paroxysmal	**337/2376**			
ePWV Continuous	337/2376	2376 (100)	1.06 (1.00–1.12)	0.056
ePWV ≥ 11.302	194/1025	1025 (43.14)	1.34 (1.03–1.73)	0.029
AF type=Persistent	**69/383**			
ePWV Continuous	69/383	383 (100)	1.09 (0.95–1.25)	0.206
ePWV ≥ 11.302	35/159	159 (41.51)	2.07 (1.13–3.79)	0.019
AF type=Chronic	**179/843**			
ePWV Continuous	179/843	843 (100)	1.09 (1.00–1.18)	0.039
ePWV ≥ 11.302	122/519	519 (61.57)	1.12 (0.76–1.63)	0.571
AF type=Unspecified	**2002/11057**			
ePWV Continuous	2002/11057	11057 (100)	1.12 (1.10–1.15)	<0.001
ePWV ≥ 11.302	1280/5565	5565 (50.33)	1.51 (1.35–1.69)	<0.001

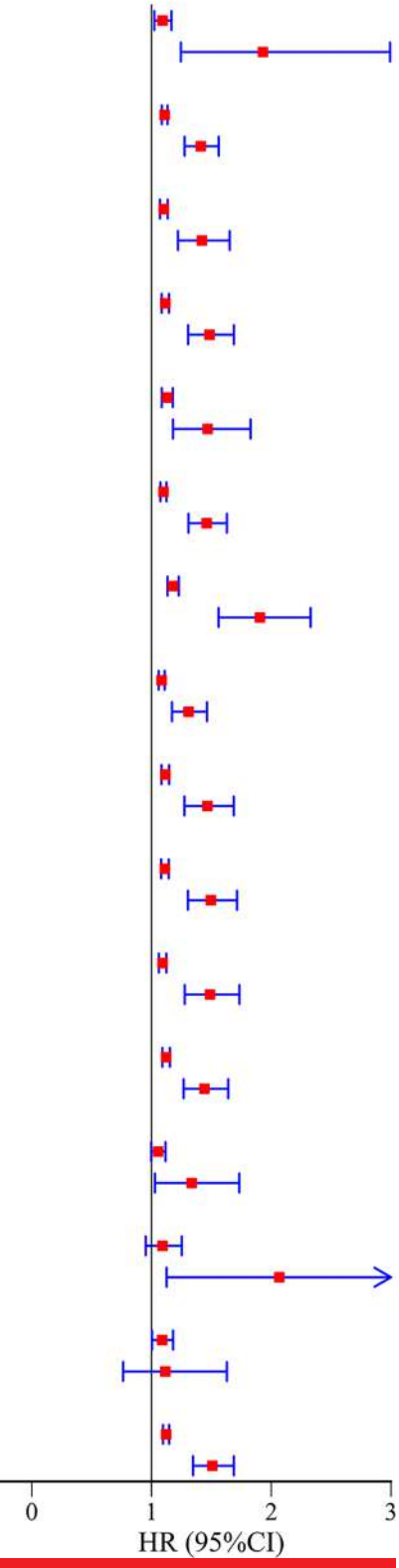

Figure 5. The relationships between ePWV and 30-day mortality risk in different subgroups. Adjusted for the same covariates as in multivariable analysis. CCI, Charlson Comorbidity Index; ePWV, estimated pulse wave velocity; SOFA, Sequential Organ Failure Assessment.

