

The efficacy of the exercise treadmill test in patients with mild cardiovascular risk
in a regional New Zealand population

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Abstract

Background: The purpose of this study was to investigate the efficacy of the exercise treadmill test in patients with mild cardiovascular risk in a regional population in New Zealand. Exercise treadmill tests are a valuable non-invasive tool to assist in the diagnosis of coronary artery disease and have been used for many years. There has been continued debate over the accuracy of the exercise treadmill test in the patient with mild cardiovascular disease due to the potential for false positive results and the subsequent cost implications further testing incurs in this group. Despite this, exercise treadmill testing remains a commonly used test in this cohort.

A large proportion of patients with mild cardiovascular risk are seen in the researcher's chest pain clinic and undergo assessment for coronary artery disease using exercise treadmill testing. Due to the current fiscal and resource constraints in the public health system it is important to know that local resources are being utilised in a safe, effective and efficient way. This research has been undertaken to understand the efficacy of the exercise treadmill test in patients with mild cardiovascular risk within a regional New Zealand hospital. It comprises a review of the literature associated with exercise stress testing, the methodology used to complete the research, the results, and finally the implications of these including limitations and recommendations.

Aim: To determine the efficacy of the exercise treadmill test in predicting the presence of coronary artery disease in patients with mild cardiovascular risk in a regional New Zealand population.

Design: A quantitative, retrospective audit was completed in an outpatient population, who were seen for assessment in the chest pain clinic. A retrospective design was chosen as it allowed historical data to be collected which could then be used to evaluate current practice, while the audit provided information on practice standards and insight into areas for quality health service improvement.

Methodology: The study was conducted on 743 consecutive patients between the ages of 35 to 85 years of age who were assessed in the chest pain clinic from 1 July 2011 to 28 February 2014. Of those, 214 were excluded as they had known disease or had been assessed for reasons other than coronary artery disease. A total of 529 eligible patients with mild, moderate or high cardiovascular risk scores and typical or atypical symptoms were included in the final analysis. The audit was completed using information from the chest pain clinic database which captures anonymous information on all patients who are seen in the chest pain clinic and records gender, cardiovascular risk, typical or atypical symptoms and outcomes of exercise treadmill test and further tests. Re-admission rates at six months were obtained using the electronic patient record system that captures all admissions to the hospital and emergency department. Major adverse cardiac events (myocardial infarction, unstable angina, and cardiac death) and any admission to

the emergency department were recorded six months after exercise testing for all patients. Descriptive and inferential statistics were used to describe data and examine relationships between the different cardiovascular risk groups. Ethical approval was obtained from the Research Ethics and Approvals Committee of the Eastern Institute of Technology and locality approval was obtained from the local District Health Board where the research took place.

Results: Of the five hundred and twenty-nine patients included in the audit, 207 had mild cardiovascular risk, 164 had moderate cardiovascular risk and 158 had high cardiovascular risk. There was a predominance of atypical symptoms in all three risk groups: mild 82%; moderate 70%; and high 62%. Positive exercise treadmill outcomes were lower in those with mild and moderate cardiovascular risk (21% and 33%) while the greatest percentage was seen in those with high cardiovascular risk (42%). Positive exercise treadmill results were generally referred for coronary angiography regardless of cardiovascular risk with a small number being discharged for general practitioner follow up, review with a cardiologist, or stress echocardiography. Coronary angiography following a positive exercise treadmill test confirmed disease in 31% of patients with mild cardiovascular risk, 81% with moderate cardiovascular risk and 80% with high cardiovascular risk. The false positive rate was greatest in those with mild risk (68%), compared to 19% and 25% in the moderate and high risk groups. In patients with atypical symptoms, disease was confirmed in 5% of patients with mild cardiovascular risk, 25% with moderate cardiovascular risk and 27% with high cardiovascular risk. By contrast, typical symptoms and a positive exercise treadmill test confirmed disease in 8% with mild cardiovascular risk, 28% with moderate cardiovascular risk and 40% with high cardiovascular risk. Of 529 patients there were 34 (6%) re-presentations to the emergency department within six months. Eleven presented with cardiac chest pain, all were waiting for angiography or stress echo which was expedited, and six were confirmed to have disease.

Conclusion: These findings suggest that due to the low diagnostic result of coronary artery disease in the person with mild cardiovascular risk and atypical symptoms, the exercise treadmill test is not efficacious, raising the question whether it is an appropriate use of the resource in this cohort or whether alternative management strategies need to be considered. Education by primary care health professionals on lifestyle and cardiovascular risk has the potential to improve health outcomes for at risk patients and reduce cardiovascular risk over time. Currently, New Zealand's public health care system is faced with fiscal and resource constraints related to the high costs associated with health care delivery and the challenge exists for district health boards to address these constraints and make service delivery as efficient as possible. While exercise treadmill test results were less accurate in those with mild cardiovascular risk and atypical symptoms this was not the case in those with typical symptoms, confirming its value in this cohort. While this research provides important information on the

chest pain clinic service it is essential to acknowledge the limitations of this study when interpreting the results. A retrospective methodology has inherent weaknesses related to selection bias which are unavoidable due to the historic nature of this design. Other factors that threaten reliability and validity need to be considered such as data entry errors and misinterpretation of test results. This research occurred at a single centre and is therefore not generalisable to other populations. Further research in a similar non-acute, outpatient population in New Zealand would be beneficial and a prospective study would provide additional methodological rigor.

Key words: Exercise treadmill test; cardiovascular risk; chest pain clinic; coronary artery disease; atypical symptoms; typical symptoms; coronary angiography

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Glossary of Abbreviations

ACS	Acute Coronary Syndrome
AMI	Acute Myocardial Infarction
CAD	Coronary Artery Disease
CA	Coronary Angiography
CABG	Coronary Artery Bypass Grafts
CCU	Coronary Care Unit
CHD	Coronary Heart Disease
CP	Chest Pain
CPC	Chest Pain Clinic
CPU	Chest Pain Unit
CVD	Cardiovascular Disease
CVR	Cardiovascular Risk
DHB	District Health Board
ECG	Electrocardiogram
ED	Emergency Department
ETT	Exercise Treadmill Test
GP	General Practitioner
MACE	Major Adverse Cardiac Events
MI	Myocardial Infarction
OU	Observation Unit
PCI	Percutaneous Coronary Intervention
PPV	Positive Predictive Value
NPV	Negative Predictive Value
RACPC	Rapid Access Chest Pain Clinic
SE	Stress Echo
TIMI	Thrombolysis in Myocardial Infarction

Chapter One

Introduction

This thesis will explore the efficacy of the exercise treadmill test (ETT) in detecting coronary artery disease in people with mild risk of coronary artery disease (CAD) at a regional New Zealand hospital. In this chapter the rationale for this research is explained and background information provided to give insight and context to the discussion that follows. An explanation of chest pain (CP), ETT, chest pain clinics (CPC), cardiovascular risk (CVR) and probability analysis is included and the research question and aims are identified. Finally, the thesis structure is summarised.

Rationale and Background

Chest pain is a common symptom associated with a variety of diagnoses from the serious to the benign. For the patient with chest pain the first medical contact may be with a general practitioner (GP) or the emergency department (ED) of the nearest hospital. Chest pain raises concern due to the possibility of myocardial infarction (MI) and it is imperative to have this investigated in a timely manner. After initial assessment the differential diagnosis (the consideration of possible causes of symptoms) will determine the direction of future care. If MI and other life threatening conditions have been ruled out the need for further investigations may be necessary to establish the likelihood of CAD in other words, are the symptoms experienced by the patient angina or can a diagnosis of non-cardiac chest pain be made safely (Parsonage, Cullen & Younger, 2013)?

The ETT is a diagnostic tool that can be used for the assessment of angina. This non-invasive test can be used to gather diagnostic and prognostic information for the patient who has the ability to exercise and has a normal resting electrocardiogram (ECG). There are many other test modalities that can be used, the availability of which depends on local resources and expertise, but the ETT is perhaps the most cost-efficient and readily available method (Gibbons et al., 2002).

Due to the ETT being the predominant tool for the investigation of stable chest pain at the researcher's hospital and the focus of the study, literature involving the ETT will predominate over other modalities, where possible.

Cardiovascular disease (CVD) is the primary cause of death in New Zealand and represents 40% of all deaths (Ministry of Health [MOH], 2007). As New Zealand has a predominantly public health care system the costs related to CVD are of national concern and there is emphasis on reducing the \$501 million dollars spent on CVD related hospitalisations in the 2011/12 financial year (National Health Committee [NHC], 2013). Coronary artery disease accounted

for 57% of these admissions and has been targeted as an area that would gain the most benefit from health and resource savings. In the latest review from the NHC (2014) they estimated a cost to the health system of \$287 million per annum from CAD alone, 8.2% of which is attributed to outpatient and ED visits. Of interest to the researcher is the recommendation that diagnostic testing in patients with a > 90% or < 10% pre-test probability of disease should be discontinued as it adds little to diagnostic accuracy (Fihn et al., 2012). Due to the significant cost of health care and the fiscal constraints in the public health system it is timely to be looking at these issues.

What is angina

Angina pectoris was first described by William Heberden, an 18th century physician who used the term to describe the breast discomfort experienced by otherwise healthy patients, when walking. He noted that symptoms disappeared with rest, and as time went on, symptoms would start to occur at night, waking the patient from their sleep and causing great distress (Van Tellinghen, 2010). This early description of chest discomfort on exertion that is relieved by rest is what is now considered the main component of typical angina.

Chest Pain By Any Other Name....

There are many possible causes of chest pain, such as musculoskeletal injury, pulmonary disease, gastro-oesophageal tract disorders, to name a few. The interesting thing about using chest pain as a descriptor for angina, which is the common term used by many health professionals, is that many people explain their chest symptoms in terms of a discomfort, heaviness, tightness, or squeezing sensation, rather than a pain (Anderson et al., 2007, McConaghy & Oza, 2013). Some describe a heavy sensation in the arms, constriction in the throat, epigastric discomfort or pain between the shoulder blades; all these symptoms may raise the suspicion of angina but do not confirm the disease is present. The National Heart Attack Alert Program Coordinating Committee (as cited in Jones & Slovis, 2010) add indigestion, heartburn, shortness of breath, light headedness, dizziness and loss of consciousness to the milieu and Lee et al. (as cited in Jones & Slovis, 2010) include sharp or stabbing pain, and pain occurring with movement or palpation. Some of these symptoms may be considered atypical but according to Jones and Slovis (2010) there is no current agreement on what constitutes atypical angina. This demonstrates the vast array of descriptions believed to be associated with typical and atypical symptoms of angina and how challenging it is to assess the patient on symptoms alone. In the researcher's thesis, the classification of typical and atypical angina follows the classification as outlined by Fihn et al. (2012), (see Table 1.1) where patients were considered to have typical angina symptoms if they described retrosternal chest discomfort, tightness, pressure, squeezing, and/or arm pain/heaviness, and if these were associated with

exertion, lasting minutes and relieved by rest. Atypical symptoms were shortness of breath, chest discomfort or pain lasting seconds or continuing for several hours that occurred at rest and was not provoked during exercise.

Despite the fact that angina is not often described as “pain” by patients, it remains the term frequently quoted by health professionals when assessing patients and for this reason it will be included in this text, but will be regarded as synonymous with the other descriptions that are typically used by patients.

Table 1.1 below shows the classification of chest pain by Fihn et al. (2012) adapted from Braunwald et al. (1994).

Table 1.1: Clinical Classification of Angina

Typical Angina (definite)	<ol style="list-style-type: none"> 1) Substernal chest discomfort with a characteristic quality and duration that is 2) Provoked by exertion or emotional stress and 3) Relieved by rest or nitroglycerin
Atypical angina (probable)	Meets two of the above criteria
Non-cardiac chest pain	Meets one or none of the typical angina characteristics

Exercise Stress Tests

One of the most compelling signs of stable angina is the provocation of symptoms with exertion which are then relieved by rest and for this reason exercise stress tests can be used to provoke symptoms while the patient is being monitored and assessed in a safe environment. Exercise treadmill testing is a well established, relatively cost effective, and non-invasive test to assist in risk stratification and the diagnosis of CAD (Banerjee, Newman, Van den Bruel & Heneghan, 2012). It is often one of the first tests used in the evaluation of the patient who presents with acute chest discomfort and assists with decisions on the management and treatment of the patient. During an ETT the patient is monitored using a twelve lead ECG at rest, throughout exercise, and several minutes immediately after exercise while the patient is recovering. There are a number of different protocols that can be used in exercise stress testing, each having pre-determined stages, incline adjustments and speed variations. The Bruce Protocol is widely used

and has seven stages each lasting three minutes before an increment in speed and inclination occurs (Hill & Timmis, 2002). This is the protocol used in the researcher's CPC and all patients will have completed ETT using this method. During the exercise test analysis of the ECG, resting heart rate and blood pressure, and its response to exercise, provocation of symptoms and exercise capacity are all vital components recorded and used in the interpretation of the test.

Selection criteria and procedure protocols for ETT are derived from the Cardiac Society of Australia and New Zealand (CSANZ) guidelines on ETT. Contraindications to exercise testing, test end points and interpretation of the test follow the American College of Cardiology and American Heart Association (ACC/AHA) guidelines (2002) for exercise testing (Gibbons et al., 2002). In the researcher's CPC a positive test is therefore based on ST segment depression or elevation of greater than or equal to one millimeter of horizontal or down-sloping change for 60 to 80 milliseconds (ms) after the end of the QRS complex. However, for the purposes of this thesis there is no differentiation between those with a symptom positive or an ECG positive result.

A negative ETT means that no ECG changes or symptoms were provoked with exercise and an equivocal result is one where there is some doubt regarding the result, be it due to symptoms or subtle ST changes at high workload. Of note, some researcher's literature uses the word indeterminate or inconclusive to describe an equivocal result.

There are several variations to the ETT, such as the use of a bicycle ergometer in place of the treadmill machine, or the use of stress echocardiography (SE) or nuclear perfusion scans. The choice of test will be dictated by a number of factors which include the availability of a particular test in the clinic, as many are expensive and require special technical expertise and therefore may not be an option in small centres.

The ability of the patient to exercise adequately is important, if not, a pharmacological agent may be used to stimulate the heart in place of exercise, such as dobutamine SE. An abnormal resting ECG makes interpretation of the ECG during exercise difficult so an additional imaging tool is required in this situation. In such cases, SE provides the additional information needed by using cardiac echocardiography imaging (ultrasound) before and immediately after exercise to look for regional wall motion abnormalities that have been induced by exercise. While these tests are common alternatives to the standard ETT they are more costly and their availability is dependent on local resources.

