NZMSJ Academic Writing Prize
Issue 10
FIRST PLACE

Risk stratification in patients presenting with chest pain who are not initially diagnosed with an Acute Coronary Syndrome

Caroline Ulrich
Trainee Intern
Dunedin School of Medicine
University of Otago

Caroline is currently a trainee intern at the Dunedin School of Medicine. Having grown up in a rural community in South Canterbury, she has an interest in rural medicine and the limitations that smaller DHBs such as South Canterbury must cope with. She has now completed two summer research projects at Timaru hospital, both dealing with ways to best serve the predominantly rurally based population of South Canterbury and hopes to further her interest in rural medicine by working at a smaller hospital when she graduates this year.

ABSTRACT

Aims: Understanding outcomes for patients presenting with chest pain, determined not to be caused by an acute coronary syndrome (non-ACS), is important to aid triage and management. The primary intention of this study was to compare the clinical outcomes of non-ACS chest pain patients, divided into high-risk and low-risk non-ACS subgroups.

Methods: The hospital medical records of patients presenting to Timaru Public Hospital with non-ACS chest pain over a 4-month period (1/1/06 – 30/4/06) were reviewed. Eligible non-ACS patients were divided into high-risk and low-risk subgroups based on the presence or absence of a history of coronary artery disease (CAD), respectively.

Results: 128 patients with non-ACS chest pain were included in the final study group. Outcomes at a minimum of 18 months of follow-up differed significantly between the high-risk and low-risk non-ACS subgroups, especially the number of re-presentations (including acute coronary syndrome (ACS) and myocardial infarction (MI)). The high-risk non-ACS subgroup and patients with ACS chest pain were very similar with regard to outcomes such as re-presentations, ACS, MI and mortality.

Conclusion: This retrospective review provides evidence that outcomes for patients with non-ACS chest pain may be influenced significantly by a prior history of CAD. Furthermore, patients considered to be high risk, based on the presence of CAD, require more active investigation and invasive management followed by aggressive risk factor modification.

The presentation of chest pain to hospital is a common occurrence. While the management of acute coronary syndrome (ACS) -related chest pain is well defined, investigating and managing patients with chest pain initially thought to be of non-ACS origin, is less clear.

There is a wide variety of causes of non-ACS chest pain which include gastro-oesophageal disorders, pleuropericardial disease, pulmonary embolism, musculoskeletal pain as well as stress and anxiety-related disorders.[1-7] Several studies have recommended a range of investigations for these patients[1,3,7-10] which may be helpful in reaching a definitive diagnosis. However, such investigations are not always appropriate or available.

A recent retrospective cohort study published by Taylor et al[11] reported outcomes of patients who had attended a rapid assessment of chest pain clinic. This clinic was set up to reduce the number of hospital attendances and admissions by patients who did not have chest pain of coronary origin. In this study, patients were classified as "low risk chest pain" if they did not have ST-segment ECG change or symptoms suggestive of myocardial ischaemia on exercise[11] – similar to the protocol used to define "non-ACS chest pain" in this study. Results showed that only 3.6% of "low risk chest pain" patients suffered cardiovascular morbidity or mortality after six years of follow-up.[11]

Interestingly, a number of studies have previously concluded that a prior history of coronary artery disease (CAD) is important prognostically in patients with chest pain,[2,4,5] and is more important for long-term prognosis than discharge diagnosis[5]. Prina et al. (2004) found that patients presenting with chest pain and a history of CAD were more likely to have an adverse cardiac event within 12 months. They concluded that this should increase the clinician's level of suspicion that the pain could be coronary in origin, even with negative preliminary investigations.[2] Conversely, other studies have shown that patients with no prior history of CAD have better outcomes with respect to cardiac morbidity and mortality.[12,13]

The primary intention of this study was to look at clinical outcomes for patients presenting to hospital with chest pain of non-ACS origin (as defined over) divided into low-risk and high-risk non-ACS subgroups based on the presence or absence of a history of coronary artery disease.

METHODS

Study Design

Timaru Public Hospital (TPH) is a provincial hospital serving a population of 55000. All patients presenting to TPH with chest pain are triaged through the cardiac care unit (CCU). This study was a retrospective review of a consecutive sample of patients presenting with chest pain, determined to be of a non-ACS cause, between January 1 2006, and April 30 2006. Ethical approval was granted by the Regional Upper South A committee to conduct the study.