Subgroups	Outcome/Total	N(%)	HR (95% CI)	P
Age<65	**720/3316**			
ePWV Continuous	720/3316	3316 (100)	1.04 (0.99–1.09)	0.155
ePWV ≥ 11.302	38/117	117 (3.53)	1.57 (1.13–2.20)	0.008
Age≥65	**4045/11343**			
ePWV Continuous	4045/11343	11343 (100)	1.08 (1.06–1.09)	<0.001
ePWV ≥ 11.302	2932/7151	7151 (63.04)	1.27 (1.18–1.37)	<0.001
Gender=Female	**2144/5867**			
ePWV Continuous	2144/5867	5867 (100)	1.07 (1.05–1.09)	<0.001
ePWV ≥ 11.302	1475/3424	3424 (58.36)	1.25 (1.12–1.40)	<0.001
Gender=Male	**2621/8792**			
ePWV Continuous	2621/8792	8792 (100)	1.08 (1.06–1.10)	<0.001
ePWV ≥ 11.302	1495/3844	3844 (43.72)	1.34 (1.22–1.47)	<0.001
SOFA<4	**1467/5275**			
ePWV Continuous	1467/5275	5275 (100)	1.06 (1.03–1.09)	<0.001
ePWV ≥ 11.302	1023/3034	3034 (57.52)	1.17 (1.02–1.34)	0.026
SOFA≥4	**3298/9384**			
ePWV Continuous	3298/9384	9384 (100)	1.08 (1.06–1.10)	<0.001
ePWV ≥ 11.302	1947/4234	4234 (45.12)	1.36 (1.25–1.48)	<0.001
CCI<6	**1118/6674**			
ePWV Continuous	1118/6674	6674 (100)	1.14 (1.11–1.18)	<0.001
ePWV ≥ 11.302	547/2236	2236 (33.50)	1.72 (1.48–2.00)	<0.001
CCI≥6	**3647/7985**			
ePWV Continuous	3647/7985	7985 (100)	1.05 (1.04–1.07)	<0.001
ePWV ≥ 11.302	2423/5032	5032 (63.02)	1.18 (1.09–1.28)	<0.001
Heart failure=No	**2252/8272**			
ePWV Continuous	2252/8272	8272 (100)	1.09 (1.06–1.11)	<0.001
ePWV ≥ 11.302	1354/3807	3807 (46.02)	1.39 (1.25–1.55)	<0.001
Heart failure=Yes	**2513/6387**			
ePWV Continuous	2513/6387	6387 (100)	1.07 (1.05–1.09)	<0.001
ePWV ≥ 11.302	1616/3461	3461 (54.19)	1.27 (1.15–1.39)	<0.001
Vasoactive drug use=No	**2657/8140**			
ePWV Continuous	2657/8140	8140 (100)	1.07 (1.04–1.09)	<0.001
ePWV ≥ 11.302	1857/4624	4624 (56.81)	1.34 (1.20–1.48)	<0.001
Vasoactive drug use=Yes	**2108/6519**			
ePWV Continuous	2108/6519	6519 (100)	1.11 (1.08–1.13)	<0.001
ePWV ≥ 11.302	1113/2644	2644 (40.56)	1.34 (1.21–1.49)	<0.001
AF type=Paroxysmal	**691/2376**			
ePWV Continuous	691/2376	2376 (100)	1.07 (1.03–1.11)	0.001
ePWV ≥ 11.302	388/1025	1025 (43.14)	1.37 (1.14–1.64)	0.001
AF type=Persistent	**135/383**			
ePWV Continuous	135/383	383 (100)	1.10 (1.00–1.21)	0.046
ePWV ≥ 11.302	72/159	159 (41.51)	1.63 (1.08–2.47)	0.021
AF type=Chronic	**350/843**			
ePWV Continuous	350/843	843 (100)	1.06 (1.00–1.12)	0.059
ePWV ≥ 11.302	240/519	519 (61.57)	1.04 (0.79–1.38)	0.788
AF type=Unspecified	**3589/11057**			
ePWV Continuous	3589/11057	11057 (100)	1.08 (1.06–1.10)	<0.001
ePWV ≥ 11.302	2270/5565	5565 (50.33)	1.31 (1.20–1.42)	<0.001