The ETT has been used as an assessment tool for many years and there has been continual debate over its accuracy to diagnose CAD especially in those with mild CVR. According to Askew and Chareonthaitawee (2013) the low risk patient with atypical symptoms or pain that does not raise suspicion of a cardiac origin should not be referred for stress testing. Gibbons et

al. (2002) recommend its value is best seen in those with a moderate pre-test probability of CAD. Despite this, it remains a prevalent screening tool in those with mild CVR. This may, in part, be explained by what Jones and Slovis (2010) describe as a fear of litigation experienced by emergency physicians in the United States of America (USA) who might miss a diagnosis of MI in a low risk patient. The authors explain that there has not been any evidence to date, to safely identify a low risk cohort that can be safely discharged from ED without some form of stress testing. Based on this premise there may be inappropriate decisions made on testing or unnecessary admissions to hospital which not only have financial and resource implications but also consequences for the patient who may experience undue anxiety related to further investigations. This may not necessarily be the case in the New Zealand health care context as complaints towards health practitioners are covered by the Health and Disability Commissioner Act 1994. This Act was established to “promote and protect the rights of health consumers and disability services consumers, and, to that end, to facilitate the fair, simple, speedy, and efficient resolution of complaints relating to infringements of those rights” (Health and Disability Commissioner Act 1994, 2014, p. 11). As a result of this Act there is no avenue for litigation in New Zealand.

Chest Pain Clinics

The very nature of a CPC or observation unit (OU) as they are sometimes known is to screen patients for the presence of significant CAD. In many parts of the world these units are attached to the ED or coronary care unit (CCU) and assessment is done to exclude an acute coronary syndrome (ACS) in patients attending the ED with unstable chest pain. Unlike most CPCs reviewed in the literature, the researcher works in a CPC that is not connected to an ED or CCU, instead the clinic is attached to the outpatient department of a regional hospital. Referrals are accepted and triaged by the cardiologist and then booked for outpatient assessment and ETT at the CPC. Most referrals originate from GPs who wish to have their stable patient with chest pain investigated to confirm or rule out CAD. A thorough history and physical assessment is undertaken by the CPC specialist nurse and ETT performed if it is safe to do so. Selection criteria and procedure protocols are derived from the CSANZ (2010) guidelines on exercise testing. The contraindications, test end points, and interpretation of test results are guided by the ACC/AHA (2002) guidelines for exercise testing using the criteria for a positive test, as described in the previous section. In the researcher’s CPC if the test induced symptoms in the patient without ST changes it is classed as a positive test result. In the case of a patient exercising for >9 minutes with no symptoms and ST changes of < 1mm, then the ETT is considered equivocal. Once the ETT has been completed, the specialist nurse discusses the results with the cardiologist and together they decide on a plan of care. If results prove negative a letter is written to the referring GP and the patient is discharged. If the test is equivocal or

positive it is likely another test will be ordered; either exercise/dobutamine SE or coronary angiography (CA) and a letter is written to the GP outlining this decision. Treatment options are often recommended at this time, if the patient has any CVR factors.

The awareness of CVR, presenting symptoms and the pre-test probability of disease are all important considerations in the assessment of patients and the interpretation of results. The CPC specialist nurses provide education on CVR and lifestyle advice irrespective of the outcome of the test.

Cardiovascular Risk

Cardiovascular disease has been growing in prevalence around the world increasing mortality and morbidity rates to a point where it is predicted to exceed the rate of death from infectious disease within the next ten years. Alarming, the prevalence of CVD has extended to the developing countries with current statistics reporting that 25% of all deaths are now attributable to CVD (Levenson, Skerrett & Gaziano, 2002). This escalation of disease is thought to be related to the rising global population, which has a predicted 60% increase from 1990 to 2020, and also to the advances in health care, which has seen a reduction in death rates and increased survival from communicable diseases increasing population growth. Simultaneously, there have been social and economic changes that have exposed populations to the risk factors associated with CVD development, namely, smoking, fat consumption and hypertension (Levenson et al., 2002; World Health Organisation [WHO], 2011).

For this reason CVR assessment is a current New Zealand health priority (MOH, 2011) and aims to capture those at increased risk of developing CVD so they receive lifestyle information and/or medications to reduce their risk. When a person presents with symptoms suggestive of CAD such as chest pain or discomfort with exertion, a high CVR may increase the likelihood that their symptoms are related to heart disease. If coronary disease is suspected, a referral is usually made for further assessment.

Knowledge of a patient's CVR is therefore an important consideration in the assessment of the patient with chest discomfort and contributes to the decision to investigate for CAD. However, CVR alone has not been found to support the use of stress testing and clinical judgement and presenting symptoms remain important components (Schrock, Li, Orazulike & Emerman, 2011).

Cardiovascular disease is particularly prevalent in western society. There are recognised risk factors associated with development of the disease, some which are modifiable and some which are not (see Table 1.2)

Table 1.2: Cardiovascular Risk Factors

Modifiable	Non-Modifiable
Diet	Age
Smoking	Gender
Physical inactivity	Family History
Hypertension	
Hypercholesterolaemia	
High Glucose Levels	

CVR tables are used to estimate a persons' risk of developing CVD over a time frame, commonly five or ten years. The risk tables are designed for use in people who have no history of coronary disease and helps guide the practitioner with treatment decisions and lifestyle recommendations. There are several risk calculators in use around the world but it is the New Zealand Guidelines Group (NZGG) CVR tables, designed for the New Zealand population, that are used in this research thesis (NZGG, 2012). The New Zealand CVR tables are based on a five year absolute risk for CVD and CVR is divided into three groups, mild, moderate and high CVR. The risk categories are assigned a percentage as follows: mild risk < 10%; moderate risk 10 - 15%; high risk > 15%. For the purposes of this research, when a patient is recorded as having a CVR of 10% they are assigned to the mild risk group; for those with a CVR of 15% they are recorded to have a moderate CVR. It is important to note that CVR categories may differ depending on the country of origin, and some research refers to low and intermediate risk, rather than mild or moderate risk. In the researcher's study the terms low and intermediate may sometimes be used in place of mild and moderate CVR but they are considered equivalent.

Probability Analysis

The treadmill test is not a perfect tool and it is known to give false positive results particularly in women and low risk patients, or false negative results in the higher risk patient (Anderson, Murphy, & Balaji, 2014). This makes interpretation challenging, often leading to more invasive and costly tests such as CA or more worryingly, potentially missing a diagnosis in the high risk patient as stated in the seminal study by Detry et al. (1975). To minimise this risk, it is important to consider the probability of the disease existing in the individual before the test has been performed. This will help determine the accuracy of the results. This assessment of pre-test probability assists in the decision to proceed with a particular diagnostic test and helps

avoid unnecessary tests. Pre-test probability is based on the patient's presenting symptoms, physical examination and presence of CVR factors. In the patient who presents with typical symptoms of angina, their pre-test probability will most likely be calculated as moderate or high, depending on gender and age, and as a result, the predictive value of the test is increased. Post-test probability confirms the probability of the target disease being likely after test results are known (Di Censo, Guyatt & Ciliska, 2005).

Researcher's Interest

The researcher of this thesis has worked as a cardiology specialist nurse for a number of years and been involved with the CPC since 2006. Over the years the researcher has assessed a large number of patients with chest pain and mild CVR, and questioned the value of this test in this cohort as the diagnostic result appeared to be low, particularly in those with atypical symptoms. There was a sense that resources may be better utilised elsewhere. This was however, anecdotal evidence, and it was the wish of the researcher to establish whether local data supported the use of ETT in this cohort.

Research Question

What is the efficacy of the exercise treadmill test in patients with mild cardiovascular risk in a regional New Zealand population?

Research Aims

To determine the efficacy of the ETT in predicting the presence of coronary artery disease in patients with mild cardiovascular risk.

Ultimately, it may be possible to use the results of the audit to assist with local planning and delivery of the outpatient CPC service.

Conclusion

This introduction has discussed the rationale for this research and provided information on the classification of chest pain, the use of ETTs, and the role of the researcher's CPC. It has given an overview of CVR and the risk scores used to classify patients. The importance of pre-test probability and prevalence of disease has been briefly discussed to demonstrate how this can enhance the accuracy of the ETT and finally the researcher's interest has been identified and the question and aims of the research outlined. The overall structure of the thesis now follows.

Thesis Structure

Chapter One

Chapter one has introduced the background and rationale for this thesis and given an explanation of the function of the CPC and the role of ETT. It has provided information on angina symptoms, the challenge of chest pain assessment and the role of CVR.

Chapter Two

This chapter reviews the literature evaluated for this thesis. It begins with an explanation of the search strategy used, followed by four areas of research focus: The first reviews the literature pertaining to the assessment of symptoms associated with CAD i.e. typical and atypical symptoms, secondly, a review of the literature on CPCs is discussed; the third section reviews research related to the use of clinical prediction tools; and finally, research focused on the ETT as a diagnostic tool is examined.

Chapter Three

The methodology used in the research is discussed and includes an explanation of the research design, the research question, the aims, setting, patient sample, and the ethical and cultural considerations taken in preparation for this research. Reliability and validity are discussed in relation to the use of ETT and the researcher's collection of data. Data analysis methods are also described.

Chapter Four

This chapter provides a description of the results and analysis of the research using both descriptive and inferential statistics. It contains six sections, cardiovascular risk and symptoms; treadmill results for all patients; management of positive and equivocal treadmill results; results of angiography; six month re-presentation rates; and finally, the presence of disease according to CVR and symptoms. Inferential statistics are then provided and highlight the CA results for those with typical and atypical symptoms

Chapter Five

A discussion of the results is contained in this chapter and is condensed into four sections which includes; symptoms, ETT results and CVR, re-presentation rates, and outcomes according to CVR and symptoms. The implications of the results are discussed and the study limitations explained.

Chapter Six

The final chapter summarises the main findings and concludes the thesis. This includes recommendations for further research.

Chapter Two

Literature Review

Introduction

In the patient with mild cardiovascular risk, screening for CAD presents some challenges. In the first instance several factors need to be considered in order to use the most reliable and cost efficient test. In New Zealand, cost efficiency is crucial to maintaining a well functioning public health system. Within the fiscal constraints of this system it is important to ensure that patients receive the best and most appropriate care utilising diagnostic tools that give accurate results. Fihn et al. (2012) discuss the importance of reducing harm and discomfort to patients and avoiding tests that give false positive or false negative results; for this reason it is essential to realise the value of this commonly used test. The ETT is best used in the patient with a normal resting ECG, who is able to exercise, and is often chosen because of its cost effectiveness and relative ease of use (Detrano, Gianrossi & Froelicher, 1989). However its diagnostic accuracy in some patients, such as those with mild or low CVR has been the subject of scrutiny for many years. Chest pain clinics were originally established to assess patients considered at low risk of ACS, who presented to ED with chest pain. The researcher's CPC is different in this regard as it involves assessment of an outpatient population with stable chest pain, referred by their GP.

This chapter will provide a review of the literature on exercise stress tests for diagnosing CAD with most of the literature sourced from international studies. A search strategy is provided and the chapter is divided into three sections. The first views the evidence regarding typical and atypical symptoms associated with CAD, the second explores the function of CPCs and the third will focus on the ETT as a tool for the assessment of CAD.

Search Strategy

There is an abundance of research related to the investigation of CAD and in the first instance several databases and search engines were used including MEDLINE, CINAHL, PUBMED, GOOGLE SCHOLAR, and GOOGLE using the terms coronary disease AND diagnosis, ischaemic heart disease AND diagnosis, ischemic heart disease OR diagnosis, cardiovascular risk assessment OR stress tests, cardiovascular risk AND stress test, diagnosing heart disease, and prognostic value of exercise tests. This research retrieved thousands of research articles, most of which were unhelpful. Free online cardiology journals produced many useful results as did hard copy journals from the hospital library. Cardiology journals and research articles are also received via email regularly, many of which were useful. The most significant contribution was acquired by reading the reference list of research papers of interest and with the use of

Google, PUBMED and the hospital librarian, these were procured with relative ease through an interloan process.

Typical and Atypical Symptoms

Patients may present with chest pain which is typical or atypical of angina. Assessment of atypical chest pain is challenging. Amsterdam et al. (2010) advise that a significant proportion of patients present with atypical symptoms which may in fact be angina equivalents. These complaints may be described as arm discomfort, jaw ache, and fatigue and are more prevalent in women, patients with diabetes and the elderly (Gibbons et al., 2002; Gulati, Shaw, & Merz, 2012; Kohli & Gulati, 2012). For this reason they need to be considered with a degree of suspicion and further assessment is usually necessary.

In the primary care setting, the first encounter for the patient is often the GP, who, after considering the differential diagnoses and ruling out ACS or other life-threatening disease, will make a clinical decision for further tests based on CVR, the resting ECG and a physical examination (McConaghy & Oza, 2013). Historically, the definition of typical symptoms was derived from the male population, as early research was based on this cohort. As a consequence, this may not reflect the experience of the female population who not only present with atypical symptoms, but also at an older age than men (Amsterdam et al., 2010). In the USA, the number of deaths per year from CVD is greater in women than men and it is possible that the consequence of suffering atypical symptoms contributes to these statistics as appropriate investigations may be overlooked or delayed (Kohli & Gulati, 2010).

Schillinger et al. (2004) undertook a study in a Viennese ED to discover the predictive value of atypical features of angina in excluding ACS and major adverse cardiac events (MACE) which they listed as any CVD related death, coronary artery bypass surgery (CABG), MI or percutaneous coronary intervention (PCI). The focus for the study was on the patient's presenting symptoms, CVR and medical history and did not include ECG assessment or admission blood tests. The reasons given for this study were the increasing limitations on health resources and the associated high cost of intensive monitoring of possible ACS patients. Researchers hoped to identify patients as having low or high risk of a coronary event and then manage them accordingly, in a more cost efficient and timely manner. This was a prospective cohort design conducted over eight months, with 1288 patients included with an acute chest pain presentation. Seven pre-determined criteria were used to classify the patient as having typical or atypical angina symptoms and included location, character, radiation of pain, appearance of pain (whether induced by exercise, sore to touch or associated with cough), dyspnoea, nausea or diaphoresis, CAD history, and whether two or more risk factors of CAD were present (smoking, diabetes, hypertension, hyperlipidaemia, family history in first degree

relative, and obesity). Likelihood ratios and the positive predictive values (PPVs) of typical and atypical symptoms were calculated to predict or exclude acute MI (AMI) and MACE (which included MI, PCI, CABG, and death from a cardiac event) within six months. They were able to collect follow-up data on all patients for AMI and death at six months, and found that 13% experienced AMI, while 19% had MACE, which included those with AMI. A PPV of 94% was seen with the presence of four or more of the atypical symptom criteria for excluding AMI (95% CI 0.91 - 0.96) and 93% PPV for excluding MACE at six months (95% CI 0.90 – 0.96). The authors concluded that when assessing low risk patients with an acute presentation of chest pain atypical symptoms were able to identify low risk patients for early discharge.

