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ORIGINAL ARTICLE

Elevated Baseline Cardiac Troponin Levels in the Elderly – Another Variable to Consider?

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Aims This study aimed to determine the frequency of baseline high-sensitivity troponin T (hs-TnT) elevation in different age groups presenting to the Emergency Department without acute coronary syndromes (ACS) or other acute illnesses known to cause to troponin elevation. We additionally sought to determine whether the relationship between age and hs-TnT was independent of co-morbidities.

Methods We retrospectively analysed data on all patients presenting to the Emergency Department (ED) between November 2010 and June 2011 in whom hs-TnT was measured. Patients presenting with acute coronary syndromes (ACS) or other acute illness known to elevate hs-TnT levels were excluded. Demographics, clinical characteristics and diagnosis were recorded, together with hs-TnT assay results.

Results Of 3219 patients with hs-TnT testing in the ED during the study period, 526 with proven/suspected ACS and 1376 with other acute medical conditions known to elevate troponin concentrations were excluded. The percentage of patients with hs-TnT concentrations elevated above the upper reference limit (>14ng/L) increased with age: <50 years (1.8%), 50-69 years (7.3%), ≥70 years (41.5%), p=0.001. Multivariate analysis identified age over 70 years (p<0.001) as the strongest independent predictor of elevated hs-TnT. Other independent predictors included atrial fibrillation (p<0.001), age 50-69 years (p<0.001) male gender (p<0.001), previous heart failure (p<0.007) and previous ischaemic heart disease (p<0.04).

Conclusions Hs-TnT elevations (>14ng/L) are common in elderly patients presenting to the ED without ACS or other acute illnesses known to cause to troponin elevation. This finding appears to be independent of the higher burden of co-morbidities in this age group.

Keywords Troponin • Elderly • Myocardial infarction • Diagnosis • Chest pain

Introduction

Cardiac-specific troponin (cTn) assays are routinely employed in the diagnosis and risk stratification of patients with acute myocardial infarction, according to current guidelines [1,2]. Dynamic changes in biomarker concentration above the 99th percentile range for a healthy reference population are considered significant, and help identify patients at higher risk of cardiovascular death in both the short and long-term [3–5].

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High sensitivity cardiac troponin (hs-Tn) assays have a lower limit of detection and allow more precise measurement of cTn levels at and below the 99th percentile [6]. Their use has been shown to improve diagnostic sensitivity and reduce the time to diagnosis for myocardial infarction [7]. However, the higher detection rate enabled by these high sensitivity assays challenges diagnostic specificity, and their use has resulted in increased numbers of patients with elevations of cTn above the 99th percentile due to chronic or acute illnesses other than myocardial infarction [8,9]. Inappropriate ''rule in'' of patients for the diagnosis of myocardial infarction may have important consequences, including investigations and therapies that are unwarranted and potentially harmful, prolonged stay in the emergency department or inappropriate admission and unnecessary patient anxiety.

Emerging data have identified increasing age as a possible cause of baseline troponin elevation in hospitalised and community-based populations [10–12]. The elderly are more likely to have cardiac risk factors, pre-existing heart disease and other chronic co-morbidities that may elevate baseline troponin levels. It is unclear, therefore, whether elevated hs-Tn levels are due to this higher burden of co-morbidity, undiagnosed cardiac disease or an age-related phenomenon unaccounted for in the original assay validation protocols. In this study we aimed to determine the frequency of baseline hs-Tn elevation in different age groups presenting to the Emergency Department without ACS or other acute illnesses known to elevate hs-Tn levels. Furthermore, we sought to determine whether age, itself, was independently associated with hs-Tn levels.

Methods

Study Population

All patients presenting to the Emergency Department with hs-TnT testing between November, 2010 and June, 2011 were retrospectively identified from our Biochemical Service database. Use of this dataset and the study protocol was reviewed by the Central Regional Ethics Committee and found to conform to the New Zealand standards for observational research. Individuals with renal impairment (eGFR $\leq$45 ml/min/1.73m^2) and those with $\geq$20% dynamic change in serial hs-TnT testing over six hours were excluded from further analysis.

Medical records on the remaining patients were reviewed independently by two separate clinicians (IW and SY) and excluded from further analysis if any of the following pre-specified clinical criteria were met: (1) presentation consistent with ACS, defined by symptoms and/or ECG changes (LBBB, new ST-segment deviation or T-wave inversion) consistent with myocardial ischaemia; (2) presentation with palpitations; (3) new onset superventricular tachyarrhythmias; (4) permanent atrial fibrillation/flutter with uncontrolled ventricular rate (>120/min); (5) cardio-respiratory arrest; (6) ventricular tachyarrhythmia; (7) acute heart failure; (8) severe valvular disease or cardiomyopathy (LVEF $\leq$30%); (9) myocarditis/pericarditis; (10) active sepsis (defined by elevated white cell count, inflammatory markers or fever); (11) pulmonary embolus or deep vein thrombosis; (12) acute cerebrovascular event; (13) severe anaemia ($\leq$ 80 g/L); and (14) cocaine/ecstasy use.

Recorded Variables

Demographic details, background cardiovascular risk factors (hypertension, hyperlipidaemia, diabetes, smoking status), relevant co-morbidities (prior cardiac, cardiovascular and/or renal disease) and final diagnoses related to the index presentation were recorded. Serum electrolytes, creatinine, estimated glomerular filtration rates and high-sensitivity cardiac-specific Troponin T were also recorded for each patient.

High Sensitivity Troponin T Assay

Hs-TnT was measured in EDTA plasma samples using the Cobas CE modular system (Roche Diagnostics); the level of detection is 5ng/L and the 99th percentile 14ng/L, with a 5% coefficient of variation at 13ng/L. Where repeat measures were available (<20% variability), the higher of the two values was considered for analysis.

Statistical Analysis

Continuous variables are expressed as means $\pm$ standard deviation. Categorical variables are expressed as absolute values and percentages of the total. Values of hs-TnT $\leq$4 ng/L were considered to be under the lower limit of detection of the assay, and for statistical analysis and graphical display were given a value of 4ng/L. Patient demographics according to age were divided empirically into three groups: <50 yrs of age, 50-69 years of age, and $\geq$70 yrs of age. Statistical significance between groups was determined by Analysis of Variance and Pearson $_X^2$ test. The distribution of hs-TnT was compared across the three age groups using Kruskil-Wallis test. Demographic and clinical predictors for hs-TnT elevation above the upper reference limit were identified by Pearson $_X^2$ test, and independent determinants of hs-TnT elevation examined using multivariate logistic regression analysis for all baseline characteristics that were significant variables in univariate analysis. Data were analysed using SPSS (v19; IBM, USA). P values <0.05 were considered significant.

Results

During the eight-month period examined, hs-TnT was measured in 3219 patients presenting to the Emergency Department. Of these 468 patients were immediately excluded because of impaired renal function (eGFR $\leq$45 ml/min/1.73m^2) and a further 147 patients because of a $\geq$20% change between measurements in serial hs-TnT testing, irrespective of clinical context (Fig. 1).

Of the remaining 2604 patients, 379 were excluded from further analysis because of confirmed/suspected ACS. A further 908 patients were excluded because of tachyarrhythmia