CLINICAL PROFILE OF PATIENTS PRESENTING WITH ACUTE CORONARY SYNDROME TO THE LADYSMITH PROVINCIAL HOSPITAL EMERGENCY DEPARTMENT

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg in partial fulfilment of the requirements for the degree of Master of Sciences in Medicine (Emergency Medicine)

Johannesburg, 2014
DECLARATION

I, Bonnard Ewanguam Mumpi declare that this research is my own work. It is being submitted for the degree of Master of Sciences in Medicine (Emergency Medicine) to the University of the Witwatersrand, Johannesburg. It has not been submitted or presented for any other degree, diploma or professional qualification at this or any other University.

The work presented in this research report was undertaken in the Division of Emergency Medicine, University of the Witwatersrand, Johannesburg.


Bonnard Ewanguam Mumpi

Date

Johannesburg

05 / 08 / 2014
DEDICATION

To Almighty God for your gift of life, intelligence, through whom everything and anything is made possible.

To my farther Urbain Mumpi and late mother Rosalie Nier for your love, education, guidance, support … which has contributed to make me a real human being, a man who cares and participates in the advancement of the cause of humanity.

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ABSTRACT

Background: Patients with acute coronary syndrome (ACS) may present with a wide range of symptoms that may easily be misdiagnosed.

Methods: This cross-sectional, hospital-based, descriptive, retrospective audit of medical records was based at the Ladysmith Provincial Hospital ED and consisted of the last 160 consecutive patients (from the date of initiation of data collection) with accessible medical records and with a final hospital discharge diagnosis of ACS.

Results: The frequency of patients presenting with ACS was approximately 53 patients per annum. There was a male to female ratio of 1.3: 1. The mean age was 55.8 years (SD 12.8 years). The study population consisted of Asian (103/160, 64.4%), black (36/160, 22.5%) and white (21/160, 13.1%). The majority of the study patients were unemployed (98/160, 61.25%), urban resident (143/160, 89.4%), not alcohol users (137/160, 85.6%), and not smokers (88/160, 55.0%). Risk factors and comorbidity included previous acute coronary syndrome (44/160, 27.5%), family history (29/160, 18.1%), previous cardiovascular surgery (10/160, 6.25%), obesity (45/160, 28.1%), hypercholesterolemia (49/160, 30.6%), diabetes (42/160, 26.25%), hypertension (76/160, 47.5%), and renal failure (27/160, 16.9%). Approximately three quarters (119/160, 74.4%) of the study patients had typical chest pain, 16.3% (26/160) had atypical chest pain, and 9.4% (15/160) had no chest pain. The median length of hospital stay was 3 days and the in-hospital mortality was 8.1 % (13/160).

Conclusion: The relatively high frequency of ACS reported in this study, when compared to other similar studies, is concerning. Also of concern in this study, is the alarming proportion of Asians that presented with ACS.
TABLE OF CONTENTS

DECLARATION .................................................................................................................. i
DEDICATION .................................................................................................................... ii
ACKNOWLEDGEMENTS .................................................................................................. iii
ABSTRACT ....................................................................................................................... iv
TABLE OF CONTENTS ................................................................................................... v
LIST OF FIGURES .......................................................................................................... ix
LIST OF TABLES ............................................................................................................ x
INTRODUCTION ............................................................................................................. 1
  1.1 Background and significance of the study ............................................................... 1
  1.2 The aim of the study ............................................................................................... 3
  1.3 Objectives .............................................................................................................. 3
LITERATURE REVIEW ................................................................................................. 5
  2.1 The frequency of ACS / MI internationally and in SA ........................................... 5
  2.2 The burden of ACS ............................................................................................... 6
  2.3 The impact of age on ACS ................................................................................... 7
  2.4 The impact of sex on ACS .................................................................................... 8
  2.5 The impact of race on ACS .................................................................................. 9
  2.6 The impact of socioeconomic status on ACS ....................................................... 10
  2.7 The impact of alcohol on ACS .............................................................................. 10
  2.8 Common risk factors for ACS ............................................................................. 12
  2.9 Specific risk factors ............................................................................................. 13
    2.9.1 HIV .................................................................................................................... 13
    2.9.2 Renal Failure .................................................................................................. 15
  2.10 Typical presenting symptoms ............................................................................. 17
  2.11 Atypical presenting symptoms and missed diagnosis ........................................ 17
4.6 Presenting features of study patients ................................................................. 40
  4.6.1 Chest pain ........................................................................................................ 40
  4.6.2 Presenting symptoms of patients with no chest pain .............................. 41
  4.6.3 Associated symptoms of all study patients ............................................. 42
  4.6.4 Radiation of pain ......................................................................................... 42
  4.6.5 Cardiogenic shock ....................................................................................... 43
  4.6.6 Cardiac failure ............................................................................................. 43
  4.6.7 ECG findings ................................................................................................. 43
  4.6.8 Laboratory findings ...................................................................................... 44
4.7 Risk factors for ACS of study patients ............................................................ 46
4.8 Age of study patients ...................................................................................... 46
4.9 Sex of study patients ....................................................................................... 47
4.10 Race of study patients .................................................................................... 47
4.11 Socio-economic and behavioural characteristics of study patients .......... 48
4.12 Management of study patients ..................................................................... 48
  4.12.1 Initial management .................................................................................... 48
  4.12.2 Early reperfusion therapy ........................................................................ 48
4.13 Outcomes of study patients .......................................................................... 49
  4.13.1 Clinical deterioration requiring ICU ......................................................... 49
  4.13.2 Length of hospital stay ............................................................................. 50
  4.13.3 Time to clinical stability ........................................................................... 50
  4.13.4 Death .......................................................................................................... 51

DISCUSSION ............................................................................................................ 52
5.1 Frequency of ACS presentation ....................................................................... 52
5.2 Clinical stability of patients on presentation ................................................ 53
5.3 Presenting clinical features ............................................................................. 53
  5.3.1 Chest pain .................................................................................................... 53
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.3.2 Associated symptoms</td>
<td>54</td>
</tr>
<tr>
<td>5.3.3 Cardiogenic shock and cardiac failure</td>
<td>54</td>
</tr>
<tr>
<td>5.3.4 ECG findings</td>
<td>55</td>
</tr>
<tr>
<td>5.3.5 Laboratory findings</td>
<td>55</td>
</tr>
<tr>
<td>5.4 Risk factor assessment</td>
<td>55</td>
</tr>
<tr>
<td>5.5 Demographic characteristics</td>
<td>57</td>
</tr>
<tr>
<td>5.6 Socio-economic and behavioural characteristics</td>
<td>58</td>
</tr>
<tr>
<td>5.7 Management</td>
<td>59</td>
</tr>
<tr>
<td>5.8 Outcomes</td>
<td>60</td>
</tr>
<tr>
<td>5.9 Limitations of the study</td>
<td>62</td>
</tr>
<tr>
<td>CONCLUSION</td>
<td>64</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>65</td>
</tr>
<tr>
<td>APPENDICES</td>
<td>82</td>
</tr>
<tr>
<td>APPENDIX 1</td>
<td>82</td>
</tr>
<tr>
<td>Ethics Clearance Certificate</td>
<td>82</td>
</tr>
<tr>
<td>APPENDIX 2</td>
<td>83</td>
</tr>
<tr>
<td>Patient Data Collection Sheet</td>
<td>83</td>
</tr>
</tbody>
</table>
LIST OF FIGURES

Figure 1: Time course of release of serum cardiac markers after acute myocardial infarction........................................................................................................................................... 24
Figure 2: Flow diagram describing the process in achieving the final study sample 36
Figure 3: Frequency histogram for SBP of study patients ........................................... 38
Figure 4: Frequency histogram for DBP of study patients ........................................... 39
Figure 5: Frequency bar chart describing chest pain of study patients .................... 41
Figure 6: Frequency bar chart describing associated symptoms of study patients .. 42
Figure 7: Frequency bar chart describing radiation of pain of study patients ........... 43
Figure 8: Pie chart describing the proportion of study patients that presented with the various subcategories of ACS ........................................................................................................... 45
Figure 9: Frequency histogram describing age distribution of study patients.......... 46
Figure 10: Frequency histogram for age group categories of study patients.......... 47
Figure 11: Frequency histogram for length of hospital stay of study patients........... 50
LIST OF TABLES

Table 1: Summary of ECG findings for the diagnosis of acute coronary syndrome . 21
Table 2: Characteristics of cardiac biomarkers for the diagnosis of acute myocardial
infarction........................................................................................................................................ 23
Table 3: ESC recommendations for reperfusion therapy....................................................... 27
Table 4: Summary of results for baseline vital signs of study patients ......................... 38
Table 5: Frequency distribution table for GCS score of study patients......................... 40
Table 6: Frequency distribution table for presenting symptoms of study patients with
no chest pain.................................................................................................................................. 41
Table 7: Selected laboratory findings of study patients .................................................. 44
Table 8: Frequency distribution for race of study patients .............................................. 48
Table 9: Frequency distribution table for number of days to clinical stability of study
patients........................................................................................................................................ 51
LIST OF ABBREVIATIONS

ACS: Acute coronary syndrome
AMI: Acute myocardial infarction
ART: Antiretroviral therapy
BP: Blood pressure
DBP: Diastolic blood pressure
CABG: Coronary artery bypass graft
CK: Creatine kinase
CK– MB: Creatine kinase muscle band isoenzyme
CAD: Coronary artery disease
CKD: Chronic kidney disease
CVD: Cardiovascular disease
DOA: Date of admission
DOD: Date of discharge
ECG: Electrocardiogram
ED: Emergency department
EP: Emergency Physician
eGFR: Estimated glomerular filtration rate
GCS: Glasgow coma scale
HAART: Highly active antiretroviral therapy
HDL: High-density lipoprotein
HR: Heart rate
ICU: Intensive care unit
LBBB: Left bundle branch block
LDL: Low-density lipoprotein

LVH: Left ventricular hypertrophy

MI: Myocardial infarction

NSTEMI: Non ST-segment elevation myocardial infarction

PCI: Percutaneous coronary intervention

PIN: Patient identification number

RBBB: Right bundle branch block

RR: Respiratory rate

SA: South Africa

SBP: Systolic blood pressure

SD: Standard deviation

STEMI: ST-segment elevation myocardial infarction

TIMI: Thrombolysis in myocardial infarction

Tn I & Tn T: Troponin I and Troponin T

UA: Unstable angina

UK: United Kingdom

USA: United States of America

VF: Ventricular fibrillation

VT: Ventricular tachycardia

WHO: World health organisation
CHAPTER 1

INTRODUCTION

1.1 Background and significance of the study

Acute coronary syndrome (ACS) refers to a spectrum of clinical events that result from acute myocardial ischaemia. It encompasses unstable angina (UA), ST-segment elevation myocardial infarction (STEMI), and non ST-segment elevation myocardial infarction (NSTEMI).\textsuperscript{1} Typically, these clinical entities are accompanied by cardiac ischaemic chest pain with electrocardiographic (ECG) changes and/or a rise in serum cardiac biomarkers.\textsuperscript{2}

Acute coronary syndrome may be typical or atypical.\textsuperscript{3} Potential ACS patients present with a wide range of symptoms of which chest pain is the chief complaint.\textsuperscript{4} ACS has various clinical manifestations.\textsuperscript{3} In its atypical presentation, it frequently presents with symptoms other than chest pain\textsuperscript{3} such as non-pain equivalent symptoms, or it may be silent.\textsuperscript{5,6} Early recognition of atypical ACS presentation, especially when chest pain is absent, presents a real challenge\textsuperscript{4} which may result in under-diagnosis or missed diagnosis,\textsuperscript{3} and therefore may delay initiation of appropriate treatment. Delay in the onset of appropriate therapy has been associated with poor outcomes.\textsuperscript{7}

According to the World Health Organisation (WHO), cardiovascular diseases (CVD) cause 12 million deaths throughout the world each year.\textsuperscript{8} Cardiovascular diseases remain the leading cause of death in the United States of America (USA), causing more than 710,000 deaths annually.\textsuperscript{9} Up to one third of patients with confirmed myocardial infarction present without chest discomfort (atypical presentation) in the
USA. In some low / middle-income countries, cardiovascular disease has also been reported as the leading cause of mortality, with ischaemic heart disease related mortality expected to increase by 120% for women and 137% for men by 2020.\textsuperscript{10}

The decision as to the most appropriate disposition (e.g. observation, referral, admission, discharge, follow up etc.) of patients suspected with ACS is one of the most challenging decisions in the emergency department (ED). Inappropriate disposition of patients may impact on morbidity, mortality, cost and ED overcrowding.