Study Population

The hospital medical records of all patients who presented to CCU with chest pain were reviewed to determine eligibility for the study. For the purpose of this study, ACS was defined as a presentation with chest pain associated with either:

1) ECG changes suggestive of ischaemia, (ST elevation or depression of >1mm in one or more leads or new T wave inversion)

or,

2) Positive cardiac enzyme Troponin T (TnT) of >0.03ng/ml during the

index admission.

All patients with a negative hospital evaluation for ACS, by the above criteria, were considered for this study. Exclusion criteria included:

1) An incomplete data set (less than two TnT results, no ECG or missing notes).

and

2) Residence outside the South Canterbury area.

The notes of patients presenting with chest pain due to ACS were reviewed to enable basic comparisons between the groups to be made. Patients admitted more than once during the four month study period with chest pain were included in this study at the first admission, and subsequent admissions were classified as re-presentations.

Study Protocol

To provide 18 months of follow-up, the review of patient notes began on November 9, 2007. The details of the index presentation including history, physical examination, demographic data, previously prescribed drugs and presence of cardiac risk factors were extracted from the hospital notes of each patient with non-ACS chest pain eligible for the study. Overall cardiovascular risk was determined by combining the total number of cardiac risk factors present in each patient with a maximum total of six. The risk factors used to determine this score were: proven history of CAD, family history of IHD/CAD, hypertension (>140/90mmHg; previously diagnosed +/- treatment), hypercholesterolaemia, diabetes (type I or II), smoker (past or present). Previous presentations and investigations for chest pain were also obtained from the notes. The final discharge diagnosis was taken from coding data. Patient notes were reviewed for any re-presentations to the CCU with chest pain, further investigations or treatment for chest pain, any new diagnoses that could account for the index presentation, and all-cause mortality.

Eligible patients with non-ACS chest pain were classified according to whether they had a definitive history of CAD or not. A history of CAD was defined as any previous: myocardial infarction (MI), percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass graft (CABG) or any combination of these. Two study subgroups were produced:

1) A low-risk subgroup of patients with no history of CAD.

2) A high-risk subgroup of patients with a history of proven CAD.

The notes of patients presenting with ACS chest pain were reviewed to extract basic demographic data (age, gender), details of any re-presentations and all-cause mortality.

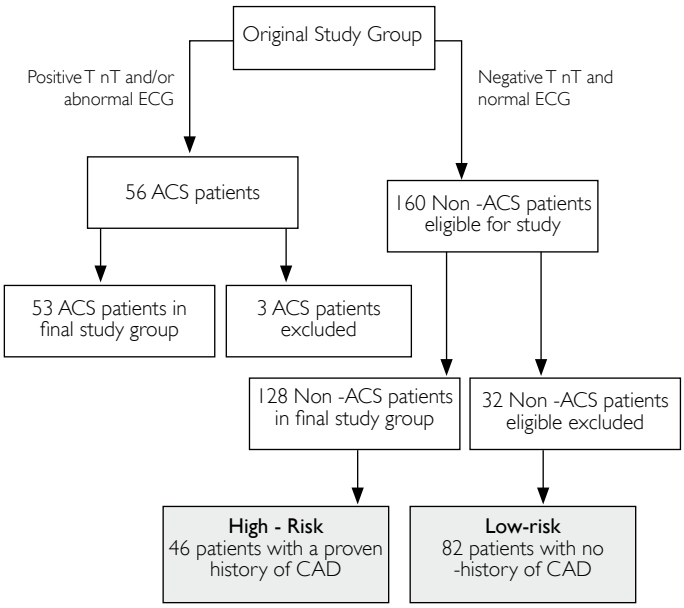
Data analysis

Nominal (categorical) data were summarised in percentages and independent-samples t-tests were used to identify statistically significant differences between the two study groups. Statistical analyses were performed using the SPSS software package (LEAD Technologies, Inc., 1989-2001).

RESULTS

During the study period, 216 patients presented to the CCU at TPH with chest pain. On review of all patient notes, a total of 160 (74%) patients were classed as having non-ACS chest pain. Of these, 26 (16%) patients were excluded due to incomplete data sets, and six (4%) were excluded due to their place of residence being outside the South Canterbury area. Of the remaining 128 patients, 46 had a proven history of CAD, 82 did not. Figure 1 shows the categorisation of the 216 patients presenting with chest pain.

