Supplementary material

Biomarker assessment

Biomarkers were selected based on biological plausibility, prior literature and availability. We included biomarkers of inflammation and oxidative stress,[3-5] myocardial injury and strain,[5-8] vascular damage,[9,10] renal dysfunction,[11] and cerebral damage.[12]

C-reactive protein (CRP) and interleukin-6 were both positively associated with an inflammatory, prothrombotic state and CRP was additionally shown to directly related to stroke risk.[3,4] Growth differentiation factor-15 was associated with stroke-related death among with troponinT and N-terminal prohormone of brain natriuretic peptide (NT-proBNP).[5,6] Moreover, NT-proBNP is released into the serum after acute ischaemic stroke, as are heart-fatty acid binding proteins (hFABPs).[8] As a marker for left atrial dilatation, insulin-like growth factor-binding protein-7 (IGFBP-7) was shown to be positively associated with left atrial size.[7] Renal markers were included, as renal insufficiency is known to influence the efficacy of anticoagulants in atrial fibrillation patients.[11] As vascular markers, angiopoietin-2 was shown to be upregulated after cerebral artery occlusion in an experimental model and endothelial cell-specific molecule-1 (ESM-1) plays a crucial role in vascular permeability after ischemic stroke.[9,10] Osteopontin acts as a direct marker of cerebral damage after ischemic stroke and was therefore also included in our analyses.[12]

Detailed description for Figure 1B

Receiver operating curves are displayed, showing the accuracy of the models to diagnose large non-cortical and cortical infarcts. Final model (area under the curve [AUC], 0.679; 95% confidence interval [CI], 0.636 to 0.722) includes hs-troponin T, osteopontin, heart fatty-acid binding protein 3, vascular disease, and atrial fibrillation on the electrocardiogram (ECG). Biomarker model (AUC, 0.662; 95% CI, 0.617 to 0.706; P=0.16 compared to the final model) includes hs-troponin T, NT-proBNP, heart fatty-acid binding protein 3, and osteopontin. The addition of the CHA_2DS_2-VASc score to the biomarker combination did not improve the AUC of 0.666 (95% CI, 0.622 to 0.710; P=0.29 compared to the final model). Clinical variables (AUC, 0.633; 95% CI, 0.589 to 0.677; P=0.001 compared to the final model) include vascular disease and atrial fibrillation on the ECG. The CHA2DS2-VASc score alone had an AUC of 0.602 (95% CI, 0.558 to 0.647; P=0.0002 compared to the final model).

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