South Africa is a low / middle-income country in which modernization and industrialization has resulted in an epidemiologic transition in disease patterns from infectious disease as the predominant cause of morbidity and mortality to more chronic illnesses such as heart disease.\textsuperscript{11} As a result of change in diet, decreased physical activity and increased tobacco use,\textsuperscript{11} cardiovascular disease is expected to become the leading cause of death in emerging countries including South Africa by 2020.\textsuperscript{10} In South Africa the annual incidence of AMI is more than 800,000. Approximately 200,000 die acutely, half of them before reaching hospital.\textsuperscript{12}

In addition to the epidemiological transition,\textsuperscript{11} SA is faced with the HIV/AIDS pandemic which is associated with an increased risk for cardiovascular disease.\textsuperscript{13} South Africa is the Sub-Saharan country housing the largest population living with HIV worldwide,\textsuperscript{13} with 6.4 million HIV infected individuals reported in the 2013 UNAIDS report.\textsuperscript{14} Moreover, antiretroviral therapy (ART) by supposedly increasing the life expectancy of HIV infected individuals may further increase the incidence of cardiovascular diseases in South Africa.\textsuperscript{13}
Early recognition of patients with ACS and in particular its atypical presentation represents a real challenge. Since time is muscle, early diagnosis and treatment will result in improved outcomes.\textsuperscript{2,7}

Acute coronary syndrome (ACS) is a common cause for admission at the Ladysmith Provincial Hospital. ACS accounts for up to 15\% of cardiac patients admitted to the Ladysmith Provincial Hospital (unpublished hospital registry). However, no study has been conducted looking at the profile of adult patients presenting with ACS to the Ladysmith Provincial Hospital.

This study provides insights with regard to the clinical profile of patients presenting with ACS to the Ladysmith Provincial Hospital, with a view to improving early, prompt diagnosis and clinical outcomes, and decreasing the likelihood of missed diagnosis.

\textbf{1.2 The aim of the study}

To determine the clinical profile of patients that presented to the Ladysmith Provincial Hospital ED and had a final hospital discharge diagnosis of ACS.

\textbf{1.3 Objectives}

1. To determine the frequency of patients that presented to the Ladysmith Provincial Hospital ED with a final hospital discharge diagnosis of ACS.

2. To describe the presenting features (vital signs, typical chest pain, atypical chest pain, non-pain equivalent or silent, associated symptoms, cardiac failure, cardiogenic shock, ECG findings, laboratory findings, etc.) of patients that
presented to the Ladysmith Provincial Hospital ED with a final hospital discharge diagnosis of ACS.

3. To describe risk factors (e.g. age, sex, race, obesity, hypertension, diabetes, renal failure, etc.) of patients that presented to the Ladysmith Provincial Hospital ED with a final hospital discharge diagnosis of ACS.

4. To describe the initial and definitive management of patients that presented to the Ladysmith Provincial Hospital ED with a final hospital discharge diagnosis of ACS.

5. To determine the short-term outcomes of patients that presented to the Ladysmith Provincial Hospital ED with a final hospital discharge diagnosis of ACS: clinical deterioration requiring ICU, length of hospital stay, time to clinical stability and death.
CHAPTER 2

LITERATURE REVIEW

2.1 The frequency of ACS / MI internationally and in SA

According to the American Heart Association 2013 statistical update which is based on 2009 death rate data in the United States of America (USA), more than 2150 Americans die of coronary vascular disease daily (about 1 death every 40 seconds). About 153 000 Americans who died of coronary vascular disease were <65 years of age and 34% of deaths attributable to CVD occurred before the age of 75 years, which is well before the average life expectancy of 78.5 years. Coronary heart disease alone caused ≈1 of every 6 deaths. Each year an estimated ≈635 000 Americans have a new coronary attack, ≈280 000 have a recurrent attack and an estimated 150 000 silent first myocardial infarctions occur each year. Approximately every 34 seconds, 1 American has a coronary event, and approximately every 1 minute, an American will die of one. In Europe, the annual incidence of ACS is estimated as 3 per 1000 inhabitants, but varies from country to country. In the United Kingdom (UK), the incidence of MI is approximately 2 per 1000 for women and 6 per 1000 for men aged 30 to 69 years.

Cardiovascular diseases are expected to become the leading cause of death in emerging countries including South Africa by 2020. In South Africa over 800,000 people suffer from AMI every year of which 200,000 die, half of them before reaching the hospital. In low to middle income countries such as South Africa, coronary artery disease (CAD) accounts for approximately 10% of healthy life years lost.
Prior to the era of the coronary care unit, in-hospital mortality of MI and ACS was estimated to be 25 - 30% worldwide. Subsequent to the introduction of coronary care units, the mortality decreased to approximately 16%. With advances in coronary revascularisation techniques, the current mortality is around 5% - 6%.

2.2 The burden of ACS

The economic costs of ACS are huge. The clinical and socio-economic implications of this disabling disease continue to increase as the prevalence of atherosclerosis continue to rise worldwide. The estimates for economic costs of coronary heart disease include not only the direct cost to the health care system but also include loss of productivity and the continual need of formal and informal long term care.

In 1999 for instance, the economic burden of coronary heart disease in the UK was estimated at 2.6 billion Euros for direct health care costs, a further 3.6 billion Euros for the provision of care for coronary artery disease subjects and 4.4 billion for loss of productivity. In the USA, the direct and indirect cost related to the burden of coronary artery diseases was estimated to be more than 165 billion dollars annually.

The significant morbidity and mortality associated with missed ACS may result in legal action against health care providers. The world has not yet recovered from the 2008 economic recession which has compelled most governments worldwide to cut social expenditures (including the health care expenditure) and implement cost-effective measures. The challenge for the clinician is to balance clinical judgement, appropriate diagnostic strategies and evidence-based principles whilst at the same time avoiding unnecessary costly therapy.
2.3 The impact of age on ACS

Elderly individuals are at higher risk of developing ACS. Consistent study reports have concluded that older patients have an increased prevalence of multiple risk factors such as a history of angina, transient ischemic attack, stroke, MI, diabetes, hypertension, congestive heart failure, CABG (coronary bypass graft) surgery, and atrial fibrillation. Hypertension is closely related to age and is an important risk factor for the development of ACS in older patients. Some studies have shown that cigarette smoking is the only factor among traditional risk factors to be inversely related to age. This suggests that smoking may not be an important risk factor for ACS in elderly patients or cigarette smoking may be associated with a shorter survival and earlier onset ACS. Elderly patients commonly delay seeking medical care. This may be due to cognitive impairment, atypical clinical presentation or the presence of comorbidities that may mask a diagnosis of ACS.22

ST- segment elevation myocardial infarction (STEMI) is more common in young patients and NSTEMI is more common in elderly patients. The higher prevalence of NSTEMI in the elderly may be explained by the higher prevalence of previous MI, multivessel disease, hypertension and ventricular hypertrophy, which may cause global subendocardial ischemia and poor myocardial perfusion.22

Cardiovascular and bleeding events are more common among the elderly. Hospital mortality is also higher among the elderly even after adjusting for confounders. Advanced age is an independent predictor of increased risk of cardiovascular events in patients with ACS.22
2.4 The impact of sex on ACS

Coronary artery disease (CAD) is the leading cause of mortality in both men and women in high-income countries, but women tend to experience CAD almost a decade later in their life.\textsuperscript{23} Men more commonly present with acute myocardial infarction (AMI) or sudden death, whereas women are more prone to present with atypical symptom and angina.\textsuperscript{24}

From a pathological point of view, men presenting with ACS are more likely to have plaque rupture, whereas atherosclerotic plaque erosions is more common in women.\textsuperscript{23} This implies that sex may influence plaque formation, plaque vulnerability and clinical presentation. Virmani et al demonstrated that fibroatheromas with a thin fibrous cap and a large necrotic core are more susceptible to plaque rupture and subsequent thrombosis than other phenotypic lesions.\textsuperscript{25} Patients presenting with plaque erosion usually have an indolent period of angina in contrast to those with plaque rupture who present more suddenly.\textsuperscript{24}

Analysis from the PROSPECT study has demonstrated that in spite of being older and having more comorbid risk factors, women diagnosed with ACS have less extensive CAD when compared to men. Several studies, including the PROSPECT study, have found that women presenting with ACS are substantially older than men, have more comorbid conditions such as diabetes and are more prone to increased risk of coronary events.\textsuperscript{23} Several other studies have also reported that men have more extensive atherosclerosis than women.\textsuperscript{25}
Women with risk factors such as diabetes and hypertension develop severe atherosclerotic lesions at least seven to eight years later when compared with their male counterpart.\textsuperscript{23} This may be consistent with the theory suggesting that oestrogen may delay plaque development, stabilize existing plaques, and prevent plaque rupture in women.\textsuperscript{26}

2.5 The impact of race on ACS

Most of the burden of cardiovascular disease mortality and morbidity is associated with modifiable risk factors.\textsuperscript{27,28} Differences in the prevalence and incidence of risk factors by race or ethnic group are substantial.\textsuperscript{29} Studies have demonstrated important ethnic-specific variations in risk factors, management and outcomes associated with atherothrombotic disease.\textsuperscript{21}

The rates of obesity are lower in Asians, but do not translate into lower rates of other comorbid conditions including diabetes mellitus.\textsuperscript{21} In fact Asians, particularly South Asian have the highest burden of diabetes mellitus.\textsuperscript{30,31} Other studies have reported that among the ethnic or racial groups, Blacks with ACS have the highest rates of acute cardiovascular mortality, whereas Asians have the lowest. Likewise, other adverse cardiovascular events seem to be higher in Blacks and lower in Asians. Overall Blacks have the lowest incidence of coronary artery disease (CAD).\textsuperscript{21} In contrast, Asians particularly South Asians have a much higher incidence of CAD.\textsuperscript{32}
2.6 The impact of socioeconomic status on ACS

Differences in socioeconomic status have been consistently linked with variations in cardiovascular disease and mortality rates.\textsuperscript{33-35} Despite a strong and consistent relationship between socioeconomic status and cardiovascular health, much still need to be understood about the ways in which socioeconomic status influences or affects health.\textsuperscript{36} Individuals with low income are more likely to smoke, to have diabetes mellitus or hypertension. This may result in accelerated atherosclerosis and subsequent higher mortality rates. A study conducted in Ontario reported 8.0% obesity, 33.0% diabetes mellitus, 49.5% hypertension and 32.3% smokers among low-income patients whereas in high-income patients the same study reported 3.1% obesity, 19.4% diabetes, 35.9% hypertension, and 27% smokers.\textsuperscript{33}

Wealth-health gradient is observed worldwide, including in countries where health care is funded by the state. The wealth–health gradient does not dependent on the socioeconomic indicator used and persists even after such cardiovascular events as myocardial infarction.\textsuperscript{33} The causes of these gradients are debatable\textsuperscript{37-39} and need clarification.\textsuperscript{36} Outcome-income gradients have been found to persist even after adjustment for traditional cardiac risk factors and cardiovascular events.\textsuperscript{33} These low income or education related effects are likely due to increased psychosocial stressors, lack of lifestyle change after ACS and limited access to medical care.\textsuperscript{40,41}

