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ORIGINAL ARTICLE

Outcomes in Patients Presenting with Symptoms Suggestive of Acute Coronary Syndrome with Elevated Cardiac Troponin but Non-obstructive Coronary Disease on Angiography

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Background Many patients provisionally diagnosed with acute myocardial infarction (AMI) have angiographically unobstructed coronary arteries. Despite other potential causes, patients are often diagnosed as AMI with psychosocial implications and medication burden. The aim of this audit was to review such patients at our centre.

Methods All patients investigated for possible AMI with coronary angiography from 2007 until 2011 at Christchurch Hospital, New Zealand, in whom cardiac troponin was elevated (with no other cause found for that elevation) but coronary angiography showed diameter stenosis <50% were reviewed. Primary outcome was two-year cardiac death and AMI (by universal definition).

Results Of the 351/6493 (5.4%) who met the inclusion criteria, 180 had normal angiograms and 171 had non-obstructive coronary disease (stenosis >0% and <50%). By two years there were two cardiac deaths (0.6%) and five AMIs (1.4%). The primary outcome rate was therefore 2.0% (2.2% for those with normal angiograms and 1.8% with non-flow limiting coronary disease, p=1.000).

Conclusion Patients who have presented with AMI symptoms, elevated cardiac troponin, and unobstructed coronary arteries on angiography are at very low risk of cardiac death (0.6%), AMI (1.4%) or either (2.0%) at two-year follow-up.

Keywords Troponin • Myocardial infarction • Acute coronary syndrome • Coronary angiogram • Coronary stenosis

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Introduction

A substantial proportion of patients (3-14%) diagnosed with acute myocardial infarction (AMI) have angiographically unobstructed coronary arteries (i.e. free from focal stenosis of ≥50% stenosis diameter) [1–5]. Most AMIs are caused by plaque rupture or disruption with subsequent platelet aggregation and coronary thrombosis [5]. However, in cases where there is no flow limiting disease, it has been postulated that AMI has occurred due to plaque disruption either with luminal occlusion and recanalisation prior to angiography or without occlusion but with accompanying distal embolisation of atherothrombotic debris or platelet aggregates [1,2]. Other potential mechanisms include endothelial dysfunction, vasospasm, coronary embolism, spontaneous dissection or even myocardial bridging [2,5].

Other causes of cardiac troponin (cTn) elevation with or without angina type symptoms include myocarditis, pulmonary embolus and Takotsubo cardiomyopathy [2,5].

Previous studies have demonstrated in patients with symptoms of acute coronary syndrome (ACS) and elevated cTn, early angiography and revascularisation, antiplatelet therapy and secondary prevention medications improve short and long-term outcomes [2,5]. Despite other potential causes for presentations with ischaemic symptoms and elevated cTn but no flow limiting disease on angiography, patients are given a diagnosis of AMI. This has implications for driving, insurance and employment as well as an important psychological and social impact. Patients are also committed to needless secondary prevention treatments which may be harmful and costly [2,5].

The aim of this study was to ascertain the prevalence, investigation, diagnosis, treatment and medium term outcomes in patients with symptoms suggestive of ACS and elevated cTn but with angiographically unobstructed coronary arteries in real world practice.

Methods

This study is a single centre audit of all patients investigated for possible ACS with coronary angiography in Christchurch Hospital, New Zealand, over five years (January 2007-December 2011) in whom cTn was elevated above the decision cut-point but coronary angiography revealed no flow limiting lesion. Christchurch Hospital is a tertiary referral centre for angiography and percutaneous intervention serving a population of approximately 500,000. Individual patients were only included once (on their first presentation) even if they were investigated on multiple occasions.

Exclusion criteria included diameter stenosis ≥50% in ≥1 coronary artery, previous revascularisation, when indication for angiography was not investigation of ACS and normal cTn levels. Patients in whom there existed objective evidence for an alternative explanation for a cTn elevation were also excluded as it is not these patients who pose a diagnostic/prognostic conundrum. These included arrhythmia with tachycardia, severe cardiomyopathy with ejection fraction <35%/heart failure, pulmonary embolus, Takotsubo cardiomyopathy, severe sepsis requiring ICU admission and severe renal failure (estimated glomerular filtration rate of <10 mL/min/1.73m2).

All patients undergoing coronary angiography were identified using the catheter laboratory database. Patient demographics and in-patient investigation results were retrieved from the hospital intranet reporting system. Hospital notes were reviewed in cases of interest.

Coronary angiograms were reported by the five operators during this time period. Patients were classified as having normal arteries or non-obstructive coronary disease (stenosis diameter of >0% but <50%).

The cTn in use during the investigation period was Abbott Architect cTnI, decision cut-point 0.03 µg/L. A minority of cases referred to us from elsewhere in New Zealand had measurement of Roche high sensitivity cTnT, decision cut-point 0.014 µg/L. Patients were categorised as having low (<0.1 µg/L), medium (0.1-1.0 µg/L), or high (>1.0 µg/L) level cTnI elevations. A dynamic change of ≥3 standard deviations in serial measurements is considered significant [6], and corresponds to an absolute change of 0.039 µg/L for Abbott Architect cTnI [7].

Baseline characteristics, investigations and treatment of eligible patients are presented in Table 1. The discharge diagnosis and discharge medications were recorded, including aspirin, clopidogrel, β blockers, angiotensin converting enzyme inhibitors/angiotensin receptor blockers and statins. The only antiplatelet agent other than aspirin available to us during this period was clopidogrel.

Patients were followed for two years for adverse events (including deaths, readmissions, in/out patient investigations and treatments such as revascularisation). Events searched for included death, cardiac death, cTn positive events, AMI (defined as per universal definition), [8] revascularisation and heart failure. Previous audit data has suggested that patients representing to centres other than Christchurch hospital or the surrounding hospitals in South Canterbury or the West Coast (who share the same intranet system) or to private practice is <1%. The primary outcome was the composite of cardiac death and AMI.

As per institutional protocol, ethics committee approval and informed consent were not sought as this was an audit.

Those with normal angiograms were compared with those with non-obstructive coronary disease. Continuous variables are presented as medians and interquartile ranges (compared using the using the Mann Whitney U test), and categorical variables as numbers and percentages (compared using the using chi square test). Comparisons were two-tailed and a p value of <0.05 was considered significant. The primary outcome was plotted on Kaplan Meier curves and groups compared using the log rank test. Cox proportional hazards modelling was used to ascertain variables predicting the primary outcome using the forward conditional method. Statistics were completed using SPSS version 20.