High-sensitivity cardiac troponin T and NT-proBNP for ruling-in and ruling-out of cardiac amyloidosis

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Background: Cardiac amyloidosis (CA) is caused by the extracellular deposition of misfolded proteins into insoluble amyloid fibrils, the 2 most common forms being transthyretin (ATTR) and immunoglobulin light chain (AL) amyloidosis. Chronic elevation of cardiac troponins and natriuretic peptides is common in CA and predicts worse outcome. The diagnostic yield of biomarkers of cardiac damage for CA has been less investigated.

Purpose: We aimed to evaluate the ruling-in/out values for the diagnosis of CA of high-sensitivity cardiac troponin T (hs-cTnT) and of N-terminal fraction of pro-B-type natriuretic peptide (NT-proBNP).

Methods: We studied 275 consecutive patients referred to two tertiary Centers in Italy (n=184) and France (n=91) with the clinical suspicion of CA due to the presence of a plasma cell dyscrasia or an unexplained left ventricular (pseudo)hypertrophy. CA was confirmed by the combination of suggestive features on imaging techniques (echocardiography, cardiac magnetic resonance, diphosphonate scintigraphy) and biopsy examination. All patients underwent a full baseline characterization including hs-cTnT and NT-proBNP. Biomarkers values corresponding to a negative likelihood ratio <0.1 or a positive likelihood ratio >10 were respectively chosen as rule-out and rule-in cut-offs for CA.

Results: CA was confirmed in 161 (59%) patients, who had either AL amyloidosis (n=96, 60%) or ATTR amyloidosis (n=65, 40%). At time of evaluation, 97 (35%) patients (34 CA vs. 63 controls, p=0.112) were hospitalized for decompensated heart failure. Patients with CA showed higher hs-cTnT (65 ng/L [44–122] vs. 31 [18–42], p<0.001) and NT-proBNP (4260 ng/L [2006–8911] vs. 1199 [468–3357], p<0.001) than those without CA. The area under the curve (AUC) values for hs-cTnT and NT-proBNP were 0.832 and 0.744 respectively (p=0.002 for the difference). The combination of the two biomarkers (AUC=0.836) improved discrimination over NT-proBNP (p=0.004), but not over hs-cTnT (p=0.423). A hs-cTnT value <15 ng/L (sensitivity=100%, negative predictive value=100%, true negatives=13, false negatives=0) and a NT-proBNP <550 ng/L (sensitivity=98%, negative predictive value=89%, true negatives=33, false negatives=4) were selected as rule-out cut-offs. A hs-cTnT level ≥80 ng/L (specificity=96%, positive predictive value=93%, true positives=71, false positives=5) was optimal for ruling in amyloidosis, while no rule-in cut-off could be selected for NT-proBNP. hs-cTnT values of either ≥80 or <15 ng/dL could effectively rule-in/out 89 (32%) patients.

Conclusions: Plasma hs-cTnT and NT-proBNP have diagnostic value in patients with suspected CA. Stand-alone hs-cTnT levels <15 or ≥80 ng/L may help to exclude or confirm the diagnosis of CA in up to one third of patients undergoing a diagnostic screening for the disease.
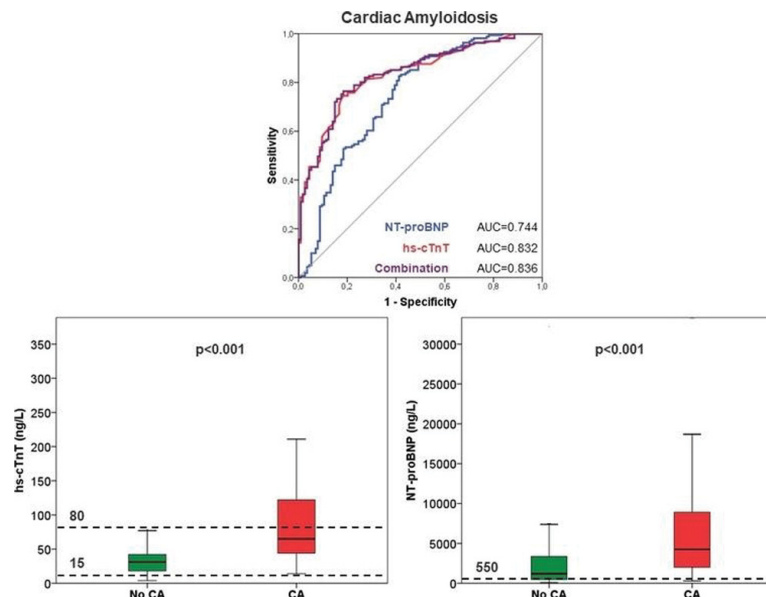
Figure 1