BY

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Dedication

To my late parents

who encouraged me to follow a career in medicine

Acknowledgements

I am delighted to acknowledge the invaluable advice, help and encouragement that I have received from a number of people during my research project. Without their gracious help, this thesis would never have been completed.

I am especially grateful to the late Professor David De Bono who offered me the opportunity to study and work in Leicester. I am grateful to him for his support in helping me get the project off the ground and for his unlimited enthusiasm throughout. His wise advice in the early months provided a solid foundation and clear direction to my research.

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It is a pleasure for me to express my appreciation to my family and friends who have been very supportive for as long as I can remember:

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Chapter 1

Introduction

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Introduction

Rationing and prioritisation

The NHS was established on the fundamental principle that health care should be available to all, free at the point of delivery and with equity of access. The prevailing belief was that improving the nation's health would ultimately reduce the cost of healthcare. In reality, costs increased due to unexpected, overwhelming and ever-increasing demands for services, leading inevitably to long wait times and waiting lists for most health care interventions.

Rationing of health services has become a necessity in order to overcome the mismatch between ever-increasing demand and limited funding for health care and the subsequent supply of services. A first step in restraining health services is *explicit rationing*. Various approaches have been tried. Managed care was developed originally in the USA in an attempt to deliver quality health care while containing costs. This was the first time quality and cost control had been closely linked and relied on modifying the actions of doctors in order to eliminate inappropriate treatments and ensure that cost-effective practices were adopted (Inglehar JK *1994*). The New Zealand Project was established to ration access to coronary bypass surgery and its scoring system is described in detail later in this thesis. A non-invasive clinical scoring system for elective coronary angiography was designed to restrict the procedure to patients who might derive benefits from subsequent revascularisation.

The NHS has tended to rely on *implicit rationing*, which is based on a cost benefit analysis – trying to achieve the most good for most people (Coombs *1990*). This is in marked contrast to a) what patients believe they should have; that is equal access to services solely on the basis of clinical need and irrespective of willingness or ability to pay (McGuire AG *1988*); and b) clinical practice, in which medical and nursing teams try to provide the best care for individual patients. In recent years, however, the NHS has initiated the development of *explicit rationing* through the development of clinical protocols and guidelines.

Containing the cost of coronary disease

The management and diagnosis of coronary artery disease consumes a considerable amount of NHS funds. Coronary angiography is considered pivotal in patient management as it determines access to coronary angioplasty and coronary bypass surgery. Attempts to hold down the overall costs of care of patients with coronary artery disease in the US have focused on access to coronary angiography, using an assessment of clinical appropriateness (Brook RH et al *1989*).

Monitoring access to coronary angiography is important, because many studies have shown that this procedure is used inappropriately. In particular, there is wide variation in the use of coronary angiography not only within the US, but also between the US and Western Europe (Guadagnoli E *1995*), with no impact on the quality of health care or on mortality from coronary disease (Kosecoff J et al *1987*).

If a reasonable approach to the rationalisation of coronary angiography is going to work, it will be necessary to develop an objective system which a) assists clinicians to provide angiography for those patients who might benefit from investigation; and b) minimises overuse of this procedure.

Objective scoring systems in coronary artery disease

An objective prioritisation scoring system would assist physicians to improve patient selection for, and ration access to, elective coronary angiography. A satisfactory system would incorporate non-invasive clinical factors that predicted the severity of coronary disease and might determine, according to the availability of public funds, a threshold for referral of patients for investigation. A reliable, user-friendly and computer-based scoring system to evaluate the extent of coronary artery disease would be extremely beneficial.

The first attempt to develop such a system was the RAND/UCLA appropriateness system. This was based on panellists' decisions regarding what constituted the appropriate use of coronary angiography using hypothetical indications or 'clinical scenarios'. The panel consisted of nine members from different clinical specialities involved in the management of coronary artery disease – representatives were drawn from across the US and from both academic and private health care facilities. Critics of this approach focused on the constitution of the panel (Bernstein SJ et al *1992*).

'Decision models' for the management of coronary artery disease relate to outcome and the costs of managing coronary artery disease. Researchers at Duke University in North Carolina evaluated the prognostic value of exercise test scores in coronary artery disease and in Canada scores were allocated to symptoms, considered a key determinant of access to cardiac procedures (Naylor CD et al *1990*).

A major development in New Zealand was the establishment of a National Health Committee, independent of the Ministry of Health. Its tasks were to determine which health services would be publicly funded, to define eligibility for services in terms of clinical practice guidelines and to devise a new system of waiting lists, enabling patients to undergo surgical procedures within a reasonable time based on clinical priority. For bypass surgery, selection criteria were based on outcome data from several major clinical trials. Regression analysis was used to determine weighting values that resulted in the highest degree of correlation between priority scores and clinician judgements of a reasonable waiting time. These weights were assigned according to the extent of coronary disease symptoms based on the Canadian Cardiovascular Society scale, exercise test results and social disability caused by coronary disease. There were many reservations about this system, some arguing that it failed to predict acute cardiac events while awaiting surgery (Seddon ME et al *1999*), others that the scoring system was too confusing.

Prioritisation remains an important issue and there will be renewed interest in scoring systems as a result of the National Service Framework (NSF March 2000) and the National Plan for the NHS, which have made the identification of those *at risk* of coronary disease, and the management of those with *known* disease, a national priority.

A brief guide to chronic stable angina

Chronic stable angina, a common manifestation of coronary heart disease, carries a good overall prognosis and annual mortality of 2-4%, whatever treatment is deployed. Angina has an overall prevalence of 3.1%, slightly more for men than for women (Colhoun H et al *1994*). Over the last few years there has been a decrease in the coronary heart disease age-adjusted mortality rate in England and Wales, between 1972 and 1989 of 33% in men and 23% in women aged 30-69 (Tunstall-Pedoe H *1991*). Angiographic studies report rates of coronary atheroma to be 20 times higher in patients with symptoms of angina than members of the general population who have no symptoms (Payne et al *1997*).

Symptomatic treatment of angina

The goal of management is to improve the quality and quantity of life by controlling symptoms. First line treatment consists of medical therapy with coronary angiography offered to determine the extent of coronary disease in patients with symptoms refractory to drugs. Angiography is pivotal to subsequent management.

In clinical practice, drug treatment is extremely effective (in most patients) at relieving symptoms. However, there have been few clinical trials, which have evaluated in any meaningful way the benefits of the various drugs prescribed for patients with angina; most studies are under-powered.

Beta-blockers, calcium antagonists, nitrates and potassium channel activators are used to treat the symptoms of angina. Although the evidence is most convincing for beta-blockers, all drugs delay the onset of ischemia or reduce the extent of silent myocardial ischaemia (Jackson G et al *1997*). Some have vaso-dilating effects, which can be beneficial, and some negative inotropic effects, which can be detrimental.

Revascularisation

Blood supply can be improved through coronary angioplasty (PTCA) and coronary artery bypass surgery (CABG); both procedures effectively control pain and can improve longevity.

Coronary angioplasty

In the wide population of patients with coronary artery disease, no prospective randomised trial has shown a prognostic benefit for coronary angioplasty over medical treatment, though there is evidence of survival benefits for patients treated with coronary bypass surgery. Indications for angioplasty as an alternative to surgery to achieve myocardial revascularisation have evolved from intervention in disease affecting one coronary artery to multi-vessel disease and multiple subtotal stenosis in a single vessel.

Immediate and long-term outcome of PTCA

The relief of angina following PTCA can be impressive, far outweighing the need for emergency surgery or the risks of re-stenosis, myocardial infarction or death. Nevertheless, for patients with stable angina, particularly affecting a single artery, medical management is equally effective at controlling symptoms.

Randomised trials comparing the long-term effects of coronary angioplasty, coronary artery bypass surgery and medical treatment have provided important information on the management of stable angina. PTCA can improve symptoms in patients with a recent myocardial infarction or strongly positive exercise test and single vessel disease (Parisi AF et al *1992*). In the RITA-2 study, initial benefits were attenuated over 2 or 3 years of follow-up and there was no reduction in the risk of myocardial infarction and death (Chamberlain DA et al *1997*). PTCA of more complex lesions is associated with immediate angiographic success and low rates of non-fatal myocardial infarction and CABG, and these benefits persist after five years of follow-up (NHLBI registry *1985-1986*). The outcome of PTCA appears to be less favourable in patients with multiple-vessel disease, CABG, hypertension and chronic heart failure (Detre K et al *1988*).

The main early complication of coronary angioplasty of acute or abrupt closure occurs in 2 to 8% of patients (Cowley MJ et al *1984*). This is usually managed by intra-coronary stent if the coronary anatomy is suitable; if this fails emergency CABG is possible, though mortality rates are much higher. Restenosis affects about 14% of patients and this can be managed by second angioplasty. Coronary angioplasty can also be carried out on coronary bypass grafts with a high initial success rate 75%-90% (Webb JG *1990*).

Coronary artery bypass surgery

Coronary artery bypass surgery is superior to medical therapy at controlling the symptoms of angina (European Coronary Surgery Study) (Varnauskas E et al *1988),* and can prolong life when disease affects the left main stem (Veteran Administration Co-operative Study of Surgery for Coronary Artery Disease, Takaro T et al *1976).* The CASS Principal Investigators reported in-hospital mortality of 1.4% (much the same today) and an overall lower annual mortality rate compared with the European Collaborative Study and the VA Study.

Chaitman et al *(1983)* studied the effects of coronary artery anatomy on prognosis. They found the combined proximal left anterior descending artery and proximal circumflex stenosis was not the prognostic equivalent of left main stem stenosis. The 5-year survival rate was 55% for the former against 46% for left main disease. Disease located in the proximal part of the left anterior descending artery has an adverse impact on survival.

The large randomised trials have shown that coronary bypass surgery has become the treatment of choice for patients with multi-vessel disease, particularly when associated with left ventricular dysfunction. Better results can be achieved by using the internal mammary artery- the patency rate is excellent for internal mammary grafts, with 10-year patency of 95% (Loop FD et al *1986*), far superior to the 50-60% rate seen in saphenous vein grafts (Bourassa MG et al *1985*).

Coronary bypass surgery versus coronary angioplasty

Comparing these strategies, mortality rates are similar except in diabetic patients, where surgery is superior (The BARI Investigators *1996*). Patients with multi-vessel disease who are clinically and angiographically suitable for CABG or PTCA are at low risk of combined death or MI and neither method is associated with a major prognostic advantage (Pocock SJ et al *lancet 1995*). Some clinicians may therefore prefer to recommend PTCA as an initial re-vascularisation strategy in younger patients, and patients with previous CABG. Observational data suggests that PTCA is recommended for two vessel disease while CABG is better for managing three vessel disease.

Methods of prioritising coronary angiography

Question marks have been raised about the appropriate use of coronary procedures because of the wide variation in their use between states in the US (Kosecoff J et al. *1987*), and also between the US and another countries (Dawson JH *1987*).

Pressures such as the growth of managed care and other types of per capita payment systems, combined with limitations on funding, have forced health policy makers to find a system that would reduce inappropriate referrals for coronary artery procedures. Coronary angiography is a good target to hold down the overall costs of care for patients with ischaemic heart disease, as this is considered a prerequisite to percutaneous coronary angioplasty and coronary bypass surgery (Eisenstein EL et al *1996*).

There have been various attempts to introduce a prioritisation process that might be applied to patients with chest pains. These involve:

1. **Individual clinical judgement**
2. **Consensus judgements**
3. **Physiological measurement**
4. **Decision modelling**

Individual clinical judgement

Some clinicians would argue that individual clinical judgement is the best way of deciding which patients warrant coronary angiography. This approach is problematic because practitioners may be biased (whether knowingly or not) in several ways. For example, GPs are more likely to refer male patients for coronary angiography (Kee F et al *1994*). An explicit process to select patients for interventions would prevent bias, however inadvertent.

Consensus judgements

Consensus has been proposed as a means of advising purchasers on which clinical indications are appropriate, and improving the level of agreement among physicians as to when a coronary angiogram should be performed and when it should not. The corner stone for all appropriateness studies was the appropriateness systems for coronary angiography (Bernstein SJ et al *1992*) that was based on the system developed by RAND/ UCLA appropriateness system, as described below.

Step 1: literature covering the effectiveness and risks of coronary procedures summarised. **Step 2**: all possible hypothetical indications ('clinical scenarios') identified- clinical and other factors considered as recommendation to carry out procedure. **Step 3:** clinical scenarios organised into 'chapters' (e.g. stable or unstable angina or acute myocardial infarction). Indications organised according to result of exercise test, ejection fraction, angina class, adequacy of medical therapy and co- morbidity. **Step 4**: an 'expert panel' of nine clinicians involved in the care of coronary patients rated the appropriateness of clinical scenarios using the modified Delphi process, individually and then as a group when each panellist was aware of his/her own *and* the group's ratings for each scenario. Indications were considered 'Appropriate' when medical benefits (such as improved mortality or morbidity) exceeded medical risks (such as procedural mortality) by a sufficient margin to make the procedure worthwhile; they were 'Inappropriate' where medical risks exceeded the medical benefits; and deemed 'Uncertain' when medical benefits equalled medical risks. Agreement among panellists was defined as a*ll members agreed that a clinical indication was appropriate, uncertain, or inappropriate.* A relaxed definition was as described above but with one extreme high and one extreme low rating excluded. Group discussion tends to improve agreement between panellists. **Step 5**: the final appropriateness rating = median of panellist's ratings.
Appropriateness methodology

CHAPTER 3: Chronic stable angina: A. Angina on mild exertion (class III, IV) and received: No or less than maximal medical therapy and Very positive exercise test and no stress imaging study, age ≥75 years Very positive exercise test and no stress imaging study, age <75 years
Typical hypothetical indications or 'case scenarios'

The outcome of appropriateness studies varies from one country to another, among centres in the same country and from one year to another (Bengston A et al *1994*, Bernstein SJ *1992*). This mainly occurs because of the difference in the constitution of each panel, and differences in health care systems.
Improvements in interventional procedures and the results of large clinical trials were probably responsible for the differences in outcome of appropriateness studies from year to year. Bernstein et al *(1997)* reported a significant increase in appropriate rates for CABG in New York from 54% (1981) to 90% (1990), but nevertheless there were no significant differences in the outcome of appropriateness for coronary angiograms between the original and subsequent studies (Noonan S.J. et al *1995*).

In all appropriateness studies asymptomatic or mild angina and less than maximal anti- angina medication were associated with uncertain or inappropriate indications for coronary angiography.

Moreover there were significant differences in outcome when different ratings were applied to the same group of patients. UK panellists rated 49%, 30%, and 21% of 320 patients appropriate, uncertain, and inappropriate respectively, whilst the US panel's ratings were 71%, 12%, and 17% respectively (Gray D at al *1993*).
Variation in outcome of appropriateness probably occurs nationally because of differences in the constitution of each panel and internationally because of differences in health care systems.

The appropriateness system has the potential to identify the *over-use* of services but doesn't contain information on detecting under-use, because it is easier to asses the former and difficult to identify the latter in retrospective studies.

There are pressures due to limited funding, and there have been major advances in the interventional management of coronary artery disease. Appropriateness and scoring systems have become established in an attempt to rationalise the use of such procedures, with priority given to patients at high risk of ischaemic-related events and those who might benefit from these procedures. Although those systems failed to detect under-use, they are an important step on the way to achieving a system nearer the optimum for rational use of these procedures.

Appropriateness methods are not without their problems. It is difficult to assess reproducibility as there are hundreds (Gray D et al *1993*) or thousands of possible clinical scenarios (Bernstein SJ et al *1993*), most of which are never seen in clinical practice. The overlaps between different scenarios make it more difficult to choose which scenario should be applied to an individual patient. The constitution of the panel may also affect the outcome (Gray D et al *1993*) as a cardiac surgeon is usually more likely than a cardiologist to rate as appropriate any given indication for coronary angiography or revascularisation procedure – in line with the principle *'never ask a barber if you need a haircut!'* In addition, this system was not intended to be able to predict the extent of coronary artery disease or post angiography management.

Physiological measurement

Duke University Medical Centre method

Mark and colleagues developed a system incorporating exercise treadmill scores in patients with coronary artery disease (Mark DB et al *1987*). A predictive formula was developed and the resultant score was predictive of five-year survival. Treadmill scores can add important prognostic information to both clinical and cardiac catheterisation data, facilitating the decision to refer patients for CABG. For example, a patient with three-vessel disease and a high risk based on the exercise test scoring system would benefit from CABG, whilst a similar patient with a low risk would not benefit from this procedure.

Naylor and colleagues in Ontario judged surgical priorities for CABG, believing that patients at high risk of adverse ischaemia events deserved greater priority. Determinants of urgency were:

Symptoms – these were considered the key urgency determinant with special priority given to those with a large amount of myocardium at risk of ischaemia. Typically, patients with mild stable angina and impaired quality of life waited less than 3 months, while those at lower risk waited up to 6 months. Unstable angina was considered 'semi-urgent'. Patients who responded to medical treatment had less priority than those with intractable symptoms.

Coronary anatomy – five patterns of disease were defined, with left main disease taking priority over multi-vessel disease including proximal LAD stenosis, three-vessel disease without proximal LAD stenosis, single vessel disease involving proximal LAD and one or two vessel disease without proximal LAD stenosis.

Non- invasive testing – risk stratification was based on the Duke University system.

MODELS FOR POLICY DECISIONS

Options and choices that are considered in the health care decision-making process might rely on the costs and benefits of such procedures. For example, angioplasty is an effective strategy in acute myocardial infarction, with one-year mortality far superior to either medical treatment or thrombolysis (Zuzanne B et al *1989*); because angioplasty is less readily available and is associated with higher costs than thrombolytic strategy, angioplasty is not an effective alternative to thrombolytic therapy.

Yet decision-modelling technology does have its downside: it is costly, time consuming and is labour intensive and demands a high degree of expertise.

New Zealand priority criteria project for coronary bypass surgery

A major development in New Zealand was the establishment of a National Health Committee (Hadron DC et al *1997*) that sought to devise a system of prioritisation to manage waiting lists, enabling patients to undergo CABG within a reasonable time. A professional advisory group consisting of cardiologists, cardiac surgeons, physicians and general practitioners developed criteria for CABG. Priority criteria were selected in line with published studies and clinicians determined suitable waiting times. Regression analysis determined weightings of correlation between priority scores and waiting times and a total score determined the overall degree of benefit.

The New Zealand priority criteria project did make some attempt to incorporate both clinical trial evidence as well as a validated set of criteria from Duke

University, preferring trial data where this was available and consensus information where it was not. When deciding who should and should not undergo bypass surgery, this methodology takes into account both non-invasive clinical scores and the scores of coronary angiography.