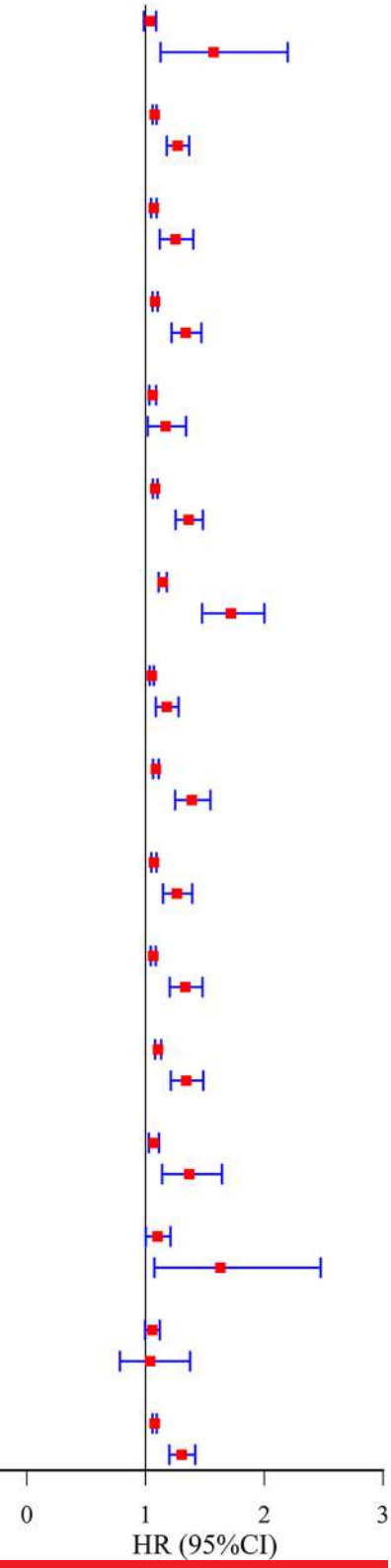

Figure 6. The associations between ePWV and 1-year mortality risk in different subgroups. Adjusted for the same covariates as in multivariable analysis. CCI, Charlson Comorbidity Index; ePWV, estimated pulse wave velocity; SOFA, Sequential Organ Failure Assessment.

hypoperfusion, ischemic episodes, endothelial dysfunction, disturbed shear stress, and atherosclerotic development.[35] Among critically ill patients, the presence of multiple organ dysfunction and systemic inflammation may amplify these effects, leading to an increased risk of adverse endpoints among AF patients with elevated ePWV.

This study possesses several strengths. First, this represents the first investigation to examine the connection of ePWV with mortality risk among AF patients, offering a novel prognostic assessment tool for this patient group. Second, the large sample size guarantees adequate statistical power, and comprehensive adjustment for potential confounding factors bolsters the reliability of the findings. Third, the use of RCS curves aids in identifying the non-linear relationship and inflection point, providing valuable insights for risk stratification. Fourth, the consistent results across multiple subgroups reinforce the robustness of the findings. Fifth, the comparison of predictive values demonstrates that combining ePWV with SOFA improves prognostic accuracy, which has significant clinical implications. Nevertheless, certain limitations should be acknowledged. First, the derivation of ePWV relied solely on baseline blood pressure data. Some factors (e.g., smoking cessation, medication use) in cohort participants during the follow-up period may influence the estimation of mortality risk. The link between ePWV trajectories based on multiple blood pressure measurements over time and mortality risk needs to be further investigated. Second, this was a single-center investigation conducted in a US population, and the applicability of the findings to other populations needs to be further confirmed. Third, this study adopted a retrospective cohort design, and the impact of recall bias inherent to retrospective research cannot be entirely avoided. Fourth, all patients in this analysis were AF patients admitted to the ICU. Further investigation is warranted to determine the correlation of ePWV with mortality risk among non-ICU AF patients. Fifth, the cutoff value for ePWV classification (11.302 m/s) in this study was based on the RCS curve. This cutoff value has not yet been validated in clinical settings, which may limit the generalizability of the ePWV classification findings. Sixth, various ePWV calculation methods exist. Variations among different calculation formulas and deviations of calculated ePWV from actual measured PWV may affect the findings.