A similar conclusion was drawn by Nawaz, Ayub and Raza (2013) who conducted a retrospective observational chart review of ED patients seen in an OU with atypical symptoms to ascertain if stress testing in a low risk cohort was necessary. Patients had no prior history of CAD and normal ECG and troponins (a protein found in the blood when heart muscle has been damaged); however, a CVR was not done, instead, patients were risk stratified according to the number of CVR factors and also the Thrombolysis in Myocardial Infarction (TIMI) risk score. The TIMI risk score was developed as a simple tool to assess the risk of death and ischaemic events in a patient presenting with unstable angina or non-ST elevation MI (NSTEMI). It is used as an adjunct to clinical assessment to help guide decision making in regard to medical therapy and management of patients (Antman et al., 2000). Exercise tests using imaging techniques were used in 48% of patients and 2.6% (2 patients) had a positive result followed by a normal coronary angiogram. The study found that due to a low rate of disease and high false-positive rate, patients could be managed safely with initial observation and early discharge thereby saving the patient from undergoing unnecessary tests and the associated costs, and avoiding the risk of a false positive result.

Vieweg, Alpert, Johnson and Hagan (1977) found ETT a reasonable predictor of CAD in men presenting with typical chest pain. The study was conducted on men with normal baseline ECG, no history of hypertension or previous CAD. All had a presentation of chest pain considered suggestive or typical of angina and all participants underwent ETT using the Bruce protocol. Coronary angiography, the gold standard for diagnosis of CAD, was performed on all of the men with positive ETTs and also on those with a negative result who had achieved at least 90% of their maximum predicted target heart rate. This resulted in the final cohort of 114 men. Two groups of patients were formed, group A with coronary disease, defined as a coronary narrowing of 70 percent or more in one or more vessels and group B without any coronary disease. Those with mild coronary disease were not included in the study. There were 69 patients in group A. Fifty-nine percent (41) had a positive ETT; 14% (10) had a negative ETT with achievement of 90% of their age predicted target heart rate; and 17% (12) had a

negative ETT without achieving 90% of their predicted heart rate. An inconclusive ETT result was seen in 8% of patients with only 50% of them achieving a 90% target heart rate. In group B, (45 patients); 9% (4) had a positive ETT result and 69% (31) had a negative result at a 90% predicted target heart rate; 18% (8) had a negative ETT but did not achieve a 90% predicted heart rate; and 4% (2) had an inconclusive test with a 90% predicted heart rate response. A positive ETT was defined as horizontal or down-sloping ST segment depression of 1mm or more 80 ms after the J point and inconclusive if the ST segment was depressed 0.5 to 0.75mm. Less than 0.5mm was deemed normal. When the researchers looked at the men in group A who had a true positive result and those with a false negative result, they established a sensitivity of 80.4% for this cohort. In group B, specificity was established to be 88.6%. They found, when they conducted a review of the literature matching their cohort, that the PPV of ETT was very similar, at 91.9% and 91.1 % respectively. While this study is over thirty years old and biased to a specific cohort, it is interesting to see the results in this traditional, high risk cohort. However, assessment of CVD is required in women and in patients presenting with atypical symptoms so it is necessary to look at the value of ETT in a varied cohort to understand its true value. In the discussion on limitations Vieweg et al. (1977) acknowledged that the high sensitivity is attributable to this highly selected population; that is, all participants were male with symptoms of chest pain and recognised that if the population studied had a lower prevalence of CAD, for example those without typical symptoms, or female participants, ETT would be less useful. They suggested that if the test was being done for anything other than the evaluation of chest pain, the predictive power would likely be reduced.

Chest Pain Clinics

Over the years, hospital admission rates for the investigation of chest pain have escalated, with greater than three million patients being admitted to hospitals in the USA for chest pain assessment in one year and over 8 million annual presentations to ED with symptoms suggestive of ACS (Blomkalns & Gibler, 2005). Due to the length of stay in hospital and the costs associated with these admissions, CPC and OUs have been developed and found to be cost efficient (Gaspoz et al., 1994; Quin, 2000). Not only did development of CPCs address the financial ramifications of hospital admissions, it also expedited assessments in low risk patients who avoided a lengthy stay in hospital and received a faster diagnostic result.

Chest pain clinics vary in design depending on location and country; most being found attached to EDs and CCUs, or in a medical outpatient area. Most units use a non-invasive test such as ETT to assist in the risk assessment and stratification of patients so that an accurate and reasonable diagnostic outcome is achieved in a timely manner. Typically, patients with a high risk of an ACS are excluded from referral to them, instead going straight to hospital admission and CA.

Over the years research has been conducted to assess the effectiveness and safety of these clinics in stratifying CVR in patients presenting to ED with chest pain. While such clinics have been in existence for many years, they have been slow to develop in New Zealand, but this is gradually changing. In a recent New Zealand study, Mazhar, Killion, Liang, Lee and Devlin (2012) reported on the safety and efficacy of a chest pain unit (CPU) established at Waikato hospital to quickly assess mild and moderate risk patients, and to exclude ACS. High risk patients were excluded from the study. A prospective audit was completed of patients presenting with chest pain during March 2005 to July 2009. All the patients were assessed using ECG, elevation of troponins and ETT, if appropriate. Three month re-admission rates and one year mortality statistics were assessed also. Of the 2358 patients seen in this study, 82% were diagnosed with non-cardiac chest pain, 74% underwent exercise testing and 2.7% were readmitted within three months, most for non-cardiac reasons. The rate of negative ETTs was 78%, positive results 13% and inconclusive 10%. Of the patients who had a positive ETT, 69% went on to have CA with the results showing a 30% false positive result. Only 1% of patients were readmitted with ACS and there were no cardiac deaths at one year in those discharged with non-cardiac pain. The median length of stay was 22 hours. This study confirmed that a CPU with ETT was a safe and effective way of managing patients with chest pain in those with mild to moderate CVR. Study limitations were not discussed in detail and there was no cost analysis other than a conclusion that savings were made. An argument could be made that due to the high number of negative tests some of the patients with mild CVR could have been discharged directly from ED, without undergoing ETT and with advice for review by their GP, thereby avoiding a 22 hour stay in hospital. Also, the definition of a positive CA was not given so it is difficult to fully appreciate the significance of the results as in some studies a positive angiogram is defined as a coronary narrowing of greater than or equal to 50% in any main epicardial coronary vessel (Jones, Pothier, Blackstone, & Lauer, 2004; Morise & Diamond, 1995) while in others it is defined as a coronary narrowing greater than or equal to 70% (Napoli, 2014; Vieweg et al., 1977). This may affect the statistical analysis and results by increasing or decreasing the number considered to have CAD. Overall, the study is positive and supports the use of the CPU in the patient presenting acutely with mild to moderate CVR.

In a similar study in Belfast, Ireland, Dougan et al. (2001) undertook a prospective study of a Rapid Access Chest Pain Clinic (RACPC) to evaluate clinical outcomes, morbidity and mortality data at three months post-discharge, and the cost-effectiveness of the RACPC service. Their study confirmed that the RACPC improved waiting times for assessment of patients, reduced unnecessary hospital admissions, and safety was not compromised. This resulted in cost savings and improved efficiency of the service.

By contrast the study conducted by Khare, Powell, Venkatesh and Courtney (2008) in the USA, analysed the costs incurred from CPC patients who had mild CVR with a positive or equivocal ETT result which then resulted in a negative CA. The study used a retrospective observational method with nine months of data and included 1194 patients who were admitted to the OU meeting the criteria of low CVR, no previous history of significant CAD, no chest pain, negative ECG for ischaemia, normal troponins on first assessment, and a normal chest xray. They were subsequently excluded if the second troponin test was elevated or if any of the other criteria had changed. Exercise stress echocardiography was the predominant form of stress test used (80.9%), followed by adenosine thallium testing (12.2%), ETT (5.1%) and dobutamine SE (1.8%). The choice of test was dictated by the availability of each test and clinical indications. Cardiologists viewed all stress test results and determined if they were positive, indeterminate or negative using established criteria. A thorough description of what constituted a positive or negative result was given.

The primary outcome was the number of patients who had positive or indeterminate stress test results and negative CA. Of those who underwent CA, 64% had a negative CA result following a positive stress test and 92% had a negative CA result following an indeterminate stress test. In a secondary analysis, they compared these data with patients who had negative stress test results and looked at clinical characteristics, all costs associated with the care, procedures and treatment for each patient, and the length of stay in the hospital. Interestingly, SE has a higher sensitivity and specificity than ETT (Arbab-Zadeh, 2012) and despite this, the rate of negative results were high. The research found that costs attributable to the positive and indeterminate group were five times greater than those with a negative result and suggested that in the low CVR population alternative risk stratification processes should be investigated.

According to Anderson et al. (2007) in the American College of Cardiology/American Heart Association (ACC/AHA) 2007 guidelines for the management of unstable angina and NSTEMI patients, it is recommended that stress tests be performed on patients within 72 hours of ED presentation. However, Napoli, Arrighi, Siket and Gibbs (2012) were concerned that a reported true positive result of stress tests in a CPU environment were as low as 2 to 7%. Their study sought to establish whether shared management of low risk patients by ED doctors and cardiologists, within a CPU context, was efficient and safe, and whether the rate of stress tests could be reduced. The main method of stress testing was nuclear stress tests followed by SE, and only 5% underwent ETT. They assessed the rate of MACE at 30 days in all patients, including those who had or did not have a stress test. This study used an observational prospective approach of consecutive patients entering an urban CPU. Apart from the study authors, all the ED doctors and cardiologists were blinded to the purpose of the study and 1063 patients were enrolled 51% which were female. The TIMI risk score and Diamond and

Forrester (D&F) CAD likelihood score was recorded for each patient. Stress testing was undertaken in 51% of the cohort and the decision for this was made predominantly by the consulting cardiologist. Of the patients who underwent stress testing only 5.7% were positive, 20.8% of those were referred for CA. Thirty day MACE was 0.1% (1 patient) and resulted in coronary revascularisation 30 days later. Results showed that the incidence of MACE was lower than that reported in previous studies and the 51% utilisation of stress tests in their CPU cohort was also lower than previous CPU research findings. Researchers concluded that this study showed that selective stress testing at physician discretion is safe and cost effective. While this is a reassuring study it is worthwhile noting that most of the stress tests were done with the addition of imaging which increases the sensitivity and specificity of these tests (Fihn et al., 2012). Not all localities have these resources available and therefore decisions are based on tests that may have lower accuracy. The authors discuss several limitations of the study such as omitting information on the character of pain and other presenting symptoms and not including information on how the doctors made decisions regarding who to exercise and who not. They also acknowledge that selection bias may have contributed to the cohort all being at low risk for ACS as those with an intermediate risk were admitted straight to hospital thus reducing the rate of ACS seen in the CPU cohort.

Patients are usually assessed in a CPC because they are experiencing some form of chest discomfort and it is these symptoms along with their level of CVR that helps guide clinicians in their care and management. Jones et al. (2004) studied the prognostic significance of chest symptoms on all cause mortality by looking at the outcomes in patients (n = 10,870) referred for a symptom-limited exercise test. The primary endpoint of all cause mortality (death from any cause) was gleaned from a social security death index. They used propensity matching to control for differences in characteristics of the different groups studied and to minimise referral and selection bias. Of eligible patients 38% were asymptomatic, 6% had typical angina symptoms, 31% had atypical angina, 17% were considered to have non-anginal chest pain and 8% had dyspnoea. The study found that in patients who had chest pain, the existence of typical angina symptoms increased the risk of mortality when compared to patients presenting with non-anginal chest pain but not in patients who had atypical chest pain. They therefore concluded that while presenting symptoms were an important consideration in whether or not to refer patients for stress testing, an increased CVR was a more significant indicator of prognosis once the exercise test results were available.

Poldervaart et al. (2013) investigated the value of stress testing after using a risk stratification tool in patients presenting to ED department with chest pain. They devised the "HEART" tool, an acronym for History, ECG, Age, Risk factors and Troponin which attributes a score (between 1-10) to each component which then places the patient into low, intermediate or high risk. They

conducted a prospective validation study of the HEART score in 248 patients who underwent exercise stress testing to assess whether knowing the score of a patient in the first instance negated the added value of the stress test in the prediction of MACE (AMI, PCI, CABG, medical management of stable CAD, and death from any cause) at six weeks post-presentation. Bicycle ergometers were the stress modality utilised, patients with abnormal ECG findings and chest pain were not included in this study. The standard interpretation of exercise ECGs using the ACC/AHA exercise treadmill guidelines (2002) was used to define positive, negative and inconclusive tests. The authors concluded that exercise ECG provided only a small contribution to risk stratification if the HEART score is known as 50% of tests were inconclusive and rates of false positives tests were high. The group receiving the most benefit would be the intermediate risk group (54.8%), a finding concordant with the recommendations of Gibbons et al. (2002). For those patients in the high risk group with a positive test there was a 50% risk of MACE, so the suggestion was that non-invasive tests were not contributory in this cohort or in the low risk group where there were no positive results and a 2.4% incidence of MACE. As for study limitations, the six week follow up for MACE was short, and a longer time period may give greater confidence in the results. These studies support the use of assessing CVR, symptoms and pre-test probability of disease before deciding the usefulness of non-invasive testing.

However, in contrast, Schrock et al. (2011) found that clinical judgement was better than risk factor assessment for determining the need for stress testing. A retrospective observational cohort design was used in this study but in contrast to the above study, a CVR score was not assigned to patients: instead the number of risk factors was documented. Also the authors documented that 22% of the cohort (n = 4026) had prior disease. They concluded that while a greater number of risk factors was associated with an abnormal stress test result in all patients, there was not a significant difference in the number of abnormal tests or a relationship between risk factors and abnormal tests and therefore recommended that clinical judgement was of most value in determining the need for stress tests.