Although clinicians accepted this project and clinical practice did change, restricted resources led to the adoption of '*cut-off points*' below which surgery would not be funded (despite the potential for health gains). This led to concerns about the potential under-use of coronary bypass surgery due to an inadequate level of funding. As a result, waiting lists for elective surgery were ultimately replaced with a booking system.

Comparison of physician and patient perspectives of rationing access to health care

It is important to recognise that physician, non-medical (lay), and patient opinions on priority setting are not necessarily the same. Although beyond the scope of this thesis, the following table draws attention to some of the differences in expectations (Table 1).

Physician perspective	Patient perspective
Want increased spending to expand use of procedures to overcome increased demand	Want right to have free access to health services without financial or other barriers whenever needed
Want principle of mobilising resources for the benefit of the individual patient according to individual need	Want to ensure own safety as long waiting list for procedures – this carries risk of increased mortality and morbidity
Want to avoid danger of becoming 'silent queue managers'	Want any explicit rationing to be made at higher level of social organisation so that all are treated equally
Want to maintain physician autonomy over management of the individual patient	Want relief of symptoms
Want to remain free to promote the interests of their patients	Want to ensure procedure indicated so that risks of unnecessary procedure avoided
Want to ensure an appropriate level of care as well as efficient and equitable allocation of available resources	Want to minimise risk of missing significant coronary artery disease by limiting access to patients who might benefit from procedures
Want to avoid cuts in medical services that would unacceptably put patients at risk to avoid gap between optimal and permitted care widening	
Want to avoid rationing of access to procedures unless all other approaches to care have been exhausted	

Table 1: Comparison of physician and patient perspectives of rationing access to health care:

Conclusion

Rationing access to coronary angiography has become a necessity as the gap between the demand for cardiac procedures and limited funds has widened to such an extent that long waiting lists are now the norm. This increases the risk of patients developing an acute cardiac event and sustaining avoidable mortality. As a result, health authorities and clinicians must optimise the use of coronary angiography, which requires the identification of patients who might, and accordingly those who will not, benefit from investigation and so reduce inappropriate use of coronary angiography in a way that is both ethically and medically acceptable.

The goal for those working in the NHS must be to achieve a balance between what clinicians want – the best for their patients – and what can be afforded (that is, what the NHS is prepared to pay), depending on competing demands for available resources. If we are to obtain the best use of finite resources, there is a need for an alternative process of selecting patients for procedures that have important revenue consequences; in chronic stable angina, this means controlling access to coronary angiography. What is needed is some means of reliably predicting the severity of coronary disease using non-invasive test results. This would have two important outcomes. First, clinicians could offer angiography to those patients who were most likely to benefit from coronary revascularisation. Second, patients who were unlikely to have coronary disease would be spared the hazards of angiography.

What is required is a new prioritisation scheme that is of practical value in managing patients with coronary disease that is acceptable to clinicians and can be widely adopted into UK practice.

Chapter 2

Methods and populations

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Methods and populations

Introduction and rationale

Rationing access to coronary angiography has become a necessity as the gap between the demand for cardiac procedures and limited funds has widened to such an extent that long waiting lists are now the norm. This increases the risk of patients developing an acute cardiac event and sustaining avoidable mortality. The widening gap between available NHS resources and the demand for coronary artery management has encouraged both health authorities and clinicians to try to optimise the use of coronary angiography and eventually reducing waiting time for this procedure; this requires the identification of patients who *might*, and those who *will not*, benefit from investigation. This should reduce the inappropriate use of coronary angiography in a way that is both ethically and medically acceptable.

To date, deciding who should and should not be offered a cardiac investigation or procedure has been built around a) the classic appropriateness systems developed by RAND; and b) a prioritisation scoring system developed in New Zealand which addressed how to prioritise patients on a waiting list for coronary bypass surgery but not coronary angiography. Both techniques have their limitations.

With appropriateness methods, it is difficult to assess reproducibility as there are hundreds (Gray D et al *1993*) and thousands of possible clinical scenarios (Bernstein SJ et al *1992*); overlaps between different scenarios make it more difficult to choose which scenario should be applied to an individual patient. The constitution of the panel may also affect the outcome. In addition, this system was not intended to be able to predict either the extent of coronary artery disease or post-angiography management.

The New Zealand priority criteria project did make some attempt to incorporate both clinical trial evidence as well as a validated set of criteria from Duke University, preferring trial data where this was available and consensus information where it was not. When deciding who should and who should not receive bypass surgery, this methodology takes into account both non-invasive clinical scores and the scores of coronary angiography.

As a result, there is no reliable system currently available to predict the severity of coronary disease that would assist the clinician to refer patients for coronary angiography using non-invasive test results. A methodology, as described below, was developed to devise a new approach to patient selection for coronary angiography.

General Methodology

Glenfield Hospital, Leicester is a tertiary referral centre for patients with coronary heart disease, being responsible for the care of about one million residents of the city and county of Leicestershire. Patients with suspected coronary artery disease are usually referred to the outpatient clinic by:

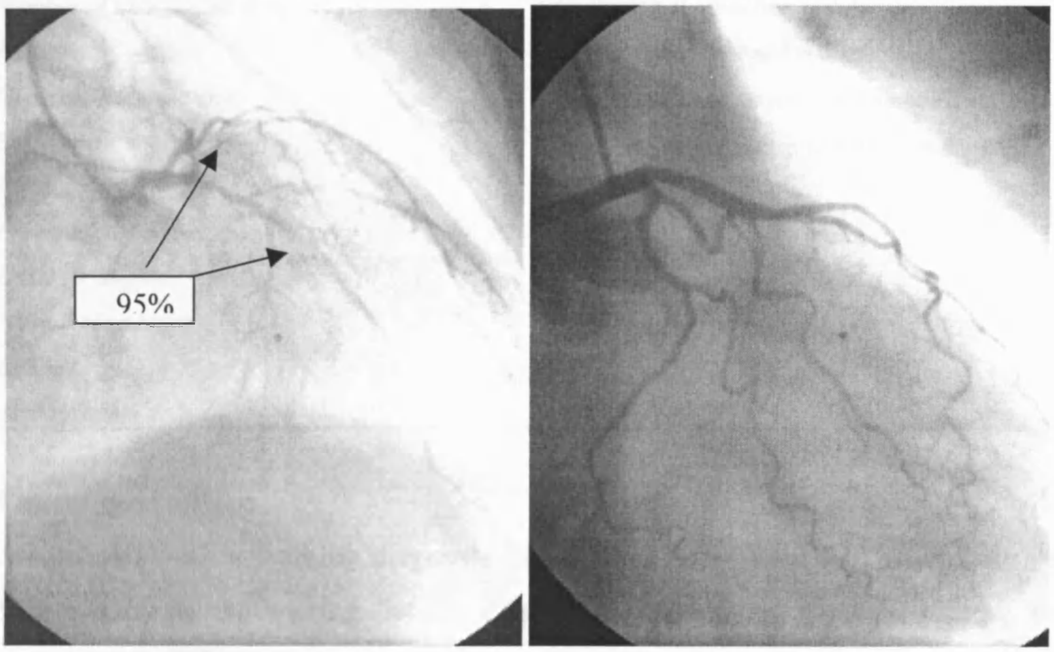
- A general practitioner to investigate symptoms suggestive of myocardial ischaemia. Investigations include non-invasive exercise testing and coronary angiography;
- A physician/cardiologist from a local district general hospital who may be able to carry out an exercise test but lacks the facilities to perform diagnostic coronary angiography.

Data collection

Basic demographic data were collected on all patients. The author collected specific data prospectively from the time of being placed on the coronary angiography waiting list, using a standard data collection form.

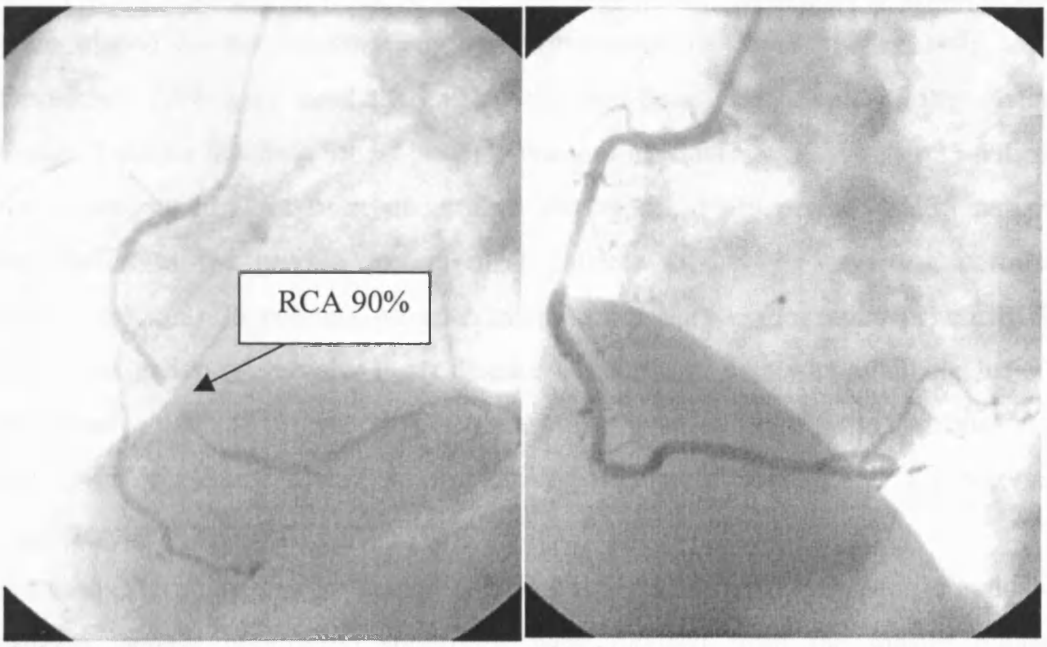
The author reviewed original coronary angiograms at the same time that Glenfield consultants reviewed the films to determine future management.

A standard approach of classifying coronary disease into one, two and three vessel disease was used when a coronary atheromatous lesion involved a major coronary artery (left anterior descending, circumflex and right coronary arteries). A more detailed classification was used to describe lesions affecting the proximal left anterior descending or left main artery. A coronary stenosis was defined as 'significant' if the diameter of coronary artery was narrowed by more than 50% and 'not significant or normal' if less than 50% (Figure 1). Coronary artery lesions were scored according to the New Zealand Criteria (Table 1), adapted from the New Zealand priority criteria project (Hadorn DC *1997*).



A: Normal left Coronary artery
(2 Vessels disease LAD, CX 95%)

B: Left coronary artery disease



C: Normal right coronary artery

D: Right coronary stenosis

Figure 1: Coronary angiography A, and C normal coronary arteries, B, and D coronary artery disease

The following clinical variables were collected:

Age	
Gender	
Symptoms:	Using Canadian Cardiovascular Society
Exercise stress test	Using the Bruce protocol
Number of anti-angina drugs	Excluding short-acting nitrates
Diabetes	Diagnosed or treated for diabetes
Hypercholesterolaemia	Plasma total cholesterol ≥ 6.5 mmol/L
Hypertension	Systolic≥ 160 or diastolic ≥100 mm Hg
Previous myocardial infarction	
Previous coronary bypass surgery	
Unstable angina	Or worsening angina
History of smoking	
Ethnic origin	
Angiographic data	

Patient populations

All patients with a working diagnosis of coronary heart disease (CHD) who had been placed on the waiting list for diagnostic coronary angiography during the period 1 July 1996 to 30 June 1997 were available for this project.

There were two master datasets. The first consisted of consecutive patients who were placed on the coronary angiography waiting list from 1 July 1996 to 31 December 1996 were used to develop the non-invasive clinical scoring system. Figure 2 shows that data for 92 patients was not available because a) in 25 patients the procedure had not been undertaken during the study period; b) 35 patients transferred to the private sector; c) 7 patients died while awaiting coronary angiography; d) 25 patients were undergoing coronary angiography primarily for the investigation of valvular heart disease. As a result, data was available for 572 consecutive patients (Figure 2). This dataset was used to find out the distribution of non-invasive clinical scores among those patients on waiting list for coronary angiography (Chapter 4).

Because each study was conducted at different times and involved specific inclusion criteria, several population subgroups were devised from the master dataset.

However all these were consecutive patients on the waiting list for coronary angiography.

Randomly-chosen consecutive patients referred between 1 October and 10 November 1996 (125 patients) were used to test the correlation between angina and the exercise test score with angiography data, and to devise the clinical scoring system based on a consensus of cardiologists at Glenfield Hospital, described in chapter 3 (Figure 3).

Consecutive patients on the waiting list between 11 November and 31 December 1996 (178 patients) were used for uni- and multi-variant analysis to devise the modified non-clinical scoring system (Chapter 4), and to assess the ability of this scoring system to predict the severity of coronary artery disease (Figure 3).
Post-angiographic data for 9 patients was missing; thus 169 consecutive patients were used to devise the new angiography scores (Chapter 6).

The second master dataset consisted of 203 consecutive patients who were listed for angiography between 1 January and 30 March 1997 .The first 100 patients were used to validate the predictive power of the non-invasive clinical scoring system (modified version) to identify severe coronary artery disease, and subsequently used to construct ROC, which was used together with the outcome of distribution of non-invasive clinical scores to set up the threshold score (Chapter 4) above which patients might be referred for coronary angiography (Figure 3).

This master dataset (203 patients) was used to validate new angio-scoring, as described in chapter 6 (Figure 4).

As all patients included in the subsets were consecutive from 1 October 1996 to 30 March 1997, 372 consecutive patients on the waiting list for coronary angiography were used for:

1 Identifying patients at increased risk of an acute cardiac event while awaiting revascularisation (Chapter 5). Survival analysis was conducted on all 139 patients awaiting coronary revascularisation (Figure 5).

2 Application of a clinical scoring system (Chapter 7) in patients with previous coronary artery bypass surgery (Figure 6)

3 Validate non-invasive clinical scores (Chapter 8) and to compare the predictive value of appropriateness systems based on RAND/UCLA systems and the non-invasive clinical scoring system (Figure 7).

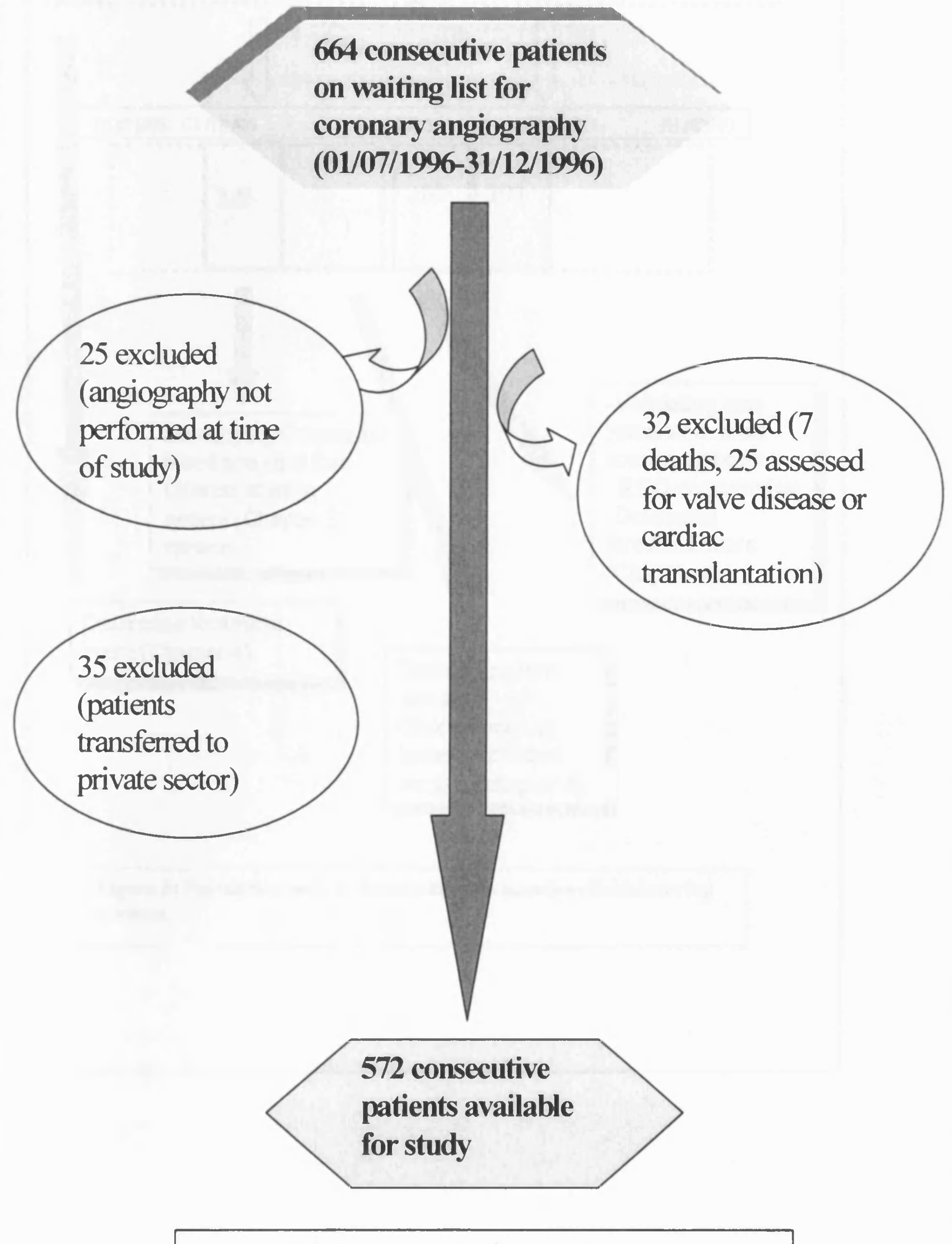


Figure 2: Patients assigned a non-invasive clinical score (first master dataset)

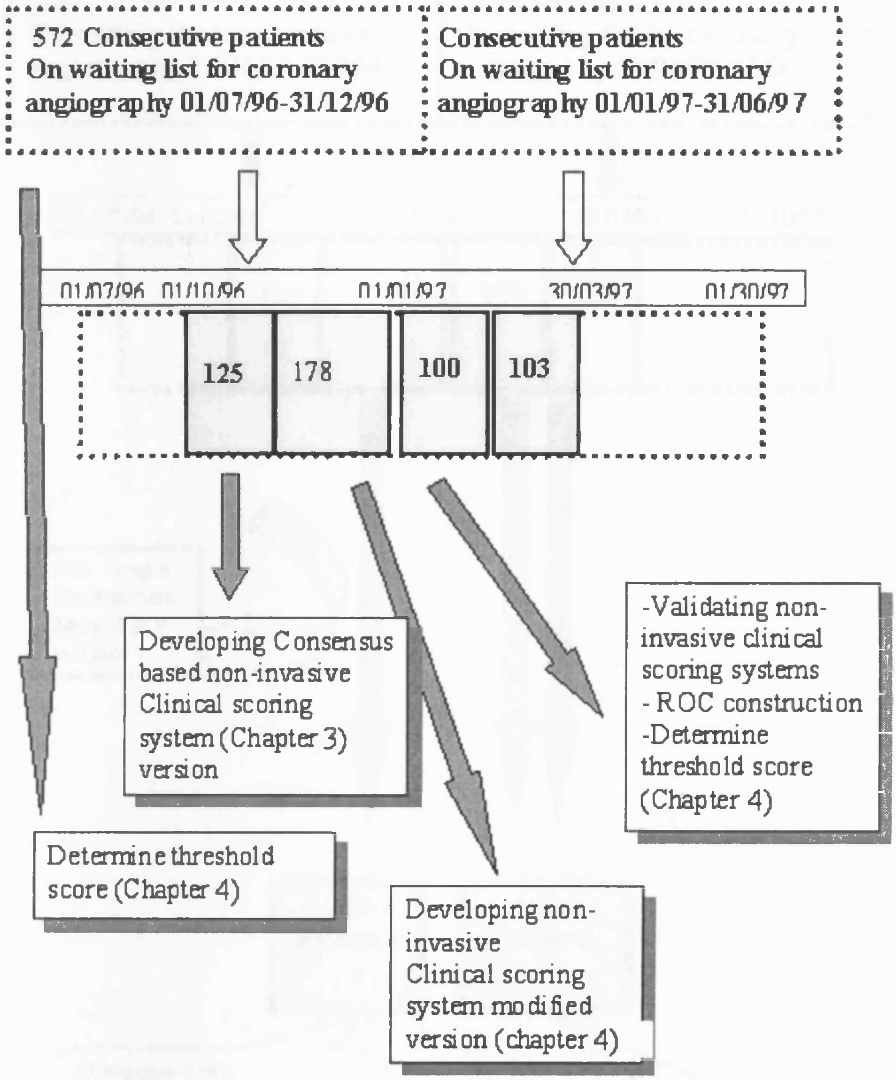


Figure 3: Population used in developing non-invasive clinical scoring systems.