2.7 The impact of alcohol on ACS

There is an association between mild regular alcohol consumption and a decreased risk for developing coronary heart disease whereas heavy alcohol intake and binge
drinking are associated with increased cardiovascular mortality.\textsuperscript{42} Mortality and morbidity related to ACS is less in non-alcohol related presentations than in patients presenting with alcohol intoxication.\textsuperscript{43} Heavy binge drinking may also be associated with myocardial infarction, but the underlying mechanisms are unclear.\textsuperscript{42} Acute myocardial infarction in young individuals has been described after heavy alcohol intake.\textsuperscript{43}

Acute ethanol intoxication may precipitate ACS via several mechanisms. Alcohol has been reported to induce coronary spasm by unknown mechanisms as long as 9 hours after drinking, even after plasma ethanol has been cleared. Low levels of prostaglandin F1-alpha and cyclic guanosine monophosphate are incriminated in the mechanism of coronary spasm induced by alcohol ingestion.\textsuperscript{42} In addition to coronary spasm, several other mechanisms have been proposed by which alcohol may trigger ACS.\textsuperscript{44} These include transient enhancement of thromboxane-mediated platelet activation, induction of changes in the normal circadian periodicity of the haemostatic system and inhibition of fibrinolysis.\textsuperscript{45}

Heavy alcohol intake is associated with an increased risk of hypertension,\textsuperscript{46} which in turn is a major risk factor for coronary heart disease.\textsuperscript{46,47} In comparison to those that abstain from alcohol, light to moderate alcohol intake is associated with a lower risk of coronary heart disease.\textsuperscript{48,49} This is likely due to increased levels of high-density lipoprotein (HDL), decreased fibrinogen and increased insulin sensitivity in individuals that consume light to moderate amounts of alcohol.\textsuperscript{50}
2.8 Common risk factors for ACS

Risk factors associated with ACS can be divided into modifiable and non-modifiable risk factors. Modifiable risk factors include obesity, smoking, use of cocaine, abnormal lipid profile, hypertension, diabetes mellitus, sedentary lifestyle, chronic kidney disease, HIV / AIDS and antiretroviral therapy (ART). Hypertension is a major public health problem, accounting for nearly 13% of all deaths across the world and 17% of all deaths in developed countries. In a study, 41% of patients with ACS were smokers, whilst another study reported an incidence of 63%. In another study, 25% of patients with ACS were obese. Other studies reported the incidence of dyslipidaemia in patients with ACS as 16%, 30.5% and 59%. Hypertension was reported in 34%, 50%, 50.8% and 75% of patients with ACS in different studies. The incidence of diabetes mellitus was reported as 16%, 23.9%, 24.3% and 38% in various studies.

Non-modifiable risk factors include family history of coronary artery disease (first degree relative: male < 55 years, female < 65 years), older age, sex (male more than female), prior manifestation of CAD (previous MI, PCI (percutaneous coronary intervention), CABG surgery, atherosclerosis in non-coronary territories (stroke), race (higher in people of Indian descent). In a study, 15.6% of patients had history of prior CABG surgery, 9.0% had a history of prior of stroke, 15.2% had prior PCI and 29.7% had prior MI. Another study reported history of PCI, CABG, stroke and MI in 26.83%, 23.06%, 11.76% and 42.89% respectively in patients that presented with ACS.
The risk for cardiovascular disease (CVD) among individuals with diabetes mellitus is 2 to 3 times higher compared to non-diabetics. Obesity and overweight are reported as independent risk factor for CVD, and are associated with higher rates of cardiovascular related deaths. Smokers have a 70% higher risk for coronary artery disease (CAD) compared to non-smokers. This risk is proportionate to the pack year history of smoking.\textsuperscript{62} A greater number of risk factors for CAD is associated with higher morbidity and mortality.\textsuperscript{2,63}

Regular physical activity reduces the risk for CAD as opposed to a sedentary lifestyle. Several other measures are known to reduce the risk for CVD. These include control of hypercholesterolaemia, obesity and hypertension.\textsuperscript{62} The INTERHEART study examined the importance of risk factors for CAD.\textsuperscript{64} The five modifiable risk factors found to be predictive of CAD were current smoking, raised apoprotein B – apoprotein A\textsubscript{1} ratio, diabetes, hypertension and psychosocial stress.\textsuperscript{64} The INTERHEART study also demonstrated that these risk factors are consistent across a wide range of cultural, ethnic and geographic regions around the globe.\textsuperscript{65}

2.9 Specific risk factors

2.9.1 HIV

South Africa is the Sub-Saharan country housing one of the largest populations living with HIV worldwide\textsuperscript{13}, with 6.4 million HIV infected individuals reported in the 2013 UNAIDS report.\textsuperscript{14} The South African department of health estimated that 18.3\% of young adults between the ages of 15 and 49 years were living with HIV in 2006,\textsuperscript{66} with more than half of all HIV positive patients residing in the KwaZulu-Natal and Gauteng provinces.\textsuperscript{67} The HIV prevalence among Black South Africans is the highest
and is estimated as 12.9%. White and Indian South Africans have an estimated HIV prevalence of 6.2% and 1.6% respectively.\textsuperscript{68}

Post-mortem studies conducted in HIV positive patients from high-income countries have demonstrated high rates of atherosclerosis related CAD compared to aged-matched HIV negative patients.\textsuperscript{69} HIV infection on its own can predispose to premature atherosclerosis by several mechanisms including endothelial dysfunction, a heightened pro-inflammatory state and dyslipidaemia such as elevated triglyceride levels and low levels of high density lipoprotein (HDL) cholesterol.\textsuperscript{18}

In addition to premature atherosclerosis, HIV is associated with a higher risk of thrombosis, as a result of various abnormalities of the coagulation and fibrinolytic systems. Furthermore, studies have reported a strong link between highly active antiretroviral therapy (HAART) and premature coronary artery disease (CAD).\textsuperscript{18} Protease inhibitors in particular have been associated with endothelial dysfunction, a prothrombotic state, insulin resistance and dyslipidaemia.\textsuperscript{70} Prolonged exposure to protease inhibitor has been associated with an increased risk for developing ACS. Even before the advent of protease inhibitor for the treatment of HIV/AIDS, post-mortem studies have reported premature CAD in HIV infected patients.\textsuperscript{18} Therefore, both HIV and antiretroviral therapy (ART) play a role in the development of CAD and ACS. Becker and colleagues in a study conducted in Soweto, South Africa found that antiretroviral therapy naive HIV positive patients with ACS were younger and had fewer traditional risk factors than HIV negative patients with ACS. HIV positive patients also had less atherosclerotic and a higher thrombotic burden. This suggests that a prothrombotic state may play a role in the pathogenesis of ACS in patients with HIV.\textsuperscript{71}
Triant et al. has reported increased rates of AMI and cardiovascular risk factors in patients with HIV. In this study, the HIV cohort had a higher prevalence of hypertension (21.2% vs. 15.9%), diabetes (11.5% vs. 6.6%), and dyslipidaemia (23.3% vs. 17.6%) than the non-HIV cohort. The study also reported AMI rates of 11.13 per 1000 patient-years for HIV and 6.98 per 1000 patient-years for non-HIV.72

2.9.2 Renal Failure

Renal failure is recognised as a well-defined risk factor of cardiovascular disease.73 There is an increased morbidity and mortality associated with percutaneous coronary intervention (PCI) in patients with chronic kidney disease (CKD).74 Patients with CKD requiring haemodialysis are also at increased risk of developing cardiac ischaemia as a result of the induced hypercoagulable state from membrane and haemodialysis circuit contact, especially if subtherapeutic doses of anticoagulation are used.73

Chronic kidney disease is considered both a coronary risk equivalent and a risk for progression of cardiovascular disease.75 The increase in cardiovascular mortality in chronic kidney disease patients may be explained by pump failure and arrhythmias. The rate of myocardial infarction (MI) is higher in patients with chronic kidney disease when compared to the general population.76 The pathophysiology includes decreased myocardial capillary density, cardiomyocyte dysfunction, increased left ventricular mass, impaired ion reutilization, anaemia, erythropoietin deficiency, abnormal calcium–phosphate homeostasis with phosphate retention, hyperparathyroidism, inflammation, hypervoleamia, and hyperhomocysteinemia.75 All of these disruptions may lead to myocardial dysfunction and fibrosis.77 Therefore, chronic kidney disease patients in the setting of ACS are more prone to develop arrhythmia, left ventricular dysfunction and subsequent death than the general
The risk of cardiovascular death in patients with moderate chronic kidney disease is similar to risk of cardiovascular death in patients with diabetes mellitus or previous myocardial infarction. The incidence of renal failure in patients with ACS has been reported as 15% and 17.4% in two studies.

Acute coronary syndrome (ACS) patients presenting with chronic kidney disease demonstrate more extensive coronary artery disease and have higher risk for heart failure, re-infarction and death than ACS patients without coronary artery disease. They are also more likely to have delayed or atypical presentations. As a result they are less likely to receive appropriate therapy than are patients without renal impairment.

Recent studies have found that patients with reduced estimated glomerular filtration rate (eGFR) have a high prevalence of coronary artery disease, myocardial infarction, and cardiovascular death than the general population. They also have a poorer outcome post ACS than those without renal impairment.

In South Africa, hypertension has been attributed as the cause of chronic kidney disease in 21% of patients on renal replacement therapy. Hypertension was also reported as the commonest cause of end-stage renal disease in 34.6% of black South African, 20.9% of people of mixed ancestry, 13.8% of Indians, and 4.3% of Whites.
2.10 Typical presenting symptoms

Although there is a consensus description about what represents typical chest pain, the equivalent definition for atypical chest pain remains less clear. The first description of typical ischemic chest pain was provided by Heberven who defined it as a painful sensation in the breast accompanied by a strangling sensation, anxiety, and occasional radiation of pain to the left arm.\(^6\) Currently, typical chest pain is described as pressure, tightness, or heaviness; it may radiate to the neck, jaw, shoulders, back, or one or both arms.\(^4\), \(^51\) It may also be accompanied by other symptoms such as shortness of breath, sweating, nausea, vomiting, dizziness,\(^7\) abdominal pain, diaphoresis, and syncope.\(^51\) In a study, 70.8% of patients presented with typical chest pain.\(^80\) Another study reported 83% of patients with typical chest pain.\(^54\)

2.11 Atypical presenting symptoms and missed diagnosis

Atypical chest pain and presentation of ACS is another confounder that may increase the incidence of missed or delayed diagnosis. Emergency Physicians (EP) are faced with this problem which is further complicated by cultural differences, ethnic differences and language barriers in various patient populations. Clinicians therefore must have a high index of suspicion for the work up of ACS with suspicious presentations.\(^2\), \(^4\)

Atypical chest pain includes signs and symptoms that do not fit the classically described complaints associated with myocardial ischaemia. The description of chest pain thought to be atypical may include sharp or stabbing pain, pain reproduced by
palpation or position change, pleuritic chest pain, burning pain or indigestion. The pain may also be described as indigestion or heartburn with associated nausea and or vomiting.\textsuperscript{4} In the absence of the pain, other symptoms termed non-pain equivalents\textsuperscript{6} may include shortness of breath, weakness, dizziness, light-headedness, loss of consciousness,\textsuperscript{81} nausea, and diaphoresis.\textsuperscript{4} ACS atypical presentations are commonly observed in women, older patients (> 75 years), and patients with diabetes\textsuperscript{7}, chronic renal failure, or dementia.\textsuperscript{82,83} Several studies have reported the incidence of atypical chest pain as between 4.7% and 33%.\textsuperscript{3,54,84-86}

As described above, the distinction between typical and atypical chest pain is blurred,\textsuperscript{6} especially given that patients and doctors may communicate in languages that are not their first language, and many nuances of description may be lost in translation.