Hermann, Weingart, Duvall, and Henzlova (2009) conducted research to assess the usefulness of routine stress tests in low risk patients, under the age of 40, who were seen in an ED with symptoms suggestive of CAD. They used a retrospective observational method that identified 220 patients between the ages of 23 to 40 years who presented to an ED with possible ACS. Patients were excluded if they had a prior history of heart disease, evidence of MI or ischaemia on ECG, a blood test showing elevated cardiac enzymes, or cocaine use. Only 6 patients (2.7%) had a positive stress test and four of those went on to CA with a negative result. Of the two remaining, one refused CA and the other had no further tests at the hospital research centre. The study found that routine stress testing, in the evaluation of this cohort of young, low risk

patients, provided no additional diagnostic value in the assessment of CAD, and that of the four tests which had been positive, suggesting presence of disease, all were false positive results. Of note, they used three different exercise modalities, radionuclide perfusion imaging 73%, ETT 22% and SE 5% and interestingly the six positive results came from the exercise radionuclide perfusion scans which have a higher sensitivity and specificity than ETT alone. Researchers in this study hypothesised that routine provocative stress testing may not be justified or add value to the management of young, low-risk patients being evaluated in an ED setting, particularly if the post-test probability of disease is no greater than the pre-test probability of disease. This was also confirmed in the study by Schillinger et al. (2004) who found that 35% of study participants under the age of 40 years old, with four or more atypical features of CAD, had a PPV of 98% (95% CI 0.96-1.0) for excluding acute MI and MACE. Hermann et al. (2009) suggest there is a need for additional study in this area particularly with regard to the use of risk stratification tools to identify those patients at very low risk of ACS. However, they also suggest that regardless of the findings it is unlikely to change practice while physicians feel at risk of missing any patient with CAD. This most likely reflects the litigious environment in the USA and possibly accounts for the continued practice of investigating patients at very low risk despite evidence to the contrary.

Hurune, O'Shea, Maguire and Hewagama (2013) found the ETT to be a useful diagnostic tool in their remote Australian location with no local cardiology service available and a high indigenous population (47.5%). In a cohort of 268 patients, they conducted a retrospective audit that looked at the effectiveness of ETT for diagnosing CAD in this isolated population. The average age of patients was 49 years but many had numerous CVR factors, unlike those patients in the Hermann et al. (2009) study. Clinical outcomes were recorded for 24 months post ETT and included subsequent CA showing evidence of CAD, re-admissions to hospital for further chest pain investigation or diagnosis of acute coronary syndrome. They found that while the indigenous patient was younger, had more chronic diseases and were more likely to be of female gender, the PPV of 48.1% and negative predictive value (NPV) 96.5% were similar in both indigenous and non-indigenous groups. However there was a higher rate of inconclusive results (< 85% predicted target heart rate achieved) in the indigenous group due to limited exercise capacity and these patients were therefore referred for SE. The overall inconclusive rate was 33.6%, with just over half of those being from the indigenous group. Positive results for the entire cohort were only 11.6% and of those who went on for CA, 52.9% were deemed positive. Risk of re-presentation at 12 and 24 months for both ACS and chest pain were increased as ETT results moved from negative to positive, and incidence was slightly higher for indigenous patients but did not reach statistical significance. The study reported the ETT in terms of its sensitivity, specificity, positive and negative predictive values. Of all patients

tested, sensitivity was 61.9% and specificity 94%. They concluded that if maximal stress (>85% target heart rate) was achieved the ETT was a worthwhile, non-invasive screening tool in this remote setting and utility compared favourably with other literature on ETT performance.

Sekhri, Feder, Junghans, Hemingway and Timmis (2007) studied the efficacy of RACPCs in Britain by comparing ACS incidence in patients with a diagnosis of angina, those diagnosed with non-cardiac chest pain, and the population in general. The study was a multi-centre cohort study from six British hospitals. It involved nearly 9,000 patients and follow up was for a median of 2.57 years. Primary endpoints were deaths due to CHD or non-fatal MI, and hospital admission for unstable angina. Unsurprisingly, the study found that patients with angina had a higher risk of death due to CHD or non-fatal ACS than the general population or those with a non-cardiac chest pain diagnosis. However, an important result was that 32.4% of patients with a non-cardiac chest pain diagnosis, also reached the primary endpoint of death due to CAD or ACS and compared to those with angina, they were younger, were of south Asian origin, and over 80% had normal ECG's. They also stated that a very small proportion of the non-cardiac patients had typical symptoms of angina and an abnormal ETT. Of interest, they do not explain why these patients were not investigated further but it may be possible no explanation could be found. Whilst the study "confirmed the prognostic validity of differential diagnosis within RACPC's" (Sekhri et al., 2007, p. 460) the results raised concern that misdiagnoses were made. The authors suggests several reasons for the apparent misdiagnosis, one being that most patients had recent onset of symptoms within 4 weeks to six months of presentation, and therefore they may have had unstable plaques that were prone to rupture causing MI. They also found there was inadequate prescribing of secondary prevention medications such as statins. It went on to highlight the need for improvement in diagnostic measures suggesting the use of risk scores and further non-invasive testing. The study did not have information on family history or lipid measurements (two important CVR factors) and a more informed CVR assessment may have reduced the small but concerning results of misdiagnosis.

Clinical Prediction Tools

In a Canadian study, Hess et al. (2012) took a different approach in their management of chest pain patients. In their study they used a prospective observational cohort methodology involving three EDs and 2,718 patients over nearly three years. They were motivated to develop a clinical prediction tool to identify patients at very low risk of CAD so they could be considered for discharge from ED rather than admitted for ongoing tests that are costly, time consuming and would potentially add little additional value to the diagnosis. Their tool identified patients over 50 years of age with no known clinical indications of CAD. In this case the patient was deemed very low risk and considered for discharge from ED for follow up on an outpatient basis within 30 days. There were 64 variables used in the assessment of patients and

these were recorded on case record forms designed specifically for the study. Primary outcomes were acute MI, coronary intervention, or death from cardiac cause, or unknown cause, within 30 days of presentation regardless of whether they occurred in the hospital, ED or after discharge. Results suggested that the clinical prediction rule used identified very low risk patients for ACS who could be discharged early. They recommended a prospective multicentre study was needed to validate the rule. Methodology included completing standardised data collection forms before any testing took place and recursive partitioning was used to develop the rule which was validated with 5,000 bootstrap replications. If using the tool, the authors stressed the need for outpatient follow up within 30 days of discharge and despite the pleasing results there was a sense of cautiousness in recommending the tool before further validated testing had taken place.

Meyer, Mooney and Sekera (2006) were also motivated to develop a care pathway protocol to discharge low risk patients safely and quickly from ED, and they did this by referring low risk chest pain patients for outpatient ETT within 72 hours as per ACC/AHA guidelines on the management of stable angina (Fihn et al., 2012). This observational study involved 979 consecutive patients and the primary outcome was the rate of death or MI in the six months following discharge and outpatient stress testing. The predominant stress test was ETT. As a secondary analysis they also looked at rates of coronary intervention and subsequent ED visits for chest pain within six months. Of those patients with low risk who had completed the six month follow up 2% had coronary intervention, 0.1% suffered an MI within one month, and 0.2% within six months, 0.7% had a normal stress test but underwent CA within six months and 0.6% returned with ongoing chest pain within six months. Admission rates were reduced from 31.2% to 26.1% and it was considered to be a safe and practicable protocol.

The seminal research of Diamond and Forrester (1979) was undertaken due to the complexity of diagnosing CHD and the limitations of the various tests available at the time. They conducted a literature review to determine the significance of the pre-test probability of CAD using patients between 30 and 70 years of age and considered gender, age and presenting symptoms to predict the likelihood of disease. Four diagnostic tests were reviewed for sensitivity and specificity and ETT was one of them. Bayes' theorem was used as analysis of conditional probability, which accounts for pre-test probability based on disease prevalence in the population in question (Diamond & Forrester, 1979). The review discussed the low predictive accuracy of positive tests in low risk individuals and the importance of gathering information on disease prevalence in the target population in addition to sensitivity and specificity to enhance predictions and assist the calculation of post-test likelihood of disease. They discussed the limitations and biases inherent in the literature reviewed and accounted for some of this by pooling rather than averaging data. Overall, they found that knowledge of pre and post-test probabilities was of value in aiding clinical diagnosis and this has informed practice since.

However, Genders et al. (2011) undertook to validate Diamond and Forrester's work by prospectively collecting data on patients presenting to hospitals with chest pain but no history of CAD and who were referred on to CA. They discovered that the original model over-estimated CVR particularly in women. They updated and reclassified the original predictions of age, gender, chest pain and included hospital setting to improve the model predictions. The methodology involved a CAD consortium from the Assessment of Imaging in Medicine (EuroAIM) so they were able to perform a large pooled analysis of the data to increase the power and external validity of the results. Validation included calibration-in-the-large, which checks that the average prediction is equal or close to the observed outcome, recalibration, and re-estimation which compares the predictor effects in the new data with those in the original data. The discussion describes the strengths and weaknesses of the study, the limitations, and clinical implications. The authors explain that the clinical value of diagnostic tests are dependent on pre-test probability and by using this revised and updated Diamond and Forrester model, a more precise estimate will be established which will improve decision making on further management. They advise that in the patient with a very low risk pre-test probability an expectant approach, with no testing, is justified and in those with high risk an invasive approach is best. In the intermediate pre-test probability patient a negative test is reassuring for ruling out significant CAD but a positive result would benefit from further testing. This model does not account for other CVR factors such as diabetes, smoking, family history, ethnicity and dyslipidaemia and it acknowledges that these will need to be considered in future models. Similarly, Patel et al. (2010) suggest that age, gender and chest pain symptoms are the strongest predictors of disease and that reducing the number of variables helps to simplify the tool for easier use.

These two studies, the original and the contemporary updated version, support the predictive power of pre-test probability. Both conclude that non-invasive testing of low pre-test probability patients give little value in determining management due to the limited accuracy of the results.

Exercise treadmill tests

Detrano et al. (1989) studied the diagnostic accuracy of the ETT by conducting a meta-analysis covering 22 years of research. This extensive study focused on exercise-induced ST segment depression as a measure of diagnostic accuracy but acknowledged the weaknesses of using this measure in isolation. Using sensitivity and specificity they calculated the mean measure of 1 mm of ST segment depression showed 68% sensitivity and 77% specificity but that a large variability was possible. So while many patients with 1 mm of ST depression who go forward for CA will have a stenosis (narrowing) in at least one vessel, it is likely to miss a significant proportion of patients with stenoses who had no ST depression on exercise testing. They

suggest that other factors such as Bayes' theorem and clinical judgement should be used to increase accuracy and they recommended further research be focused on the heart rate adjustment for ST segment depression as this looked to be an important addition to improving diagnostic accuracy.

More recently Patel et al. (2010) found that an improved risk stratification approach was necessary to increase the diagnosis of CAD by CA. Their study of over 398,000 people resulted in just over one third of participants having obstructive CAD, defined as a 70% or greater luminal narrowing of a major coronary artery or greater than or equal to 50% narrowing of the left main stem. This research was conducted by gathering data from a national cardiovascular disease registry in the USA that included 663 hospitals. They analysed results on patients with no prior history of CAD, with and without angina symptoms, who underwent CA following a non-invasive test. Several stress test modalities were included, ETT being one of them, and they correlated findings according to patient demographics, risk factors, and symptoms. In 83.9% of patients who had some form of non-invasive test prior to CA, 68.6% were positive. There was a small increase in the amount of obstructive coronary disease found in those with a positive non-invasive test compared to those who had no prior testing, 41% and 35% respectively and the rate was also higher than those with an equivocal and negative non-invasive test. Their study calculated the CVR of patients using the Framingham ten year risk score and used low, intermediate and high risk categories. The diagnostic yield of CA was higher in those with greater risk scores and for those who actually had angina symptoms. Researchers stressed that the best indicators for disease remain the traditional risks, which are being male, of older age, smoking status and the presence of diabetes, hypertension or dyslipidaemia. In light of the large number of hospitals included in this research there are several limitations that were acknowledged by the author's. These included a lack of information concerning the type of stress testing undertaken; the lack of information of patients assessed but who did not have CA; the variable interpretation of CA findings related to assessment by different physicians; and the underestimation of risk scores as lipid levels and blood pressure measurements were assigned by the authors.

Miller (2008) chose a different perspective when he evaluated the prognostic accuracy of stress tests and found that diagnostic accuracy was limited to only those patients who proceed to CA. He found that prognosis was able to be assessed in a larger cohort of patients by looking at clinical outcomes such as duration of exercise, blood pressure response to exercise, chronotropic incompetence (the inability of the heart rate to increase with exercise as expected) heart rate recovery post-exercise, and presence of ventricular ectopy. While Miller (2008) acknowledged that the diagnostic evaluation of ETT also provides prognostic information, like Detrano et al.

(1989) he suggested that to enhance the power of the results, prognostic variables during exercise testing should be considered.

Banerjee et al. (2012) acknowledged the varying information on the accuracy of non-invasive tests and conducted a systematic review and meta-analysis of prospective studies that included all types of exercise test modalities (bicycle stress tests, bicycle stress echo, treadmill tests, treadmill stress echo, and exercise myocardial perfusion scans) compared with CA, in patients with no prior history of CHD. They included 34 studies comprised of 3,362 patients and found that accuracy of exercise tests varied depending on age, clinical history, gender, the prevalence of CHD and modality of the test. As several different diagnostic modalities were reviewed, results showed that certain tests were more beneficial in certain patient groups. The overall finding was that ETT is more useful in excluding CAD than confirming it, but they felt it a worthwhile tool in individualising the diagnosis of CAD. Likelihood ratios, sensitivity and specificity were used along with pre and post-test probabilities and confidence intervals. The power of this review is in the numbers of participants overall and the variety of studies making the data more robust.