CONCLUSIONS

Elevated PWV levels indicate increased arterial stiffness. The results found that elevated ePWV levels had a connection with a higher risk of 30-day/1-year mortality among AF patients. Moreover, ePWV demonstrated predictive ability for 30-day/1-year mortality. Future research could focus on the link between ePWV trajectories based on multiple blood pressure measurements and outcomes among AF patients.

Ethics Committee Approval: Given the use of fully anonymized and de-identified clinical data extracted from a publicly accessible database, ethical review and informed consent were not required for the present investigation.

Informed Consent: Informed consent is not required for this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – N.X.; Design – N.X., Y.C.; Supervision – N.X.; Resources – Y.C.; Materials – Y.C.; Data Collection and/or Processing – Y.C.; Analysis and/or Interpretation – N.X.; Literature Search – Y.C.; Writing – N.X.; Critical Review – Y.C.

Declaration of Interests: The authors have no conflict of interest to declare.

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Supplementary Table 1. Comparative analysis for the differences in missing variables pre- and post-interpolation.

Variables	Missing values (n [%])	Pre-interpolation	Post-interpolation	Statistics	*P*
Weight, M (Q_1, Q_3)	2445 (16.68%)	80.33 (67.68, 95.60)	80.80 (68.50, 94.62)	W = 89997193.500	0.453
Heart rate, Mean (±SD)	1 (0.01%)	88.00 (±21.45)	88.00 (±21.45)	t = -0.001	0.999
Respiratory rate, Mean (±SD)	895 (6.11%)	18.96 (±5.93)	18.82 (±5.80)	t' = -1.942	0.052
SPO2, Mean (±SD)	3 (0.02%)	97.15 (±3.26)	97.15 (±3.26)	t = -0.011	0.992
WBC, M (Q_1, Q_3)	191 (1.30%)	11.00 (8.00, 15.10)	11.00 (8.10, 15.10)	W = 106111329.000	0.924
Platelet, Mean (±SD)	188 (1.28%)	192.00 (±97.08)	192.46 (±96.60)	t = 0.406	0.685
INR, Mean (±SD)	1254 (8.55%)	1.52 (±0.42)	1.52 (±0.40)	t' = -0.430	0.667
Hematocrit, Mean (±SD)	174 (1.19%)	32.39 (±6.69)	32.41 (±6.66)	t = 0.231	0.817
Glucose, M (Q_1, Q_3)	145 (0.99%)	132.00 (109.00, 165.00)	132.00 (109.00, 165.00)	W = 106473444.500	0.897
BUN, Mean (±SD)	154 (1.05%)	28.69 (±22.33)	28.63 (±22.23)	t = -0.213	0.832
RDW, Mean (±SD)	193 (1.32%)	14.99 (±2.25)	14.99 (±2.24)	t = -0.003	0.997
Anion gap, Mean (±SD)	180 (1.23%)	13.91 (±4.23)	13.90 (±4.21)	t = -0.184	0.854

SPO2, oxyhemoglobin saturation; WBC, white blood cell; INR, international normalized ratio; BUN, blood urea nitrogen; RDW, red blood cell distribution width.

Supplementary Table 2. Cox regression screening 30-day mortality-related confounders.