During the initial contact with a patient presenting with chest pain, the goals of the emergency physician are to determine the likelihood of ACS or non-ACS, exclude other life-threatening causes of chest pain\textsuperscript{6} and appropriate disposition (admit, discharge with appropriate counselling, etc.) of the patients. The greatest pitfall during assessment of ACS patients in the absence of chest pain is the failure to consider the diagnosis of cardiac ischaemia.\textsuperscript{4}

The rates of missed diagnosis of ACS vary from 2% to 4% in centres in the USA.\textsuperscript{4} Factors associated with inadvertent discharge of patients with missed cardiac ischaemia include younger age, atypical symptoms, women, non-white race, physician inexperience, failure to detect ischaemia on initial ECG, failure to obtain an ECG.\textsuperscript{87,88} Missed and delayed diagnosis of ACS is associated with high morbidity
and mortality. Patients discharged from the ED with a missed diagnosis of ACS have been reported to have mortality rates ranging between 10% and 25%.

In an attempt to identify patients with low-risk chest pain, several studies have proposed different predictive models, including the Thrombolysis In Myocardial Infarction (TIMI) risk score, Sanchis rule, and the Vancouver rule. Despite the development of multiple risk stratification systems, none of these predictive models allows one to safely discharge patients home. It is important for a physician to understand that many early risk stratification models were derived using high risk patients and therefore, do not equate low risk presentations as “no risk.”

2.12 Complications of ACS

Complications associated with ACS comprise haemodynamic disturbances and mechanical complications. The later includes mitral valve regurgitation, cardiac rupture, ventricular septal rupture, right ventricular infarction, pericarditis, left ventricular aneurysm, left ventricular thrombus, and post-infarction infarct extension. Haemodynamic disturbances include arrhythmias such as ventricular tachycardia (VT) and ventricular fibrillation (VF), conduction disturbances and heart failure. Heart failure may be accompanied by hypotension, pulmonary congestion, low output status and cardiogenic shock. Cardiac failure rates of 5.8%, 14%, 16% and 26% have been reported in different studies. Studies have reported cardiogenic shock rates of 4.1%, 4.5%, and 7.3%.
2.13 ECG findings

As early as 1917, myocardial infarction related changes were identified on ECG, allowing the ante-mortem recognition of coronary occlusion for the first time. A decade later, ECG became an integrated part of the work up of a patient that presented with chest discomfort. The characteristics of common ECG abnormalities in various locations are summarised in table 1.

The ECG continues to be the most important, cost-effective and immediately available initial test in identifying coronary occlusion and in the decision-making process for emergency reperfusion therapy as it allows categorising ACS as STEMI or NSTEMI / UA. However, the accuracy of ECG remains less optimal. The sensitivity and specificity of the ECG depend on the number and extent of abnormalities.

Alternative diagnosis or pseudo-infarction patterns in patients presenting with ST-segment elevation include early repolarization, pericarditis, left bundle branch block (LBBB), left ventricular aneurysm morphology, brugada syndrome and left ventricular hypertrophy (LVH).

Subendothelial ischaemia can lead to ST-segment depression and T-wave inversion. Among patients with ST-segment depression, approximately 25% eventually develop STEMI and the remaining 75% may demonstrate NSTEMI. Q wave > 0.04 second and at least one quarter of the height of the corresponding R wave is termed a significant Q wave. Small Q waves, referred to as septal Q waves, may be normal when present in leads II, III, and aVF and leads I and aVL. Classically, ECG changes
occur in STEMI, but a completely normal ECG may also be present in a patient with myocardial ischaemia. A new or presumably new LBBB is considered equivalent to ST-segment elevation. But this principle has been questioned as a study has demonstrated that less than half of patients with presumably new LBBB actually had AMI.

Table 1: Summary of ECG findings for the diagnosis of acute coronary syndrome

<table>
<thead>
<tr>
<th>ECG findings</th>
<th>Lesion</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive predictive value (%)</th>
<th>Negative predictive value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ST-segment elevation greater in lead III than in lead II plus ST-segment depression of &gt; 1 mm in lead I, lead aVL, or both</td>
<td>Right coronary artery</td>
<td>90</td>
<td>71</td>
<td>94</td>
<td>70</td>
</tr>
<tr>
<td>Absence of the above findings plus ST-segment elevation in leads I, aVL, V₅, and V₆ and ST-segment depression in leads V₁, V₂, and V₃</td>
<td>Left circumflex coronary artery</td>
<td>83</td>
<td>96</td>
<td>91</td>
<td>93</td>
</tr>
<tr>
<td>ST-segment elevation in leads V₁, V₂, and V₃ plus any of the features below:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST-segment elevation of &gt; 2.5 mm in lead V₁, right bundle branch block with Q wave, or both</td>
<td>Proximal LAD coronary artery</td>
<td>12</td>
<td>100</td>
<td>100</td>
<td>61</td>
</tr>
<tr>
<td>ST-segment depression of &gt; 1 mm in leads II, III, and aVF</td>
<td>Proximal LAD coronary artery</td>
<td>34</td>
<td>98</td>
<td>93</td>
<td>68</td>
</tr>
<tr>
<td>ST-segment depression of ≤ 1 mm or ST-segment elevation in leads II, III, and aVF</td>
<td>Distal LAD coronary artery</td>
<td>66</td>
<td>73</td>
<td>78</td>
<td>62</td>
</tr>
</tbody>
</table>


The diagnosis of chest pain secondary to ACS remains challenging and problematic, particularly in patients initially thought to be at low risk for developing cardiac
ischaemia. Moreover, diagnostic and therapeutic challenges arise again particularly when the ECG is normal or nearly normal, or when it is abnormal at the base line because of underlying conditions. The 12-lead ECG may be non-diagnostic in patients with acute MI secondary to an occlusion of the left circumflex coronary artery or right coronary artery. Indeed, 26% to 60% of patients may have a normal ECG on presentation. A 15 lead ECG (includes V4R, V8 and V9) may diagnose right ventricular and posterior left ventricular infarction and therefore increases the diagnostic sensitivity of the ECG. Ideally, within 10 minutes upon arrival at the ED, providers should obtain a 15-lead ECG.

In the absence of left ventricular hypertrophy or left bundle branch block, ST-segment elevation in acute myocardial infarction is defined as ≥ 1 mm elevation measured at the J point in any 2 contiguous leads except in leads V2 and V3. In these two leads (V2/V3) the ST-segment elevation should be ≥ 2.5 mm in men under the age of 40 years, ≥ 2mm in men over the age of 40 years, or ≥ 1.5 mm in women.

The ACCESS study and a study conducted by Lemos et al in 41 countries have reported the incidence of NSTEMI as 59% and 60% respectively. The above two studies also reported the incidence of STEMI as 41% and 40% respectively. Other studies reported an incidence of STEMI of 15% and 27%. The PURSUIT study reported 39.1% of patients with ST-segment depression, 16.4% with ST-segment elevation and 49.1% with T wave inversion in the American cohort, and 56%, 12.7% and 51.4% respectively in the non-American cohort. Other studies reported 2%, 2.4% and 6% incidence of LBBB among ACS patients.
2.14 Cardiac biomarkers

Cardiac biomarkers play an important role in the diagnosis of acute coronary syndrome. Characteristic of the most used serum cardiac biomarkers and their release kinetics are presented respectively in table 2 and figure 1. The challenge in diagnosing ACS is further escalated, given the fact that cardiac biomarkers (troponin I and T (Tn I and Tn T) and creatine kinase isoenzyme (CK-MB)) are insensitive during the first 4 to 6 hours,\(^7\) contributing to under recognition of atypical ACS and subsequent poor outcomes.\(^{103,104}\)

**Table 2: Characteristics of cardiac biomarkers for the diagnosis of acute myocardial infarction.**

<table>
<thead>
<tr>
<th>Serum cardiac marker</th>
<th>Test first becomes positive (hours)</th>
<th>Peak level (hours)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive predictive value (%)(\dagger)</th>
<th>Negative predictive value (%)(\dagger)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CK</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single assay</td>
<td>3 to 8</td>
<td>12 to 24</td>
<td>35</td>
<td>80</td>
<td>20</td>
<td>90</td>
</tr>
<tr>
<td>Serial assays</td>
<td></td>
<td></td>
<td>95</td>
<td>68</td>
<td>30</td>
<td>99</td>
</tr>
<tr>
<td><strong>CK-MB</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single assay</td>
<td>4 to 6</td>
<td>12 to 24</td>
<td>35</td>
<td>85</td>
<td>25</td>
<td>90</td>
</tr>
<tr>
<td>Serial assays</td>
<td></td>
<td></td>
<td>95</td>
<td>95</td>
<td>73</td>
<td>99</td>
</tr>
<tr>
<td><strong>Troponin I and T</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measured 4 hours after onset of chest pain</td>
<td>4 to 10</td>
<td>35</td>
<td>96</td>
<td>56</td>
<td>91</td>
<td></td>
</tr>
<tr>
<td>Measured 10 hours after onset of chest pain</td>
<td>8 to 28</td>
<td>89</td>
<td>95</td>
<td>72</td>
<td>98</td>
<td></td>
</tr>
</tbody>
</table>

CK — creatine kinase, CK-MB — creatine kinase muscle band

Reprinted with permission from Achar SA, Kundu S, Norcross WA. Diagnosis of acute coronary syndrome. Am Fam Physician 2005(1); 72:119-26.\(^{95}\) Copyright © 2005 by the American Academy of Family Physicians.
Figure 1: Time course of release of serum cardiac markers after acute myocardial infarction.


2.15 Management of ACS

The goals of treatment for ACS include identification of patients with ST elevation MI for early reperfusion therapy, relief of chest discomfort, treatment of life-threatening complications such as VF, VT, unstable tachyarrhythmia’s and prevention of major adverse cardiac events (MACE). The treatment strategy for ACS patients is based on duration and persistence of symptoms, the initial ECG, cardiac history and findings on physical examination. The American Heart Association and the
European Society of Cardiology have both recommended guidelines for the management of ACS.\textsuperscript{1,2,5,90,105}

Initial therapy in the management of patients with ACS includes administration of oxygen to maintain saturation above 94%, aspirin, nitroglycerine and morphine if pain is not relieved by nitroglycerine. Acute relief of pain reduces myocardial oxygen demand and attenuates the hyperactive catecholamine state.\textsuperscript{105} In addition to pain relief, nitroglycerine also acts as a vasodilator.\textsuperscript{106} Oxygen administration has been shown to reduce ST-segment elevation in anterior infarction.\textsuperscript{107, 108} The second international study of infarct survival (ISIS-2) has shown the efficacy of aspirin in reducing death from MI.\textsuperscript{106} Aspirin has additional benefits when given with thrombolytic agents\textsuperscript{109} and reduces nonfatal AMI by 30% and vascular death by 17% in high-risk patients.\textsuperscript{110}

The management of STEMI relies on the “open artery theory” which stipulates that a prompt and complete restoration of blood flow limits infarct size, preserves left ventricular (LV) function and improves survival rates.\textsuperscript{106} Pharmacological therapy (fibrinolysis) and mechanical means (PCI) are the two methods currently available for restoring coronary perfusion.\textsuperscript{106,111}

The following is a summary of the recent European Society of Cardiology (ESC) guidelines regarding the principles of early reperfusion therapy:\textsuperscript{90}

- Fibrinolytic therapy is recommended within 12 hours of symptom onset in STEMI patients without contraindications to fibrinolytic therapy, if an experienced team cannot perform primary PCI within 120 min of first medical contact.
• In STEMI patients presenting early (<2 h after symptom onset) with a large infarct and low bleeding risk, fibrinolysis should be considered if time from first medical contact to balloon inflation is >90 min.

• If possible, fibrinolysis should start in the prehospital setting.

• A fibrin-specific agent (tenecteplase, alteplase, reteplase) is recommended over non-fibrin specific agents.

• Oral or intravenous aspirin must be administered.

• Clopidogrel is indicated in addition to aspirin.

• Transfer to a PCI-capable centre following fibrinolysis is indicated in all patients after fibrinolysis.

• Rescue PCI is indicated immediately when fibrinolysis has failed (<50% ST-segment resolution at 60 min).

