Heart, Lung and Circulation (2016) xx, 1–5
1443-9506/04/$36.00
http://dx.doi.org/10.1016/j.hlc.2016.07.015

ORIGINAL ARTICLE

Long Term Prognostic Value of a Negative Work-Up for Acute Coronary Disease in Emergency Department Chest Pain Patients Without Known Coronary Artery Disease: A Cohort Study

Q1 **Anne-Maree Kelly, MD FACEM FFCP*, Sharon Klim, BN**

Joseph Epstein Centre for Emergency Medicine Research at Western Health, Melbourne, Vic, Australia

Received 16 March 2016; received in revised form 12 July 2016; accepted 22 July 2016; online published-ahead-of-print xxx

Background To determine the rate of all cause and cardiac death, new myocardial infarction (MI) or coronary revascularisation at over three years from index visit in emergency department chest pain patients without known coronary artery disease (CAD) at index presentation who had a negative electrocardiogram (ECG) and biomarker workup for acute coronary syndrome (ACS).

Methods An unplanned sub-study of a prospective observational study of consecutive adult patients presenting to the ED with atraumatic chest pain (or equivalents). The primary outcome of interest was the predictive performance of a negative ECG and biomarker work-up for ACS for all cause and cardiac mortality over more than three years' follow-up in patients not known to have pre-existing CAD presenting to the ED with chest pain. Secondary outcomes were rate of new MI or revascularisation not related to the index visit.

Results 237 patients were studied. Median age was 52 (IQR 42 – 62) and 55.3% were male. Median follow-up was 48 months. There were seven deaths (3%, 95% CI 1.4 – 6%), one of which was potentially cardiac in origin with cause of death given as pulmonary hypertension and cardiac failure (0.4%, 95% CI 0.02 – 2.3%). There was one confirmed MI (0.6%, 95% CI 0.03 – 3.8%). The rate of revascularisation not related to the index visit was 3.1% (95% CI 1.1 – 7.4%).

Conclusion Patients who present to ED with potentially cardiac chest pain but do not have known CAD, have non-ischaemic ECGs and troponin assays below the 99th percentile are at low risk of cardiac death or MI in long-term follow-up. This challenges the recommendation for routine functional or anatomic testing.

Keywords Prognosis • Chest pain • Coronary artery disease • ED

Introduction

Q2 Emergency department (ED) based processes to identify patients presenting with chest pain who are at low risk of acute coronary syndrome (ACS) or adverse cardiac events have been shown to have a low rate of, and high negative predictive value for, major adverse cardiac events (MACE) in short-term follow-up [1–4]. Less is known about the predictive performance of these processes in longer term follow-up, particularly in the subgroup of patients without known pre-existing coronary artery disease (CAD). Current guidelines suggest that patients with a negative ACS work-up should have provocative functional testing (e.g. exercise stress test, myocardial perfusion imaging or stress echocardiography)

*Corresponding author at: JECEMR, Sunshine Hospital, Furlong Road, St Albans 3021, Vic, Australia, Email: anne-maree.kelly@wh.org.au

Please cite this article in press as: Kelly A-M, Klim S. Long Term Prognostic Value of a Negative Work-Up for Acute Coronary Disease in Emergency Department Chest Pain Patients Without Known Coronary Artery Disease: A Cohort Study. Heart, Lung and Circulation (2016), http://dx.doi.org/10.1016/j.hlc.2016.07.015

or anatomical imaging (e.g. CT coronary angiography (CTCA)) to identify 'silent' CAD [5]. However if the rate of events in long-term follow-up is low and not cardiac-related, there may be a case for testing of selected patients only.

The aim of this study was to determine the rate of all cause and cardiac death, new myocardial infarction (MI) or coronary revascularisation, at over three years from index visit in patients without known CAD at index presentation who had a negative ECG and biomarker work-up for ACS in the ED.

Methods

Design and Setting

This is an unplanned sub-study of a prospective observational study of consecutive adult patients (aged over 18 years) presenting to the ED of two community teaching hospitals between 19 January 2009 and 30 June 2009 with chest pain.