	Univariable Cox regression		Bidirectional stepwise regression	
Variables	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
Age	1.48 (1.42-1.55)	<0.001	1.31 (1.25-1.38)	<0.001
Gender				
Female	Ref		Ref	
Male	0.75 (0.69-0.81)	<0.001	0.93 (0.85-1.01)	0.086
Race				
White	Ref		Ref	
Black	1.00 (0.84-1.20)	0.961	0.76 (0.64-0.91)	0.003
Others	1.12 (0.99-1.26)	0.076	1.14 (1.01-1.29)	0.037
Unknown	1.69 (1.52-1.87)	<0.001	1.44 (1.29-1.60)	<0.001
Diabetes				
No	Ref			
Yes	0.99 (0.91-1.08)	0.829		
Heart failure				
No	Ref		Ref	
Yes	1.31 (1.21-1.41)	<0.001	0.83 (0.76-0.90)	<0.001
AIS				
No	Ref		Ref	
Yes	1.47 (1.33-1.64)	<0.001	1.62 (1.45-1.81)	<0.001
Sepsis				
No	Ref			
Yes	1.20 (1.09-1.31)	<0.001		
AKI				
No	Ref		Ref	
Yes	1.69 (1.56-1.84)	<0.001	1.29 (1.18-1.42)	<0.001
AF type				
Paroxysmal	Ref		Ref	
Persistent	1.30 (1.00-1.68)	0.049	1.11 (0.85-1.44)	0.450
Chronic	1.57 (1.31-1.89)	<0.001	1.16 (0.96-1.39)	0.118
Unspecified	1.32 (1.17-1.48)	<0.001	1.23 (1.09-1.38)	0.001
SOFA	1.58 (1.53-1.63)	<0.001	1.37 (1.31-1.44)	<0.001
CCI	1.51 (1.46-1.56)	<0.001	1.28 (1.22-1.33)	<0.001
Weight	0.79 (0.76-0.83)	<0.001	0.84 (0.80-0.89)	<0.001
Heart rate	1.29 (1.24-1.33)	<0.001	1.12 (1.08-1.16)	<0.001
Respiratory rate	1.38 (1.34-1.43)	<0.001	1.15 (1.10-1.19)	<0.001
SPO2	0.77 (0.74-0.79)	<0.001	0.90 (0.87-0.94)	<0.001
Temperature	1.08 (1.04-1.12)	<0.001		
WBC	1.09 (1.08-1.11)	<0.001		
Platelet	1.16 (1.12-1.20)	<0.001	1.11 (1.08-1.15)	<0.001
Calcium	0.96 (0.93-1.00)	0.059		
INR	1.29 (1.24-1.33)	<0.001	1.07 (1.03-1.11)	<0.001
Hematocrit	1.01 (0.97-1.05)	0.528		
Glucose	1.13 (1.11-1.16)	<0.001	1.05 (1.02-1.08)	<0.001
BUN	1.40 (1.37-1.43)	<0.001	1.08 (1.04-1.12)	<0.001
RDW	1.45 (1.41-1.49)	<0.001	1.20 (1.16-1.24)	<0.001
Anion gap	1.51 (1.47-1.55)	<0.001	1.15 (1.11-1.19)	<0.001
Ventilation				
No	Ref		Ref	
Yes	1.87 (1.61-2.19)	<0.001	1.74 (1.48-2.04)	<0.001

	Univariable Cox regression		Bidirectional stepwise regression	
Variables	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
Vasoactive drugs				
No	Ref		Ref	
Yes	1.32 (1.22-1.42)	<0.001	1.09 (0.99-1.20)	0.070
RRT				
No	Ref		Ref	
Yes	2.69 (2.42-2.98)	<0.001	1.16 (1.03-1.31)	0.017
Antiarrhythmic				
No	Ref		Ref	
Yes	0.71 (0.65-0.78)	<0.001	0.79 (0.73-0.87)	<0.001
Anticoagulant drugs				
No	Ref		Ref	
Yes	1.51 (1.40-1.63)	<0.001	1.11 (1.02-1.21)	0.014
Antiplatelet drugs				
No	Ref		Ref	
Yes	0.43 (0.40-0.47)	<0.001	0.54 (0.50-0.59)	<0.001

AIS, acute ischemic stroke; AKI, acute kidney injury; SOFA, Sequential Organ Failure Assessment; CCI, Charlson comorbidity index; SPO2, oxyhemoglobin saturation; WBC, white blood cell; INR, international normalized ratio; BUN, blood urea nitrogen; RDW, red blood cell distribution width; RRT, renal replacement therapy; HR, hazard ratio; CI, confidence interval; Ref, reference.