Figure 1. Flow chart of 216 patients presenting to the CCU with chest pain



Baseline demographic characteristics of the two non-ACS groups and the ACS group are shown in Table 1. There was a statistically significant difference in mean age between the low-risk and high-risk non-ACS groups (95% CI of the difference = -16.5 to -5.9, p <0.0001). There was also a statistically significant difference between the low-risk non-ACS and ACS groups (95% CI of the difference = -16.2 to -5.7, p <0.0001). There was no difference in age between the ACS and high-risk non-ACS groups.

Table 1. Baseline demographic characteristics of all patients.

	Low-risk	High-risk	ACS
Number of patients	**82**	**46**	53
Mean age (range), yr	**60.2 (21-89)**	**71.4 (47-90)**	71.2 (38-93)
Female (%)	**45 (55%)**	**21 (46%)**	24 (45%)
Male (%)	**37 (45%)**	**25 (54%)**	29 (55%)

Cardiovascular risk factors present in both non-ACS chest pain patient groups are shown in Table 2. There was a statistically significant difference in mean cardiovascular risk between the low-risk and high-risk non-ACS subgroups (p<0.0001). Table 3 shows previously prescribed medications of all non-ACS chest pain patients.

Table 2. Cardiovascular risk factors of all non-ACS patients.

	Low-risk	High-risk
Positive family history IHD (%)	36 (**44%**)	25 (**54%**)
Preexisting hypertension (%)	38 (**46%**)	30 (**65%**)
Preexisting hypercholesterolaemia (%)	40 (**49%**)	25 (**54%**)
Preexisting Diabetes Mellitus (%)	12 (**15%**)	12 (**26%**)
Current Smoker (%)	11 (**13%**)	4 (**9%**)
Ex-smoker (%)	22 (**27%**)	29 (**63%**)
Mean cardiovascular risk *	1.95	3.73

IHD = Ischaemic Heart Disease

* Overall cardiovascular risk was determined by combining the total number of cardiac risk factors present in each patient, with a maximum total of six.

Table 3. Previously prescribed drugs of all non-ACS patients

Drug	Low-risk	High-risk
Nitrate	5%	37%
Beta-blocker	21%	59%
Calcium channel blocker	11%	17%
Diuretic	5%	37%
Aspirin	22%	78%
ACE inhibitor	7%	30%
AT II receptor blocker	0	13%
Antacid	4%	4%
H2-antagonist	1%	2%
Proton Pump Inhibitor	18%	43%
Statin	16%	72%
Fibrate	1%	0

ACE = Angiotensin Converting Enzyme; AT = Angiotensin

Mean length of stay for evaluation was 1.31 days (SD 1.71, range 0 to 8) in the low-risk non-ACS subgroup, and 1.37 days (SD 1.25, range 0 to 5) in the high-risk non-ACS subgroup. Discharge diagnoses for both groups are shown in Table 4.

All patients were followed for at least 18 months. The average duration of follow-up was 623 days (SD 30.8, range 561 to 670) in the low-risk subgroup, and 622 days (SD 29.3, range 560 to 692) in the high-risk subgroup. The difference in the mean number of re-presentations (Table 5) was significant between the low-risk and high-risk non-ACS subgroups (95% CI of the difference -1.928 to -0.759, p<0.0001). Similarly, between the low-risk non-ACS subgroup and ACS group (95% CI of the difference -1.067 to -0.278, p=0.001). There was no significant difference between the high-risk non-ACS subgroup and the ACS group (95% CI of the difference -0.120 to 1.536, p=0.093). Table 5 shows the outcomes of patients at a minimum of 18 months follow-up. Causes of mortality in the low-risk non-ACS subgroup included: two of unknown cause, and one small cell carcinoma of lung. In the high-risk non-ACS subgroup, causes of mortality included: three of unknown cause, one electromechanical dissociation, and one bronchopneumonia secondary to myelodysplasia.

Table 5. Outcomes during minimum 18-month follow-up.

Outcome	Low-risk	High-risk	ACS
No. representing to CCU (%)	17 (21%)	22 (48%)	23 (43%)
Mean no. representations	0.31	1.7	0.98
No. representing with ACS (%)	1 (1%)	8 (17%)	12 (23%)
All-cause Mortality (%)	3 (4%)	5 (11%)	9 (17%)

DISCUSSION

Approximately 800 patients present annually with chest pain to CCU at Timaru Public Hospital. Based on this study, 74% of these patients will have non-ACS chest pain. While the percentage of patients determined to have non-ACS chest pain is larger than that found in other studies,[1-3] this reflects the criteria used to determine patients eligible for the study. A number of patients who may have had unstable angina, despite normal ECG and serial cardiac enzymes, were included in the non-ACS chest pain group.