• Emergency PCI is indicated in the case of recurrent ischaemia or evidence of re-occlusion after initial successful fibrinolysis.

• Primary PCI is indicated in acute severe heart failure / cardiogenic shock patients, unless the expected PCI related delay is excessive and the patient presents early after symptom onset.

• Angiography with a view to revascularization (of the infarct-related artery) is indicated after successful fibrinolysis.

• Optimal timing of angiography for stable patients after successful fibrinolysis is 3–24 hours.

Fibrinolytic therapy is contraindicated in patients with NSTEMI / UA. According to the ESC guidelines for patients without persistent STEMI, high risk NSTEMI / UA should undergo coronary angiography within 24 hours of symptom onset, whereas low risk
NSTEMI / UA should undergo coronary angiography within 72 hours of symptom onset.51

**Table 3: ESC recommendations for reperfusion therapy**

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reperfusion therapy is indicated in all patients with symptoms of &lt;12 h duration and persistent ST-segment elevation or (presumed) new LBBB.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Reperfusion therapy (preferably primary PCI) is indicated if there is evidence of ongoing ischaemia, even if symptoms may have started &gt;12 h beforehand or if pain and ECG changes have been stuttering.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Reperfusion therapy with primary PCI may be considered in stable patients presenting 12–24 h after symptom onset.</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Routine PCI of a totally occluded artery &gt;24 h after symptom onset in stable patients without signs of ischaemia (regardless of whether fibrinolysis was given or not) is not recommended.</td>
<td>III</td>
<td>A</td>
</tr>
</tbody>
</table>

ECG = electrocardiogram, i.v. = intravenous, LBBB = left bundle branch block, PCI = percutaneous coronary intervention.

*Class of recommendation.

*Level of evidence.

2.16 Patient outcomes after ACS

Indicators that can be used to assess patient outcomes after ACS include time to clinical stability, length of hospital stay, and mortality rate (in-hospital mortality rate). A median length of hospital stay post ACS of 8 days was reported in a Swiss study. This study also showed that a longer length of hospital was associated with a higher mortality. The PURSUIT study reported mean length of hospital stay post ACS of 8 days and 10 days in the American and non-American cohorts respectively. The first and second SYMPHONY studies have reported median time to clinical stability of 3.6 days and 3.7 days respectively. The in-hospital mortality rate at a study conducted at the University of Michigan has been reported as 6.9% whilst another North American study reported an in-hospital mortality rate of 6.3%. Other studies reported in-hospital mortality rates between 3.27% and 5.3%.
CHAPTER 3  
METHODOLOGY

3.1 Ethical considerations

Permission to conduct this study was granted by the Ladysmith Provincial Hospital management, and by the KwaZulu-Natal Health Research Committee. Ethics clearance was obtained from the Human Research Ethics Committee (medical) (HREC (medical)) of the University of the Witwatersrand (clearance certificate M 120801 – Appendix 1, p 82). In accordance with the principles of patient confidentiality, patient-identifying information was not recorded in the data collection sheet and a unique patient identification number (PIN) was assigned to all patients studied, starting from 001. PIN was known only to the researcher allowing for patient confidentiality to be respected at all times. Scanned medical records were stored in a password-protected folder in a password-protected computer only accessible to the researcher. Patient identifying information was blocked out and replaced with a unique PIN number for each patient prior to scanning. This folder will be deleted at the end of the study.

3.2 Design of the study

This is a cross-sectional, hospital-based, descriptive, retrospective audit of medical records.
3.3 Site of the study

The study was conducted at the Ladysmith Provincial Hospital in KwaZulu-Natal. All of the patients included in the study initially presented to the ED. These patients were further managed either in the adult ICU, high care ward or medical ward.

3.4 The study population

The study population consisted of adult patients that presented to the Ladysmith Provincial Hospital ED and had a final hospital discharge diagnosis of ACS.

3.5 Inclusion criteria

- All patients with a final diagnosis of STEMI.
- All patients with a final diagnosis of NSTEMI.
- All patients with a final diagnosis of UA.

3.6 Exclusion criteria

- Patients diagnosed as stable angina.
- Patients with an initial diagnosis of ACS but later reviewed to another diagnosis (e.g. pulmonary embolism, acute pericarditis, dissecting aortic aneurysm).
- Patients whose medical records could not be accessed.
3.7 Data collection

- The researcher, who had spent about four hours informally researching methodologies regarding retrospective data collection from medical records, collected all available data. The researcher did not attend any formal certified training course regarding retrospective data collection from medical records.
- The researcher was not blinded to the study aims and objectives.
- The study supervisor was frequently consulted during the period of data abstraction.
- Data collection was initiated on 1st June 2013.
- Eligible patients, meeting study criteria and who presented to the Ladysmith Provincial Hospital ED before 1st June 2013 at 00:00 were included in the study.
- The researcher reviewed Ladysmith hospital ED registers.
- The researcher also reviewed intensive care unit, high care ward and the medical ward registers to identify patients with ACS that were misdiagnosed in the ED and later diagnosed in these wards.
- All the above registers had documented as standard hospital protocol, the final patient diagnoses before transfer out of the ED or before discharge from the ICU, high care ward and medical ward.
- 138 patients were required as per sample size calculation (see below).
- A sample size of 160 patients was agreed upon to account for a possible 15% of medical records with incomplete data entry.
• In anticipation that approximately 30% of patient records may not be available due to missing files, 210 potential patient names and patient file number, with diagnosis that met study criteria were selected from the above registers.

• Medical records of these patients were requested and obtained from the hospital records department.

• The respective wards and available doctors were contacted in an attempt to find medical records that could not be found at the hospital records department.

• Patients whose medical records could still not be accessible were excluded from the study.

• For ease of later reference, all medical records that met study criteria were scanned and stored in a password-protected folder in a password-protected computer only accessible to the researcher. Patient identifying information was blocked out and replaced with a unique PIN number for each patient prior to scanning. This folder will be deleted at the end of the study.

• Data from available medical records meeting the study criteria were abstracted and entered into a specifically designed data collection sheet (Appendix 2, p 83 - 85).

•Captured data included age, sex, race, duration of hospital stay (calculated from date of admission to the date of discharge), risk factors for ACS, presenting complaints at the ED, vital signs (BP, HR, RR, GCS), presenting ECG, initial laboratory data (CK-MB, troponin T, haemoglobin, urea, creatinine and total cholesterol), initial management, reperfusion therapy, and patient outcomes (step-down, step-up, time to clinical stability and death).
• The set of vital signs recorded on presentation before any therapeutic intervention was performed, were recorded in the data collection sheet as the vital signs on presentation. If more than one set of vital signs was recorded on initial presentation, the set of results that was closest to the normal range was used. Any set of vital signs reported as spurious by the attending clinician or regarded as spurious by the researcher were excluded.

• Any other conflicting data entries (which were few) was assessed by the researcher, who taking the rest of the patient assessment and also the considerations of the most qualified attending clinician into account, decided as to which data to enter in to the data collection sheet.

• Missing data: Negative findings were not recorded in the archived medical records for most of the following subsets of categorical data: presenting features of study patients (chest pain, associated symptoms, radiation of pain, etc....), risk factors for ACS of study patients, socio-economic and behavioural characteristics of study patients, management of study patients, outcomes of study patients, etc.... Where these negative findings were not recorded in the medical records, they were regarded as negative findings by the data abstractor (researcher).

• To assess for inter-rater reliability, data from a sample of 25 randomly selected medical records was re-abstracted by an independent person with previous experience in data abstraction from medical records. He was blinded to the study methodology and to the information obtained by the researcher.
3.8 Sample size estimation

Acute coronary syndrome (ACS) accounts for about 10% of patients presenting to the Ladysmith Provincial Hospital ED per annum (hospital registry, 2000 - 2012). Assuming an ACS prevalence of 10%, a 5% margin of error, and a 95% confidence level, the minimum sample size required was calculated as 138 using the online Raosoft sample size calculator. One hundred and sixty subjects were enrolled in the study to account for a possible 15% of medical records with incomplete data entry.

3.9 Data analysis

All data recorded in the data collection sheets were entered into an electronic data spreadsheet for analysis (Microsoft® Excel®). STATA ® version12 software was used to perform all statistical analyses. Categorical (gender, race, risk factors, presenting features, death) and continuous (age, duration of hospital stay, vital signs, laboratory data, time to clinical stability) data have been described in the next chapter. Means, standard deviations, medians, ranges, flow diagrams, tables, histograms, bar charts and pie charts have been used where appropriate.
CHAPTER 4

RESULTS

4.1 Inter-rater reliability

Eight randomly selected variables from the data collection sheets were assessed. These selected data from a sample of 25 randomly selected medical records was re-abstracted by an independent person with previous experience in data abstraction from medical records. He was blinded to the information obtained by the researcher. The average intraclass correlation coefficient was 0.93 (95% CI, 0.79 – 0.98).

4.2 Final study sample

One hundred and ninety seven consecutive patients from the sample of 210 names selected from the four registers (ED, ICU, high care and medical ward) were required to make up the eligible 160 patients that met study criteria. A total of 37 patients (18.8%) were excluded from the study. Out of this number, 29 patients (14.7%) had no accessible medical records. Five patients (2.5%) were initially assessed as ACS in the ED, but had their final discharge diagnosis reviewed to stable angina. Another three patients (1.5%) were initially assessed as ACS in the ED, but had their final discharge diagnoses reviewed to pericarditis. Therefore, assuming that the 29 patients without available medical records would have had a final hospital discharge diagnosis of ACS, the false positive diagnosis rate for ACS at the Ladysmith Provincial Hospital ED over the study period was 4.1% (8/197).
4.3 General description of the final sample

A total of 160 patients were included in the study. This comprised of 103 Asians (66 males, 37 females), 36 Blacks (15 males, 21 females) and 21 Whites (9 males, 12 females). The overall sex distribution comprised 90 males and 70 females. A male to female ratio of 1.3: 1.
4.4 Frequency of patients presenting with ACS to the ED

Assuming that the 29 patients for whom no medical records could be found had a final hospital discharge diagnosis of ACS, a total of 189 patients presented with ACS to the Ladysmith Provincial Hospital ED over the study period. These 189 patients presented from 1 November 2009 to 31 May 2013, a period of 43 months. This represents a frequency of approximately 53 patients per annum.

From the 160 patients with available hospital records, 3 patients (1.9 %) were not initially diagnosed with ACS in the ED (false negative diagnosis rate). Two patients were later diagnosed with UA in the medical ward and the other patient was diagnosed with NSTEMI in the ICU. All three patients were male, had no chest pain on presentation and were aged 57, 69 and 77 years respectively. Two patients had concurrent pneumonia and the third patient was misdiagnosed as acute pericarditis. However all three patients were eventually diagnosed with ACS within 10 hours of presentation to hospital and all of them survived and had good short-term outcomes.

4.5 Clinical stability of patients on presentation

4.5.1 Summary of vital signs of study group on presentation to the ED

The results for baseline vital signs of study patients (systolic blood pressure, diastolic blood pressure, heart rate and respiratory rate) are summarised in Table 4.
Table 4: Summary of results for baseline vital signs of study patients

<table>
<thead>
<tr>
<th>Vital sign</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>66</td>
<td>230</td>
<td>132.9±27.4</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>43</td>
<td>140</td>
<td>84.2±16.9</td>
</tr>
<tr>
<td>Heart Rate (beats per minute)</td>
<td>38</td>
<td>147</td>
<td>87.3±19.2</td>
</tr>
<tr>
<td>Respiratory Rate (breaths per minute)</td>
<td>12</td>
<td>40</td>
<td>21.3±19.2</td>
</tr>
</tbody>
</table>

SD=Standard Deviation

4.5.2 Systolic Blood Pressure (SBP)

![Frequency histogram for SBP of study patients](image)

Figure 3: Frequency histogram for SBP of study patients

The frequency histogram for systolic blood pressure of study patients is shown in Figure 3. The median SBP for the study population was 122 mmHg and ranged between 66 and 230 mmHg. The mean (SD) was 132.9 (27.4) mmHg. The majority of the study patients had a SBP between 120-139 mmHg (43/160, 26.9%). Two study patients had a SBP of > 220 mmHg (2/160, 1.3%).
4.5.3 Diastolic Blood Pressure (DBP)

The frequency histogram for diastolic blood pressure of study patients is shown in Figure 4. The median DBP for the study population was 83.5 mmHg and ranged between 43 and 140 mmHg. The mean (SD) was 84.2 (16.9) mmHg. The majority of the study patients had a DBP between 60-99 mmHg (121/160, 75.6%). Two study patients had a DBP of > 120 mmHg (2/160, 1.3%).