Participants

Adult patients presenting with non-traumatic chest pain (or equivalents) and undergoing evaluation for potential ACS were eligible for inclusion in the parent study. For this sub-study, additional inclusion criteria were absence of known coronary artery disease at index ED visit, no ischaemic ECG features and all troponin assays during the index ED evaluation being below the 99th percentile for the test. Known coronary artery disease was as reported by the patient (confirmed where possible from medical records) and defined as any of: previous myocardial infarction (MI), physician-diagnosed angina, percutaneous coronary intervention, coronary artery bypass grafts or coronary angiogram showing stenosis >50%. Patients were not eligible for inclusion if they had clearly ischaemic ECG features identified by the treating clinician at initial assessment (including STEMI), they did not have a troponin assay or ECG performed within 24 hours of pain onset, there was a clear non-ACS diagnosis made by the treating clinician at initial assessment, they had a serious arrhythmia pre-hospital or at ED presentation (including cardiac arrest), language barrier or lack of telephone details precluded follow-up or they were aged under 18 years. Patients were also excluded if they declined consent to follow-up or records could not be found.

Data Collection

Clinical and investigational data regarding the index presentation were collected on a piloted data collection form. Data collected included demographics, cardiac risk factors, history of CAD, cardiac failure, atrial fibrillation or peripheral vascular disease, clinical features at ED presentation, use of warfarin, aspirin or statins, results of biochemical analyses including cardiac biomarkers, ECG findings, interventions during hospitalisation and in-hospital clinical course. In the parent study, patients were contacted by telephone at 7 and 30 days after the index ED visit to determine occurrence of defined MACE (defined as all cause and cardiac death, new MI or coronary revascularisation).

Regarding long-term follow-up, we chose to determine patient outcome as at 31 March 2013, representing approximately four years from the index ED visit. The choice of this date was arbitrary. Initially a review of the medical record was undertaken during 2014 to determine if the patient had died (including whether the cause of death was cardiac, non-cardiac or unknown) or treatment for a new MI coronary revascularisation had occurred in the study health service during the follow-up period. If complete data was not available covering the relevant period, patients were contacted by telephone. If patients could not be contacted by telephone, a death registry search (Victorian Registry of Births, Deaths and Marriages) was undertaken. For patients who had died and the cause of death was unclear, clarification was made by contact with their family doctor. Deaths of unknown cause were assumed to be cardiac.

The primary outcome of interest was the predictive performance of a negative ECG and biomarker work-up for ACS for all cause and cardiac mortality. Secondary outcomes were the rate of new MI or revascularisation.

The troponin assay used was TnI-Ultra by Siemens Diagnostics performed on an Advia Centaur analyser. The test has a reported range of 0.006 to 50 microg/l. Co-efficient of variation is 10% at TnI 0.03 microg/l, 5.3% at 0.08 microg/l and 4.1% at 0.18 microg/l. The 99th percentile is 0.04 microg/l (95%CI 0.03 – 0.05 microg/l) (manufacturer's information). Timing of biomarkers was in accordance with the Australasian guidelines for contemporary troponin assays at the time of the index presentation [5]. Tests are taken at presentation and three to four hours later as long as the latter test is more than six hours from symptom onset. If a patient presented more than six hours from symptom onset, a single assay was deemed sufficient to rule out ACS.

Analysis and Sample Size

Data analysis is descriptive. Continuous variables are reported as medians and interquartile ranges (IQR). Categorical data is reported as proportions, with 95% confidence intervals where relevant. Mortality is reported for the whole sample. Myocardial infarction or revascularisations are only reported for patients with full follow-up. No sample size calculation was undertaken as this was an unplanned post-hoc study.

Ethical Approval

The project was approved by the institution's low risk ethics panel as a quality assurance project under the National Health and Medical Research Council (Australia) guidelines [6]. Patient consent for data collection from medical records was not required. Participants provided verbal consent to telephone follow-up.

Results

Two hundred and thirty seven patients met inclusion criteria. Sample derivation is shown in Figure 1. Median age was

Please cite this article in press as: Kelly A-M, Klim S. Long Term Prognostic Value of a Negative Work-Up for Acute Coronary Disease in Emergency Department Chest Pain Patients Without Known Coronary Artery Disease: A Cohort Study. Heart, Lung and Circulation (2016), http://dx.doi.org/10.1016/j.hlc.2016.07.015