Our study had some limitations:

1) Being a retrospective study we relied on the completeness of hospital notes for historical data.
2) The study population was predominantly European, therefore our findings may not be generalisable in locations where there is greater

Table 4. Discharge diagnoses of all non-ACS patients.

	Low-risk	High-risk
Chest Pain of undetermined cause	30 chest pain NOS 9 non-cardiac chest pain 2 musculoskeletal chest pain 2 atypical chest pain 1 sinus tachycardia **= 44 (54%)**	9 chest pain NOS 3 non-cardiac chest pain 1 musculoskeletal chest pain **= 13 (28%)**
Gastrointestinal-biliary cause	4 GORD 3 gastritis 2 oesophagitis **= 9 (11%)**	1 GORD 1 gastritis 1 epigastric pain NOS **= 3 (7%)**
Respiratory cause	1 LRTI 3 pleuritic chest pain 1 infective exacerbation asthma **=5 (6%)**	2 LRTI **= 2 (4%)**
Coronary artery disease	4 angina 8 unstable angina **= 12 (15%)**	17 angina 6 unstable angina **= 23 (50%)**
Other	3 LVF/CHF/RVF 2 PAF 2 recurrent SVT/WPW 2 pericarditis 1 PE 1 angina 2° anaemia 1 mechanical pain (due to displaced spinal screws) **= 12 (15%)**	1 LVF 1 PAF 1 VT 1 angina 2° anaemia 1 aortic stenosis **= 5 (11%)**

NOS = Not Otherwise Specified; GORD = Gastro-oesophageal Reflux Disease; LRTI = Lower Respiratory Tract Infection; LVF = Left Ventricular Failure; CHF = Congestive Heart Failure; RVF = Right Ventricular Failure; PAF = Paroxysmal Atrial Fibrillation; VT = Ventricular Tachycardia; PE = Pulmonary Embolism; SVT = Supraventricular Tachycardia; WPW = Wolff-Parkinson-White.

ethnic diversity.

3) An inability to extend follow-up to the community meant that a complete picture of healthcare resource utilisation by these patients was not able to be achieved.

This study shows that patients presenting with chest pain initially diagnosed as non-ACS can be divided into low-risk and high-risk subgroups based on the presence or absence of a prior proven history of CAD. This supports the conclusion, of Launbjerg et al. (1994), that patients of higher risk can be more readily identified from the medical history than discharge diagnosis.[5]

Patients in the high-risk non-ACS subgroup were very similar in terms of age and gender balance to those patients who were initially found to have ACS chest pain. Patients in the low-risk non-ACS subgroup were significantly younger than both the high-risk non-ACS subgroup and the ACS group. The proportion of females was higher in the ACS group, which is consistent with other studies of patients with chest pain of non-coronary origin.[1,2,6]

Greater than half of the low-risk non-ACS subgroup had a discharge diagnosis of chest pain of undetermined origin, whereas 50% of the high-risk non-ACS subgroup had a diagnosis of either angina or unstable angina. The low-risk non-ACS subgroup did, however, have a high percentage (15%) of other diagnoses (Table 4.) that have previously been shown to carry significant morbidity and mortality.[4]

At a minimum of 18-months follow-up, outcomes were significantly different between the low-risk subgroup and the high-risk non-ACS subgroups (Table 5). The high-risk non-ACS subgroup had a greater number of patients re-presenting with chest pain, a higher mean number of re-presentations, and a greater number of patients presenting with ACS and MI, all of which are comparable to the ACS group. These findings are consistent with the conclusion made by Prina et al that in any patient who has a past medical history of cardiac disease, clinical suspicion of an ACS must remain high even in the absence of ischaemic ECG changes or raised cardiac enzymes.[2] This concept is further supported by the 2007 ACC/AHA Guidelines for the Management of Unstable Angina/Non-ST Elevation Myocardial Infarction. Here a history of CAD, including MI, is listed as a feature indicative of a high likelihood that the signs and symptoms the patient presents with are due to ACS secondary to CAD.[14]

Structured scoring systems to determine the subsequent risk of cardiac events, such as the Thrombolysis in Myocardial Infarction (TIMI) risk score, would be a useful way of objectively determining risk in patients presenting with chest pain, even in those who are thought to not have ACS. Both an objective history of CAD and cardiovascular risk factors (>3) are included in this risk score, and it is therefore likely to help identify patients with high-risk non-ACS chest pain (as defined in this study) and improve outcomes for these patients. Furthermore, the implementation of an algorithm for patients suspected of having ACS, such as that published in the 2007 ACC/AHA Guidelines[14], could be a useful addition to the use of a structured risk scoring system. Both of these tools would provide a structured protocol for the identification and management of patients with chest pain and most likely lead to improved outcomes for all patients.