![Figure 4: Frequency histogram for DBP of study patients](image)

4.5.4 Heart Rate (HR)

The median heart rate for the study population was 85 beats per minute and ranged between 38 and 147 beats per minute. The mean (SD) was 87.3 (19.2) beats per minute. The majority of the study patients had a heart rate between 70-89 beats per minute (75/160, 46.9%).
4.5.5 Respiratory Rate (RR)

The median respiratory rate for the study population was 20 breaths per minute and ranged between 12 and 40 breaths per minute. The mean (SD) was 21.3 (4.2) breaths per minute. The majority of the study patients had respiratory rates between 20 to 24 breaths per minute (114/160, 71.3%).

4.5.6 Glasgow coma scale (GCS)

All study patients had only a single GCS score recorded in the ED presentation form. Two study patients presented with confusion. The GCS score was 13 for both of these patients (table 5).

Table 5: Frequency distribution table for GCS score of study patients

<table>
<thead>
<tr>
<th>GCS score</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>2</td>
<td>1.3</td>
</tr>
<tr>
<td>15</td>
<td>158</td>
<td>98.7</td>
</tr>
<tr>
<td>Total</td>
<td>160</td>
<td>100</td>
</tr>
</tbody>
</table>

4.6 Presenting features of study patients

4.6.1 Chest pain

Approximately three quarters (119/160, 74.4%) of the study patients had typical chest pain, 16.3% (26/160) had atypical chest pain, and the remaining 9.4% (15/160) had no chest pain, as shown in Figure 5.
4.6.2 Presenting symptoms of patients with no chest pain

From a total of 15 study patients who reported no chest pain, their presenting symptoms were as follows. The majority (10/15, 66.7%) had dyspnoea only and the remaining five had a combination of dyspnoea, fatigue, fainting, dizziness, sweating, nausea, and vomiting, as shown in Table 6.

Table 6: Frequency distribution table for presenting symptoms of study patients with no chest pain

<table>
<thead>
<tr>
<th>Presenting Symptoms</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnoea only</td>
<td>10</td>
<td>66.7</td>
</tr>
<tr>
<td>dyspnoea, fatigue</td>
<td>2</td>
<td>13.3</td>
</tr>
<tr>
<td>fainting, dizziness, sweating, nausea</td>
<td>1</td>
<td>6.7</td>
</tr>
<tr>
<td>vomiting, fatigue</td>
<td>2</td>
<td>13.3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>15</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>
4.6.3 Associated symptoms of all study patients

The majority of the study patients (31/160, 19.5%) had dyspnoea, others had no associated symptoms (20/160, 12.6%), nausea (15/160, 9.4%), sweating (15/160, 9.4%), nausea and vomiting (12/160, 7.6%) and dizziness (10/160, 6.3%). The rest of the study patients had combinations of some of the following: dyspnoea, dizziness, malaise, nausea, vomiting, abdominal pain, body weakness, numbness, palpitation, sweating, and fainting. Figure 6 show the frequency distribution of associated symptoms for all study patients.

4.6.4 Radiation of pain

The majority of the study patients had radiation of pain to the left arm (50/160, 31.3%), left shoulder (18/160, 11.3%), and the back (9/160, 5.6%) only. Some had no radiation of pain (14/160, 8.8%). The remaining study patients had radiation of
pain to a combination of the back, left arm, left shoulder, jaw, neck and left side of the body. This frequency distribution is shown in Figure 7.

Figure 7: Frequency bar chart describing radiation of pain of study patients

4.6.5 Cardiogenic shock

Only six patients in the study group (6/160, 3.8%) developed cardiogenic shock.

4.6.6 Cardiac failure

Almost twenty per cent of the study patients (31/160, 19.4%) developed cardiac failure as a consequence of ACS. None of the study patients had echocardiography performed at Ladysmith Provincial Hospital due to unavailability.

4.6.7 ECG findings

Sixty-two patients (38.8%) presented with ST segment elevation and 4 patients (2.5%) presented with presumably new LBBB. The other 94 study patients (58.7%) were classified as NSTEMI / UA.
From the 94 patients that presented with NSTEMI / UA, 11 patients (11.7%) had a normal ECG, 6 patients (6.4%) had ECG features of a RBBB, 44 patients (46.8%) had ST segment depression and 61 patients (64.9%) had T wave inversion on their ECG.

From the study population, 35/160 patients (21.9%) had significant Q waves, suggesting previous or established STEMI. Eleven of these were found in patients diagnosed with acute NSTEMI / UA, suggesting previous STEMI.

4.6.8 Laboratory findings

Table 7: Selected laboratory findings of study patients

<table>
<thead>
<tr>
<th>Laboratory Finding</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated Troponin T</td>
<td>103</td>
<td>64.4</td>
</tr>
<tr>
<td>Elevated Creatine Kinase – Muscle Band (CK-MB)</td>
<td>86</td>
<td>53.8</td>
</tr>
<tr>
<td>Missing data</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Elevated Creatinine</td>
<td>28</td>
<td>17.5</td>
</tr>
<tr>
<td>Anaemia (Haemoglobin &lt; 12 mg/dl)</td>
<td>12</td>
<td>7.5</td>
</tr>
<tr>
<td>Elevated Total Cholesterol</td>
<td>46</td>
<td>28.8</td>
</tr>
<tr>
<td>Missing data</td>
<td>6</td>
<td>3.8</td>
</tr>
</tbody>
</table>
Table 7 summarises selected laboratory findings of all the study patients. The highest recorded value during the first twelve hours of presentation was included. One hundred and three patients (64.4%) had elevated troponin T, 86 patients (53.8%) had elevated CK-MB, 28 patients (17.5%) presented with elevated creatinine, 12 patients (7.5%) presented with anaemia (haemoglobin < 12 mg/dl) and 46 patients (28.8%) presented with elevated total cholesterol.

All of the 66 patients (41.3%) with ST segment elevation / presumably new LBBB had elevated troponin T within twelve hours of presentation. Thirty-seven (23.1%) patients without ST segment elevation had raised troponin T and were diagnosed as NSTEMI. Therefore 57/160 patients (35.7%) were diagnosed as UA.

**Figure 8: Pie chart describing the proportion of study patients that presented with the various subcategories of ACS**
4.7 Risk factors for ACS of study patients

The prevalence of previous acute coronary syndrome (ACS) was 27.5% (44/160), family history 18.1% (29/160), previous heart surgery 6.3% (10/160), obesity (BMI > 30 kg/m²) 28.1% (45/160), hypercholesterolemia 28.8% (46/160), diabetes 26.3% (42/160), hypertension 47.5% (76/160), and renal failure 16.9% (27/160). Hypertension was the most frequent risk factor among the study patients. Only 6% of study patients had documented HIV test results therefore it was not included in the study.

4.8 Age of study patients

The ages of the study patients ranged from 17 to 87 years with a mean age (standard deviation (SD)) of 55.8 (12.8) years. The age distribution is shown by the frequency histogram in Figure 9.

Figure 9: Frequency histogram describing age distribution of study patients
After categorising the ages into age groups, the distribution is shown in Figure 10.

![Frequency histogram for age group categories of study patients](image)

**Figure 10: Frequency histogram for age group categories of study patients**

The majority of the patients were in the age group of 45-54 years (50/160, 31.3%), followed by the 55-64 year age group (43/160, 26.9%), and then the 35-44 year age group (22/160, 13.8%). More than three-quarter (76.4%) of study patients were aged < 65 years; and those aged ≥ 65 years were only approximately 24%.

### 4.9 Sex of study patients

The majority of study patients were male (90/160, 56.25%).

### 4.10 Race of study patients

The majority of the study patients were Asian (103/160, 64.4%) and there were more black patients (36/160, 22.5%) than white patients (21/160, 13.1%) as shown in Table 8.
Table 8: Frequency distribution for race of study patients

<table>
<thead>
<tr>
<th>Race</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asian</td>
<td>103</td>
<td>64.4</td>
</tr>
<tr>
<td>Black</td>
<td>36</td>
<td>22.5</td>
</tr>
<tr>
<td>White</td>
<td>21</td>
<td>13.1</td>
</tr>
<tr>
<td>Total</td>
<td>160</td>
<td>100</td>
</tr>
</tbody>
</table>

4.11 Socio-economic and behavioural characteristics of study patients

The majority of the study patients were unemployed (98/160, 61.3%), urban resident (143/160, 89.4%), referred from private practice (37/160, 23.1%), not alcohol users (137/160, 85.6%), and not smokers (88/160, 55.0%).

4.12 Management of study patients

4.12.1 Initial management

All study patients were initially administered oxygen. The majority were given aspirin (145/160, 90.6%) and nitrates (145/160, 90.6%). The majority of study patients were also given enoxaparin and clopidogrel (141/160, 88.1%), whilst less than half of the patients (69/160, 43.3%) were given morphine.

4.12.2 Early reperfusion therapy

Sixty-two patients (38.8%) presented with ST segment elevation and 4 patients (2.5%) presented with presumably new LBBB. Therefore 66 of the study patients were considered for early reperfusion therapy. However, only 65% (43/66) of these
patients received early reperfusion therapy. The other 23 patients (35%) presented beyond the cut off time period and were therefore not considered for early reperfusion therapy. Of the 43 patients that were eligible for early reperfusion therapy, 40 patients (93.0%) received thrombolytic therapy (2 patients (5.0%) received alteplase and 38 patients (95.0%) received streptokinase). Due to timing and the long distance to the nearest PCI facility, primary PCI was not considered for any of these patients. The other three patients had contra-indications to the use of thrombolytic agents and were hence transferred emergently to the PCI facility. Seven of the forty patients that received thrombolytic agents (19.5%), did not have appropriate resolution of the ST segments. All of these patients were transferred to the PCI facility for rescue PCI.

As per Ladysmith Provincial Hospital protocol, all patients presenting with ACS (STEMI / NSTEMI / UA) must be referred to an appropriate facility for coronary angiography in order to delineate coronary anatomy. Over the entire study period, eight patients (4.1%) referred from Ladysmith Provincial Hospital for coronary angiography underwent coronary artery bypass grafting (personal communication with cardiology ward staff at Grey’s Hospital).

4.13 Outcomes of study patients

4.13.1 Clinical deterioration requiring ICU

About 26.3% (42/160) deteriorated clinically and were transferred from the medical ward to the ICU.
4.13.2 Length of hospital stay

Figure 11: Frequency histogram for length of hospital stay of study patients

The median number of days in hospital was 3 days and ranged from 1 to 16 days. The mean (SD) number of days spent in hospital was 3.6 (2.0) days. Figure 11 shows the frequency histogram for length of hospital stay. The majority of patients stayed in hospital for three days (49/160, 30.6%).