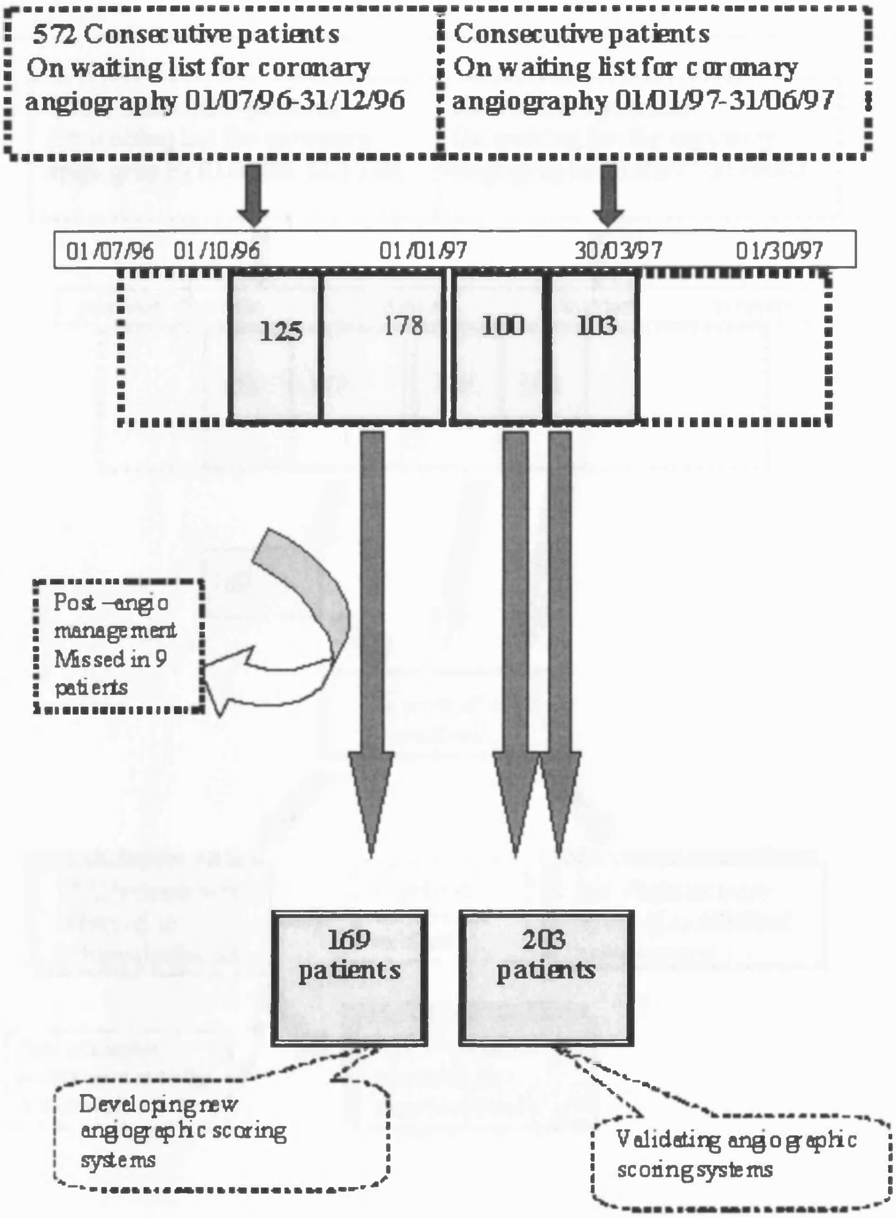


Figure 4: Population used to develop and validate the new angio-scoring system (Chapter 6).

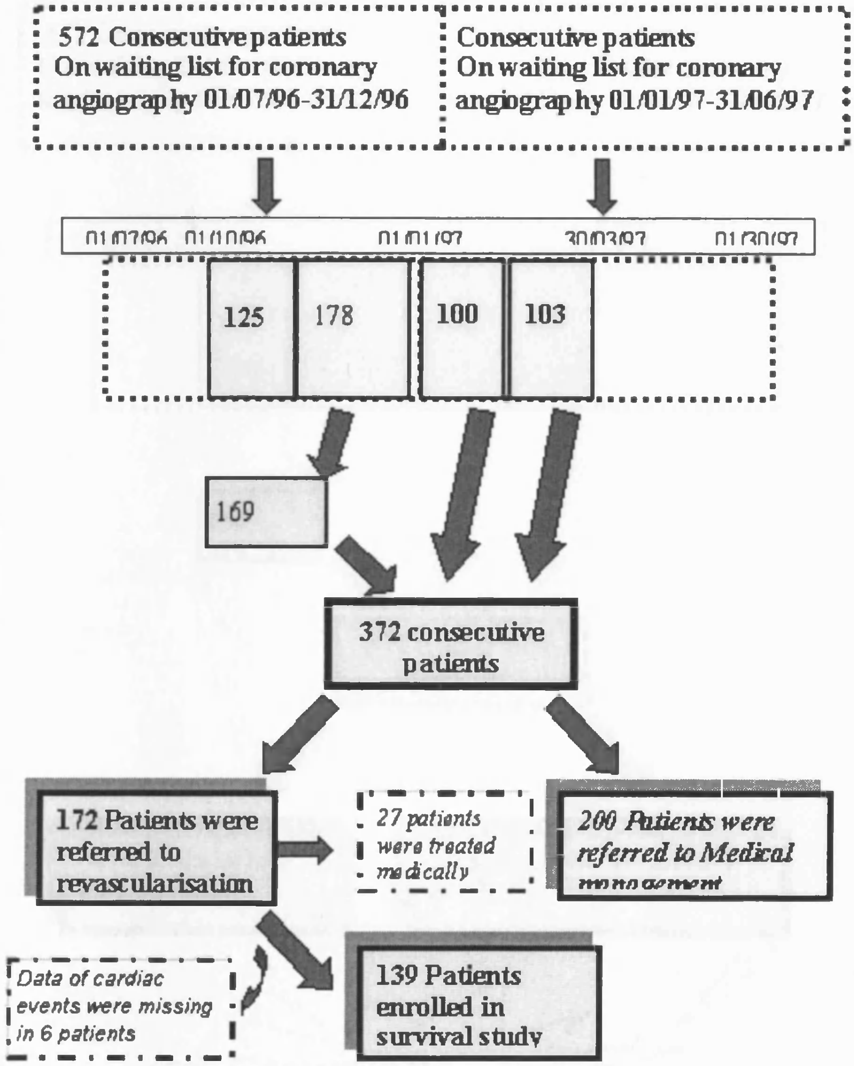


Figure 5: Population used to conduct survival analysis (Chapter 5)

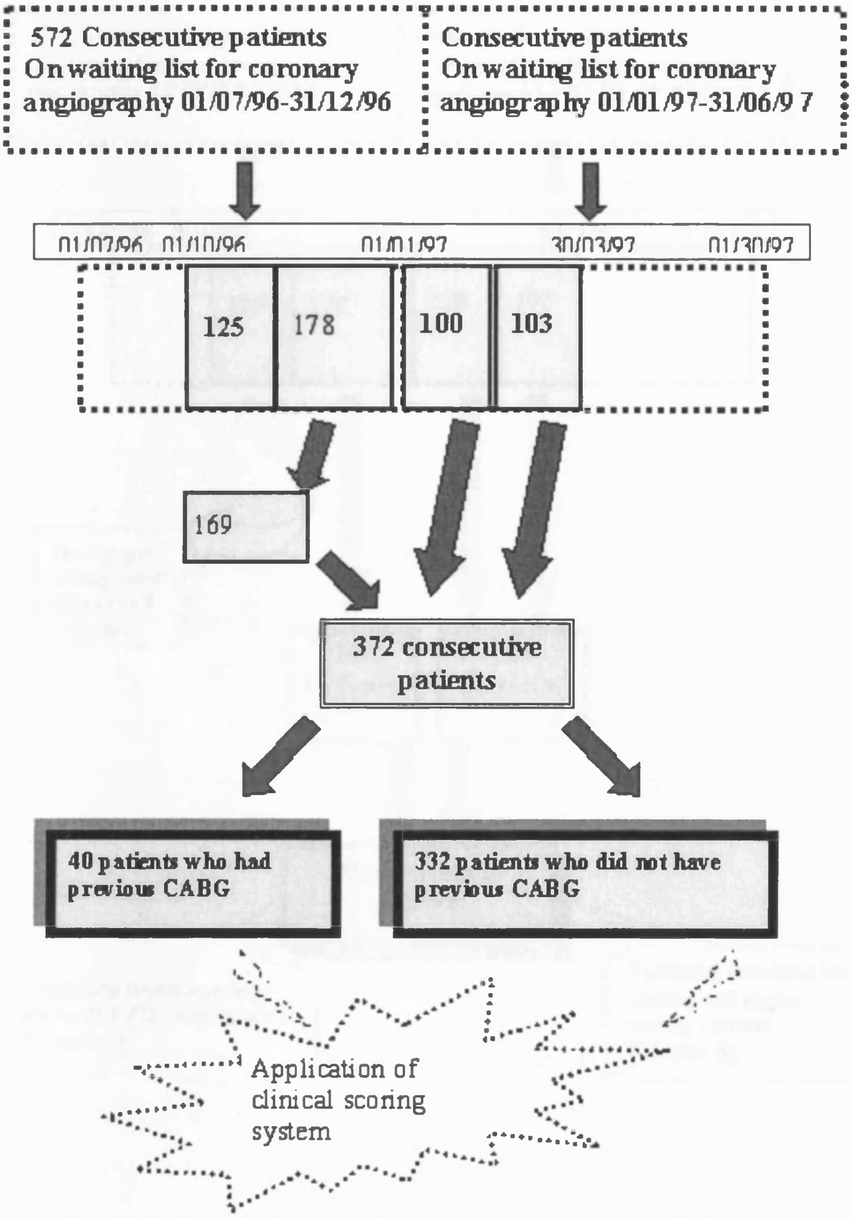


Figure 6: Population used to test non-invasive clinical scoring system in patients with previous coronary bypass syrgery (Chapter 7)

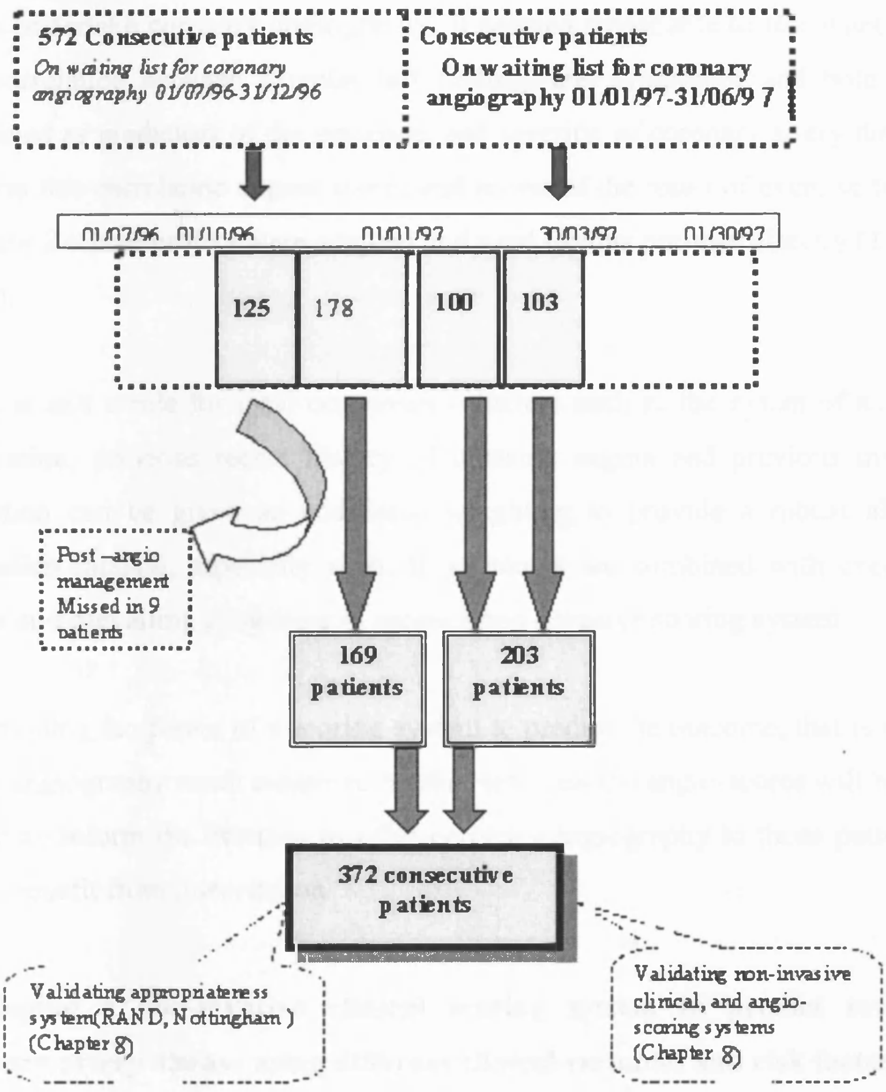


Figure 7: Population used to test non-invasive clinical scoring system with existing appropriateness scoring system (Chapter 8)

Method adopted to develop a non-invasive clinical scoring system based on consensus.

Various appropriateness and prioritisation systems have been developed based on the result of the exercise test and symptoms as a means of determining whether or not to undertake coronary angiography. It seemed reasonable to test whether there was correlation between exercise test findings and symptoms, and both of these combined as predictors of the presence, and severity, of coronary artery disease. To perform this correlation angina scores and scores of the result of exercise tests from the New Zealand project were adapted and used for this purpose directly (Tables 2,3 and 4).

There is still a role for local consensus – factors such as the extent of anti-angina medication, previous recent history of unstable angina and previous myocardial infarction can be given an additional weighting to provide a robust alternative evaluation method, especially when these scores are combined with exercise test scores and prevailing symptoms to create a non-invasive scoring system.

Ascertaining the power of a scoring system to predict the outcome, that is the result of the angiography result measured by the New Zealand angio-scores will be helpful as it may inform the decision to offer coronary angiography to those patients who might benefit from intervention.

Developing a non-invasive clinical scoring system to predict severity of coronary artery disease using different clinical variables and risk factors.

Based on the hypothesis that a scoring system might be developed that would predict the severity of coronary artery disease, clinical variables and risk factors were identified using uni- and multi-variant analysis. Significant variables that predicted the severity of coronary artery disease were given weight and incorporated with scores of symptoms and of exercise tests.

The predictive power of previously reported systems based on consensus and other methods were compared with a novel system devised by the author. Validation was carried out on a separate group of patients.

Statistical methods

The Kruskal-Wallis test was used to test for correlations between the exercise test result, symptoms and angiography scores. Uni-variate and multi-variate analyses were used to identify variables to develop models that predicted the severity of coronary artery lesions measured by the New Zealand scoring system in Chapter 4, and the new angio-scoring system. Pearson's test was used to test the correlation between non-invasive clinical and angiography scores in Chapter 3. Receiver-operator curves were used to plot sensitivity against specificity. The area under the curve was used to identify group of patients referred for a revascularisation procedure after angiography (Chapters 6 and 7). Student's *t- test* was used to test the predictive power of non-invasive clinical scores in patients who received revascularisation procedures (Chapter 7).

Kaplan-Meier analysis and log rank tests were used to evaluate survival rate, and to compare the survival between two groups of patients with non-invasive test scores either side of the threshold score (Chapter 5).

The Chi-square test was used in Chapter 8 to test for differences in non-invasive clinical scores between appropriate, uncertain, and inappropriate rated groups of patients according to RAND/UCLA, and Nottingham appropriateness ratings; and to compare appropriateness ratings and non-invasive clinical scores with angiography scores as measured by the New Zealand or new angio-system.

Exercise test, angina and coronary disease scoring systems

Scoring systems developed by other authors (as shown below) were applied in various chapters. Scores for exercise test results, severity of angina symptoms and the extent of coronary disease defined at coronary angiography are described in Tables 2, 3 and 4 below.

Exercise stress test	Test result	Score
Bruce Stage 4	Negative	0
Bruce Stage 3	Mildly positive	8
Bruce Stage 2	Positive	12
Bruce Stage 1	Very positive	22

Table 2: Scores for the result of the exercise test were adapted from the New Zealand project (Hadron DC et al *1997*)

Angina class on current medication	Scores
Class I: angina on strenuous exertion	1
Class II: angina on walking or climbing stairs rapidly	2
Class III: angina on walking one or two level blocks	8
Class IVA: Unstable angina, rest pain	18

Table 3: Symptom scale according to Canadian Cardiovascular Society criteria and scored according to the New Zealand project (Hadron DC et al *1997*).