Supplementary Table 3. Cox regression screening 1-year mortality-related confounders.

	Univariable Cox regression		Bidirectional stepwise regression	
Variables	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
Age	1.51 (1.46-1.56)	<0.001	1.23 (1.19-1.28)	<.001
Gender				
Female	Ref			
Male	0.77 (0.73-0.82)	<0.001		
Race				
White	Ref		Ref	
Black	1.13 (1.00-1.27)	0.048	0.87 (0.77-0.98)	.023
Others	0.93 (0.85-1.02)	0.143	0.96 (0.87-1.05)	.385
Unknown	1.25 (1.15-1.36)	<0.001	1.16 (1.06-1.26)	.001
Diabetes				
No	Ref		Ref	
Yes	1.10 (1.03-1.16)	0.003	0.81 (0.76-0.87)	<.001
Heart failure				
No	Ref		Ref	
Yes	1.54 (1.45-1.63)	<0.001	0.91 (0.86-0.97)	.005
AIS				
No	Ref		Ref	
Yes	1.32 (1.21-1.43)	<0.001	1.28 (1.17-1.39)	<.001
Sepsis				
No	Ref			
Yes	1.04 (0.97-1.11)	0.253		
AKI				
No	Ref		Ref	
Yes	1.33 (1.26-1.41)	<0.001	1.17 (1.10-1.25)	<.001
AF type				
Paroxysmal	Ref		Ref	
Persistent	1.27 (1.05-1.52)	0.012	1.07 (0.89-1.29)	.497
Chronic	1.57 (1.38-1.78)	<0.001	1.16 (1.02-1.32)	.026
Unspecified	1.16 (1.07-1.26)	<0.001	1.16 (1.07-1.26)	<.001
SOFA	1.34 (1.31-1.38)	<0.001	1.25 (1.21-1.29)	<.001
CCI	1.62 (1.58-1.66)	<0.001	1.45 (1.41-1.50)	<.001
Weight	0.76 (0.73-0.79)	<0.001	0.81 (0.77-0.84)	<.001
Heart rate	1.23 (1.20-1.26)	<0.001	1.09 (1.06-1.12)	<.001
Respiratory rate	1.35 (1.32-1.38)	<0.001	1.12 (1.09-1.15)	<.001
SPO2	0.77 (0.75-0.79)	<0.001	0.91 (0.88-0.94)	<.001
Temperature	1.11 (1.08-1.14)	<0.001	1.03 (1.00-1.06)	.097
WBC	1.08 (1.06-1.09)	<0.001		
Platelet	1.18 (1.15-1.20)	<0.001	1.10 (1.07-1.13)	<.001
Calcium	1.01 (0.98-1.04)	0.546		
INR	1.24 (1.21-1.27)	<0.001	1.06 (1.03-1.09)	<.001
Hematocrit	0.97 (0.94-0.99)	0.020	1.10 (1.06-1.13)	<.001
Glucose	1.10 (1.07-1.12)	<0.001	1.05 (1.02-1.07)	<.001
BUN	1.39 (1.37-1.42)	<0.001	1.10 (1.07-1.13)	<.001
RDW	1.48 (1.46-1.52)	<0.001	1.26 (1.23-1.29)	<.001
Anion gap	1.44 (1.41-1.47)	<0.001	1.08 (1.05-1.12)	<.001
Ventilation				
No	Ref		Ref	
Yes	1.18 (1.08-1.30)	<0.001	1.25 (1.14-1.38)	<.001