4.13.3 Time to clinical stability

Clinical stability was defined as the first day that patients met two or more of the following criteria: resolution or improvement of symptoms, systolic blood pressure (SBP) > 90 mmHg, heart rate 50 – 100 beats per minute and Killip class < II (i.e. no clinical evidence of left ventricular failure). Time to clinical stability was calculated by subtracting the date of admission from the first date the patient achieved clinical stability.
Table 9: Frequency distribution table for number of days to clinical stability of study patients

<table>
<thead>
<tr>
<th>Time to clinical stability (in days)</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>42</td>
<td>31.6</td>
</tr>
<tr>
<td>2</td>
<td>59</td>
<td>44.4</td>
</tr>
<tr>
<td>3</td>
<td>23</td>
<td>17.3</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>3.8</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>1.5</td>
</tr>
<tr>
<td>7</td>
<td>2</td>
<td>1.5</td>
</tr>
<tr>
<td>Total</td>
<td>133</td>
<td>100</td>
</tr>
</tbody>
</table>

The frequency distribution of time to clinical stability (in days) is shown in Table 9. The median number of days to clinical stability for 133 of the study patients was 2 days and ranging from 1 to 7 days. The mean (SD) number of days to clinical stability was 2.1 (1.1). The majority of the study patients achieved clinical stability within 2 days (101/133, 75.9%). The other 27 patients either demised or were transferred to the referral centre prior to achieving clinical stability.

4.13.4 Death

A total of 13 study patients died prior to hospital discharge (8.1%, 13/160).
CHAPTER 5

DISCUSSION

This was a retrospective, cross-sectional, hospital-based study of 160 consecutive patients with accessible medical records who presented to the Ladysmith Provincial Hospital ED. Difficulty in retrieving medical records and extracting data from medical records were some of the constraints of the study.

5.1 Frequency of ACS presentation

A total of 189 patients presented with ACS to the Ladysmith Provincial Hospital ED over the study period. This is assuming that the 29 patients for whom no medical records could be found had a final hospital discharge diagnosis of ACS. These 189 patients presented from 1 November 2009 to 31 May 2013, a period of 43 months. This represents a frequency of approximately 53 patients per annum. The known false positive and false negative diagnosis rates of ACS at the Ladysmith Provincial Hospital ED over the study period was 4.1% and 1.9% respectively. However this does not account for patients who may have been misdiagnosed or prematurely discharged from the ED. In large volume hospitals in Canada, an average frequency of approximately 24 patients per year presenting with ACS was reported.\textsuperscript{33} The ACCESS South African study reported an average frequency of 22 patients per annum.\textsuperscript{57} These reported figures represent less than half of that found in this study. The higher frequency of ACS reported in this study, when compared especially to the South African cohort of the ACCESS study, is concerning and needs to be further investigated with regards to population risk factor control measures and possibly genetic and environmental factors. In contrast, another study reported a frequency of
255 patients per annum (22 patients per month). This is about 5 times higher than findings from this study.

5.2 Clinical stability of patients on presentation

The majority of patients enrolled in the study had a normal GCS of 15/15 (98.75%). The median systolic BP was 122 mmHg and ranged from 66 mmHg to 230 mmHg. The overall median diastolic BP was 83.5 mmHg and ranged from 43 mmHg to 140 mmHg. The overall median heart rate was 85 beats per minute and ranged from 38 beats per minute to 147 beats per minute. The overall median respiratory rate was 20 breaths per minute and ranged from 12 breaths per minute to 40 breaths per minute. A study reported a median systolic BP of 130 mmHg and ranged from 118 mmHg to 152 mmHg, a median diastolic BP of 80 mmHg and ranged from 70 mmHg to 86 mmHg. The same study also reported a median heart rate of 71 beats per minute and ranged from 60 beats per minute to 80 beats per minute, and a median respiratory rate of 20 breaths per minute and ranged from 18 breaths per minute to 21 breaths per minute. These results are very similar to findings from this study.

5.3 Presenting clinical features

5.3.1 Chest pain

Approximately three quarters of the study patients (74.4%) presented with typical chest pain. In a study, 70.8% of patients presented with typical chest pain. Another study reported 83% of patients that presented with typical chest pain. Nearly one quarter (24.6%) of the study patients had an atypical presentation. The reported incidence in other studies was between 33.3% and 47%. Of all the
study patients with atypical presentations, 9.4% presented without chest pain (silent presentation). This was similar to 8.4% reported by Brieger et al, in the GRACE study. Stern et al\textsuperscript{116}, Canto et al\textsuperscript{117} and Milner et al\textsuperscript{118} reported incidence of 21.7%, 26.5% and 30% respectively. Dyspnoea was the most common symptom (66.7%) in patients with no pain in this study. Dyspnoea was also reported to be the most common presenting symptom in patients without chest pain (49%) in the GRACE study.\textsuperscript{58}

5.3.2 Associated symptoms

Most of the study patients presented with dyspnoea as the commonest associated symptom (19.5%). Dyspnoea was also reported as the most common associated symptom (51%) by Arslanian-Engoren and colleagues in a study conducted on women and men presenting with ACS.\textsuperscript{56} Nausea alone or associated with vomiting represented the second most common associated symptom of the study patients (18.8%). This was in contrast with the GRACE study which found that diaphoresis was the second most common symptom (26.2%) on presentation.\textsuperscript{58} Radiation to the left arm was reported in 31.3% of study patients. This was similar to 25 % reported by Arslanian-Engoren et al.\textsuperscript{56}

5.3.3 Cardiogenic shock and cardiac failure

Approximately 4% of the study patients presented with cardiogenic shock, which was similar to other studies.\textsuperscript{54,58} A significant proportion of the study patients presented with cardiac failure (19%). The reported incidence in other studies was between 5.8% and 26%.\textsuperscript{56,92,93}
5.3.4 ECG findings

The majority of the study patients presented with NSTEMI / UA (58.8%), which was similar to the ACCESS study (59%)\textsuperscript{57} and the study conducted in 41 countries by Lemos et al (60%).\textsuperscript{52} Likewise, 38.8% of study patients presented with STEMI. The above two studies found a similar incidence of 41% and 40% respectively.\textsuperscript{52,57} The reported incidence in other studies was between 15% and 27%.\textsuperscript{53,99}

The prevalence of ST-segment elevation / presumably new LBBB among study patients was 38.8%. The prevalence for ST-segment elevation in this study is about three times higher than the 12.7% reported in the non-American cohort of the PURSUIT study.\textsuperscript{100} Amongst patients that presented with NSTEMI / UA, 46.8% had ST segment depression and 64.9% had T wave inversion on their ECG. The non-American cohort of the PURSUIT study also reported a 56.2% prevalence of ST segment depression and a 51.4% prevalence of T wave inversion.\textsuperscript{100}

5.3.5 Laboratory findings

Almost two thirds of study patients tested troponin positive (64.4%), which was similar to the 69.3% reported by Mukherjee and colleagues in a study on the impact of combination evidence-based medical therapy on mortality in patients with ACS.\textsuperscript{53} The reported incidence by Antman and colleagues was 95% in the TIMI IIIb study\textsuperscript{119} and was 31% in the study by Goncalves et al.\textsuperscript{120}

5.4 Risk factor assessment

The overall comorbidity and risk factors associated with ACS in this study reflected those described in the literature. HIV as a risk factor could not be analysed in this
study given that most files did not have HIV result recorded. A study has reported AMI rates of 11.13 per 1000 patient-years for HIV and 6.98 per 1000 patient-years for non-HIV. 

Almost half of the study patients (47.5%) had hypertension. Four other studies had a reported prevalence of hypertension of 34%, 50%, 50.8% and 75%. Hypercholesterolemia was the second most frequent comorbidity and accounted for 30.6% of study patients. The reported incidence in other studies was 16%, 30.5% and 59%. Obesity was the third most frequent comorbidity and found in 28% of study patients. This was similar to 25% reported by El-Menyar et al. About 26% of study patients had diabetes mellitus. Similar findings were reported in the ACCESS study (23.9%) and in the Grace (24.3%) study. Other studies reported figures of 16% and 38%. About seventeen percent (16.9%) of patients had renal failure, which was similar to 15% reported by El-Menyar and colleagues and 17.4% reported by Meier and colleagues in the University of Michigan study.

About a quarter (27.5%) of study patients had known prior CAD. The reported incidence in other studies was 26.9%, 37% and 43.7%. Only 18.1% of the study patients had a positive family history of CAD, which was similar to 21% reported by Lemos et al. This was higher than 13% reported by El-Menyar et al in the Gulf RACE study, but lower than 31.2% reported by Gurm et al. Only 6.3% of patients had previous heart surgery (CABG), which was similar to 7.1% reported by Lincoff and colleagues in the non-US cohort of the PURSUIT study. Other studies reported a prevalence of between 4% and 13%.
5.5 Demographic characteristics

The mean age was 55.8 ± 12.8 years, which was similar to the mean age of 58.0 ± 12.1 years reported in the ACCESS study. Matetzky et al also reported a similar mean age of 57 ± 12.8 years in their acute myocardial infarction study conducted in an Israeli population. In contrast, Eagle et al reported a higher mean age of 65 ± 13 years in the validated prediction model of all forms of ACS study, which was conducted in 14 different countries. Gonçalves and colleagues also reported a higher mean age of 63.4 ± 10.8 years. In this study, the youngest patient was 17 years old and the oldest was 87 years old. A similar finding of 18 – 90 years was reported in the study by Bhattacharyya and colleagues. Matetzky and colleagues reported a range of 28 – 74 years in their study. Arslanian-Ergoren et al and Schamroth et al also reported the youngest patient in their study as 17 years.

The overall sex distribution in this study was 56% males and 44% females. Amongst Asians, about two thirds were male whereas amongst Blacks and Whites more than half were female. Mukherjee and colleagues reported an overall gender distribution of 63% male and 37% female. The ACCESS study reported an overall 76% male and 24% female gender distribution. Another study found the gender distribution to be 75% male and 25% female. The higher proportion of females amongst Blacks and Whites in this study is a concern and needs to be further investigated.

Although Asians only comprise about 2.5% of the South African population, the majority of the study patients with ACS were Asian (103/160, 64.4%). There were more Black patients (36/160, 22.5%) than White patients (21/160, 13.1%). In the United States of America, a study reported the majority of patients with ACS were
white (75%), followed by black patients (7%), and Asian patients represented only 3%. Another study also found Asians to be at higher risk for CAD. The alarmingly high prevalence of ACS amongst Asians in this study is concerning and warrants further investigation. Vigorous education programmes, modifiable risk factor control measures and possibly genetic predisposition testing need to be promulgated at a governmental level.

5.6 Socio-economic and behavioural characteristics

The majority of patients (89.4%) came from urban areas; only 10.6% came from rural areas. This is consistent with a rapid change in the spectrum and pattern of cardiovascular diseases and risk factors associated with urbanisation in African countries. This reaffirms the epidemiologic transition in South Africa. A substantial proportion of study patients (61.25%) were unemployed. This rate of unemployment is substantially high given the current unemployment rate of 25.6% in South Africa as per Statistics South Africa’s second quarter year 2013 report and also given the fact that more than three-quarters (76.4%) of study patients were aged < 65 years. The high unemployment rate in this study may be partly due to the 24% of patients who were 65 years and older, most of whom were retired. It is also likely that most people that are employed have medical insurance and are more likely to present to private health care facilities. Despite being high, the unemployment rate was similar to 60.6% reported by Alter et al in a Canadian study on socioeconomic status and mortality after acute myocardial infarction and 66% reported by Pitsavos et al. It was lower than 48.7% reported by Kronish et al.
Forty five percent of study patients were smokers, which was similar to the 44% reported in the ACCESS study. Other studies reported an incidence of 41% and 63%. Only 16.4% of patients admitted to alcohol use. Hansen et al in a Danish study on alcohol intake and acute coronary syndrome reported a prevalence of 10.2%.

5.7 Management

Eighty eight percent of patients in this study were administered both enoxaparin and clopidogrel. The ACCESS study reported that 73.3% of all patients in South Africa received low molecule weight heparin (enoxaparin). Other studies reported frequencies of 41.7% and 88.4%.