Degree of coronary artery obstruction (% Diameter occluded)	Scores
No significant coronary obstruction (≥50%)	0
1 Vessel disease (50-74%)	8
>1 Vessel disease (50-74%)	9
1 Vessel disease (≥75%)	9
1 Vessel disease (≥90%)	14
2 Vessel diseases (50-89%)	15
2 Vessel diseases (both≥90%)	15
1 Vessel disease (≥90%) proximal left anterior descending artery	19
2 Vessel disease (≥90%) left anterior descending artery	19
2 Vessel disease (≥90%) proximal left anterior descending artery	19
3 Vessel disease	19
3 Vessel disease (≥90%)in at least one	19
3 Vessel disease (75%) proximal left anterior descending artery	19
3 Vessel disease (≥90%) proximal left anterior descending artery	27
Left Main (50%)	27
Left Main (75%)	32
Left Main (≥90%)	36

Table 4: Angiography scores adapted from the New Zealand project (Hadron DC et al).

Chapter 3

Developing a non-invasive clinically-based scoring system for elective coronary angiography: A consensus approach

Chapter 3

Developing a non-invasive clinically-based scoring system for elective coronary angiography: A consensus approach

Factors such as the progressive prescription of anti-angina medication, history of unstable angina or myocardial infarction are significant landmarks during any patient's coronary career. It ought to be possible to determine whether these and other factors such as prevailing symptoms and results of non-invasive tests could, with suitable weighting, be incorporated into a novel, robust evaluation method or model predictive of the presence and severity of coronary disease.

This hypothesis was tested in the following study.

METHODS

Patient population

All patients with a working diagnosis of coronary heart disease (CHD) who had been placed on the waiting list for diagnostic coronary angiography during the period 1 July to 31 December 1996 were studied. Data was validated using a subset of 125 consecutive patients chosen at random from the original patient population. Population has been described in Chapter 2 (Figures 2 and 3).
Not every patient referred for investigation was included in the study. For example, some patients were investigated primarily with a view to valve replacement, others as part of a transplant work-up.

Data collection

A standard data abstraction form was designed. Upon referral, each patient was placed on the coronary angiography waiting list and the author completed basic demographic and clinical data prospectively (Clinical variables collected are shown below).

Age
Gender
Symptoms: classified according to the Canadian Cardiovascular Society
Exercise stress test using the Bruce protocol
Number of anti-anginal drugs (excluding short-acting nitrates)
Diabetes defined as a recorded diagnosis or treatment for diabetes
Hypercholesterolaemia defined as plasma total cholesterol $\geq$ 6.5 mmol/L
Hypertension defined as recorded diagnosis or systolic $\geq$ 160 mm Hg or diastolic $\geq$100 mm Hg
Previous myocardial infarction
Previous coronary bypass surgery
Unstable angina (or worsening angina)
Ethnic origin
History of smoking
Angiographic data after review of the original angiograms, scored according to the New Zealand

A standard approach of classifying coronary disease into one, two and three vessel disease was used when a coronary atheromatous lesion involved a major coronary artery (left anterior descending, circumflex and right coronary arteries). A more detailed classification was used to describe lesions affecting the proximal left anterior descending or left main artery. A coronary stenosis was defined as 'significant' if the diameter of coronary artery was narrowed by more than 50% and 'not significant or normal' if less than 50%.

Statistical methods

The Kruskal-Wallis test was used to test the correlation between the exercise test scores, scores that were assigned according to the severity of symptoms (according to the Canadian Cardiovascular Society criteria), and angiography scores adapted from The New Zealand project (Tables 2, 3 and 4).

Pearson's correlation test was used to test the correlation between the non-invasive clinical scoring system and angiography scores. Because the data of the exercise test and symptoms were not truly parametric, the Kruskal-Wallis test was used to test the correlation between the exercises test result, symptoms and angiography score (see Chapter 2).

The correlation between exercise test scores, angina symptoms and the sum of these was tested in a subset of 125 consecutive patients who underwent coronary angiography. Because the variables tested were not truly continuous, the Chi-square test was applied.

Model Development

The model was developed in two stages: a training set comprising the entire study population, and a validation set comprising a subset of patients chosen at random from the original study population.

The extent of each patient's angina symptoms, result of an exercise test and findings at coronary angiography were awarded scores as shown in tables 2-4 (Chapter 2); scores were adapted from the New Zealand study.

Characteristics of study recruits

Patient characteristics are shown in table 5. 75% of the study population (125 consecutive patients) were men. Patients older than 60 year constituted 60% of the sample. One, two or more than two anti-angina drugs were being used to treat symptoms in 26%, 43% and 25% of patients respectively. 6% of patients were on no active anti-angina drugs at the time of referral for investigation.

21% of patients had a history of acute myocardial infarction and 19% of previous coronary bypass surgery.

Patients characteristics	% (n=125)
Gender	
Male	75
Female	25
Age	
<60	40
60-74	53
>74	7
Smoker	11
Diabetes	10
Hypertension	21
Hypercholesterolaemia	27
Symptomatic angina	95
Anti-Anginal drugs	
None	6
1 drug	26
Two drugs	43
>Two drugs	25
Exercise Test	
Not done	16.8
Positive	78.4
Negative	4.8
Previous myocardial infarction	21
Previous angioplasty or bypass graft	19
Outcome	
Medical management	46
CABG	22
PTCA	32

Table 5 - Patient characteristics

Correlation between exercise test and angiography scores

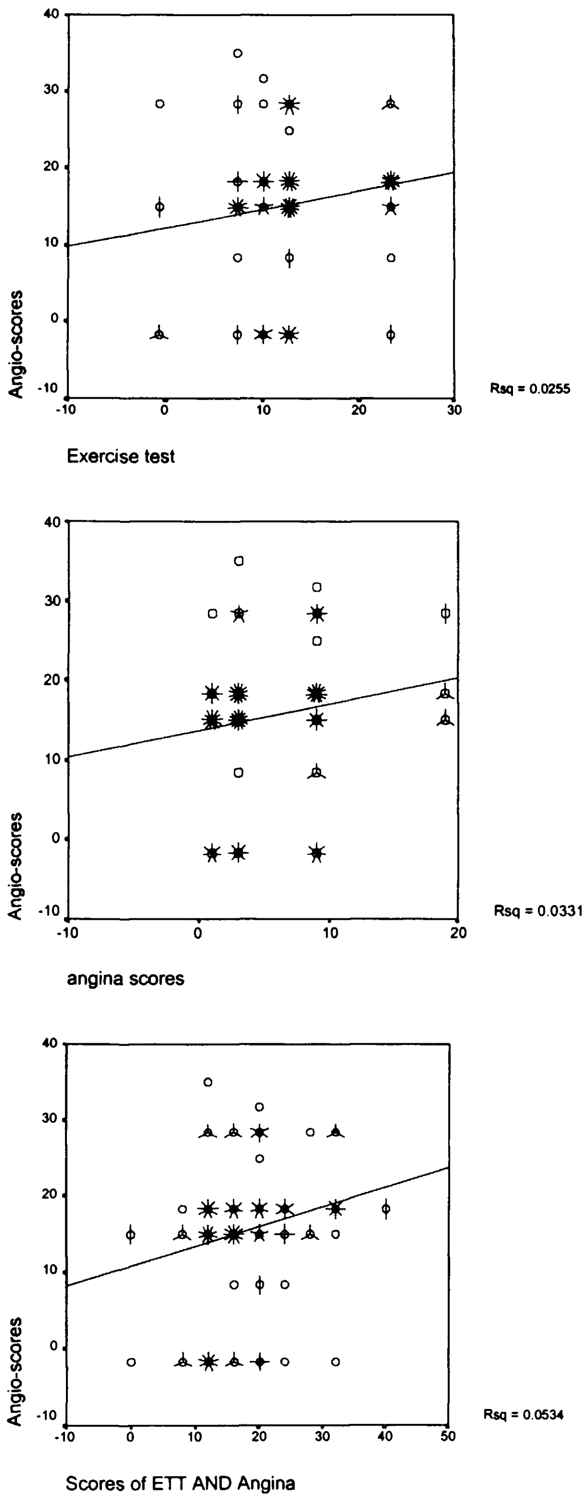
Exercise testing was performed in 83% of patients. 20%, 40% and 17% were considered positive at stage I, stage II and stage III respectively. 5% of tests were considered negative. There was no significant correlation between exercise test and angiography scores (Chi-square 5.1 for four degrees of freedom; p=0.28; Figure 8).

Correlation between angina score and angiography scores

6 patients (4.8%) were asymptomatic. 23 (18%), 45 (36%), 43 (34%) and 8 patients (6%) had angina of Canadian Cardiovascular Society Class I, Class II Class III, and Class IVA respectively. There was no significant correlation between the angina and angiography scores (Chi-square 4.3 for 3 degrees of freedom; p=0.24).

Correlation between the combined scores of exercise test and angina with angiography score

Figure 8 shows that there was a weak but significant correlation (correlation coefficient 0.244; p =0.006).



(A petal represents one case)

Figure 8: Correlation between angina scores, exercise scores and their sum, with the angiography scores.

Outcome of initial mapping of waiting list patients to a clinical scoring system

Because there was only weak correlation between the sum of the exercise test and symptom severity score and the scores for severity of coronary artery disease, an alternative scoring system seemed necessary. Other variables, which would strengthen the identification of severity of coronary disease, seem to be essential. An alternative model was deemed necessary.

Modifications to the New Zealand system

The New Zealand project was designed for patients undergoing elective coronary bypass surgery. Consequently, it is probably not a surprise to find that the model was lacking in predictive power, so modifications to the New Zealand criteria – in order to be suitable for patients who were referred for elective coronary angiography – were considered.

It was decided to try to incorporate the results of non-invasive tests into the model, so scores for coronary angiography were combined with other factors (such as exercise test results, symptoms and social scores) to rank patients on a waiting list for coronary bypass surgery. The power of non-invasive clinical factors to predict the 'outcome', that is the result of coronary angiography, has to be evaluated as the decision to proceed to revascularisation procedures mainly relies on the anatomical map of coronary artery disease. Thus if non-invasive clinical factors can predict the angiographic result it will be helpful to offer coronary angiography for those patients who might benefit from this procedure.

With adequate weighting factors applied, it was hypothesised that these factors might improve the model's ability to predict the extent and severity of coronary artery disease, an essential step into ascertaining priority for investigation. This is explored in the following section.

Weightings applied

Weightings for the severity of angina and exercise test results were adapted directly from the New Zealand and Duke criteria, with additional weighting applied for patients who could not exercise. Because the population was comprised predominantly of those attending the outpatient department, the weighting applied

for patients with Canadian Cardiovascular Society class IV angina was that assigned to class IVA, the appropriate classification for patients with angina at rest but managed medically (without admission to hospital) (Appendix 2).
By local consensus, additional weighting was given according to the extent of anti-angina medication m – more severe coronary artery disease needs more anti-angina medication to control the symptoms; thus scores of 5, 10, 15 and 20 were assigned to patients who were taking one, two, three and more than three anti-angina drugs. Symptoms suggestive of progressive angina or change of angina class towards a higher class tend to increase the likelihood of sustaining an acute cardiac event so this factor was given a score of 10 (Table 6).

Myocardial infarction occurs in the vast majority of cases due to underlying atherosclerotic coronary artery disease. A weighting factor of 10 was added if there was a history of myocardial infarction.

Scores for each clinical criterion were summed and multiplied by a scaling factor of 1.25 in order to convert the scores to a scale with a maximum of 100.

Data on the social impact of symptoms were omitted, since the data collection form was designed before the New Zealand project had been published. This is not a major problem because, to some extent, social scores reflect the severity of symptoms and quality of life (Brown NB et al *1989*).

Data describing the extent of coronary artery disease were omitted because these only become available once angiography has been performed. Clinical criteria were used to predict the severity of coronary disease.
The outcome was a consensus-based non-invasive clinical scoring system (original version) Table 6.

Statistical tests

Because non-invasive clinical scores proved to have a normal distribution, the Student's *t- test* was used to measure the difference in non-invasive clinical scores between patients who had normal or insignificant coronary artery disease and those who had significant coronary artery disease. Pearson's correlation test was used to test the non-invasive clinical scores and the angiography scores. Bi-variate analysis regression function was used to test the power of non-invasive clinical scores in predicting the angiography scores.

RESULTS

Patients with minor coronary disease

22 patients had normal coronary arteries or a coronary stenosis of less than 50% (generally considered *non-obstructive* or *insignificant*). These patients had an angiography score of less than 8. The mean non-invasive clinical score for this group of patients was 23.5 ± 8.6.

Patients with significant coronary disease

The mean non-invasive clinical score for patients with a coronary stenosis of more than 50% in at least one of the major coronary arteries was 30.7±10.5. The angiography score was equal to or more than 8.

Student's *t-test* showed that there was a significant difference in the non-invasive clinical scores between these two groups of patients (p=0.002). The Pearson correlation test showed there was significant correlation between the original version of the non-invasive clinical score and the angiography score, but this correlation was weak (Pearson correlation 0.308, p=0.0001). The mean angiography score was 15.2 ± 8.5 and the mean non-invasive clinical score was 29.5 ±10.5. Thus the non-invasive clinical score predicted successfully the presence of coronary artery disease (Figure 9).

Using the bi-variate analysis regression function, the power of the non-invasive clinical score to predict the severity of coronary artery disease was assessed. Non-invasive clinical scores were weak but significant predictors of the angiography score (ANOVA test, adjusted R^2= 0.088, P=0.0001). This test supported the concept that combined clinical scores are significantly correlated with angiography scores.

Heading	Details	Score s
Angina	Class I: angina on strenuous exertion	**0**
	Class II: angina on walking/climbing stairs rapidly	**2**
	Class III: angina on walking 1-2 level blocks	**8**
	Class IVA: unstable angina/rest pain	**18**
Exercise Test	Bruce stage IV positive or Stage III Negative	**0**
	Stage III positive (mild positive)	**8**
	Stage II positive	**12**
	Stage I positive (Very positive)	**22**
	Unable to exercise	**10**
Number of anti-angina drugs	None (excluding GTN)	**0**
	One	**5**
	Two	**10**
	Three	**15**
	>Three	**20**
Previous MI		**10**
Unstable or Progressive angina		**10**
Total scores		**80**

Table 6: Non-invasive clinical scoring system (original version)

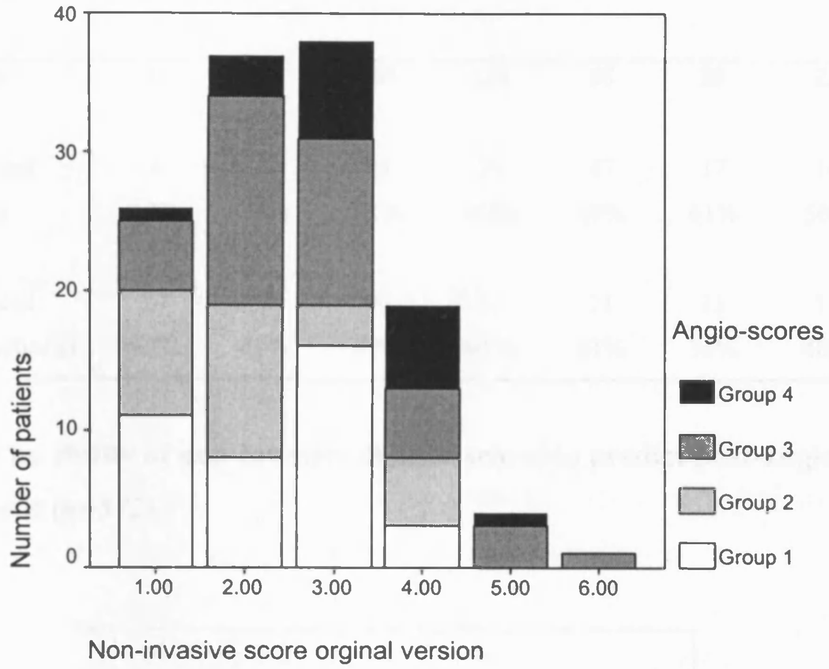


Figure 9: Correlation between original non-invasive clinical scores and severity of coronary disease estimated by New Zealand angio-scores *(n=125).*

Correlation between clinical scores and post-angiographic management

This was validated in the original cohort of 572 consecutive patients who underwent coronary angiography during the period of 1st of July -31st of December 1996 * (Figure 2). Non-invasive clinical scores according to the original system were assigned to each patient. The ability of the non-invasive scoring system to predict the outcome was validated in this group of patients (Table 7 and Figure 10).

There was a linear correlation between the clinical scores and post-angiography management. As the clinical scores increased from 0 to 49, the proportion of patients who were referred for revascularisation also showed a steady increase from 13% to 69%, but as the scores rose above 49, the proportion of such referrals declined slightly from 69% to 55%.

* This group of patients include a group of 125 consecutive patients used to develop the scoring system.

Score	0-9	10-19	20-29	30-39	40-49	50-59	60-69	≥70
No. Patients	31	74	184	128	68	28	25	34
Recommended Intervention	4 13%	29 39%	94 51%	77 60%	47 69%	17 61%	14 56%	19 55%
Recommended Medical treatment	27 87%	45 61%	90 49%	51 40 %	21 31%	11 39%	11 46%	15 45%

Table 7: The ability of non-invasive clinical scores to predict post-angiography management *(n=572)*.

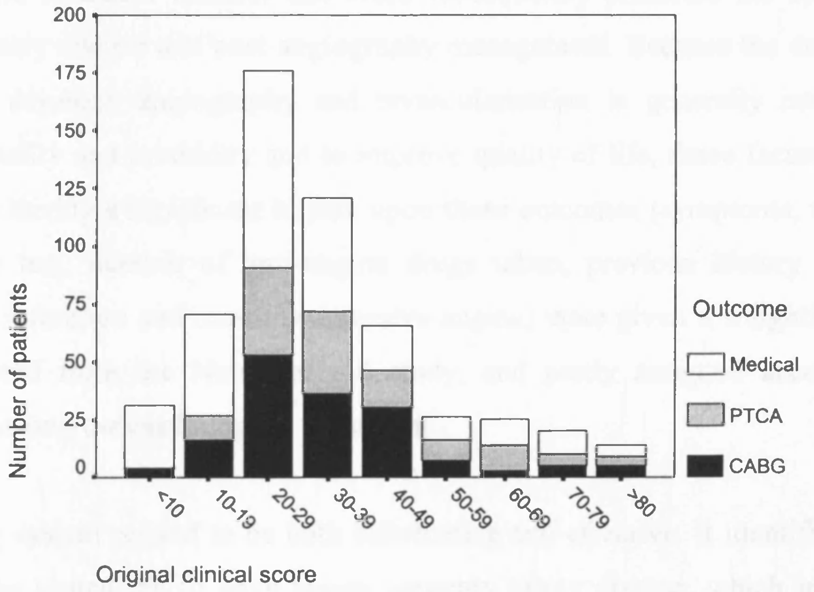


Figure 10: Relation between original clinical scores and post angiography management *(n=572)*.

