Supplementary methods

Subjects and study design

This study is a retrospective analysis of data deposited in the prospective registry of our government-initiated comprehensive stroke center between January 2010 and January 2018. Patients underwent brain magnetic resonance imaging (MRI) scans, including T2-weighted gradient echo imaging, for the evaluation of cerebral microbleed (CMB) immediately upon admission to the emergency room. Patients were enrolled in the study if they met the following inclusion criteria: (1) had acute ischemic stroke associated with atrial fibrillation and (2) had CMB on brain MRI. We excluded patients if they (1) died during hospitalization; (2) could not be treated with antithrombotic therapy due to contraindications; (3) were treated with a combination of oral anticoagulants (OAC) and antiplatelet at discharge; or (4) whose antithrombotic treatment changed during follow-up period (from OAC to antiplatelet or *vice versa*) (Supplementary Figure 1).

The patients were divided into groups according to their prescribed antithrombotic therapies, which were determined by their physicians after the index stroke. We allowed the use of any type of antithrombotic medication (antiplatelets, vitamin K antagonist, or non-vitamin K antagonist oral anticoagulants). Two blinded neuroimaging specialists identified the number and location of CMBs. The CMB burden was classified as either exactly one CMB or as multiple CMBs (≥2 CMBs). The location of CMBs was defined as strictly lobar or deep/mixed. The infratentorial location of CMB was considered deep CMB. The assessment of CMB number and location showed excellent inter-rater agreement (κ=0.917). Baseline characteristics, underlying stroke risk factors, and laboratory data were collected from all subjects.

Outcome measurements

The primary outcome measurement was the incidence of recurrent stroke (ischemic or hemorrhagic) at any time before the end of the 2-year follow-up. Subjects were grouped according to their antithrombotic therapy. Key secondary outcomes included the incidence of recurrent ischemic stroke, intracerebral hemorrhage, all-cause death, and major adverse cardiovascular events (a composite of stroke, acute myocardial infarction, or vascular death) over the following 2 years. We prospectively obtained clinical outcomes from all patients during hospitalization, routine clinic visits, or via telephone interviews with patients or their caregivers.

Statistical analysis

We compared the differences between groups using Student's t-tests or Kruskal-Wallis tests for continuous variables. We used chi-square tests or Fisher's exact tests for categorical variables. We used propensity scores and stabilized inverse probability of treatment weighting (IPTW) to balance possible confounders. An absolute standardized difference was calculated before and after IPTW; a value of <0.1 was considered as a low imbalance between the groups. The event rates of clinical outcome measures were estimated using the weighted Kaplan-Meier method and compared between the groups using the IPTW log-rank test. The weighted Cox proportional hazard regression was used to calculate the hazard ratios and 95% confidence intervals for primary and secondary outcomes, according to the antithrombotic medication received. A two-sided *P*-value of <0.05 was considered to indicate statistical significance. Statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA) and R software version 3.3.1 (R Foundation, Vienna, Austria).

Ethics statement and data availability

An Institutional Review Board of Chonnam National University Hospital approved this study. Written informed consent was obtained from all patients or their legal representatives prior to their enrollment in the prospective stroke registry. All the clinical and laboratory investigations described in this study were conducted according to the principles outlined in the Declaration of Helsinki. All supporting data within the article are available upon reasonable request from a qualified investigator.