	Univariable Cox regression		Bidirectional stepwise regression	
Variables	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
Vasoactive drugs				
No	Ref			
Yes	1.02 (0.97-1.08)	0.444		
RRT				
No	Ref		Ref	
Yes	2.43 (2.24-2.64)	<0.001	1.24 (1.12-1.36)	<.001
Antiarrhythmic				
No	Ref		Ref	
Yes	0.74 (0.69-0.79)	<0.001	0.85 (0.79-0.91)	<.001
Anticoagulant drugs				
No	Ref		Ref	
Yes	1.47 (1.39-1.56)	<0.001	1.17 (1.10-1.25)	<.001
Antiplatelet drugs				
No	Ref		Ref	
Yes	0.48 (0.45-0.51)	<0.001	0.63 (0.59-0.67)	<.001

AF, atrial fibrillation; AIS, acute ischemic stroke; AKI, acute kidney injury; SOFA, Sequential Organ Failure Assessment; CCI, Charlson comorbidity index; SPO2, oxyhemoglobin saturation; WBC, white blood cell; INR, international normalized ratio; BUN, blood urea nitrogen; RDW, red blood cell distribution width; RRT, renal replacement therapy; HR, hazard ratio; CI, confidence interval; Ref, reference.

Supplementary Table 4. Test for multicollinearity among covariates

30-day mortality		1-year mortality	
Variables	**VIF**	**Variables**	**VIF**
Age	4.265	Age	4.3361
Gender Male	1.1921	Race Black	1.068
Race Black	1.0655	Race Others	1.0516
Race Others	1.062	Race Unknown	1.0607
Race Unknown	1.0803	DiabetesYes	1.2847
Heart_failure Yes	1.2168	Heart_failure Yes	1.2265
AIS Yes	1.1283	AISYes	1.1256
AKI Yes	1.1387	AKIYes	1.1444
AF_type Persistent	1.1926	AF_type Persistent	1.1854
AF_type Chronic	1.46	AF_type Chronic	1.4322
AF_type Unspecified	1.6022	AF_type Unspecified	1.5647
SOFA	2.1828	SOFA	1.6514
CCI	1.3691	CCI	1.5158
Weight	1.4101	Weight	1.3265
Heart_rate	1.2714	Heart_rate	1.301
Respiratory_rate	1.2192	Respiratory_rate	1.247
SPO_2	1.1012	SPO2	1.1303
Platelet	1.1444	Temperature	1.1253
INR	1.176	Platelet	1.1425
Glucose	1.0813	INR	1.1491
BUN	1.4672	Hematocrit	1.237
RDW	1.2381	Glucose	1.123
Anion_gap	1.4373	BUN	1.5557
Ventilation Yes	1.0777	RDW	1.2979
Vasoactive_drugs Yes	1.5678	Anion_gap	1.49
RRT Yes	1.3991	Ventilation Yes	1.1052
Antiarrhythmic Yes	1.1014	RRTYes	1.3795
Anticoagulant_drug Yes	1.1727	Antiarrhythmic Yes	1.1039
Antiplatelet_drugs Yes	1.188	Anticoagulant_drug Yes	1.1412
ePWV	4.0545	Antiplatelet_drugs Yes	1.178
		ePWV	4.1204

VIF, variance inflation factor; AIS, acute ischemic stroke; AF, atrial fibrillation; SOFA, Sequential Organ Failure Assessment; CCI, CharIson comorbidity index; SPO2, oxyhemoglobin saturation; INR, international normalized ratio; BUN, blood urea nitrogen; RDW, red blood cell distribution width; RRT, renal replacement therapy.
A VIF value ≥10 indicates the presence of multicollinearity.

Supplementary Table 5. Comparison between AF patients and non-AF patients

Variables	Total (n=51733)	AF (n=14659)	Non-AF (n=37074)	*P*
30-day mortality, n (%)				<.001
No	44733 (86.47)	12072 (82.35)	32661 (88.10)	
Yes	7000 (13.53)	2587 (17.65)	4413 (11.90)	
1-year mortality, n (%)				<.001
No	38677 (74.76)	9894 (67.49)	28783 (77.64)	
Yes	13056 (25.24)	4765 (32.51)	8291 (22.36)	
ePWV, Mean (±SD)	10.18 (±2.74)	11.39 (±2.61)	9.70 (±2.65)	<.001
ePWV, n (%)				<.001
<11.302	34819 (67.31)	7391 (50.42)	27428 (73.98)	
≥11.302	16914 (32.69)	7268 (49.58)	9646 (26.02)	

AF, atrial fibrillation; ePWV, estimated pulse wave velocity.