The Student's *t-test* was used to assess the predictions for the group of patients referred for intervention. Leven's test for equality of variance showed that patients referred for revascularisation had a mean non-invasive clinical score of 31.7 ±10.1 versus 27.4±10.4 for those advised to continue medical treatment ($p= 0.02$) (Appendix 3).

DISCUSSION

Clinicians are used to providing, at an instinctive level, an estimate of risk of coronary heart disease and of the probability of anatomically significant coronary atheroma. Unfortunately, this process introduces at best an element of inequity in the selection of patients for invasive investigation. Formal scoring systems remove this, providing an explicit means of deciding who should and should not be investigated and provides a sound means of limiting access to coronary angiography to those patients most likely to benefit. There is a danger that, if misapplied, such systems could be introduced as a mechanism to ration access to angiography.

The aim of this study was to develop a prioritisation scheme using a non-invasive clinical scoring system, based on consensus among cardiologists at the Glenfield Hospital; and to assess whether this score subsequently predicted the severity of coronary artery disease and post-angiography management. Because the decision to proceed to coronary angiography and revascularisation is generally intended to reduce mortality and morbidity and to improve quality of life, those factors widely accepted as having a significant impact upon these outcomes (symptoms, results of an exercise test, number of anti-angina drugs taken, previous history of acute myocardial infarction and recent progressive angina) were given a weighting value partly adapted from the New Zealand study, and partly assigned according to consensus among the cardiologists in the unit .

The scoring system proved to be both informative and effective. It identified many of those who turned out to have severe coronary artery disease, which in clinical practice is of considerable value. In addition, it identified many of those who were subsequently referred for a coronary revascularisation procedure. It may prove worthwhile trying to refine and improve the predictive model further. Inclusion of multiple risk factors enhanced the prediction of the severity of coronary artery disease as well as post -angiography management.

This clinical scoring system has the potential to become a practical tool to assist clinicians in the evaluation of patients with ischaemic-sounding chest pain. Used appropriately, it could enable clinicians to offer coronary angiography only to patients who might benefit from coronary angiography. In time, this could lead to a more rational and structured approach to investigation, shorter waiting lists for angiography and eventually shorter delays on the list. Although this model was successful in that it achieved its intended aims, no scoring system is ever perfect, largely because of the complexity of individuals and the great variability of response to coronary artery disease. There are obvious limitations of the current system. For example, it does not take into account well-recognised ‘coronary risk factors’ that are often recorded by doctors when evaluating patients with chest pains which might be angina; these factors include hypercholesterolaemia, hypertension, diabetes mellitus, a family history of coronary artery disease and ethnic origin. There is no doubt that these increase the likelihood of a patient with chest pains having angina as its cause, there is no good evidence that they might predict the severity of coronary artery disease. The relatively small size of the study population may be considered too small by some clinicians and another dataset needs to be identified to prove the utility of the model beyond doubt.

Further refinements were considered necessary to improve the scoring system to overcome some of its limitations. These are described in the next chapter.

Chapter 4

Developing a non-invasive, clinically-based scoring system for elective coronary angiography: A predictive model approach

Chapter 4

Developing a non-invasive, clinically-based scoring system for elective coronary angiography: A predictive model approach

The preceding chapter reported on the development of a scoring system, which incorporated the findings of non-invasive tests, whether using ratings based on a consensus of cardiologists at Glenfield Hospital, or those developed for the New Zealand project. While informative, it lacked utility. Consequently, it proved necessary to develop one scoring system to predict the severity of coronary artery disease as well as to predict post-angiography management.

METHODS

Patient population

A group of 178 consecutive patients on a waiting list for elective coronary angiography was used to develop non-invasive clinical scoring system, and a group of 100 consecutive patients was used to validate this system.

The patient population has been described in Chapter 2 'Methods' (Figure 4).

RESULTS

Patient population

73% of the patient group (178) were men and 64% were older than 60 years. Symptoms were treated by one, two or more than two anti angina drugs in 27%, 43% and 23% of patients respectively. 7% of patients were not taking anti-angina drugs at the time of referral for investigation. The following risk factors for coronary artery disease were found: smoking 7%, diabetes 16%, hypertension 26% and hypercholesterolaemia 26% (Table 8).

Patients characteristics		% (n=178)
Gender	Male	73
	Female	27
Age	<60	36
	60-74	58
	>74	6
Smoker		7
Diabetes		16
Hypertension		26
Hypercholesterolaemia		26
Symptomatic angina		95
Anti-angina drugs	None	7.
	1 drug	27
	Two drugs	43
	Three drugs	16
	> Three drugs	7
Symptoms (Angina)	No angina	5
	Angina Class I	17
	Angina Class II	34
	Angina Class III	37
	Angina Class IV	7
Exercise Test	Not done	5
	Positive stage III	15
	Positive stage II	41
	Positive stage I	20
	Patient could not perform	6
	Negative	13
Previous infarction		57
Previous PTCA/CABG		22
Outcome	Medical management	53
	CABG	25
	PTCA	22

Table 8: Characteristics of patients with suspected coronary artery disease who underwent coronary angiography.

Uni-variate analysis

A series of variables were studied by uni-variate analysis to test their ability to predict the angiography scores according to the New Zealand system. Table 9 shows that there were significant differences in mean angiography scores according to age. Table 10 shows the ability of a variety of variables to predict angiography scores. Factors associated with significantly higher mean angiography scores were gender (males); increasing age; diabetes mellitus; a previous myocardial infarction and previous coronary bypass surgery. Although statistically hypercholesterolaemia was not significant predictor of severe coronary artery disease, it was a clinically good predictor.

Variables, which did not statistically predict significant coronary artery disease, were unstable angina, smoking, hypercholesterolaemia, hypertension, and severity of symptoms (Table 10).

		Mean Difference	Std. Error	Sig.	95% Confidence Interval	
AGE					**Lower limit**	**Upper limit**
<50 years	50-64 years	-6.0134	2.1138	.019	-11.2321	-.7947
	>64 years	-7.0763	2.1301	.005	-12.3352	-1.8174
50-64 years	<50 years	6.0134	2.1138	.019	.7947	11.2321
	>64 years	-1.0629	1.3496	.734	-4.3948	2.2690
>64 years	<50 years	7.0763	2.1301	.005	1.8174	12.3352
	50-64 years	1.0629	1.3496	.734	-2.2690	4.3948

- *The mean difference is significant at $p<0.05$ level*

Table 9: ANOVA test showing the power of age to predict angiography scores.

Variables		Mean angiography scores	SD (standard deviation)	P value
Sex	Male	16.8	10.3	0.001
	Female	11	7.5	
Diabetes	Diabetic	18.8	8.9	0.012
	Non-diabetic	14.7	6.5	
Previous MI	History of MI	18.8	6.3	0.000
	No history of MI	13.4	9.2	
Previous CABG	Previous CABG	19.8	6.2	0.000
	No previous CABG	14.3	8.8	
Unstable angina	Yes	15.1	9.1	0.816
	No	15.4	7.9	
History of Smoking	Yes	15.2	4.5	0.997
	No	15.2	9.1	
Hypercholesterolaemia	Yes	17	8.3	0.099
	No	14.6	8.8	
Hypertension	Yes	15.5	8.9	0.836
	No	15.2	8.7	
Symptoms	Class I, II	14.9	8.7	0.512
	Class III, IV A	15.7	8.7	

Table 10: Uni-variate analysis of non-invasive clinical factors in patients with suspected coronary artery disease who underwent coronary angiography.

Multivariate analysis and logistic regression

Previous myocardial infarction, gender, age, hypercholesterolaemia and diabetes mellitus predicted the severity of coronary artery disease in multivariate analysis. Unstable angina did not feature, perhaps due to the other factors (Table 11).

Variables	Cumulative Adjusted R^2	Coefficient	Standard error
Previous MI	0.84	4.26	1.24
Sex	0.134	5.69	1.33
Age (years)	0.176	0.21	0.06
Hypercholesterolaemia	0.223	4.31	1.29
Diabetes	0.247	4.31	1.29

Table 11: Model providing the best prediction of the severity of coronary artery disease according to the New Zealand angiography scoring system.

Consequently, the above variables were included with the exercise test and angina scores in the clinical scoring system. Hypercholesterolemia was included because it was clinically significant in predicting severe coronary artery disease.

Each variable was assigned a weighting factor that reflected the extent to which each factor was able to predict the angiography score and subsequent management. These weights were based on the statistical analysis and on a consensus of Cardiologists in the unit. This resulted in the modified scoring system as shown in Table 12.

	Details	Score
Angina	Class I: angina on strenuous exertion	0
	Class II: angina on walking or climbing stairs rapidly	2
	Class III: angina on walking one or two level blocks	8
	Class IVA: unstable angina, rest pain	18
Exercise Test	Bruce stage IV positive or Stage III Negative	0
	Stage III mild positive	8
	Stage II positive	12
	Stage I very positive	22
	Unable to exercise	10
Age	50-64	4
	>64	8
Sex	Male	10
Diabetes		7
Hyperchol*		7
Previous MI		8

* = *Hypercholesterolaemia*

Table 12: Modified non-invasive clinical scoring system

Validation of the modified scoring system

Because coronary angiography scores are not continuous variables, patients were allocated to the following groups:

Group 1: (n=44)	*angiography scores <14*	*normal or minimal or mild disease*
Group 2: (n=45)	*angiography scores 15-18*	*moderately severe coronary disease*
Group 3: (n=45)	*angiography scores 19-26*	*severe coronary disease*
Group 4: (n=44)	*angiography scores 27-36*	*very severe coronary disease*

Patients in groups 3 and 4 have a pattern of coronary artery disease that is widely accepted as being appropriate for revascularisation. Figure 11 show the distribution of non-invasive scores among these four groups.

Non-invasive clinical score of less than 30

29% of all patients had a score of less than 30. 13% had severe disease (groups 3 and 4) and 86.5% had mild or moderate coronary artery disease (groups 1 and 2).

Non-invasive clinical score of 30-39

62 patients were assigned to this group of scores, 35 patients (56%) had severe coronary artery (angiography scores group 3 and 4).

Non-invasive clinical score 40-49

51 patients had a score of 40-49. 73% of these had severe coronary disease (groups 3 and 4) and 27 % had mild or moderate coronary disease (groups 1 and 2).

Non-invasive clinical score greater than 49

7% of all patients had a score greater than 49. 77% of these had severe coronary disease (groups 3 and 4), and 23% mild or moderate coronary disease (groups 1 and 2).

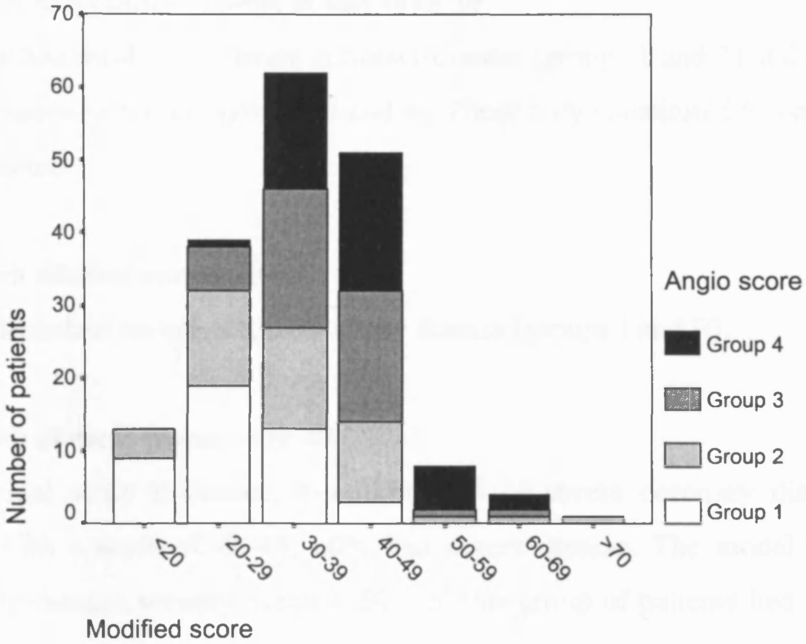


Figure 11: Ability of modified scoring system to predict the angiography scores *(n=178).*

CONCLUSION

Using a non-invasive clinical scoring system based on multivariate analysis, it seems possible to predict, with reasonable accuracy, the severity of disease that will be found at coronary angiography. With experience, of course, a clinician may well develop a 'feel' for the likelihood of disease based on individual risk factors. Combining a patient's medical history, symptomatology and exercise test results into a mathematical model should add a sufficient degree of sophistication and accuracy when applied by those less experienced.

No predictive model can be developed in isolation and it is always necessary to ensure that its claims are reliable by careful validation. The model developed above was validated on a further set of patients.

Validation of the clinical scoring system (Modified version)

The ability of the scoring system to predict the angiography score was evaluated in a group of 100 consecutive patients (population discussed in Chapter 2). Because the angiography scores are not truly continuous, the angiography scores were again divided into four groups as described above.

Patients who had clinical scores of less than 30

The majority had mild or moderate coronary disease (groups 1 and 2) and only 31% had severe coronary disease (groups 3 and 4). These only constituted 5% of the total group of patients.

Patients with clinical scores 30-39

30 % of patients had severe coronary artery disease (groups I and II).

Patients with clinical scores over 40

As the clinical score increased, the likelihood of severe coronary disease also increased. With a score of 40-49, 60% had severe disease. The model tended to over-estimate disease severity because 20% of this group of patients had normal or minimal coronary disease.

When the score was in the range 50-59, 63% had severe disease and at 60 or over 100% (Figure 12).

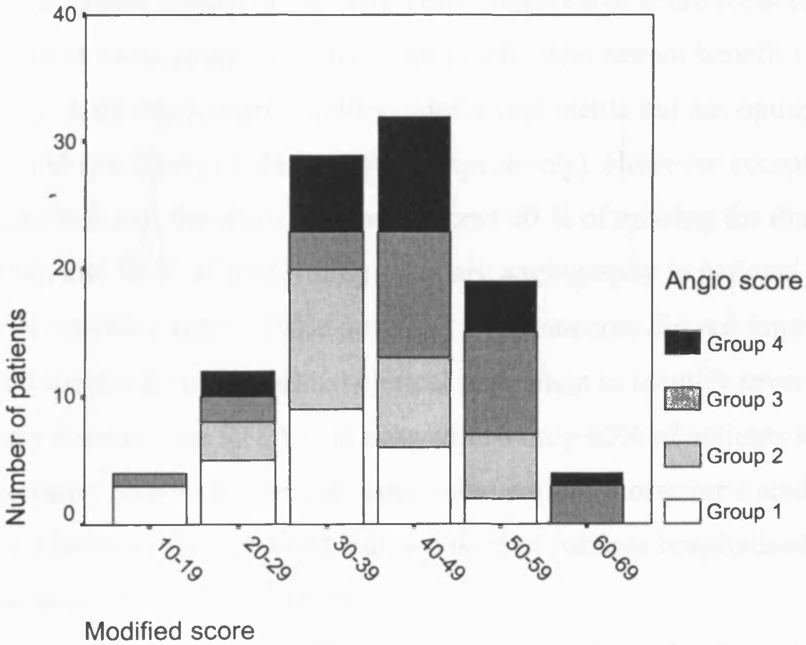


Figure 12:The ability of the modified scoring system to predict the severity of coronary artery disease *(n=100)*.

Determine the threshold score:

Receiver operator characteristics curve

It was necessary to evaluate the scoring system in order to identify how valuable this system might be in predicting such severity of coronary artery disease that it is usually widely accepted that intervention is indicated on prognostic grounds.

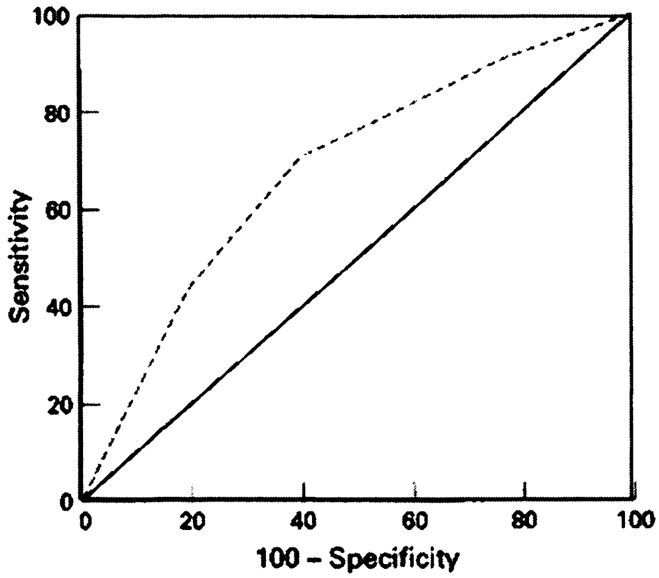
Sensitivity and specificity for various scores in a group of 100 consecutive patients on waiting list from 1 January onward (see chapter 2) were measured for both the original and the modified scoring system and the ROC was drawn for both. Figure 13 shows that the modified scoring system was slightly better than the original, as the ROC curve moved 'upwards and to the left' in the graph.

A non-invasive clinical score (modified version) of 20 had a sensitivity of 98% but a specificity of only 6%; a score of 30 had sensitivity of 89% and specificity of 22%; and a score of 40 had sensitivity of 71% and specificity of 60%.

As a threshold scores increases the risk of mis-diagnosing coronary artery disease increases as well (False negative), but a decrease in threshold score reduces the number of patients undergoing coronary angiography who cannot benefit from it (False positive). A threshold score of 40 yielded a reasonable but not optimal level of sensitivity and specificity (70%, and 60 %respectively). However acceptance of such score, assumes that the clinician has to accept 40 % of missing the diagnosis (false negative), and 30 % of performing coronary angiography in patients with normal or mild coronary artery (False positive). This outcome did not improve the sensitivity and specificity of individual clinical judgement to identify severe coronary artery disease. The RITA trial showed that only 62% of patients had significant coronary artery disease warranted intervention. Moreover a study conducted by Albertson P et al showed that two third of patients hospitalised with chest pain had normal coronary arteries.