Southard, Baker and Schaefer (2008) compared ETT with SE to assess the sensitivity of ETT to predict significant CAD and support the recommendations that ETT is a valuable initial test to risk stratify patients presenting with chest pain. They identified 3,680 patients who had completed an ETT and SE via a retrospective review of patient records with data spanning over seven years. They excluded patients with non-diagnostic results and categorised the remaining 3,098 patients into two groups, one achieving six minutes or greater of exercise and the other not achieving six minutes of exercise, both using the Bruce Protocol. The two groups were further divided according to whether the stress test result was positive or negative. Those patients with a negative ETT but a positive SE made the final cohort and were then assigned into a subset based on whether CA was performed. The patients who had significant CAD on angiography were classified as those with a true false positive ETT. Results showed that in patients with chest pain and a normal baseline ECG, who are able to exercise for at least six minutes on ETT, the false negative results were generally found in patients without critical CAD disease. They therefore concluded that the ETT is an adequate and reliable test in this cohort and SE, being a more expensive test, should be used in those patients with abnormal resting ECGs or in those unable to exercise adequately. This research demonstrates the significance of achieving an adequate workload (six or more minutes) to increase the sensitivity of the test.

Clinical guidelines are another consideration when reviewing literature on exercise testing although they vary in recommendations depending on the country of origin. Gibbons et al. (2002) found a wide variation in the diagnostic accuracy of ETT in their review of the 2002

ACC/AHA guideline update on exercise testing. A meta-analysis was performed on studies totalling 11,691 patients with no prior history of MI and reported a mean sensitivity of ETT of 67%, and specificity of 72%. They acknowledged a workup bias in many of the studies reviewed where patients were included in the study based on their test results. However, they stressed that the analysis still provided the most reasonable account of the diagnostic accuracy of ETT. They also reported a few studies without workup bias which demonstrated a sensitivity of 50% and specificity of 90% indicating there is a reasonable variation in the accuracy of stress testing. These guidelines recommend ETT as the initial test for evaluating CAD in patients with moderate CVR. By contrast, the National Institute for Health and Clinical Excellence (NICE) guidelines for chest pain assessment (2010) state that the ETT should not be used to diagnose or refute stable angina in any patients without a known history of CAD. This difference of opinion reflects the complex nature of diagnosing CAD and the myriad of confounders that need to be considered when undertaking assessments on patients who present with different clinical histories and CVR factors.

Conclusion

To conclude, this literature review has comprised a number of studies selected to assist in the understanding of the ETT as a diagnostic tool for the assessment of patients presenting with chest pain. For patients with mild CVR there are differing opinions as to the usefulness of the ETT for diagnosing CAD related, in part, to the predictive value of the ETT as a modality for identifying CAD, and the pre-test probability of disease of the patient being assessed.

Evaluation of presenting symptoms is important as research suggested that atypical symptoms in a low risk patient did not have a high diagnostic yield and was associated with a high false-positive rate (Nawaz et al., 2013; Schillinger et al., 2004). With this in mind, it is also important to be aware of atypical symptoms that may represent “angina equivalents” seen most often in women and patients with diabetes, as these warrant further investigation (Amsterdam et al., 2010). The assessment of CVR and pre-test probability helps to identify this higher risk cohort.

The development of CPCs based in ED departments have been found to be a safe and economic alternative to hospital admission for the early evaluation of acute CP patients with mild CVR (Dogan et al., 2001; Gaspoz et al., 1994; Mazhar et al., 2012). However it is important to be aware of the potential for misdiagnosis (Sekhri et al., 2007) and to reduce this possibility assessment of CVR should be undertaken and pre-test probability considered (Banerjee et al., 2012; Hess et al., 2012; Meyer et al., 2006; Patel et al., 2010).

The following chapter will describe the methodology used by the researcher to understand the efficacy of the ETT in the mild CVR population from a regional New Zealand population.

Chapter Three

Methodology

Introduction

Nursing research is no longer a foreign concept found only within the auspices of academic institutions, rather it is a practice open to all nurses who have questions to answer about the care they deliver within their area of practice. Evidence-based nursing emerged to strengthen and support the decisions that nurses made about patient care, to ensure that practice is based on sound, systematic inquiry and, as stated by Polit and Beck (2008) “The ultimate goal of research is to develop, refine, and expand a body of knowledge” (p. 3). Thus, evidence-based nursing (EBN) has the capacity to empower nurses to foster inquiry into the concerns that are important to nurses in order to improve patient care.

Depending on the type of question being asked a quantitative or qualitative methodology may be followed. Quantitative research is useful when asking questions related to nursing interventions, assessment measures or diagnostic tools and often the results are given as numerical data. Qualitative research is more subjective and used when trying to understand the experience of study participants within a certain context; it is therefore more philosophical and nothing is predefined (DiCenso et al., 2005; Hughes, 2006). Both methodologies are of equal importance in research and provide insights which are complimentary to each other, as well as of independent value, when used alone (Bowling, 2002).

This thesis uses a quantitative research design to acquire information on the efficacy of a diagnostic test. This chapter will describe the research design and rationale, and pertinent aspects of the methodology.

Research Design

There are a variety of research designs used in quantitative research, the choice dictated not only by the research question being asked but also the strength of the chosen design to deliver the most robust evidence to answer that question. A retrospective design has been chosen for this research question as it provides the researcher with the ability to look at experiences that have occurred in the past to understand or find reasons for outcomes in the present time and to determine whether correlations result. This is referred to as correlational research, which is used to look for connections between two variables (Polit & Beck, 2008). A retrospective audit was conducted to achieve this approach.

Retrospective research uses different approaches or designs depending on exactly what is being studied and what components of data are being scrutinised. Information is often collected from databases and medical records (National Emergency Medical Services for Children Data

Analysis Resource Centre [NEDARC], n.d.). According to Disenco et al. (2005), when studying the value of a diagnostic test, it is necessary to identify a cohort of people who may have the target condition in question, and conduct the test first using the new tool and then using the gold standard (the accepted reference standard for an accurate diagnosis). An evaluation of the new test can then be made by comparing the two. However, the purpose of the researcher's study is to determine the efficacy of a well-known tool, used to assist in the diagnosis of CAD. As identified in the literature review, there are conflicting opinions of the usefulness of this test, particularly in populations with a low pre-test probability of disease. With this in mind and the reality of fiscal and resource constraints in the New Zealand public health system the author wishes to determine the efficacy of the ETT in patients with mild CVR using local data.

A retrospective audit was chosen to achieve this as it was an appropriate method to answer the question and was manageable in the time frame given for the completion of this thesis. Audits aim to monitor standards, assess and improve quality of health care delivery and ensure cost effective use of resources. They therefore have the potential to change clinical practice and provide quality assurance measures to do this (Bowling, 2002).

The ETT as a diagnostic tool has certain limitations, one being the risk of a false positive result which invariably leads to further, and usually costly, testing. The accuracy of ETT in a population with mild CV risk has not only been questioned for this reason but also because of its risk of creating unnecessary anxiety for the patient given a false positive result. It may potentially affect the patients' immediate ability to work, as in the case of a taxi driver or construction worker who requires a class 2 drivers' licence, and even insurance cover may be at risk (Gibbons et al., 2002). These limitations therefore need to be taken into account when reviewing the efficacy of the ETT.

Setting

To complete this research the CPC database at the researcher's hospital has been accessed to gather retrospective information on patients who attended the chest pain clinic from 1 July 2011 to 28 February 2014.

The chest pain clinic is situated in the medical outpatient department of a regional New Zealand hospital. The assessment and treadmill procedures are performed in the treadmill room of the ECG department. One specialist cardiac nurse and one ECG physiologist are in the room with the patient. The ECG physiologist is responsible for obtaining informed consent of the patient, applying the ECG electrodes and explaining the ETT protocol to the patient. While the patient is exercising the physiologist controls the ETT machine and, in collaboration with the nurse, writes the initial interpretation of the result which is attached to the automated print out, at test completion. The specialist nurse is responsible for the patient assessment prior to starting the

ETT which involves a physical examination and recording the clinical history of presenting symptoms. At completion of the test the specialist nurse discusses the results with the cardiologist and a plan of care is decided. The nurse then explains this to the patient and dictates a letter to the referring doctor outlining the results and recommendations.

The database is stored on an Excel spreadsheet and records CVR, gender, typical or atypical symptoms, results of the ETT (positive, negative or equivocal), and outcomes of any further tests. The database lists patients by National Health Index (NHI) codes rather than names; these codes are unique to each person in New Zealand and used to ensure safe and secure sharing of patient's demographic information among health professionals (MOH, 2013). The recorded data are anonymous and NHI identifiers have not been used in the results of this research. In order to assess the safety of the ETT results a search of the patient's electronic medical records was completed for the six months following ETT and presented with the results. The rationale for this is that if a patient received a negative result, and then presented to ED with a cardiac event a short time later (in this case within six months), this would possibly indicate a false negative test and would decrease the accuracy of the test result. The hospital uses an electronic patient record system called Concerto which records patient presentations and admissions to hospital, laboratory and radiology records and all hospital generated clinic letters.

Data from the chest pain clinic are entered by the two specialist nurses who work in the clinic, one of them being the author of this thesis. It is a District Health Board (DHB) Excel database created for the purposes of auditing the nurse-led clinic and is unique to and only accessible to the cardiology department. Only the two specialist nurses involved in the CPC enter data and both nurses follow the same guidelines when defining the patient's CVR, symptoms and ETT outcomes. Following completion of this research, data specifically collected and used for the purpose of this research will be deleted or destroyed securely in the paper shredding bins provided by the DHB.

Sample

All patients from 35 to 80 years of age were included over the period July 2011 to February 2014. All patients underwent ETT and results were entered into the Excel database. This time period allowed for the collection of 6 month data following completion of ETT, on all patients. Those patients with high, intermediate and mild CVR were included, the advantage being that this provided a balanced cohort and allowed comparisons of results to be made.

Inclusion criteria.

All patients from the age of 35 years to 80 years, who completed an ETT in the CPC setting, for the assessment of stable CAD, were included. The New Zealand CVD risk assessment table includes patients from age 35 years to 74 years of age. This table was used to risk-stratify all

the CPC patients. Patients greater than 74 years of age were included because they are considered to have a high CVR based purely on age (NZGG, 2012).

Exclusion criteria.

Patients with known CAD, or with an abnormal resting ECG such as left bundle branch block (LBBB) which makes interpretation of results difficult, were excluded, as was any patient unable to perform an ETT. Occasionally patients are seen in the CPC for assessment of other disorders such as syncope or as workup for consideration of internal cardiac defibrillators (ICD) and these patients were also excluded.

Ethical Considerations

Ethical considerations are fundamental to research especially so if the research involves human participants. Ethical concerns are also fundamental to nursing practice and it is guided in New Zealand by the Nursing Council of New Zealand's code of conduct (2012) and New Zealand Nurses Organisations (NZNO) (2010) code of ethics which list beneficence, non-maleficence, justice, confidentiality, veracity and fidelity, as underpinning the work of the nurse. It is also important to be mindful of these principles when undertaking research as there is an obligation to ensure research participants are protected from being exploited or disadvantaged, that they are not exposed to undue risk or harm and that they maintain self-determination and control (Polit & Beck, 2008). Resnik (2011) also describes the need for objectivity, integrity, honesty, respect and carefulness when conducting research and these values need to be ever present in the research process.

Locality approval was granted from the local DHB where the audit took place and ethical approval was received from the Research Ethics and Approvals Committee (REAC) of the Eastern Institute of Technology (EIT) (see Appendices 1 & 2).

Cultural Safety

It is of great significance to all health care professionals that health inequalities exist in New Zealand and that Māori rates of mortality are two to three times greater than non-Māori from all causes including cardiovascular disease (Blakely & Simmers, 2011). Three principles derived from the Treaty of Waitangi and relating to Māori health are important components of New Zealand health care. They are partnership, participation and protection and they should underpin all health care planning and delivery to ensure that Māori have control over their health needs, are involved in the delivery of Māori health care services and that disparities are reduced while cultural values are maintained (Medical Council of New Zealand, 2006). The DHB where this research was conducted has a low population of Māori per capita and consequently few Māori are seen in the CPC. No ethnicity has been captured in the data

although it has to be acknowledged that if there was a patient whose ethnicity increased their CVR this was accounted for in their risk score. On consultation with the hospital ethical review board Māori consultation was not required.

Reliability and Validity

Reliability and validity are two criteria used to determine the quality of quantitative research. Reliability is an assessment of the accuracy and the consistency of the research results and is often applied to the methods that are used to measure variables (Polit & Beck, 2008).

Reliability is demonstrated when the same results are derived when the tool is used by different researchers, known as inter-rater reliability, or when it is used on different days or at different times, which is known as test-retest reliability (Roberts & Priest, 2006). The ability of the research tool to give consistent information is vital to determining its reliability.

The researcher's CPC uses the Bruce Protocol for all ETTs so individual results can be compared reliably. Other methods to assess reliability and validity of the ETT have been published. Banerjee et al. (2012) used the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) instrument in their meta-analysis of exercise stress testing to gauge quality and potential bias for the studies they reviewed. Their analysis included five different types of exercise testing, the exercise ECG being one of them. They concluded that the accuracy of all exercise stress tests vary, depending on the type of test, the characteristics of the patient being tested, and the prevalence of disease in the population. They recognised that pre-test probability was a key element of how well the test would perform in diagnosing CAD as has been reported in other research studies (Napoli, 2014). They suggest that the choice of test for each individual is important, as the consequences of the results have implications not only for the management of the patient but also on fiscal resources.

Validity, on the other hand, looks at whether the research measures what it says it measures or whether other influences are contributing to the results. It provides confidence that study results are applicable to other populations and that the study participants are representative of the population being studied at that time (Roberts & Priest, 2006). Sample size contributes to validity as a larger cohort will decrease the possibility of sampling error.

The risk of bias is an important consideration as it affects the quality and rigour of research results. There are many factors that affect bias such as an inadequate or unbalanced sample, incorrect data collection, entry and analysis, or having an inadequate study design. To reduce the incidence of bias the researcher needs to be aware of it, acknowledge when it exists and take it into account when interpreting results (Polit & Beck, 2008).

Sensitivity and Specificity

Understanding the sensitivity and specificity of a diagnostic test helps determine the accuracy and validity of test results. Sensitivity is the number of patients with disease having an abnormal test result, and specificity is the number of patients without disease having a normal or negative test result (Gibbons et al., 2002). The PPV of a test is determined by the sensitivity, so the PPV of a positive (abnormal) test result, is the percentage of patients who have an abnormal test and are found to have disease. The NPV is therefore the percentage of patients that have a negative test and do not have disease. Positive and negative predictive values are related to prevalence of disease in the target population (Parikh, Mathai, Parikh, Chandra & Thomas, 2008).

