



stroke who underwent brachial-ankle pulse wave velocity (baPWV) assessment at a tertiary referral center. The measurement of baPWV is a common examination performed during cardiovascular evaluation for patients visiting our cardiovascular center. However, some patients may not undergo baPWV evaluation owing to the following reasons: 1) patient refusal and 2) inadequate patient conditions for the measurement, such as hand tremor, amputated extremities, arterio-venous fistula, or peripheral arterial occlusive disease. To increase the reliability of the baPWV value, participants with the following conditions were excluded ( $n = 146$ ): (1) ankle-brachial index  $>1.4$  or  $<0.9$ , (2) atrial fibrillation or other uncontrolled arrhythmias, (3) dysfunction of heart valves greater than a mild degree, (4) pericardial effusion more than minimal, and (5) congenital heart disease. Finally, 2,917 women were recruited in this study. This study complied with the provisions of the Declaration of Helsinki as revised in 2013. The study protocol was approved by the Institutional Review Board (approval number, 10-2021-103). The requirement for informed consent was waived owing to the retrospective study design.

### Data collection

Clinical data, including body mass index, and information on the history of hypertension and diabetes mellitus were collected. Obesity was defined as a body mass index of  $\geq 25 \text{ kg/m}^2$ .<sup>11</sup> Hypertension was defined based on a diagnosis of hypertension, current prescription of antihypertensive medications, or systolic/diastolic blood pressure of  $\geq 140/90 \text{ mmHg}$ . Venous blood samples were obtained from the antecubital vein after overnight fasting for approximately 12 hours. The following blood sample parameters were evaluated on the same day of baPWV measurement: common blood cell count, including white blood cell count and hemoglobin; creatinine; lipid levels including triglyceride, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol; serum glucose and glycated hemoglobin; and C-reactive protein. Glomerular filtration rate (GFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation.<sup>12</sup> Left ventricular (LV) ejection fraction was assessed using the biplane Simpson method based on the apical view of transthoracic echocardiography. Past medication history was identified, which included information on renin-angiotensin system inhibitor, beta-blocker, calcium channel blocker, and statin use.

### baPWV measurement

On the day of baPWV measurement, participants were prohibited from consuming alcohol, smoking cigarettes, and consuming caffeine-containing beverages. Regularly administered drugs were continued without interruption. baPWV was measured after an approximate 5-minute period of bed rest. The examinations were conducted in a silent enclosed space under constant temperature and humidity. baPWV was conducted using a commercially available device (VP-1000 analyzer; Colins, Komaki, Japan).<sup>13,14</sup> The pressure

waveforms of the brachial and tibial arteries were acquired after wrapping the blood pressure cuff around both upper arms and ankles with plethysmographic and oscillometric pressure sensors. Time intervals between pressure waveforms of the brachial and tibial arteries (pulse transit time) were examined, and baPWV was calculated automatically with a height-based formula to estimate arterial path length. We used the mean of the right and left baPWV values for analysis. baPWV was conducted by one experienced operator. The coefficient of variation of the intraobserver variability for baPWV measurement was 5.1% in our previous study.<sup>15</sup>

### Clinical events

The primary endpoint, major adverse cardiovascular event (MACE), was a composite of clinical events consisting of all-cause death, nonfatal myocardial infarction, coronary revascularization, and stroke. Cardiovascular death included sudden cardiac death and death resulting from acute myocardial infarction, heart failure, stroke, cardiovascular procedures, cardiovascular hemorrhage, or other cardiovascular causes. Unexplained sudden death was also considered cardiac death. Myocardial infarction was defined based on clinical symptoms, electrocardiogram findings, elevated cardiac troponin, and occlusive artery lesions confirmed on coronary artery imaging. Coronary revascularization was defined as undergoing percutaneous coronary intervention and coronary bypass surgery. Stroke was defined as sudden neurological deficits examined by neurologists and as a defect confirmed via brain imaging. Data on clinical events were obtained mainly through medical chart reviews, and clinical events of participants who did not visit our hospital for more than 6 months were assessed through telephone interviews. For those who could not be contacted by telephone, we requested data from the National Statistical Office of Korea to ascertain their death.

### Statistical analysis

Data are presented as numbers (percentages) for categorical variables and as mean  $\pm$  standard deviation for continuous variables. The participants were stratified into two groups according to MACE for univariable comparison. Means were compared using the Student *t* test for continuous variables, and the prevalence was compared using the chi-square test between the two groups for categorical variables. Multivariable Cox regression analyses were performed to identify the association between baPWV and MACE. Variables with  $P < 0.10$  in the univariable analyses were included as independent variables in the multivariable analysis. The receiver operating characteristic (ROC) curve with area under curve analysis and the Youden index was used to acquire the baPWV cutoff value for predicting MACE.<sup>16</sup> We performed Kaplan-Meier survival curve analysis to determine the cumulative incidence according to baPWV and conducted comparisons using the log-rank test. Propensity score (PS) matching analysis and inverse probability of treatment weighting (IPTW) analysis using calculated PS were performed to