Other benefits of scoring system will be discussed throughout the thesis but briefly the referral system may be simplified, and variation in using coronary angiography reduced

A



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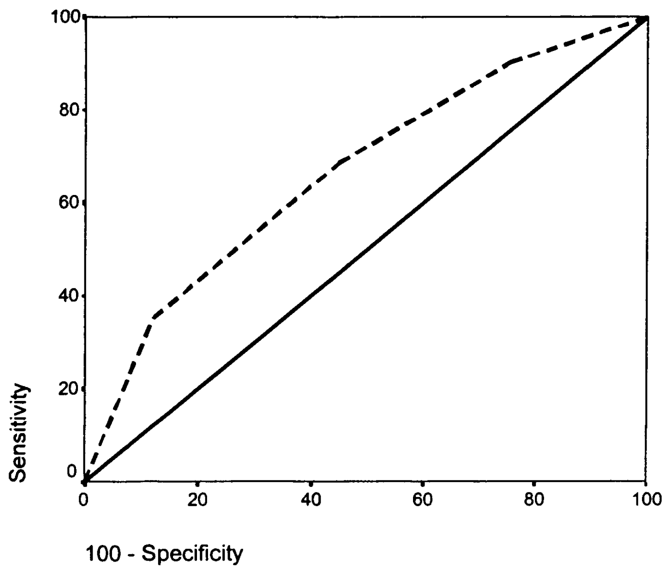

Figure 13: Receiver-operating characteristic curve for *A) modified non-invasive clinical scoring system (Leicester system) B) the original non-invasive clinical scoring system (Leicester system) (n=100)*

Cumulative frequency curve for clinical scores

Non-invasive clinical scores (using the modified system) were given to individual patients from all those put on the waiting list for coronary angiography. It was noted that more than half had a score of less than 30 and about three-quarters a score of less than 40 (Table 13).

Table 14 shows the cumulative proportion of patients who were referred for intervention and the declining proportion for whom medical management was the best option as non-invasive clinical scores increased.

Non invasive clinical scores	Cumulative Percent (Modified scores)
Scores ≥ 80	2.1
Scores ≥ 70	5.4
Scores ≥ 60	9.3
Scores ≥ 50	14.8
Scores ≥ 40	26.5
Scores ≥ 30	48.6
Scores ≥ 20	80.7
Scores ≥ 10	94.7
Scores ≥ 0	100

Table 13: Cumulative distribution of non-invasive clinical score

Non-invasive score	Group A	Group A Cumulative	Group A Cumulative %	Group B	Group B Cumulative	Group B Cumulative %
<10	4	4	1.3	27	27	9.9
10-19	29	33	11	45	72	26.6
20-29	94	127	42	90	162	60
30-39	77	204	68	51	213	79
40-49	47	251	83	21	234	86
50-59	17	268	89	11	245	90
60-69	14	282	94	11	256	95
70-79	10	292	97	10	266	98
>80	9	301	100	5	271	100

Table 14: Cumulative percentage of patients with coronary artery disease referred for either intervention (Group A) or medical management (Group B).

Discussion

The aim of this study was to develop a scoring system using easily obtainable clinical variables that predicted the severity of coronary artery disease and the revascularisation group in post angiography management. Others have attempted to identify clinical variables that might help predict coronary angiographic findings and the decision to refer for revascularisation or to continue medical management.

There were small studies testing the predictive power of deferent clinical and risk factors of coronary artery disease. A meta-analysis of 24 studies by Yamada et al (20) considered the exercise test and other clinical variables predicted that coronary artery disease shows that gender, chest pain symptoms, age, hypercholesterolaemia, positive exercise test, diabetes mellitus, smoking history, hypertension and family history of coronary artery disease are significant predictors of the presence of coronary artery disease. These findings are similar to those found in the study reported here, with the exception of symptoms (Yamada H et al 97).

The outcome was as follows:

Gender: in this study gender was confirmed as a significant predictor of severity of coronary artery disease and the same results were found in all 14 studies that enrolled this factor in their multivariate analysis. In addition, it was predictive of the extent of coronary artery disease in terms of number of arteries involved in 6 of 8 studies.

Age: was identified in this study as a significant predictor for coronary artery disease. Meta analysis showed age to be an independent predictor of coronary artery disease in 16 of 21 studies.

Symptoms: symptoms scored according to the Canadian Cardiovascular society did not predict the severity of coronary artery disease; this contradicted the results of meta-analysis which showed that symptoms were a good predictive variable for coronary artery disease in 14 of 15 studies that considered this variable, only one study scaled the symptoms according to Canadian Cardiovascular Association; it was a good predictor for the extent of coronary artery disease in 7 of 10 studies.

Diabetes Mellitus: this was a significant predictor in this study. It was a good predictor in only 4 studies of 11 studies, which considered this variable, and it was a good predictor of the extent of coronary artery disease in 5 of 9 studies.

Hypercholesterolaemia: uni-variate analysis in this study showed that hypercholesterolaemia was not a significant predictor of the severity of coronary artery disease but it was in multivariate analysis. Compared to the result of meta-analysis hypercholesterolaemia was predictive in 6 studies of 10 studies and was a good predictor of the extent of coronary artery disease in 3 of 8 studies.

Previous myocardial infarction: this study found that a history of myocardial infarction was a significant predictor of the severity of coronary artery disease. This factor was considered only in 5 studies and was a good predictor for the extent of coronary artery disease in 4 of them; many studies excluded this variable.

One of the objective methods developed by Mark and colleagues from Duke University evaluated the prognostic value of the exercise test in coronary artery disease (Mark DB et al *1987*). Three factors were found to be helpful – maximum ST displacement, angina during the test and total exercise time. The treadmill scores added important prognostic information to both clinical and cardiac catheterisation data, making the decision to refer for surgery more easy; for example a patient with three vessel disease and a poor exercise test score may benefit from coronary surgery, while a similar patient with a more favourable exercise test outcome may not benefit from surgery.

No scoring system is ever perfect, largely because of the complexity of individuals and the great variability of response to coronary artery disease. The model developed here was no exception. Applying different threshold scores changed the sensitivity and specificity of the score. For example, a threshold score of 40 yielded a reasonable sensitivity of 71% and specificity of 60% in predicting a degree of coronary artery disease that would be appropriate for revascularisation; on the other hand, a score of less than 40 increased sensitivity at the cost of reduced specificity a score of 30 had sensitivity of 89% and specificity of 22%. If a threshold score of 30 was accepted, the group with clinical score of 30-39 will approximately double the number of patients eligible for coronary angiography (26.5% of population achieved clinical scores ≥ 40). 48.6% of the population achieved clinical scores ≥ 30; this percentage of patients would not be referred for coronary angiography with present funding.

The Glenfield unit performs about 1000 elective coronary angiograms each year – more could be performed but purchasers have not provided unlimited funds. Extrapolation from the British Cardiac Society recommendation, a target of 1500 revascularisation (coronary angioplasty, coronary bypass surgery)/million people would probably require 3000-4000 coronary angiographs. As the catchment's area of Leicestershire one million people or so, about 3000-4000 (NSF march 2000) coronary angiograms may be warranted annually. It is a simple matter to achieve this target – simply asking General Practitioners to refer more patients would suffice. This, however, would be an entirely inappropriate approach for two reasons. First, the number of patients whose coronary angiograms were normal would increase and the procedure is not risk-free. Second, it is not a sensible way to manage public funds.

How might such a target be best achieved? This can be achieved by applying a non-invasive clinical scoring system for all patients with suspected coronary artery disease to select patients who are eligible for this procedure. According to the hospital records about 1000 elective coronary angiographs are done annually (excluding patients proceeding to coronary angioplasty, unstable patients, and urgent patients). Thus it is necessary to increase the number of procedures 3 or 4 times to achieve the target. Because of fixed capacity we have to choose the patients who are more likely to reap the benefits of this procedure, by assigning clinical scores to all individual patients we choose the patients who have the highest scores. According to this study only a quarter of patients who were assigned clinical scores has to be referred to coronary angiography in order to allow other patients who might see the benefits of this procedure to be enrolled on waiting list. A threshold score of 40 or more seems about right for two reasons. First, a score of over 40 increased the likelihood of finding severe coronary disease through angiography. Second, a score below 40 seemed to identify a group of patients who may be referred for continued medical management, while scores over 40 largely identified those who might be referred for revascularisation. When capacity increases with the availability of additional resources the threshold score can be reviewed and a lower score adapted.

The presence of multiple risk factors enhanced the prediction of the severity of coronary artery disease and increases the risk of dying in patients with coronary artery disease not involving left main coronary artery disease managed by medical treatment (Detre K *1984*). If this non-invasive clinical scoring system were introduced into practice at all levels locally, regionally, and nationally it could achieve 1) an improvement in the quality of health services by offering coronary angiography for patients who might benefit from investigation while avoiding the risk of performing unnecessary procedures on patients who cannot benefit; 2) more rational access to coronary angiography by setting up a dynamic threshold that can be modified on the basis of sensitivity and specificity to identify severe coronary artery disease;.3) shorter waiting lists in the short term, and perhaps in the future no waiting list at all.

Clinical scoring systems are coming of age, making clinical decision-making more transparent and forcing a rethink about the implicit rationing that plagues much of the NHS. Doctors may not relish the idea of calculating a risk score but systems such as proposed in this chapter may be introduced principally because clients prefer an objective, overtly fair system to one which is physician-dependent and translucent.

Chapter 5

Identifying patients at increased risk of having a major cardiovascular event while awaiting investigation and revascularisation

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Identifying patients at increased risk of having a major cardiovascular event while awaiting investigation and revascularisation

The waiting list for coronary angiography and coronary revascularisation is under ever-greater pressure because both expanded indications for revascularisation and advances in technology increase the number of patients who warrant investigation. There is a significant variation in waiting list size when comparing developed countries; in New Zealand, for example, the mean time on a surgical waiting list varies between two months for urgent cases to 22 months for a routine procedure. Waiting times are not static – they rose from 304 days in 1990 to 617 days in 1993 (Agnew TM et al *1994*).

Questions related to this issue focus on whether a long waiting list is associated with an increased risk of avoidable morbidity or even mortality. Risk stratification has been proposed as a means for identifying groups of patients who are at needless risk if investigation or treatment is delayed. In a Swedish study, 29% of patients on a waiting list for revascularisation were admitted to hospital due to some acute cardiac event. Acute myocardial infarction and cardiac deaths may occur in 3.8 % (Bengston A et al *1996*). In Canada, the wait time for coronary bypass surgery is short, with a median of just 17 days; acute cardiac events including mortality occur in about 0.4 % of cases. (Naylor CD et al *1995*). In the UK, acute cardiac events occurred in 23% while awaiting coronary angioplasty; there was a high risk of acute cardiac events in patients with unstable angina, high tri-glyceride concentrations and young age (Chester M et al *1995*).

The aim of this section was a) to test the hypotheses that the risk of a major cardiovascular event – that is death, myocardial infarction or unstable angina – while awaiting investigation by coronary angiography or treatment with coronary bypass surgery or coronary angioplasty could be predicted from knowledge of the results of non-invasive tests and associated clinical scores; and b) to determine whether a threshold score might be defined as a guide to who should and should not, undergo coronary angiography.

METHODS

The names of all patients scheduled for coronary angiography between 1 July 1996 and 30 June 1997 were obtained at the time of referral. Patients were identified from the cardiac catheter laboratory logbook (Chapter 2).

The medical records of all patients who were referred for revascularisation were scrutinised and the outcome of the investigation, that is referral for coronary artery bypass surgery or percutaneous coronary angioplasty, was recorded. The frequency and timing of all acute cardiovascular events (defined as death, acute myocardial infarction or admission to hospital with unstable or progressive angina) that occurred between the date of acceptance for intervention and the date of admission for the procedure was also recorded. The following clinical information was also recorded onto a standard data abstraction form: symptoms, exercise tolerance test result, age, and history of previous myocardial infarction, diabetes mellitus and gender. Scores were assigned using the non-invasive clinical scoring system described in a previous chapter (Chapter 4).

Calculation of the non-invasive risk score

The following data were prospectively collected before putting patients on waiting list for coronary angiography: age, gender, previous acute myocardial infarction, hypercholesterolaemia (serum cholesterol ≥6.5 mmol/L or taking lipid lowering agent), history of diabetes mellitus, symptoms (graded according to Canadian Cardiovascular Society scale) and the result of an exercise tolerance test (chapter 3).

Statistical methods

Simple statistical methods in terms of mean and median were used to compare groups of patients who had a cardiac event and groups of patients who didn't have a cardiac event. The Kaplan-Meier analysis and log rank test were used to evaluate the survival rate and to compare the survival between two groups of patients with non-invasive test scores either side of a putative threshold score (see chapter 2).

RESULTS

Study population

372 consecutive patients with suspected coronary artery disease underwent coronary angiography during the study period 1 October 1996 – 30 March 1997 (Figure 5). Of these, 172 consecutive patients were referred for a revascularisation procedure. The outcome data for 6 patients was not available. No offer of revascularisation was made to 27 patients, because the procedure was either considered unnecessary (because symptoms were controlled by medication, coronary anatomy was deemed unsuitable for the intervention or the patient had decided against intervention) or contra-indicated (due to poor left ventricular function); continued medical management was recommended. Thus, the study population comprised 67 patients who were awaiting bypass surgery and 72 awaiting angioplasty. 20 patients sustained acute cardiac events and 119 did not (Table 15).

	GROUP A (Patients sustained acute cardiac events)	GROUP B (Patients did not sustain acute cardiac events)
Median age	67	63.5
Mean age ±SD	63.5± 6.6	61. ±7.9
Male	15(75%)	88 (73%)
Smoker	4 (20%)	41 (35%)
Diabetes	2(10%)	27 (17%)
Hypercholesterolaemia	7(35%)	43 (27%)
Hypertension	3 (15%)	35 (30%)
Previous MI	9(45%)	75 (48%)
Previous Unstable angina	14 (70)	66 (42%)
No angina	0	3 (2.5%)
Angina I	1 (5%)	5 (4.2%)
Angina II	2 (10%)	34(28.6%)
Angina III	15 (75%)	65(54.6%)
Angina IV	1 (5%)	12(10.1%)
ETT Positive		
Not done/unable	1	19 (16%)
Stage I	7 (35%)	24 (20.2%)
Stage II	13 (65%)	55 (46.2 %)
Stage IH	0	14 (11.8 %)
Stage IV	0	7 (5.9%)
Non Invasive Score <30	1 (5%)	18 (15%)
30-39	3 (15%)	32 (27%)
>40	16 (80%)	70 (58%)

Table 15: Characteristics of patients who had a cardiovascular event (*group A, n=20)* and those who did not (*Group B, n=119*).

Waiting times for procedures

The waiting times were as follows (Table 16):

a) Coronary angiography: mean 89 ± 69 days; median 48 days.

b) Coronary artery bypass surgery: mean 326 ± 218 days; median 280 days (range 7 to 864 days);

c) Coronary angioplasty: mean 185 ± 151 days; median 144 days (range 5 to 669 days).

Waiting time from referral to *(days)*:	PTCA	CABG	Coronary angiography
N	72	67	139
Mean	185	326	89
Median	144	280	48
Std. Deviation	151	218	69

Table 16: Waiting times (days) for coronary procedure

Acute cardiac events while waiting for coronary angiography

Only five patients developed acute cardiac events while awaiting coronary angiography. The median clinical score for those who had an event was 45, and 41 for those whose wait was uneventful.

Events that occurred while awaiting investigation

There were no deaths or non-fatal myocardial infarctions that occurred during the monitoring period. One patient, with a non-invasive risk score of 42, was not offered surgery because of unsuitable coronary anatomy, and died 160 days after coronary angiography. Five patients (3% of all patients) had unstable or progressive angina. These events occurred at a median of 12 days and mean of 15 ±6 days between being listed for coronary angiography and having the investigation (Table 17, 18).

	Wait for Investigation (days)	Wait for revascularisation (days)	'Day cardiovascular events occurred '	Non-invasive score
1	23	58	14	26
2	16	51	9	40
3	20	28	10	45
4	60	102	30	56
5	14	38	12	52

Table 17: Acute cardiovascular events that occurred in patients awaiting coronary angiography.

	Mean ±SD	Median
Waiting time for coronary angiography	26 ± 13	20
Waiting time for Intervention	55 ± 20	51
Cardiac Events sustained	15 ± 6	12
Non Invasive scores	44 ± 8	45

Table 18: Characteristics of patients who had acute cardiac events while waiting investigation.

Acute cardiac events while waiting for coronary revascularisation

Non-invasive clinical scores of patients awaiting revascularisation

Of 139 patients, 20 patients developed acute cardiac events while awaiting revascularisation; their characteristics are shown in table 14. The mean and median non-invasive clinical scores were higher in the group of patients who had some cardiac event (Table 19). There was a significant difference in non-invasive clinical scores between the group of patients who had cardiac events and those who did not (p=0.017).

Group of patients		With acute cardiac events (Group A)	No Acute cardiac events (Group B)
N		20	119
Mean		45.65	39.55
Median		44.00	40.00
Std. Deviation		9.07	10.70
Minimum		31	13
Maximum		62	73
Percentiles	25	38.75	32.00
	50	44.00	40.00
	75	56.00	46.00

Table 19: Distribution of non-invasive clinical scores in those who did and who did not develop some acute cardiac event while waiting revascularisation.

Acute events that occurred while awaiting revascularisation

20 patients developed acute cardiac events whilst awaiting revascularisation. One patient had an acute myocardial infarction (his non-invasive score was 42), 17 experienced unstable angina and there were 2 deaths attributed to a cardiac cause.

The mean waiting time between being put on the waiting list and sustaining a cardiac event was 147 ± 88 days with a median of 128 days. Having a major cardiovascular event while awaiting treatment did reduce the waiting time – the median waiting time for patients who sustained a cardiac event was 140 days, compared with 190 days for patients who did not have a cardiac event. The mean waiting time was 197 ± 184 days in those who suffered an event and 263 ± 200 whose wait was uneventful (Table 20).

	Group of patients	Median days	Mean ±SD days
Waiting time between being put on waiting list to sustained acute cardiac event	*Group A (sustained Acute cardiac events*	128	147±88
Waiting time between being put on waiting list to revascularisation	*Group A (sustained Acute cardiac events*	140	197±184
	Group B (did not sustain Acute cardiac events)	190	263±200

Table 20: Waiting time between being put on waiting list and sustaining acute cardiac events and revascularisation procedures.

The mean age of patients who had a cardiac event was greater than patients who did not experience an event (67 vs. 63.5) but this was not statistically significant (p=0.12).

