A multiple biomarker strategy for diagnosis and prognosis of acute heart failure in older patients presenting to the emergency department

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PURPOSE

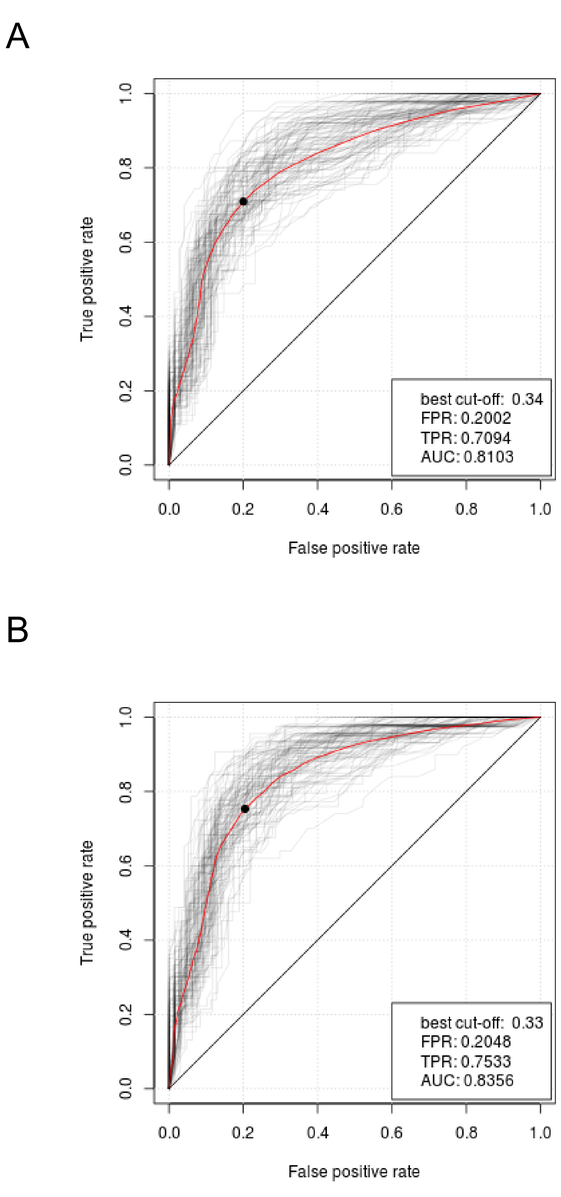
Biomarkers can help to identity acute heart failure (AHF) as the cause of symptoms in patients presenting to the emergency department (ED). Older patients may prove a diagnostic challenge due to co-morbidities. Therefore we prospectively investigated the diagnostic and prognostic performance of N-terminal pro-B-type natriuretic peptide (NT-proBNP) alone or in combination with other biomarkers for acute HF upon admission at the ED.

METHODS

We consecutively enrolled 302 non-surgical patients ≥ 70 years presenting to the ED. In addition to NT-proBNP, mid-regional pro-adrenomedullin (MR-proADM) and mid-regional pro-atrial natriuretic peptide (MR-proANP) or C-terminal pro-endothelin-1 (CT-proET-1) and ultra-sensitive C-terminal pro-vasopressin (Copeptin-us) were measured at admission. Two cardiologists independently adjudicated the final diagnosis of AHF after reviewing all available baseline data (excluding NT-proBNP, MR-proADM, MR-proANP, CT-proET-1 and Copeptin-us). All patients were followed up for cardiovascular-related death within the following 12 months.

RESULTS

AHF was diagnosed in 120 (40%) patients (age 81±6 years). Adding MR-ADM to NT-proBNP levels improved C-index (0.84 versus 0.81; P=0.045), and yielded IDI (3.3%; P=0.002), NRI (17%, P<0.001) and continuous NRI (33.3%; P=0.002). Adding CT-proET-1 to NT-proBNP levels improved C index (0.86 versus 0.81, P=0.031), and yielded robust IDI (12.4%; P<0.001), NRI (31.3%, P<0.001) and continuous NRI (69.9%; P<0.001). No other dual or triple biomarker combination showed a significant improvement of both C-index and IDI (fig. 1). Cox regression analysis revealed a 1.99-fold risk of death (95% CI 1.61 to 2.45, *P*<0.001) for an increment of the log-transformed MR-proADM concentration by 1 unit after adjustment for cardiovascular risk factors (fig. 2, table 1).