The exercise treadmill test.

There have been a plethora of studies looking at the diagnostic accuracy of the ETT for diagnosing CAD and there are several factors that affect accuracy which need to be considered when interpreting results. The meta-analysis by Detrano et al. (1989) was designed, in part, to assess exercise stress tests for diagnostic accuracy for predicting CAD, as confirmed by angiography, and to establish factors associated with sensitivity and specificity of the test. These factors include the possible causes of ST segment depression, such as electrolyte disturbances or metabolic factors rather than changes related to ischaemia. Also, the technical variations in measuring ST segments need to be known e.g. the significance of up-sloping ST segment changes, the use of the j point rather than the 80ms point for measuring ST changes or whether the resting ECG is abnormal and how this should be interpreted when, and if, there are alterations with exercise. Other factors to be considered are the placement of the ECG leads on the patient because slight variations may affect the ECG recording. The protocol used for the test needs to be known as does the criteria used to end the test, such as symptom limitation, achievement of target heart or whether ST changes have occurred. The ETT duration and achievement of target heart rate are important components of the ETT as they provide information on the reliability of ETT results (Gibbons et al., 2002). If 85% of maximal target heart rate has not been achieved it means the heart may not have been stressed adequately to assess for ischaemia and reliability of the result is reduced. These performance indicators are considered at the time of assessment in the researcher's CPC and assist with the interpretation of the test results. In order to address these issues of accuracy, guidelines have been developed to assist in standardising the use of these tools. The CPC adheres to the safety and performance guidelines for clinical exercise stress testing developed by the CSANZ (2010). It also uses the ACC/AHA 2002 guideline update for exercise testing (Gibbons et al., 2002) as a guide in the interpretation and management of patients.

A significant number of referrals received from GPs to the CPC request an ETT to rule out a cardiac cause to the patient's symptoms, and while Banerjee et al. (2012) found that the ETT was more useful for excluding coronary disease than confirming it, the implications of stress testing for reassurance need to be considered in this context. The reasons for discharging a patient with a positive ETT result have not been explored for this research but typically include such cases where the patient has achieved a very high workload (> 12 minutes of exercise on Bruce Protocol) suggesting significant prognostic disease is unlikely, or had no provocation of symptoms at very high workload.

Occasionally, the decision is made to refer a patient for another non-invasive test in preference to CA, for example SE. The decision for this is often based on the need for further clarification and reassurance if the ETT result is not unequivocal, for example when symptoms are atypical particularly in a low risk patient or if symptoms were not provoked in a high risk patient.

Accuracy of results.

In order to understand the value of the audit results the collection, interpretation and accuracy of the researcher's information need to be known.

The Excel database.

To reduce the risk of data entry errors only the two nurses involved in the CPC enter information on the Excel database. They follow the same guidelines and protocols for gathering the information, conducting the tests and determining results. However, there is a risk that information may inadvertently be recorded incorrectly, and this would be difficult to ascertain and weakens the data's reliability. To minimise this risk the nurse inputs the data immediately after the CPC appointment is completed so the data entry is not arduous and mistakes are less likely to happen. An additional threat to reliability is the number of cardiologists involved with interpretation and decision making of the ETT results. There are four cardiologists in the department and while they all practice in a similar fashion and follow the same clinical indicators for assessment and management of the CPC patients, it is possible that there are variations in outcomes due to varying opinions. However, for much of the time, the same cardiologist reviews the test and this has provided a greater degree of consistency in the results.

Patient data.

Patients are under a degree of anxiety when coming into the CPC. Not only are they being assessed for coronary heart disease but they are undergoing an exercise test on a treadmill machine that most have never experienced before. It is possible that some patients may therefore forget important information such as family history or fail to describe symptoms accurately not wanting to make a fuss or cause concern which may then affect assessment of

CVR or recording of symptoms. This potential bias known as ‘participants’ lack of candor’ needs to be acknowledged and to minimise this risk the environment is as friendly and relaxed as possible and the doctor’s referral letter is often helpful as a prompt for the nurse when assessing the patients presenting symptoms (Polit & Beck, 2008).

Management of Data

Data is initially hand-written on a clinic sheet by the nurse conducting the test. It captures gender, CVR, presenting symptoms (typical or atypical) and results of the test and management. It is then transferred into the database which is accessed by the CPC nurse who enters the data and this is done using the secure cardiology portal. The paper copy is discarded securely in a paper shredder container in the department.

Data Analysis

Descriptive statistics have been used to describe data and then inferential statistics were used to examine relationships between groups in the data. In order to do this, all patients with a negative ETT were removed from the data set while those with a positive or equivocal result were retained. Associations between symptoms and degree of CVR with CA results were explored using crosstabs and Pearson’s Chi-square tests. Column proportions were compared using z-tests ($\alpha = 0.05$) with Bonferroni corrections applied to adjust the p-values for multiple testing (IBM SPSS Statistics Version 22).

Conclusion

This chapter has described the methodology used to determine the efficacy of ETT in patients with mild CVR from a regional New Zealand population. The research question, aims, sample and setting have been provided and the rationale for a retrospective audit design explained as well as the management and analysis of data. The ethical and cultural considerations have been outlined and the importance of reliability and validity in the research process examined. The following chapter will provide the results of the audit.

Chapter Four

Results

Introduction

This chapter will discuss the results of the retrospective audit at the researcher's hospital from 1 July 2011 to 28 February 2014. The descriptive results are in six sections with corresponding graphs representing data at the end of each section. All patients, regardless of CVR have been included so comparisons can be seen. The first section reviews the association between CVR and presentation with typical or atypical symptoms. Section two discusses ETT results in all CVR groups. Section three looks at the equivocal and positive ETT results in all CVR groups and the referrals for further tests or discharge. Section four presents the CA results followed by a flowchart to demonstrate the distribution of patients referred for CA. Section five looks at readmission rates for all patients. Section six summarises the overall percentage of patients with disease according to CVR and symptoms. A description of the inferential statistics concludes this chapter.

Section One: Cardiovascular Risk and Symptoms

There were a total of 529 patients included in the final analysis of which 207 had mild CVR, 164 had moderate CVR and 158 had a high CVR. Only a small number of mild CVR patients (18%) had typical symptoms, compared to 29% and 35% in the moderate and high risk groups (see Figure 4.1). Atypical symptoms therefore, were more prevalent in all CVR groups (73% overall) with the greatest percentage in those with mild risk (82%). While this indicates that those patients with a higher CVR tended to have more typical symptoms, the number was still less than half of the total high risk population. The experience of atypical symptoms was similar between male and females, 71% and 74% respectively. Of the total audited cohort 39% were women, and the greatest number had mild CVR (51%). Women otherwise made up 33% and 28% respectively, in moderate and high CVR groups.

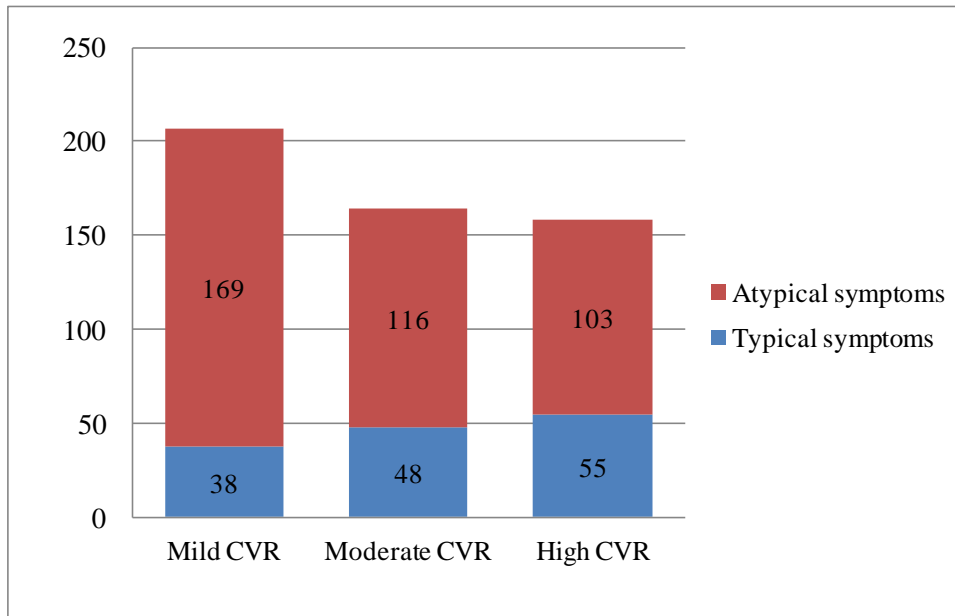


Figure 4.1: Total Participant Numbers (CVR & Symptoms)

Section 2 Treadmill Results in all CVR Patients

Rates of negative ETT's were greatest in the mild and moderate CVR cohorts (72% and 62% respectively). In the high CVR group less than half were negative (47%). Positive results showed an incremental increase with the degree of CVR: mild, moderate and high CVR respectively, 21%, 33%, and 42% (Figure 4.2). There were a small number of equivocal and normal results in each cohort which were either referred for SE or CA but most were discharged.

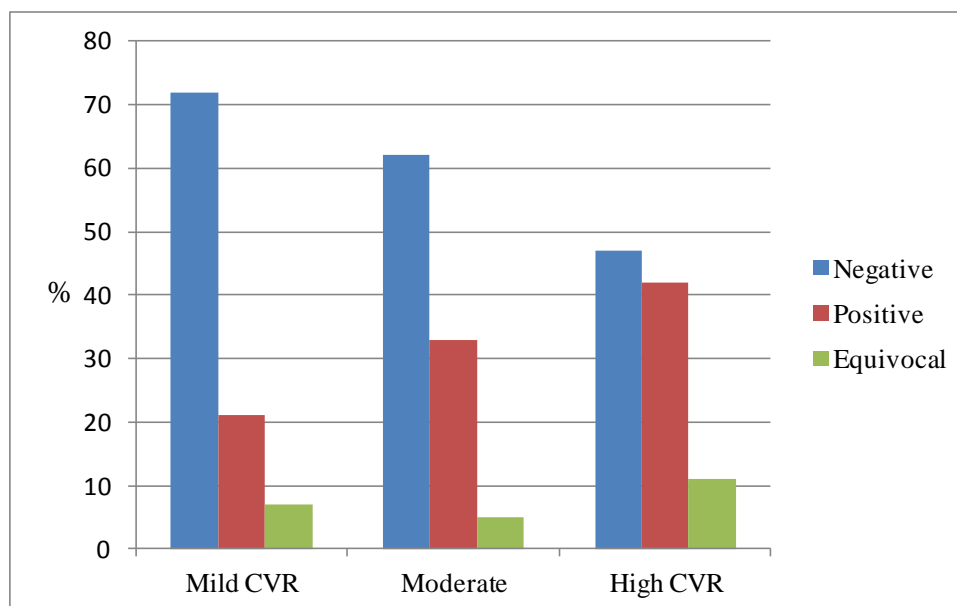


Figure 4.2: Total ETT Results

Section 3: Equivocal and Positive Treadmill Results and Management

As seen in Figure 4.3, most positive ETT's were referred to CA, 76% overall. Eleven percent of patients underwent SE and of those, one went on to CA and mild disease was confirmed. The remaining 13% were either discharged for GP follow up, or returned for three month review with a cardiologist for re-evaluation of symptoms. Of these patients none required any further investigation.

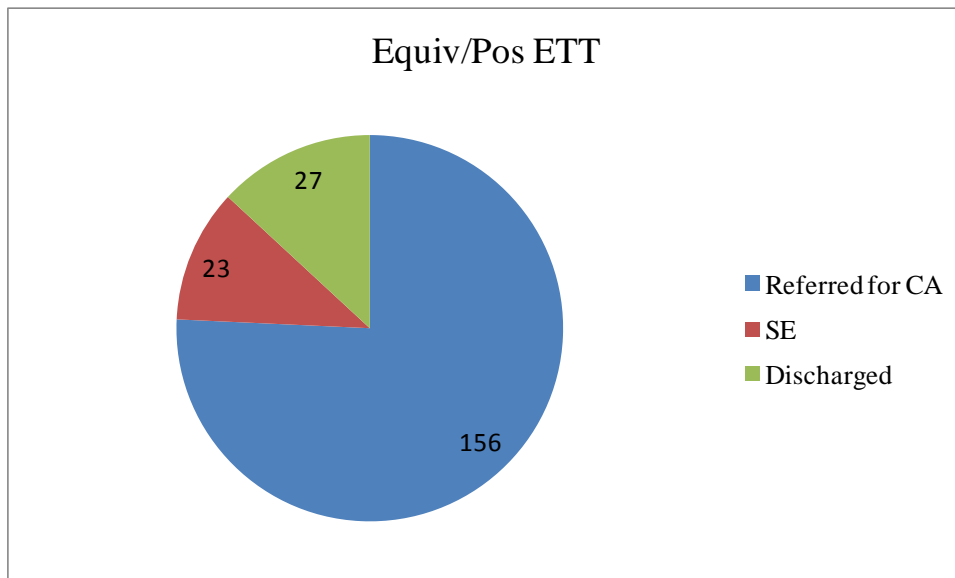


Figure 4.3: Management of Equivocal and Positive Treadmill Results

Section 4: Angiography Results

Revascularisation, either PCI or CABG was undertaken for obstructive (flow-limiting) disease. Medical management was used when CAD was confirmed but was not obstructive.

In the mild CVR group 35 patients had CA, most (91%) were referred from positive ETT's, three from equivocal results. Twenty four (68%) were normal, and 11 (31%) had disease. In those with disease, six required revascularisation and five received medical treatment. There was a false positive rate of 68%. In the moderate group, 52 underwent CA with 84% referred due to a positive ETT. Ten (19%) were normal, 42 (81%) had disease. Of those with disease, 28 required revascularisation and 14 received medical treatment. There was a 19% false positive rate in this cohort. In the high CVR group 69 patients underwent CA, 84% referred from positive ETT's. Fourteen (20%) were normal and 55 (80%) had disease, 35 had revascularisation and 20 received medical treatment. There was a 25% false positive rate. Of the total cohort who had a CA, 70% had confirmed disease. Figure 4.4 shows the percentage of confirmed disease for each of the CVR groups.