CONCLUSION

For patients presenting to hospital with chest pain of non-ACS origin, this study suggests that stratification into high-risk and low-risk subgroups is useful. The presence or absence of a prior history of CAD is a simple method of making these respective classifications and could be achieved using a structured risk scoring system such as TIMI. Low-risk non-ACS patients were unlikely to represent with an adverse cardiac event, but high-risk non-ACS patients had outcomes comparable to patients with ACS chest pain. In particular, the high rate of representations is indicative of the need to carefully investigate and follow patients considered to be at high risk.

ACKNOWLEDGEMENTS

This project was kindly funded as a summer studentship project by the Timaru Postgraduate Society.

REFERENCES

1. Panju A, Farkouh ME, Sackett DL, et al.
Outcome of patients discharged from a coronary care unit with a diagnosis of "chest pain not yet diagnosed".
Can Med Assoc J. 1996; 155:541-6.

2. Prina LD, Decker WW, Weaver AL, et al.
Outcome of patients with a final diagnosis of chest pain of undetermined origin admitted under the suspicion of acute coronary syndrome: a report from the Rochester Epidemiology Project.
Ann Emerg Med. 2004; 43:59-67.

3. Launbjerg J, Fruergaard P, Hesse B, et al.
Long-term risk of death, cardiac events and recurrent chest pain in patients with acute chest pain of different origin.
Cardiology. 1996; 87:60-6.

4. Launbjerg J, Fruergaard P, Jacobsen H, et al.
Long-term cardiac mortality in patients admitted with noncoronary chest pain under suspicion of acute myocardial infarction.
Cardiology. 1993; 82:36-41.

5. Launbjerg J, Fruergaard P, Madsen JK, et al.
Ten-year mortality of patients admitted to coronary care units with and without myocardial infarction.
Cardiology. 1994; 85:259-66.

6. Mikhail MG, Smith FA, Gray M, et al.
Cost-effectiveness of mandatory stress testing in chest pain center patients.
Ann Emerg Med. 1997; 29:88-98.

7. Fruergaard P, Launbjerg J, Hesse B, et al.
The diagnoses of patients admitted with acute chest pain but without myocardial infarction.
Eur Heart J. 1996; 17:1028-34.

8. Manini AF, Gisondi MA, van der Vlugt TM, Schreiber DH.
Adverse cardiac events in emergency department patients with chest pain six months after a negative inpatient evaluation for acute coronary syndrome.
Acad Emerg Med. 2002; 9:896-902.

9. Polanczyk CA, Johnson PA, Hartley LH, et al.
Clinical correlates and prognostic significance of early negative exercise tolerance tests in patients with acute chest pain seen in the hospital emergency department.
Am J Cardiol. 1998; 81:288-92.

10. Hillis GS, Oliner C, O'Neil BJ, et al.
Coronary artery disease in patients with chest pain who have low-risk clinical characteristics and negative cardiac Troponin I.
Am J Emerg Med. 2001; 19:118-21.

11. Taylor GL, Murphy NF, Berry C, Christie J, Finlayson A, MacIntyre K et al.
Long-term outcome of low-risk patients attending a rapid-assessment chest pain clinic.
Heart. 2008;94:628-32.

12. Foussas SG, Adamopoulou EN, Kafaltis Na, et al.
Clincial characteristics and follow-up of patients with chest pain and normal coronary arteries.
Angiology. 1998; 49:349-54.

13. Lichten PR, Bargheer K, Wenzlaff P.
Long-term prognosis of patients with anginalike chest pain and normal coronary angiographic findings.
JACC. 1995; 25:1013-8.

14. Anderson JL, Adams CD, Antman EM, Bridges CR, Califf RM, Casey DE Jr, Chavey WE II, Fesmire FM, Hochman JS, Levin TN, Lincoff AM, Peterson ED, Theroux P, Wenger NK, Wright RS.
ACC/AHA 2007 guidelines for the management of patients with unstable angina/non–ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non–ST-Elevation Myocardial Infarction): developed in collaboration with the American College of Emergency Physicians, American College of Physicians, Society for Academic Emergency Medicine, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons.
J Am Coll Cardiol 2007;50:e1–157.