Supplementary Table 6. The results of Cox regression between ePWV and 30-day/1-year mortality risk among non-AF patients.

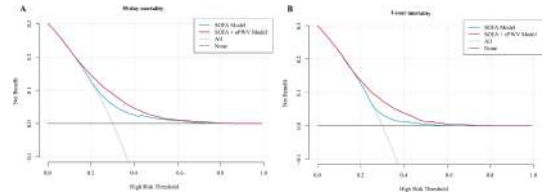
		Unadjusted model		Adjusted model	
Outcomes	**Variables**	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
30-day mortality	ePWV	1.37 (1.34-1.41)	<0.001	1.20 (1.14-1.27)	<.001
1-year mortality	ePWV	1.43 (1.40-1.46)	<0.001	1.09 (1.05-1.14)	<.001

AF, atrial fibrillation; ePWV, estimated pulse wave velocity; HR, hazard ratio; CI, confidence interval; Ref, reference;
Multivariable Cox regression model adjusted for (1) 30-day mortality: age, gender, race, heart failure, AIS, AKI, AF type, SOFA, CCI, weight, heart rate, respiratory rate, SPO2, platelet, INR, glucose, BUN, RDW, anion gap, ventilation, vasoactive drugs, RRT, antiarrhythmic, anticoagulant drugs, and antiplatelet drugs; (2) 1-year mortality: age, race, diabetes, heart failure, AIS, AKI, AF type, SOFA, CCI, weight, heart rate, respiratory rate, SPO2, temperature, platelet, INR, hematocrit, glucose, BUN, RDW, anion gap, ventilation, RRT, antiarrhythmic, anticoagulant drugs, and antiplatelet drugs.

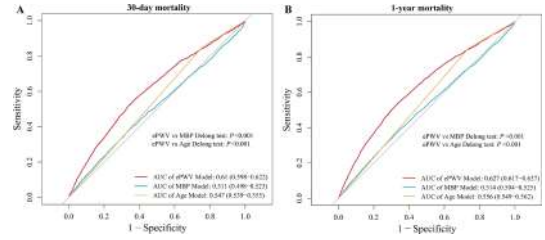
Supplementary Table 7. Comparison of the predictive performance of the SOFA + ePWV model and the SOFA model for mortality risk

Outcome	Predictive statistic	Point estimate (95% CI)	*P*
30-day mortality	NRI (Categorical)	0.031 (0.022-0.039)	<.001
	NRI (Continuous)	0.425 (0.383-0.466)	<.001
	IDI	0.038 (0.034-0.041)	<.001
1-year mortality	NRI (Categorical)	0.095 (0.083-0.108)	<.001
	NRI (Continuous)	0.427 (0.393-0.461)	<.001
	IDI	0.057 (0.053-0.061)	<.001

SOFA, Sequential Organ Failure Assessment; ePWV, estimated pulse wave velocity; NRI, net reclassification improvement; IDI, integrated discrimination improvement.



Supplementary Figure 1. Decision curve analysis of the ePWV + SOFA model and the SOFA-only model for 30-day/1-year mortality. (A) Decision curve analysis for 30-day mortality; (B) Decision curve analysis for 1-year mortality. ePWV, estimated pulse wave velocity; SOFA, Sequential Organ Failure Assessment.



Supplementary Figure 2. The receiver operating characteristic (ROC) curve of the predictive performance of ePWV and its components on 30-day/1-year mortality. (A) predicting 30-day mortality risk; (B) predicting 1-year mortality risk. ePWV, estimated pulse wave velocity; MBP, mean blood pressure; AUC, the area under the curve.