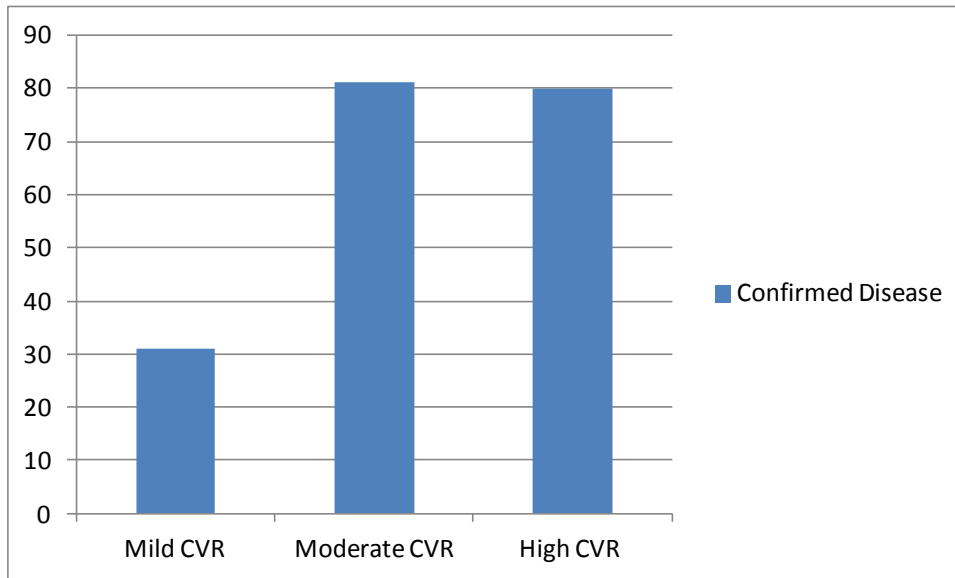


Figure 4.4: Disease confirmed on angiography

Distribution of Patients referred for CA

As a means to clarify the research data, the following page (Figure 4.5) provides a flow chart of all patients in the audit, including ETT results, typical and atypical symptoms, referral to CA, and confirmation of disease, within each of the CVR groups.

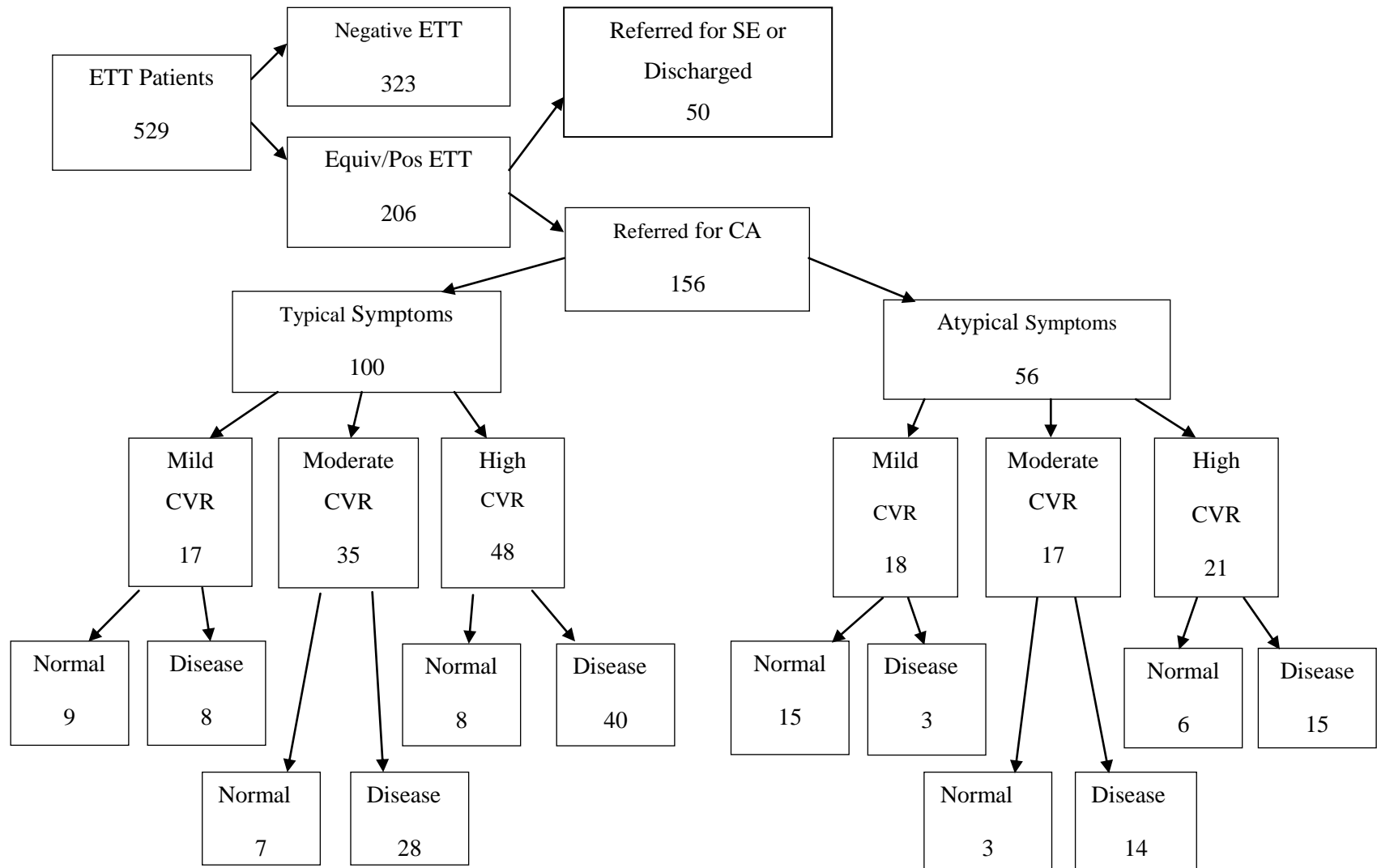


Figure 4.5: Distribution of patients referred for CA and results

Section 5: Six Month Re-presentation Rate

A total of 34 (6%) patients re-presented to ED within six months of ETT from the total cohort of 529 patients. Eleven of those patients were believed to have had a cardiac cause to their presentation, the rest presented due to injury or non-cardiac symptoms (Figure 4.6). There were no MACE presentations.

Of the 11 patients who had cardiac chest pain, nine were already waiting CA, which in most cases, was expedited, and disease was confirmed in six patients. Two were waiting for SE. The SE was expedited in one patient and the result was negative: the other had CA instead, which was normal.

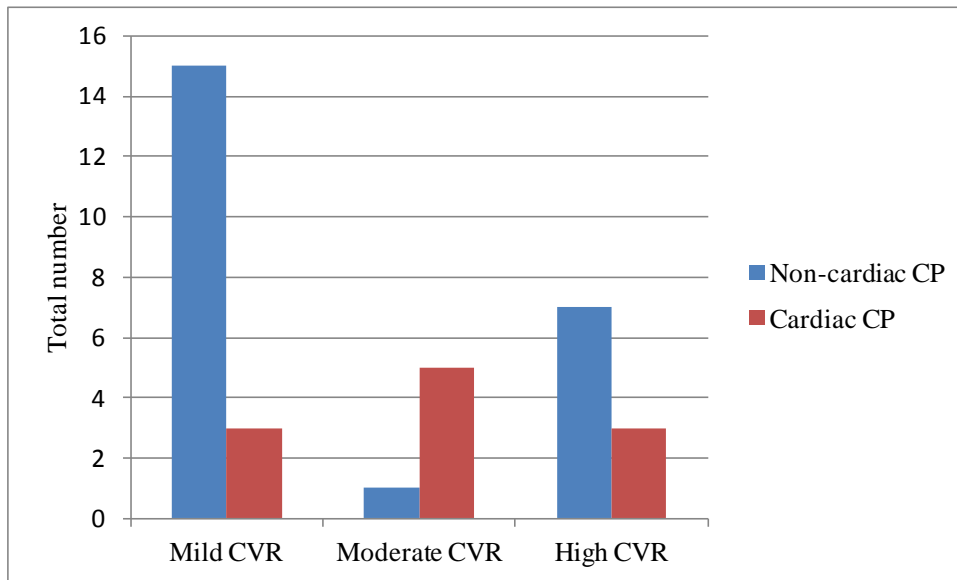


Figure 4.6: Re-presentations Rates per CVR Group

Section 6: Coronary Artery Disease Based on CVR and Symptoms

In the mild CVR group 8 (8%) of patients with typical symptoms were found to have disease compared to only 3 (5%) of patients with atypical symptoms. In the moderate CVR group 28 (28%) of patients with typical symptoms had disease compared to 14 (25%) with atypical symptoms. In the high CVR group 40 (40%) of patients with typical symptoms had disease compared to 15 (27%) with atypical symptoms (Figure 4.7).

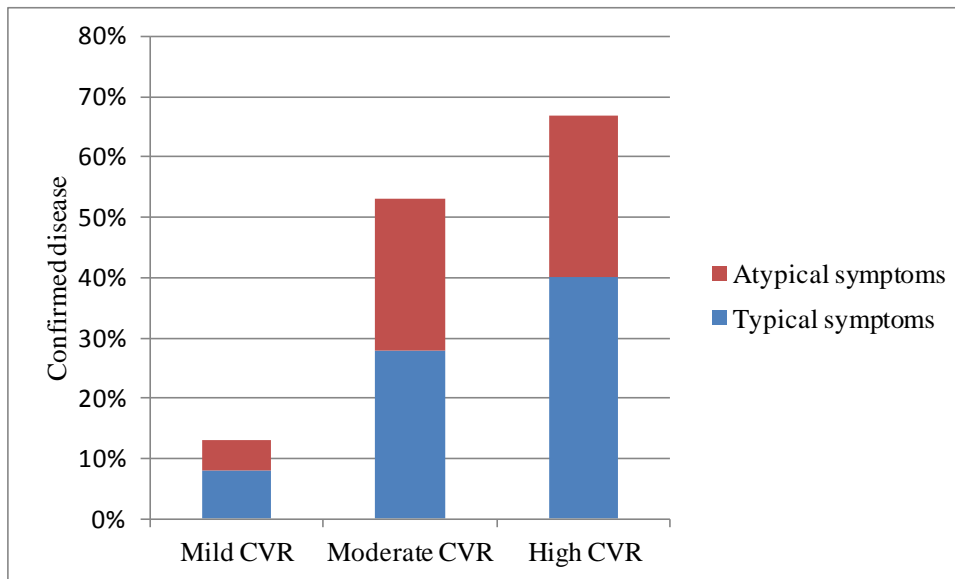


Figure 4.7: Percentage of Patients with Disease Based on CVR and Symptoms.

Inferential Statistics Results

Of the 529 individuals in the study, 323 had a negative treadmill test and were subsequently removed from the data set. Of the 206 individuals remaining, 156 were referred for CA. The percentage of those having an angiogram with negative results was significantly different (Person's Chi-square, $P < 0.001$) for those with atypical (42.9%) and typical symptoms (24.0%). Tables 1 and 2 below show the CA results for all CVR groups according to atypical and typical symptoms. Within each of these groups (i.e. those with atypical symptoms and those with typical symptoms) it was found that a significantly larger percentage of individuals with mild CVR score had negative angiogram results when compared to those with moderate or high CVR scores (Tables 4.1 & 4.2). The angiogram outcome percentages for the moderate and high scores were not significantly different (Tables 4.1 & 4.2).

Table 4.1. Angiogram outcome percentages according to CVR score and atypical symptoms

Angiogram Result	CVR score			Total
	mild	moderate	high	
Negative	15 _b	3 _a	6 _a	24
	83.3%	17.6%	28.6%	42.9%
Positive	3 _b	14 _a	15 _a	32
	16.7%	82.4%	71.4%	57.1%
Total	18	17	56	56

Each subscript letter denotes a subset of CVR categories whose column proportions do not differ significantly from each other at the $\alpha = 0.05$ level.

Table 4.2. Angiogram outcome percentages according to CVR score and typical symptoms

Angiogram Result	CVR score			Total
	mild	moderate	high	
Negative	9 _b	7 _a	6 _a	24
	52.9%	20.0%	28.6%	24.0%
Positive	8 _b	28 _a	15 _a	76
	47.1%	80.0%	71.4%	76.0%
Total	17	35	21	100

Each subscript letter denotes a subset of CVR categories whose column proportions do not differ significantly from each other at the $\alpha = 0.05$ level.

Conclusion

In conclusion, these results have looked at the outcomes of the mild, moderate and high CVR groups in regard to typical and atypical symptoms, results of ETT and referrals for CA. The results of CA have been identified in regard to symptoms and CVR and a report of re-presentations has been presented. To clarify patient characteristics, a flow chart displaying the breakdown of all patients in the audit referred for CA according to CVR and symptoms, was provided. Inferential statistics were presented using Pearson's Chi-square, ($P < 0.001$) to show associations between symptoms and CVR, with CA results. A discussion of the results follows in Chapter Five.

Chapter Five

Discussion

Introduction

This chapter will discuss the results of the retrospective audit. The first section covers atypical and typical symptoms and how these influenced ETT results. The second looks at ETT results in relation to CVR, the third discusses the re-presentation of patients, and the fourth section discusses the outcomes related to CVR and symptoms. Finally, the implications of these results are outlined and study limitations discussed.

Atypical and Typical Symptoms

Overall, across all CVR groups, the percentage of patients with a negative angiogram was significantly different (Pearson's Chi-square, $P < 0.001$) for those with atypical (42.9%) and typical (24%) symptoms. Similarly, the presence of atypical symptoms was associated with a lower diagnostic yield of CAD across all CVR groups (57%) compared to those with typical symptoms (76%). The presence of disease was also associated with a higher CVR, a finding consistent with other research (Christman et al., 2014; Patel et al., 2010; Vieweg et al., 1977). In contrast, patients presenting to ED with acute chest pain, Hermann et al. (2009) found that typical symptoms were no more likely to be associated with ischaemia on stress testing than atypical symptoms. Very few of the studies reviewed for this thesis reported on the classification of angina per se, the description given was "chest pain" without reference to typical or atypical features of ischaemia. The omission of this information has been reported to occur in approximately 60% of studies on the accuracy of stress testing (Detrano et al., 1989) and is an important limitation to consider when interpreting findings as the assessment of typical and atypical symptoms assists in the risk stratification of patients.

Exercise Test Results and Cardiovascular Risk

There were a significant number of negative ETTs in each CVR group, most in those with mild and moderate CVR, a finding also demonstrated in other research (Arbab-Zadeh, 2012; Khare et al., 2008; Mazhar et al., 2012; Nawaz et al., 2013; Newman et al., 2008; Morise, 2000).