A score of 40 seemed empirically to distinguish between those who had and those who did not have an acute cardiac event (Table 21). 64 patients had a non-invasive clinical score of less than 40; only 4 patients (6 %) had a cardiac event. 76 patients had a score in excess of 40, 16 (21%) of whom had a cardiac event (log-rank test P=0.0059). Kaplan-Meier survival curves were generated to test the impact of this as a threshold risk score (Figure 13). It shows that the events-free curve in patients with score of greater than 40 is better than in patients who had scores of less than 40.

Score	Frequency	Percent	Cumulative Percent
31	1	5.0	5.0
34	1	5.0	10.0
36	1	5.0	15.0
37	1	5.0	20.0
40	1	5.0	25.0
41	3	15.0	40.0
42	1	5.0	45.0
43	1	5.0	50.0
45	1	5.0	55.0
46	3	15.0	70.0
56	4	20.0	90.0
60	1	5.0	95.0
62	1	5.0	100.0
Total	20	100.0	

Table 21: The distribution of non-invasive clinical scores among patients who had a cardiac event while awaiting revascularisation procedure.

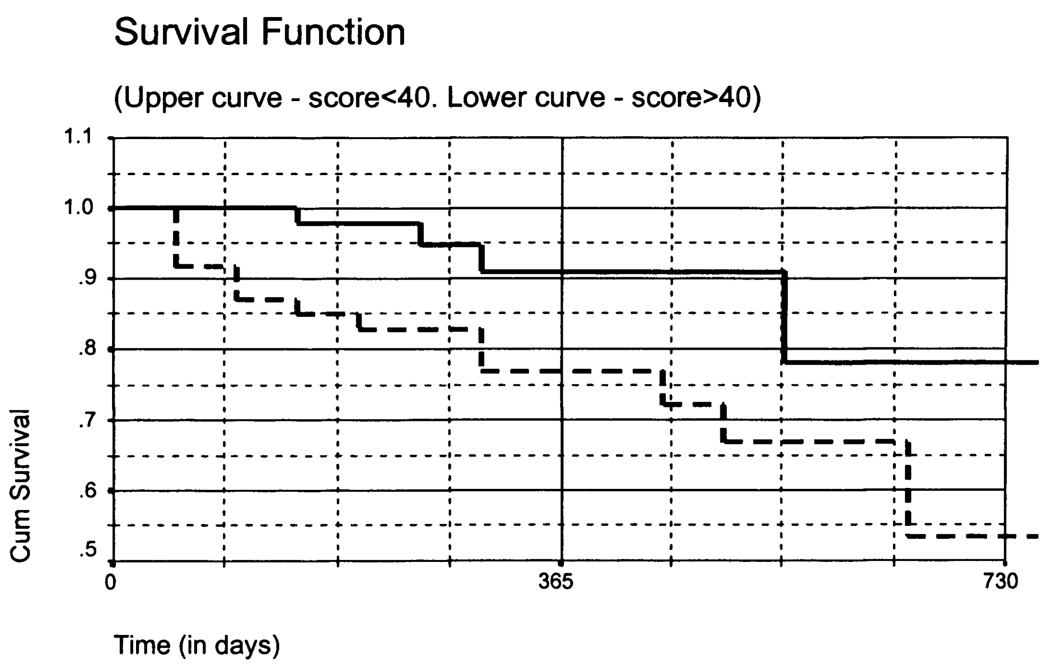


Figure 13: Kaplan-Meier analysis (events-free) comparing the groups of patients with a non-invasive clinical scores of less than and equal to or more than 40.

Two different curves were constructed in order to assess whether the threshold might discriminate between the group of patients who developed acute cardiac events while waiting for revascularisation and the group which did not; there was significant deference in developing acute cardiac events between these groups (p=0.0059).

Waiting for revascularisation is likely to increase the risk of sustaining an acute cardiac event. The waiting time from the date of referral to the date of performing intervention was categorised into groups consisting of 30 days and uni-variate analysis used to assess the effect of waiting time on the occurrence of acute cardiac events. There was no significant correlation between waiting for intervention and the occurrence of acute cardiac events (Chi-Square value = 5 the minimum expected is 0.58; p= 0.75) (Table 22).

	Value	Df	Asymp. Sig. (2-sided)
Chi-Square	5.004	8	.757
Likelihood Ratio	6.013	8	.646
Linear-by-Linear Association	2.203	1	.138
No. of Valid Cases	139		

All cells have an expected count of less than 5. The minimum expected count is 0.58.

Table 22: Correlation between waiting time and sustaining an acute cardiac event.

DISCUSSION

The chances of any patient sustaining a fatal cardiovascular event while awaiting a coronary intervention is slim – in this study mortality was less than 1%. The risk of death on a surgical waiting list seems to vary from country to country. In Canada, death rates seem exceptionally low at 0.4% (Naylor C.D. et al *1990*) whilst in the UK rates range from 1.6 – 2.4% (Billing J.S. et al). Despite a relatively short waiting time of 63 days in the Netherlands, mortality is around 2.2%. Reports from New Zealand suggest a mortality of 2.6% (Seddon ME et al *1999*).

The risk of cardiovascular morbidity, however, cannot be ignored – in this study from a large health authority in the UK; one in seven developed an acute myocardial infarction or unstable angina. Even so, this is considerably lower than in New Zealand where the risk of cardiac events was 22% (Seddon ME et al *1999*)

With unstable angina occurring in about 3% of patients and death and myocardial infarction even less likely. These results compare favourably with findings from the US where death has been reported in 2%, myocardial infarction in 1% and unstable angina in 7% (Rosanio S et al *1999*).

As in the US (Rosanio S et al), patients who experienced a cardiac event had a significantly shorter time waiting for intervention than those who did not. The most likely explanation for this is greater priority being afforded to patients who have the misfortune to sustain an acute event. In New Zealand, considerable effort has been applied to devising a priority scheme for those patients who have been listed for revascularisation. The scores generated by the New Zealand scheme are not reliable indicators of risk of morbidity or mortality (Seddon ME et al *1999*) so an alternative approach is essential. Using the technique developed in this study, it does seem possible to discriminate between those at high and low risk – a threshold score of 40 is a useful identifier as any patient with a score in excess of 40 can be reassured that the risk of an acute event is slim. With ever-greater emphasis on reducing waiting times for interventions, surgeons need a reasonable marker of risk because crude mortality rates have been used as an indicator of quality of care. Analysis of the Euro SCORE multinational database of 19030 patients (which was set up to establish the risk profile of adults undergoing cardiac surgery) identified 29 risk factors. These include most of the risk factors included in the non-invasive clinical scoring system reported in this thesis, as well as other risks factors associated with cardiac surgery mortality, preoperative patient characteristics, the type and extent of surgical procedures and factors related to the type and severity of coronary disease (Roques F et al *1999*).

One weakness of the Leicester risk assessment method is the relatively small size of the study sample. This produced only a small number of acute events in patients on a waiting list. Nevertheless, the results of this study provide a novel approach to stratifying risk and are worthy of further study – this is being undertaken and will include an analysis to establish whether a lower score can be an even more powerful discriminator.

Long waiting lists for coronary angiography and coronary bypass surgery are generally assumed to be associated with a high mortality and increased cardiac events. In the UK, NHS waiting time has increased from a mean of 115 days to over 300 days between 1979 and 1988, with a mortality rate of about 2.5%. In the private sector, where waiting is by mutual agreement, waiting times have remained the same at about 17 days for coronary angiography and 23 days for coronary bypass surgery; no deaths have been reported in this patient group (Marber M et al *1991*).

The results of the study presented here shows that there was no risk of death during the first 4 months of waiting for revascularisation, so patients can be reassured that having to wait (at least for four months) does not increase the danger. Non-fatal acute myocardial infarction seems a rare event too. However, prolonged waiting does increase the chances of an acute event, notably for unstable angina (which can affect about one in seven patients).

A threshold score of 40 successfully discriminates between a group of patients who might be at high risk of morbidity and mortality. Having a non-invasive risk score of less than 40 should prove reassuring to the clinician and patient because few events occur in these patients. Perhaps surgeons might seek to revise their waiting lists to push those who score more than 40 to the top as they seem to develop more events as the wait time exceeds 2 months.

If a scoring system were applied to clinical practice, the management of coronary artery disease could well be improved and the waiting time for investigation and revascularisation procedures could be adjusted according to the clinical score. Those with a score greater than 40 might be singled out for earlier treatment, or at least the delay could be minimised. At the end of the day, clinicians need to be aware that adding patients to a procedures list is not the most efficient way to manage patients. If the purpose of investigation and treatment is to avoid acute cardiac events and not just relieve symptoms, prioritisation seems inevitable.

Chapter 6

Developing a new angiography scoring system

Chapter 6

Developing a new angiography scoring system

A clinician needs to know whether a patient has coronary artery disease or not as a prelude to deciding whether revascularisation may be necessary. At present, only the coronary angiogram will provide a definitive answer. There are many other circumstances where it would be helpful for clinicians if a scoring system were available that would provide a reliable, robust and reproducible estimate of the likelihood of severe coronary artery disease. Ideally, there would be a close correlation between the estimated or derived score and some marker of disease severity such as the number of stenosis, the number of arteries involved, the specific artery involved or some prognostic index such as left main stem involvement.

Attempts to evaluate the severity of disease have been made before by a team in New Zealand (Hadron DC et al *1997*) based on the impact of anatomical lesions on mortality and morbidity and risk stratification estimated by a team at Duke University in North Carolina (Mark DB et al *1987*). Some observers have raised concerns about the angiography score developed by the New Zealand group (Hadron DC et al *1997*); for example, the scoring system appears to be linear but the scores themselves are not equally distributed, so the *same* score can be achieved by several different stenoses while *different* scores are shared by relatively few stenoses. Consequently, it does seem desirable to develop a new angiography scoring system to overcome these obstacles.

A new angiography scoring system is required; this ought to be based on well-established knowledge. Three examples are: a) morbidity and mortality risk increases in accordance with the coronary artery involved – each artery affects a specific area of myocardial tissue and so each artery carries a different risk; b) risk is dependent upon the extent of the coronary stenosis, a mild stenosis of 50% may cause few symptoms and perhaps less risk than a severe stenosis of 90% (Harris PJ et al *1980*); and c) prognosis is adversely affected by the number of involved vessels (Emond M et al 1994, Detre M et al 1981). A scoring system, which takes these and other factors into account, is warranted (Proudfit W.J. et al *1983*, Takro T et al *1976*).

METHOD

Study Population

The study population *has been explained in detail in Chapter 2 (Figure 4).*

Two groups of consecutive patients were chosen. The first group of 169 consecutive patients was used to develop a model to predict post-angiography management while a second group of 203 consecutive patients was used for validation purposes.

Data collection:

The author reviewed the original coronary angiograms and collected the data about post-angiography referral at the same time that Glenfield consultants reviewed the films to determine future management (for more detail see Chapter 2).

Development of a predictive model

Based on morbidity and mortality studies (see Chapter 1) and on New Zealand angiographic scores based on well-validated studies, the new angiography scoring system was developed and validated by the author in the following sequence (Figure 8):

Step 1: Each coronary angiogram was reviewed and the number and distribution of coronary lesions recorded. A risk factor score was given to the affected artery in accordance with standard practice (Conti CR et al *1979*, Naylor CD et al *1990,* and CASS Principal Investigators *1983*). Prognosis and risk of future cardiovascular events was estimated from the following:

- *Significant stenosis in right, circumflex or left descending artery* *= risk factor score of 2;*
- Significant stenosis in proximal left descending artery = risk factor score of 3;
- Significant stenosis involving the left main artery = risk factor score of 9;
- Significant stenosis in more than one vessel = highest risk scored.

Each patient was assigned a final risk factor score.

Step 2: The extent of coronary artery disease was given a further score. Only the most severe lesion in each artery was considered. The scores for all arteries involved were summed together:

- Stenosis is occluding 50 to 74% of the lumen = score of 1;
- Stenosis occluding 75%-89% of the lumen = score of 2;
- Stenosis occluding 90% or more of the lumen = score of 3.

Step 3: A final angiography score was calculated as follows:

- Sum the scores of Steps 1 and 2;
- Multiply the result by 3.

A scaling factor of 3 was necessary to allow comparison of this new angiographic score with that developed by the New Zealand team. This factor was based on the following:

- The angiography scores for coronary artery disease according to the New Zealand system (Naylor CD et al) were divided by the new system's steps 1 and 2 above.

Worked example 1:

90% lesion in Right Coronary Artery

New Zealand score = 14.

New scoring system risk score 2 plus extent score 3 = 2 + 3 = 5.

New Zealand score divided by new score 14/5 = 3.

Worked example 2:

90% lesion in Left Main Coronary artery disease

New Zealand score = 36

New scoring system risk score 9 plus extent score 3 = 9 + 3 = 12.

New Zealand score divided by new score 36/12 = 3

A major limitation of the New Zealand system was the result of basing the score on lesions affecting only the major coronary arteries (that is left main, left anterior descending, circumflex and right coronary arteries); lesions in branch vessels (such as the obtuse marginal and diagonal arteries) were not included. The clinical decision-making process usually takes into account all lesions in any vessel. Branch vessels, especially if supplying a large amount of myocardium, do influence whether a patient is offered surgery and so cannot be ignored. To overcome this, any lesion in a branch artery was assigned the same score as its parent major coronary artery minus 3 points. (Figure 13)

Worked example 3:

90% lesion in the proximal left anterior descending artery will score

a) Step 1 = 3 points;

b) Step 2 = 3 points;

c) Step 3 = multiply by factor of 3:

Angiography score = (3) plus (3) multiplied by (3) = 18

Worked example 4:

75% coronary lesion in an obtuse marginal vessel (a branch of the circumflex artery) will score

a) Step 1 = 2;

b) Step 2 = 2;

c) Step 3 multiply by factor of 3;

d) Step 4 = Minus 3 as branch vessel involved:

Angiography score = (2) plus (2) multiplied by (3) minus (3) = 9

A complication can arise when atheroma affects both the left main coronary artery and *another* major coronary vessel. If the left main artery is affected together with a *left-sided* vessel (left anterior descending artery or circumflex), only the lesion in the left main artery is taken into account because the left main artery is responsible for feeding both of these left-sided arteries. If the left main artery is affected together with the *right* coronary artery, *both* the left main *and* the right coronary lesions have to be taken into account.

Severity of coronary artery stenosis

	50-74%	**74-89%**	**≥90%**
Severity score	**=1**	**=2**	**=3**

Diagonal O. Marginal	(1+1) 3=6	(1+2) 3=9	(1+3) 3 =12
LAD CX RCA	(2+1) 3=9	(2+2) 3 =12	(2+3) 3=15
Proximal LAD	(3+1) 3=12	(3+2) 3=15	(3+3) 3=18
Left Main	(9+1) 3=30	(9+2) 3=33	(9+3) 3=36

General equation = (Scores of step 1+step 2) 3

Figure 13: illustration of new angio- scoring system

RESULTS

Statistical Methods

The SPSS statistical package version 8 was used. Basic medical statistics were used Pearson's correlation test and the Chi-Square test. The area under the receiver-operator curve was evaluated.

Using performed repeatability tests:

1) Intra-class correlation coefficients to test the repeatability of angiographic scoring systems in predicting referral for revascularisation.

The following equation was used for this purpose (Denis A 1999):

$$r_i = \frac{mSS_B - SS_T}{(m-1)SS_T}$$

Where SS_B within group sum of squares,

SS_T total sum of squares,

m number of observations based on ANOVA outcome.

2) Agreement between New Zealand and the new angiography scoring system was tested by using Inter-ratter reliability test (Denis A 1999).

Correlation between angiography scores and post-angiography management

74 (44%) of the 169 patients were recommended to continue with medical management; 54 (32%) were referred for coronary angioplasty and 41 (24%) for bypass surgery(Table 23).

The new angiography scoring system

The new scoring system as described above was tested first to evaluate the severity of coronary stenosis.

***Angiography scores less than 12** (normal or mild coronary artery disease)*

33 patients were assigned scores 0-9. 32 (97%) of these were recommended to continue medical treatment and only one was referred for coronary angioplasty (Table 21). Those patients in this group who continued medical treatment constituted 43.8% who were not offered revascularisation (Table 23).

***Angiography scores of 12 to 21**(moderate coronary artery disease)*

74 patients were assigned angiography scores of 12-21. 28 patients (37%) continued to receive medical treatment; 41 (55%) were referred for angioplasty and 7 were offered bypass surgery. Those patients who had coronary angioplasty constituted 75.9% (54 patients) those referred for the procedure (Table 23).

__Angiography scores of 24 to 45__ (severe coronary artery disease)

62 patients were assigned angiography scores of 24-45. 14 patients (22%) continued to receive medical treatment; 12 (19%) were offered coronary angioplasty and 36 (58%) bypass surgery. Those patients who had coronary bypass procedures constituted 88% who were referred for the procedure (Table 23).

Thus a score of less than 12 was associated with a recommendation to continue medical treatment; scores between 12-21 increased the likelihood of being offered coronary angioplasty; and a score over 21 increased the likelihood of being offered coronary bypass surgery (Figure 14).

New angio-scores * Post angiography management Crosstabulation

			Post angiography management			
			Medical	PTCA	CABG	Total
New angio-scores	0 - 9	n	32			32
		% within Severety of stenosis	100.0%			100.0%
		% within Outcome	43.2%			18.9%
		% of Total	18.9%			18.9%
	12 - 21	n	28	42	5	75
		% within Severety of stenosis	37.3%	56.0%	6.7%	100.0%
		% within Outcome	37.8%	77.8%	12.2%	44.4%
		% of Total	16.6%	24.9%	3.0%	44.4%
	24 - 45	n	14	12	36	62
		% within Severety of stenosis	22.6%	19.4%	58.1%	100.0%
		% within Outcome	18.9%	22.2%	87.8%	36.7%
		% of Total	8.3%	7.1%	21.3%	36.7%
Total		n	74	54	41	169
		% within Severety of stenosis	43.8%	32.0%	24.3%	100.0%
		% within Outcome	100.0%	100.0%	100.0%	100.0%
		% of Total	43.8%	32.0%	24.3%	100.0%

Table 23:The power of new angiography scores to predict post-angiography management ***(n = 169).***

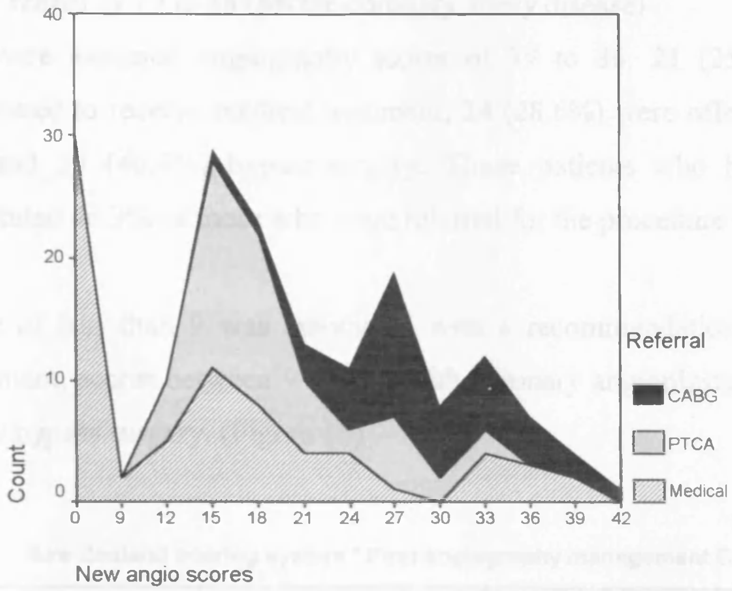


Figure 14:The power of new angiography scores to predict post-angiography management *(n =169).*

The New Zealand angiography scoring system

The New Zealand angiography scoring system was evaluated in the same population.