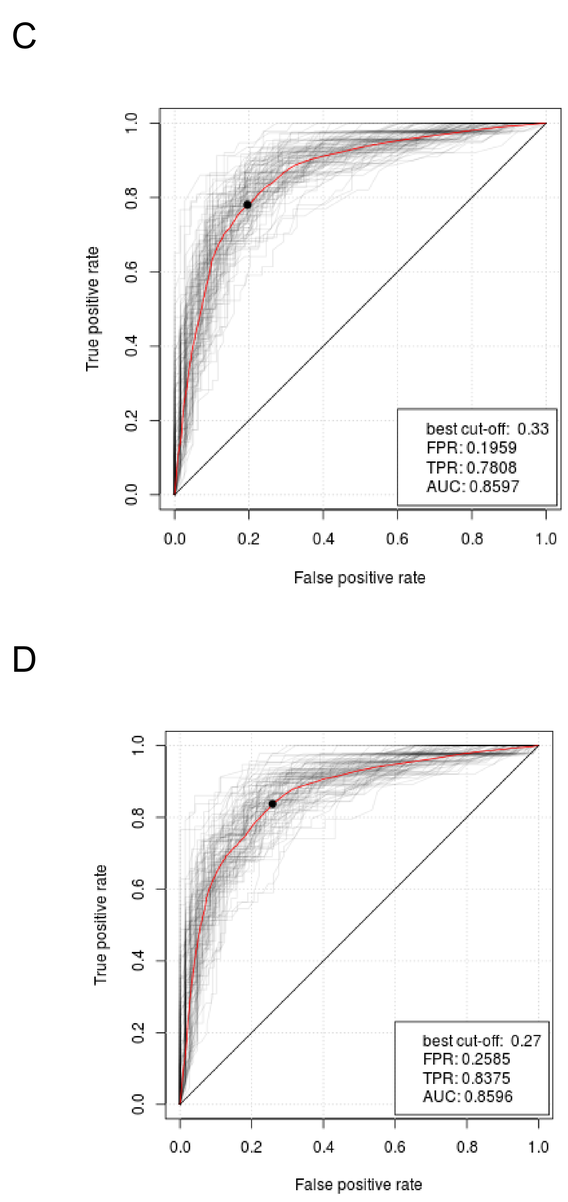


Figure 1 Receiver-operating characteristic (ROC) curves demonstrating diagnostic accuracy for HF. All following models contain age and sex as covariates. Note that no interaction effects with either age or sex are considered. Only additive effects are considered. ROC showing the diagnostic performance for the diagnosis of HF provided by NT-proBNP (A), NT-proBNP and MR-proADM (B), NT-proBNP and CT-proET-1 (C), and NT-proBNP, CT-proET-1 and MR-proADM (D). FPR indicates the false positive rate, TPR the true positive rate and AUC the area under the curve. Grey curves represent ROC curves based on bootstrap samples, the red curve indicates the aggregated estimate over all bootstrap estimates.

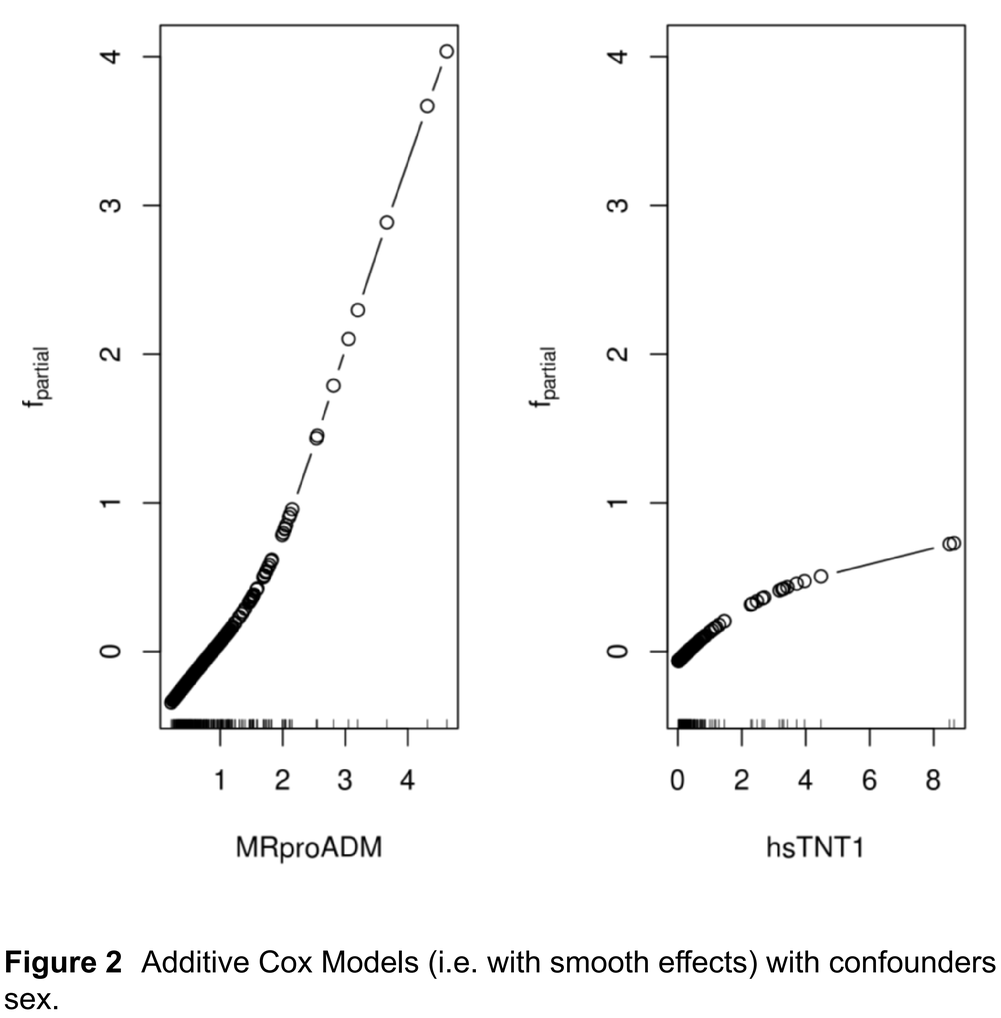


Figure 2 Additive Cox Models (i.e. with smooth effects) with confounders age and sex.

Table 1 Linear Cox Model

	β	Hazard Ratio	CI (lower)	CI (upper)	Standard Error	z value	P value
Age	0.11	1.12	1.04	1.20	0.04	3.16	0.002
Sex: male	-0.01	0.99	0.45	2.19	0.40	-0.02	0.985
MRproADM, nmol/L	0.69	1.99	1.61	2.45	0.11	6.46	<0.001
hs-cTNT, ng/mL	1.17	3.22	0.97	10.68	0.61	1.91	0.056

CONCLUSIONS

In older patients presenting to the ED, the addition of CT-proET-1 or MR-proADM to NT-proBNP improves diagnosis of HF. Both dual biomarker approaches offer significant risk reclassification improvement over NT-proBNP. MR-proADM improves the prognostic performance in AHF.

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