Approximately two-third of eligible patients (65%) underwent early reperfusion therapy, which was similar to the 70% reported by Eagle et al in the Australian, Canadian, New-Zealand and European cohorts of the GRACE study. Thirty five percent of patients who potentially could have received early reperfusion therapy were deemed not eligible. These patients presented to the Ladysmith Provincial Hospital ED after the cut-off time for early reperfusion and all of them had established Q waves on presentation. They were all transferred to the referral cardiology unit. The ACCESS study reported a similar percentage of patients (39%) who did not receive early reperfusion therapy. Of the patients that underwent early reperfusion therapy, 93% received thrombolysis. The GRACE study reported that 49% in Europe, 67% in Australia and New Zealand and 31% in Canada underwent thrombolysis. A much higher percentage of patients in this study received thrombolytic therapy as Ladysmith Provincial hospital does not have a PCI
facility and also the closest PCI facility is a distance away. Only 10 patients (15.2%) were referred early to the PCI referral centre. Three patients had contra-indications to the use of thrombolytic agents and seven patients required rescue PCI.

Although alteplase and other newer tissue plasminogen activator agents are regarded as thrombolytic agents of choice in the USA\textsuperscript{2} and Europe,\textsuperscript{106} the majority of patients (94%) who underwent thrombolytic therapy in this study received streptokinase and only 6% were thrombolysed with alteplase. Alteplase does have marginal benefits in terms of side effects and speed of onset, but is associated with higher bleeding rates and cost when compared to streptokinase.\textsuperscript{128} Alteplase and the other newer tissue plasminogen activator agents are not widely available at the Ladysmith Provincial Hospital. All patients treated with streptokinase were premedicated with hydrocortisone and promethazine prior to thrombolysis so as to minimise the risk of anaphylactic reactions.

Over the entire study period, eight patients (4.1%) referred from the Ladysmith Provincial Hospital for coronary angiography underwent coronary artery bypass grafting (personal communication with cardiology ward staff at Grey’s Hospital). Other studies reported CABG figures of 3.63%\textsuperscript{61}, 14.6%\textsuperscript{57} and 18.3%.\textsuperscript{120}

5.8 Outcomes

The overall median time to clinical stability of study patients was 2 days, with a range between 1 and 7 days. The first and second SYMPHONY studies have reported median times to clinical stability of 3.6 days (with a range between 2.2 and 5.1 days) and 3.7 days (with a range between 2.6 and 5.5 days) respectively.\textsuperscript{113} About 26.3%
of study patients deteriorated clinically and were transferred from the medical ward to the ICU. There were no data in the literature to compare step-up to the ICU of patients who had deteriorated. The overall median number of days spent in hospital (length of hospital stay) was 3 days. This was slightly more than the 5 days reported by the American cohort of the PURSUIT study.\textsuperscript{100} The Swiss study found the median length of hospital stay post ACS to be 8 days,\textsuperscript{112} whereas in the non-American cohort of the PURSUIT study, the median length of hospital stay was 10 days.\textsuperscript{100} The shorter length of hospital stay reported in this study is probably due to the fact that patients at Ladysmith Provincial Hospital are generally discharged earlier due to patient overcrowding and bed pressures.

There was an in-hospital mortality rate of 8.1%, which is slightly more than 6.9% reported by Meier et al in a University of Michigan study on ACS patients\textsuperscript{61} and 6.3% reported by Arora in a ACS study conducted in the North America.\textsuperscript{114} Overall in-hospital mortality rates of 5% and 5.3% were reported respectively by Brieger et al in the GRACE study\textsuperscript{58} and by Brilakis et al in the quality of care for ACS patients with known atherosclerotic disease study.\textsuperscript{93} The overall in-hospital mortality rate in the Gulf RACE study was 3.27%.\textsuperscript{54} Even though Ladysmith Provincial Hospital does not have PCI and CABG capacity, the mortality rates were not much higher than those reported in first world countries. This may reaffirm that thrombolytic therapy may be as effective as other forms of reperfusion therapy. Ladysmith hospital also adheres strictly to the American Heart Association guidelines on the management of ACS and is also in constant consultation with a team of highly skilled cardiologists at its referral hospital.
5.9 Limitations of the study

Clearly, a retrospective analysis holds less weight than a prospective study. As such this study is subject to known limitations regarding spurious findings, missing data and conflicting data.

It is important to emphasise that because of the nature of the presentation of ACS especially in its atypical form, clinicians may fail to even consider the diagnosis of ACS, resulting in under-diagnosis and under-reporting of the actual frequency of ACS. In this study ED, ICU, high care and medical ward registers were screened to identify patients presenting with ACS that were missed in the ED and later diagnosed in these wards. The known false positive and false negative diagnosis rates of ACS at the Ladysmith Provincial Hospital ED in this study was 4.1% and 1.9% respectively. However, this study does not account for patients who may have been misdiagnosed or prematurely discharged from the ED.

Electrocardiograms are routinely carried out on all patients presenting to the Ladysmith Provincial Hospital ED with a complaint of pain anywhere from the nose to the pubic symphysis and also on all patients older than 45 years of age. This would also have minimized the chances of missed ACS. However some patients with atypical presentation of UA / NSTEMI and to a lesser extent STEMI may still not have been recognized and erroneously discharged from the ED. Therefore, it is recognized that the reported frequency of ACS presenting to the ED in this study may be underestimated.
Important data pertaining to HIV status, ED time of evaluation, the time of onset of symptoms, or time to reperfusion therapy were not documented in the majority of study patients. Likewise, medical records on most of patients referred to Grey’s hospital for further management were not available. Medical records of 29 patients (14.7%) could not be accessed.

Moreover, this is a single centre study conducted in a public hospital in a medium sized town of South Africa. Consequently, the findings of this study may not be applicable to the private setting or to other geographic parts of South Africa.

There are also some limitations pertaining to the reviewing of medical records in general that are relevant to this study. Firstly, the researcher, who was not blinded to the study aims and objectives, abstracted all the data from the medical records. Secondly, the researcher did not receive formal training or certification in methods of data abstraction. The researcher did however spend about four hours researching various methods of data collection prior to the process of collecting data. Thirdly, although inter-rater reliability was assessed, the abstractors (researcher) performance was not formally monitored.
Despite the many limitations of this retrospective study, valuable information has been gained. Firstly, the higher frequency of ACS reported in this study, when compared to other similar studies, is concerning. Secondly, the alarming prevalence of ACS amongst Asians in this study population is also concerning. Both of these warrant further investigation. Vigorous education programmes, modifiable risk factor control measures and possibly genetic predisposition testing must be promulgated at a governmental level. Thirdly, although Ladysmith Provincial hospital is situated in a low / middle-income country and does not have PCI and CABG capacity in close proximity, the mortality rate and length of hospital stay are comparable to those reported in high-income countries.
REFERENCES


29. Cooper R, Cutler J, Desvigne-Nickens P. Trends and disparities in coronary heart disease, stroke, and other cardiovascular diseases in the United States:


70. Hsue PY, Waters DD. What a cardiologist needs to know about patients with human immunodeficiency virus infection. Circulation 2005; 112:3947-57.


APPENDICES

APPENDIX 1

Ethics Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49  Dr BE Mumpi

CLEARANCE CERTIFICATE  M120801

PROJECT
Clinical Profile of Patients Presenting with Acute Coronary Syndrome in the Ladysmith Provincial Hospital Emergency Department

INVESTIGATORS  Dr BE Mumpi

DEPARTMENT  Department of Family Medicine

DATE CONSIDERED  31/08/2012

DECISION OF THE COMMITTEE*
Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE  25/03/2013

Chairperson
(Professor PE Cleland-Jones)

*Guidelines for written ‘informed consent’ attached where applicable.
cc:  Supervisor:  Dr C van Loggenberg

DECLARATION OF INVESTIGATOR(S)
To be completed in duplicate and ONE COPY returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/we fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. I agree to a completion of a yearly progress report.
PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES.
## APPENDIX 2

### Patient Data Collection Sheet

<table>
<thead>
<tr>
<th>Patient identification number (PIN):</th>
<th>Patient hospital number:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</table>

### Demographic data

<table>
<thead>
<tr>
<th>Age:</th>
<th>Sex: M / F</th>
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</table>

<table>
<thead>
<tr>
<th>Race:</th>
<th>Black</th>
<th>Asian</th>
<th>White</th>
<th>Coloured</th>
<th>Other:</th>
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### Socio-economic status

<table>
<thead>
<tr>
<th>Employment</th>
<th>employed</th>
<th>unemployed</th>
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<tr>
<td></td>
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<td></td>
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<table>
<thead>
<tr>
<th>Residence</th>
<th>Urban</th>
<th>Rural</th>
<th>International</th>
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</thead>
<tbody>
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<td></td>
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<td></td>
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</table>

<table>
<thead>
<tr>
<th>Referring centres</th>
<th>Self</th>
<th>Clinics</th>
<th>Peripheral hospital</th>
<th>Private</th>
<th>Other</th>
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</thead>
<tbody>
<tr>
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<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Alcohol use</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Risk factors

<table>
<thead>
<tr>
<th>Smoking</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HIV status</th>
<th>positive</th>
<th>negative</th>
<th>Unknown</th>
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</thead>
<tbody>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>for HIV positive</th>
<th>on HAART</th>
<th>not on HAART</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Previous ACS</th>
<th>Family history</th>
<th>Previous heart surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Obesity (weight / BMI)</th>
<th>Hypercholesterolaemia</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Renal failure</th>
<th>Other (specify)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### ED date and time of evaluation

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Vital signs on presentation

<table>
<thead>
<tr>
<th>SBP</th>
<th>DBP</th>
<th>HR</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### GCS on presentation

<table>
<thead>
<tr>
<th>GCS on presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>
### Presenting symptoms and signs

<table>
<thead>
<tr>
<th>Typical chest pain</th>
<th>Atypical chest pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associated symptoms (specify)</td>
<td></td>
</tr>
<tr>
<td>No chest pain</td>
<td>Radiation of pain (specify)</td>
</tr>
<tr>
<td>Signs of cardiogenic shock</td>
<td>Signs of cardiac failure</td>
</tr>
</tbody>
</table>

### ECG findings

| Normal ECG | |
| ST elevation | |
| ST depression | |
| Presumably new LBBB | |
| RBBB | |
| T inversion | |
| Q wave | |
| Other | |

### Laboratory findings

- Cardiac biomarkers (specify time from onset of symptoms):
  - Troponin T:
  - CK-MB:
- Urea and creatinine: Haemoglobin:
- Total cholesterol:

### Echocardiography done

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
</table>

If yes (echocardiographic features of ACS, e.g. wall motion abnormalities): Y / N
<table>
<thead>
<tr>
<th><strong>Patient management</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Site of care</strong> &amp; <strong>Length of stay</strong></td>
</tr>
<tr>
<td>ED &amp;</td>
</tr>
<tr>
<td>ICU &amp;</td>
</tr>
<tr>
<td>High care &amp;</td>
</tr>
<tr>
<td>Medical ward &amp;</td>
</tr>
<tr>
<td><strong>Other significant events: e.g. cardiac arrest / CPR / defibrillation</strong></td>
</tr>
<tr>
<td><strong>Initial treatment (specify time from presentation)</strong></td>
</tr>
<tr>
<td>Aspirin &amp; Nitrates</td>
</tr>
<tr>
<td>Oxygen &amp; Morphine</td>
</tr>
<tr>
<td>Adjunctive therapy (specify) &amp;</td>
</tr>
<tr>
<td><strong>Reperfusion therapy: Y / N</strong></td>
</tr>
<tr>
<td>Thrombolytics (specify agent) &amp;</td>
</tr>
<tr>
<td>PCI &amp;</td>
</tr>
<tr>
<td>CABG surgery &amp;</td>
</tr>
<tr>
<td><strong>Patient outcomes</strong></td>
</tr>
<tr>
<td>Step-down &amp;</td>
</tr>
<tr>
<td>Step-up &amp;</td>
</tr>
<tr>
<td>Time to clinical stability &amp;</td>
</tr>
<tr>
<td>Death &amp;</td>
</tr>
</tbody>
</table>