Negative tests have been found reliable in ruling out significant CAD in patients with a normal resting ECG who achieve at least six minutes of exercise on the Bruce Protocol (Southard et al., 2008; Morise, 2000). A negative ETT result can be helpful for both the patient and doctor as it provides reassurance that CAD is unlikely and allows the doctor to pursue other causes of symptoms, if necessary.

Positive ETT results were greater in those with moderate and high CVR as has been demonstrated by Schrock et al. (2011) who studied the influence of CVR on stress test

outcomes and found as CVR increased so did the incidence of positive stress test results. The majority of positive ETTs were referred for CA regardless of CVR and disease was confirmed more often in those with moderate and high CVR. The false positive rate, that is, the rate of positive ETTs who did not have disease on CA, was much higher in the mild CVR group at 62%, compared to 19% and 25% in the moderate and high CVR groups respectively. This parallels the study by Khare et al. (2008) who reported a 64% false positive rate in an acute care setting of low risk patients. Interestingly, in the researcher's audit there was a 47% rate of confirmed disease in the mild CVR group with typical symptoms suggesting that use of the ETT in this cohort is valuable. The quantity of true positive ETTs confirmed through CA reflects the sensitivity of the ETT, and this was 81% and 80% in the moderate and high CVR groups respectively. This result is consistent with the 78% sensitivity of ETT cited by Hill and Timmis (2002) and the mean range of 68% sensitivity reported by Gibbons et al. (2002). However, when there is bias in study design it causes variations in sensitivity and specificity and therefore this needs to be considered when interpreting results. Apart from a very small number of negative and equivocal ETTs, only the positive ETTs were routinely referred for CA. This type of selection bias results in higher sensitivity and lower specificity and Arab-Zadeh (2012) suggest that stress test results showing 80% sensitivity are unreliable due to this type of selection bias. The most important way to reduce bias is for the researcher to be aware of it and account for it when interpreting results (Polit & Beck, 2008). Due to the inherent limitations of a retrospective methodology in terms of selection bias this needs to be considered when interpreting the researcher's results. The study limitations will be discussed later in this chapter.

Patient Re-presentation Rates

No patients presented with MACE and the overall re-presentation rate was 6%. Most re-presentations occurred in those with mild CVR, and 83% were for non-cardiac complaints such as injury or musculoskeletal pain. Amsterdam et al. (2010) discussed the problem of recidivism in acute CPU patients with a negative ETT suggesting up to 26% of patients re-present. However, the cohort examined by Amsterdam et al. were unstable, acute patients which may account for the higher number found in this study. A randomised trial by deFilippi et al. (2001) studied re-admission rates in low risk patients with chest pain to see whether re-admissions would be reduced if a definitive answer (by CA) was given at the time of assessment rather than simply being advised of a negative ETT. The results showed that in those who underwent CA and had a negative outcome there were fewer repeat visits to ED and fewer hospital admissions compared to those patients that had a negative or non-diagnostic ETT (10% vs. 30%, $p = 0.0008$). It could be argued that in patients with mild CVR, performing angiography, an invasive, costly and clinically risky procedure, for the sake of reassurance alone is not ethical practice or a fiscally responsible use of resources.

Outcomes According to both CVR and Symptoms

The most significant finding in the researcher's audit has been the low incidence of CAD confirmed in those with mild CVR, particularly those with atypical symptoms (17%). While the ETT is a safe and cost efficient diagnostic tool compared to other stress test modalities this research suggests it adds little value in a very low risk cohort. This finding is consistent with other research (Fihn et al., 2012; Genders et al., 2011; Gibbons et al., 2002) but despite this, very low risk patients are still undergoing stress test evaluation, a practice that Hermann et al. (2009) suggest may be related to the fear of litigation. However, there are differences of opinion and according to Banerjee et al. (2012) stress testing is best utilised in the low to moderate risk cohort as confidence in results is lowered when the prevalence of disease is high. Likewise, Morise (2000) suggest stress tests are valuable in patients with a mild probability of disease because the high number of negative results and strong negative predictive value in addition to the low number of positive results means the test reassures both the patient and doctor that disease is unlikely. The above authors believe that due to the availability and relative low cost of ETT it is likely to continue being used in a low risk cohort.

These differences of opinion are also found in international guidelines, for example the recommendation that ETT should not be performed in patients with no prior history of CAD (NICE, 2010) whereas the current ACC/AHA guidelines for exercise testing recommend the use of ETT in those with a moderate pre-test probability of disease due to its limited value in those with very low and very high risk (Gibbons et al., 2002).

Implications

The results of this research suggest that the ETT has limited efficacy in patients with mild CVR and particularly those with atypical symptoms. Firstly, the implications of this need to be considered in the context of New Zealand public health care resources. There is an ever increasing demand for health resources in a system that has a limited ability to meet all need. Funding is an ongoing issue for most DHBs and the requirement to allocate health care in an appropriate and fiscally sound way continues to confront management. One of the challenges this presents for DHBs is how to utilise current resources appropriately and efficiently, while still considering the implications for patients. Fihn et al. (2012) explain the importance of "...minimising the expense, discomfort, and potential harms of any tests or procedures... avoiding procedures that are likely to yield false positive or false negative results or that are unnecessary or inappropriate" (p. e57). While performing an ETT in a mild CVR patient with atypical symptoms may be questionable from the perspective of efficient use of resources it is also important to consider the implications of performing inappropriate diagnostic tests for the patient. It is the researcher's experience that patients feel a degree of anxiety when attending an

appointment for ETT. This may be related to their ability to complete the exercise component of the test adequately, or concern over the possible results and what this might mean for their future. This negative effect may be exacerbated if the test is falsely positive which then means further tests are required. These downstream effects are important and need to be considered when deciding whether an ETT assessment is appropriate and in the patient's best interest (Bossuyt & McCaffery, 2009).

Secondly, this research gives the triaging clinician a level of confidence to decline requests for ETT in patients with mild CVR and atypical symptoms. Similarly, primary care referrers may be reassured by the very low incidence of CAD identified in this cohort and have more confidence in pursuing a non-cardiac diagnosis in such patients. Consequently, with fewer referrals, the CPC waiting list would be reduced resulting in greater responsiveness of service provision for those at higher risk of CAD who would be able to be seen sooner.

Study Limitations

A number of limitations have been identified with this research. As a retrospective study it has inherent weakness such that randomisation and blinding of diagnostic results is not possible, and the selection of patients may therefore be biased. Sensitivity may be increased and specificity decreased as a result (Detrano et al., 1989). The patients included in this study were taken from a list of consecutive patients between July 2011 to February 2014, and those who did not meet the inclusion criteria were excluded. The information provided in the CPC database was recorded from the patient assessment at the time of ETT and is dependent on the interpretation by the specialist nurse at that time and the decisions of the cardiologists involved in the discussion. As two specialist nurses operate the clinic, and four cardiologists are available to review results, there may be variations between them in terms of classification of symptoms or ETT results. To minimise this, and standardise data, all clinicians follow the same guidelines and protocols for assessment and interpretation of symptoms and ETT results.

Cardiovascular risk scores are used to estimate the probability of CVD over a given time frame. The categorisation of CVR scores varies depending on the country of origin and many different scoring systems exist with slight variations. As stated previously, New Zealand CVR tables are based on a five year absolute risk whereas others may use a 10 year CVR prediction. When comparing New Zealand data with international data it is necessary to be aware of this difference in order to compare groups accurately.

As this audit was performed in a single location in a regional city of New Zealand generalisability is difficult to achieve. While reliability and validity enhance the possibility to generalise the information from one population to another it is not possible in this audit due to its retrospective design and single centre location (Polit & Beck, 2008).

Finally, it is necessary to keep in mind that the literature reviewed for this thesis mainly involved acute presentation patients managed in a CPC attached to ED, not a stable outpatient cohort such as in this audit. The discussion of risk in these acute cohorts often refers to a low or medium risk of ACS rather than a five or ten year risk of CVD. This means that true comparisons are difficult to make. It could be argued that a person whose risk of ACS is low is perhaps likely to have an overall mild CVR but it is not possible to be sure of this. In many research reviews CVR was not measured using a CVR calculator, instead lists of risk factors were given. Results, therefore, need to be interpreted with this limitation in mind.

Conclusion

In conclusion, this discussion has summarised the main results of this retrospective audit and outlined the limitations of the approach and methodology. The results are consistent with prior research but opinions differ on the significance of these findings and therefore conclusions are difficult to draw. It is important to understand that practice is influenced by the health care system of the country it takes place in and this will ultimately affect the provision of services and the decisions regarding patient care. While the results of this audit suggested that ETT assessment of mild CVR patients presenting with atypical symptoms is not efficacious, it remains a useful diagnostic tool for those with typical symptoms at all levels of cardiovascular risk.

Chapter Six

Summary and Conclusions

Introduction

This final chapter will summarise the thesis by chapters. A conclusion will be presented followed by recommendations for clinical practice and suggestions for further research in this area.

Summary

The aim of this research was to determine the efficacy of the ETT in predicting the presence of CAD in patients with mild CVR in order to answer the question “What is the efficacy of the ETT in patients with mild CVR in a regional New Zealand population?”. A secondary aim was to see if the results of the audit could be used to assist in the planning and delivery of the researcher’s CPC. To achieve this a retrospective audit of the researcher’s outpatient CPC was conducted and 529 patients met the inclusion criteria and were included in the study.

The first chapter introduced the rationale and background for this research in order to provide a context for the information that followed. An explanation of the role of ETT, the classification of angina and the role of the researcher’s CPC for the assessment of patients with chest pain was outlined. Cardiovascular risk assessment and probability analysis were discussed in relation to the risk stratification of patients and the researcher’s interest in this study was explained.

The second chapter reviewed literature related to the assessment of patients for CAD, including the evaluation of atypical and typical symptoms, the role of CPC in the assessment of patients, and the ETT as a diagnostic tool. This revealed mixed opinions on the value of ETT in patients with mild CVR with some researchers supporting it as a valid test in those with mild risk as it ruled out CAD and provided reassurance (Banerjee et al., 2012; Morise, 2000), while others were concerned that the risk of a false positive result outweighed the benefits of reassurance (Fihn et al., 2012; Genders et al., 2011; Gibbons et al., 2002; Hermann et al., 2009). The literature review highlighted the differing opinions of the value of the ETT for diagnosing CAD making conclusions about its efficacy challenging.

The third chapter described the methodology used in the implementation of this thesis and included: A discussion on the importance of reliability and validity to determine the quality of quantitative research; the use of sensitivity and specificity to identify the accuracy of a diagnostic test such as the ETT; and an explanation of the CPC Excel database and collection of patient information to provide evidence of the accuracy of the researcher’s results. The management and analysis of data was described.

The fourth chapter provided the results of the retrospective audit using descriptive and inferential statistics in reference to presentation of symptoms, ETT results, CA results, six month re-presentation rates and confirmation of CAD based on CVR and symptoms. It found that 62% of all ETTs were negative, and a high proportion of patients had atypical symptoms (73% overall). The percentage of positive ETT results increased with CVR, and the greatest number of those were seen in the high CVR group (42%). Coronary artery disease was confirmed more often in patients with typical symptoms and in those with a higher CVR.

In the fifth chapter the results were discussed and the implications of these considered in the context of the New Zealand public health care system. The study limitations concluded the chapter.

Conclusion

To conclude, this audit has answered the research question and suggests that the efficacy of the ETT in the mild CVR patients with atypical symptoms is limited but in those with typical symptoms it is a reasonable test to perform. The interpretation of these results need to be considered with the limitations of the study in mind as the power of research lies within a robust and rigorous methodology and, as previously discussed, a retrospective study has inherent weaknesses that have to be accounted for. The benefits of audit are seen in the opportunity to measure and review practice so improvements can be made that not only have the potential to benefit patients but also advance service delivery (Bowling, 2002). This audit has demonstrated this potential as it has provided evidence to assist the process of quality assurance so service delivery can be improved and patient care enhanced.

Recommendations

The recommendations for clinical practice, as a result of this audit, are to reconsider the use of ETT as a diagnostic tool for CAD in the patient with mild CVR and atypical symptoms. The challenge is to provide an economical and safe CPC service to patients who will gain the most benefit from the process taking into account the diagnostic value of the ETT for the patient and the best use of resources. In a public health care system that is facing fiscal and resource constraints it is essential to provide care that is efficient and effective and benefits all those who require the service.

The opportunity exists to inform other clinicians of the results of this audit so they have the confidence to look at alternative options of care for the mild CVR patient with atypical symptoms, resulting in an improved management strategy and reduction in stress for the patient, and making resources available to those it will most benefit.

Further Research

To validate the results of this audit further research is needed in a comparative New Zealand outpatient setting to see if the study's results translate to a similar centre. A prospective methodology would be advantageous to improve the reliability and validity of the study and reduce the limitations found in retrospective designs.

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Appendix 1: DHB Locality Approval



Fax: (03) 546 1288
Phone: (03) 546 1247

*Medical Outpatients
Nelson Hospital*

Private Bag 18
Nelson 7042, New Zealand

13 May 2014

cc BBK – research file

Sarah Cheeseman
Cardiac Liaison Nurse
Nelson Hospital

Dear Sarah

Thank you for your letter regarding your plans to undertake a retrospective audit of patients who have undergone a process through the chest pain treadmill clinic here at Nelson Hospital.

This audit activity is an appropriate use of existing clinical data and your steps to ensure all data is anonymised is essential.

This does not require ethics approval. I understand your audit is fully supported by Cardiology head of Department.

Yours sincerely

Dr Bruce King
Clinical Director Medical Systems
BBK:SUE

Appendix 2: EIT Research and Ethics Approval



Reference Number 25/14

30 June 2014

Sarah Cheeseman
MN Student
C/- School of Nursing
EIT

Dear Sarah

I am pleased to inform you that notification of your research project "*Master's Thesis*" was received and endorsed by the Research Ethics & Approvals Committee at their meeting held on 27 June 2014.

You are reminded that should the proposal change in any significant way, then you must inform the Committee. Please quote the above reference number on all correspondence to the Committee.

The Committee wishes you well for the project.

Yours Sincerely

Jeanette Hfield
Secretary - Research Ethics & Approvals Committee

Cc: Bob Marshall

Eastern Institute of Technology

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