***Angiography scores of 0 to 9** (normal or mild coronary artery disease).*

40 patients were assigned scores 0 to 9; 31 (86%) of these were recommended to continue medical treatment and 5 patients (14%) were referred for coronary angioplasty. Those patients in this group who had medical treatment constituted 41.9% who were not offered revascularisation (Table 24).

***Angiography scores of 14 and 15** (moderate coronary artery disease)*

49 patients were assigned angiography scores of 14, 15. 22 patients (44.9%) continued to receive medical treatment; 25 (51%) were referred for angioplasty and 4 were offered bypass surgery. Those patients who had coronary angioplasty constituted 46.3 % of those who were referred for the procedure (Table 24).

Angiography scores of 19 to 36 (severe coronary artery disease)

84 patients were assigned angiography scores of 19 to 36. 21 (25%) of these patients continued to receive medical treatment; 24 (28.6%) were offered coronary angioplasty and 39 (46.4%) bypass-surgery. Those patients who had coronary bypass constituted 46.3% of those who were referred for the procedure (Table 24).

Thus a score of less than 9 was associated with a recommendation to continue medical treatment, scores between 9 and 15 with coronary angioplasty and over 19 with coronary bypass surgery. (Figure 15)

New Zealand scoring system * Post angiography management Crosstabulation

			Post angiography management			
			Medical	PTCA	CABG	Total
New Zealand scoring system	0 - 9	n	31	5		36
		% within New Zealand scoring system	86.1%	13.9%		100.0%
		% within Outcome	41.9%	9.3%		21.3%
		% of Total	18.3%	3.0%		21.3%
	14, 15	n	22	25	2	49
		% within New Zealand scoring system	44.9%	51.0%	4.1%	100.0%
		% within Outcome	29.7%	46.3%	4.9%	29.0%
		% of Total	13.0%	14.8%	1.2%	29.0%
	27 - 36	n	21	24	39	84
		% within New Zealand scoring system	25.0%	28.6%	46.4%	100.0%
		% within Outcome	28.4%	44.4%	95.1%	49.7%
		% of Total	12.4%	14.2%	23.1%	49.7%
Total		n	74	54	41	169
		% within New Zealand scoring system	43.8%	32.0%	24.3%	100.0%
		% within Outcome	100.0%	100.0%	100.0%	100.0%
		% of Total	43.8%	32.0%	24.3%	100.0%

Table 24: Predictive power of New Zealand angiography scores of post-angiography management *(n=169).*

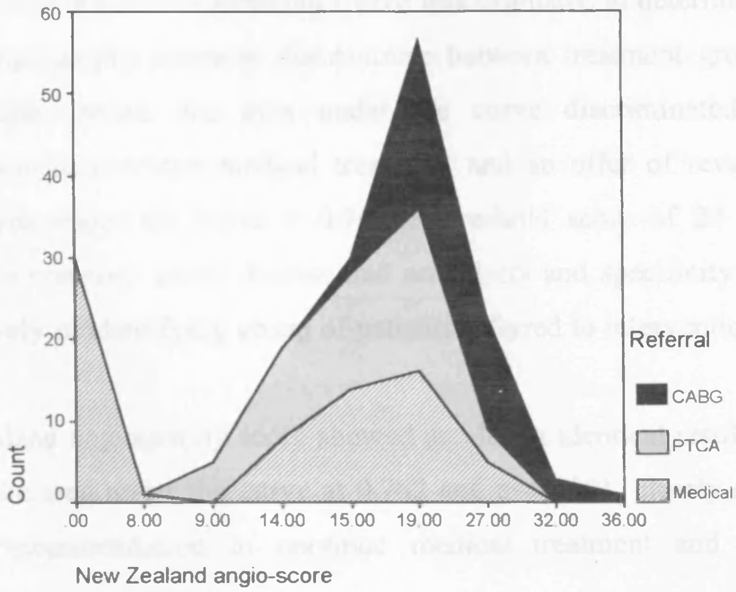


Figure 15: The power of New Zealand angiography scores to predict post-angiography management *(n=169).*

Statistical evaluation

The ability of each scoring system to identify post-angiography management

The new angiography score and post-angiography management were significantly associated (Chi-Square test 103.5 p=0.000 (minimum expected count 7.7); Gramer's V association factor[1] =0.55).

These results suggest that there was significant and positive correlation between the new angiography score and post-angiography management – the greater the angiography score, the more likely was a referral for a revascularisation procedure.

The New Zealand angiography scores and post-angiography management were very similar (Chi-Square test 65 p=0.000 (minimum expected count 8.7); Gramer's V association factor =0.44). These results suggest that there was significant and positive correlation between the New Zealand angiography scores and Post-angiography referral.

(Gramer's V of 0 implies certainty that a patient will be recommended to continue with medical treatment alone and Gramer's of 100 implies certainty that a patient will be offered revascularisation).

The area under the Receiver Operating Curve was evaluated to determine the power of the new angiography score to discriminate between treatment groups. For the new angiography score, the area under the curve discriminated between a recommendation to continue medical treatment and an offer of revascularisation ($p<0.0001$; area under the curve = 0.767). Threshold score of 24 that used to identify severe coronary artery disease had sensitivity and specificity of 0.51, and 0.81 respectively in identifying group of patients referred to intervention (Appendix 4).
The New Zealand angiography score showed an almost identical result to that seen above, with the area under the curve at 0.762 and $p<0.0001$, clearly discriminated between a recommendation to continue medical treatment and an offer of revascularisation.

Patients with a score of 24 or above according to the new angio-scoring system and a score of 19 using the New Zealand scoring system were generally accepted by the clinicians as *appropriate* for revascularisation procedures. These scores yielded similar sensitivity (077 and 0.75 respectively) and specificity (0.56 and 0.62 respectively) in their ability to predict referral for revascularisation.

Validating the new angiography scoring system:

Patient population

203 consecutive patients with suspected coronary artery disease were put on a waiting list for and who underwent coronary angiography at Glenfield Hospital during the period 1 January to 30 March 1997. (See Chapter 2, Figure 4)

The new angiography scoring system

Angiography scores of less than 12*(normal or mild coronary artery disease)*

41 patients were assigned scores 0 to 12; 41 (95.3%) of these were recommended to continue medical treatment and only two patients were referred for coronary angioplasty (Table 25) No patient was referred to coronary bypass surgery. Those patients in this group who had medical treatment constituted 41.8% who were not offered revascularisation.

Angiography scores of 12 to 21 (moderate coronary artery disease)

71 patients were assigned angiography scores of 12 to 21. 29 patients (40.3%) continued to receive medical treatment; 35 (48.6%) were referred for angioplasty and 8 (11.1%) were offered bypass surgery. Those patients who had coronary angioplasty constituted 66% of 53 patients those who were referred for the procedure.

Angiography scores of 24 to 45 (severe coronary artery disease)

88 patients were assigned angiography scores of 24 to 45. 28 patients (31.8%) continued to receive medical treatment; 16 (18.2%) were offered coronary angioplasty and 44 (50%) bypass surgery. Those patients who had bypass surgery constituted 84.6% of those were referred for the procedure (Table 25).

Thus a score of less than 12 was associated with a recommendation to continue medical treatment, scores between 12-21 with coronary angioplasty and over 21 with coronary bypass surgery (Figure 16).

New angio-scores * Post angiography management Crosstabulation

			Post angiography management			
			Medical	PTCA	CABG	Total
New angio-scores	0 - 9	n	41	2		43
		% within Severety of stenosis	95.3%	4.7%		100.0%
		% within Outcome	41.8%	3.8%		21.2%
		% of Total	20.2%	1.0%		21.2%
	12 - 21	n	29	35	8	72
		% within Severety of stenosis	40.3%	48.6%	11.1%	100.0%
		% within Outcome	29.6%	66.0%	15.4%	35.5%
		% of Total	14.3%	17.2%	3.9%	35.5%
	24 - 45	n	28	16	44	88
		% within Severety of stenosis	31.8%	18.2%	50.0%	100.0%
		% within Outcome	28.6%	30.2%	84.6%	43.3%
		% of Total	13.8%	7.9%	21.7%	43.3%
Total		n	98	53	52	203
		% within Severety of stenosis	48.3%	26.1%	25.6%	100.0%
		% within Outcome	100.0%	100.0%	100.0%	100.0%
		% of Total	48.3%	26.1%	25.6%	100.0%

Table 25: Distribution of scores based on the new angiography scoring system and the prediction of post-angiography management *(n=203)*.

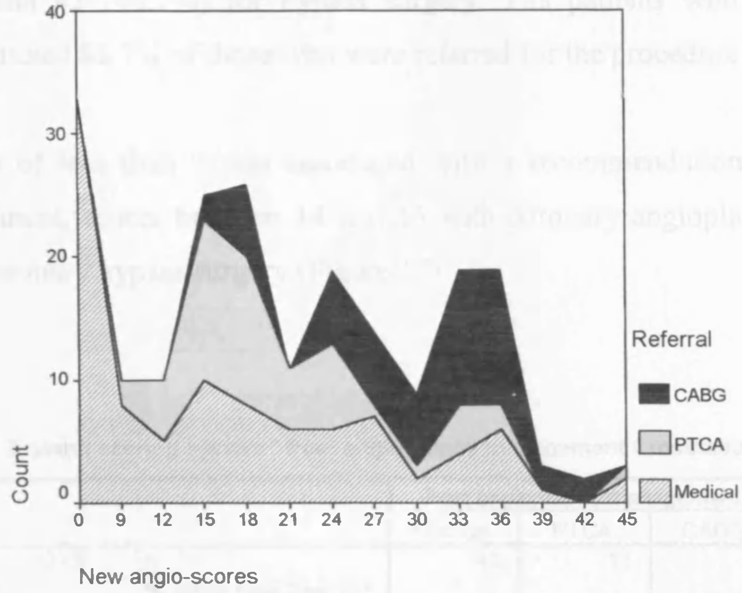


Figure 16: The power of new angiography scores to predict post-angiography management ***(n=203).***

The New Zealand angiography scoring system:

Angiography scores 0 to 9 *(normal or mild coronary artery disease)*

54 patients were assigned scores of 0 to 9; 42 (77.8%) of these were recommended to continue medical treatment and 11 patients (20.8%) were referred for coronary angioplasty (see table below). Only one patient (1.9%) was referred for coronary bypass surgery. Those patients in this group who had medical treatment constituted 42.9 % who were not offered revascularisation (Table 26).

Angiography scores of 14, 15 *(moderate coronary artery disease)*

57 patients were assigned angiography scores of 14, 15. 26 patients (45.6%) continued to receive medical treatment; 23 (40.4%) were referred for angioplasty and 8 (14%) were referred to bypass surgery. Those patients who had coronary angioplasty constituted 43.4% who were referred for the procedure (Table 26)

Angiography scores more than 19-36 *(severe coronary artery disease)*

92 patients were assigned angiography scores of 19-36. 30 (32.6%) of these patients continued to receive medical treatment; 19 (20.7%) were referred to coronary

angioplasty and 43 (46.7%) for bypass surgery. The patients who had bypass surgery constituted 82.7% of those who were referred for the procedure (Table 26).

Thus a score of less than 9 was associated with a recommendation to continue medical treatment, scores between 14 and 15 with coronary angioplasty and over 19-36 with coronary bypass surgery (Figure 17).

New Zealand scoring system * Post angiography management Crosstabulation

			Post angiography management			
			Medical	PTCA	CABG	Total
New Zealand angio-scoring system	0 - 9	n	42	11	1	54
		% within New Zealand scoring system	77.8%	20.4%	1.9%	100.0%
		% within Outcome	42.9%	20.8%	1.9%	26.6%
		% of Total	20.7%	5.4%	.5%	26.6%
	14, 15	n	26	23	8	57
		% within New Zealand scoring system	45.6%	40.4%	14.0%	100.0%
		% within Outcome	26.5%	43.4%	15.4%	28.1%
		% of Total	12.8%	11.3%	3.9%	28.1%
	27 - 36	n	30	19	43	92
		% within New Zealand scoring system	32.6%	20.7%	46.7%	100.0%
		% within Outcome	30.6%	35.8%	82.7%	45.3%
		% of Total	14.8%	9.4%	21.2%	45.3%
Total		n	98	53	52	203
		% within New Zealand scoring system	48.3%	26.1%	25.6%	100.0%
		% within Outcome	100.0%	100.0%	100.0%	100.0%
		% of Total	48.3%	26.1%	25.6%	100.0%

Table 26: Distribution of scores based on the New Zealand angiography scoring system and the prediction post angiography *(n=203)*.

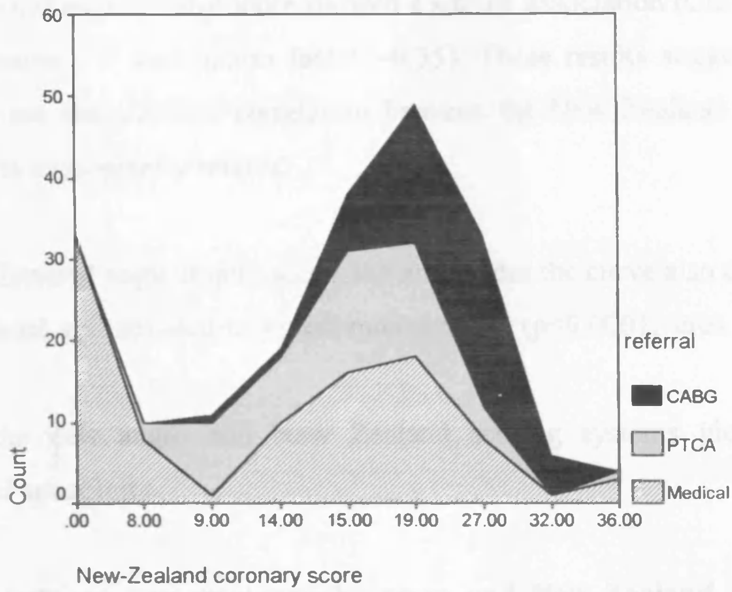


Figure 17: The power of New Zealand angiography scores to predict post-angiography management*(n=203).*

Statistical evaluation

The ability of each scoring system to identify post-angiography management

The new angiography score and post-angiography management were significantly associated (Chi-Square = 86.6 (minimum expected count 11); Gramer's V association factor =0.46). These results suggest that there was significant and positive correlation between the new angiography scores and post-angiography referral.

The area under the Receiver Operating Curve was evaluated to determine the power of the new angiography score to discriminate between treatment groups. For the new angiography score, the area under the curve discriminated between medical and revascularisation management ($p<0.0001$; area under curve area = 0.73). Threshold score of 24 that used to identify severe coronary artery disease had sensitivity and specificity of 0.57, and 0.71 respectively in identifying group of patients referred to intervention (Appendix 4).

These results suggest that the new angiography scores can discriminate between the referral for medical treatment and an offer of revascularisation.

The New Zealand angiography score showed a similar association (Chi-Square 51.5 p<0.0001; Gramer's V association factor =0.35). These results suggest that there was a significant and positive correlation between the New Zealand angiography scores and post-angiography referral

For the New Zealand angiography score, the area under the curve also discriminated between medical and revascularisation management (p<0.0001; area under curve area = 0.72).

As before, the new angio and New Zealand scoring systems yielded similar sensitivity and specificity.

Correlation between new angiography score and New Zealand angiography scores

Simple bi-variate analysis was used to test the correlation between both angiography scores in a test population of 169 patients. The new system yielded scores for the severity of coronary artery stenosis that were almost identical to the scores of the New Zealand system (Pearson correlation was significant p= 0.001 correlation coefficient r =0.91; adjusted r square 0.83).

Simple bi-variate analysis was used to test the correlation between both angiography scores in a validation population of 203 patients. The new system yielded scores for the severity of coronary artery stenosis that were almost identical to the scores of the New Zealand system (Pearson correlation was significant p=0.001; adjusted r square 0.83; correlation coefficient 0.95).

Repeatability tests:

1) Intra class correlation:

The intra class correlation coefficient was calculated as outlined above (Denis A 199) and was used to test the repeatability of the New Zealand and New angio-scoring system to identify those referred for revascularisation. The intra-class correlation coefficient for the new angio scores was consistently higher at $r\ i = 0.83$ and 0.82) than for the New Zealand angio-scoring system at $r\ i = 0.77$, 0.79 (repeatability tests were based on the result of ANOVA test table 27).

A) new angiographic scores

		Sum of squares	df	Mean Square	F	Sig
Group of 203 patients	Between Groups	4.13	1	4.14	18.19	0.000
	Within groups	45.71	201	0.227		
	Total	49.85	202			
Group of 372 patients	Between Groups	8.36	1	8.36	36.77	0.000
	Within groups	84.11	370	0.227		
	Total	92.47	371			

B) New Zealand angiographic scores

		Sum of squares	df	Mean Square	F	Sig.
Group of 203 patients	Between Groups	5.70	1	5.70	26.03	0.000
	Within groups	44.01	201	0.22		
	Total	49.71	202			
Group of 372 patients	Between Groups	9.95	1	9.95	44.61	0.000
	Within groups	82.52	370	0.223		
	Total	92.47	371			

Table 27: The outcome of ANOVA test -used for repeatability tests, *a) the new angiographic scores* and b*) the New Zealand angiographic scores.*

2) Inter-ratter reliability test:

Agreement between New Zealand and the new angiography scoring system was tested in groups of 203 and 372 consecutive patients by using the Inter-ratter reliability test. This showed substantial agreement with a Kappa score of 0.64, and 0.76 respectively in both groups of patients (Table 28)

	N of valid cases	Value	Asymp Std.Error	Approx. T	Approx. Sig.
Measurement of agreement (Kappa)	203	0.638	0.45	12.9	0.000
	372	0.76	0.030	20.3	0.000

Table 28: Inter-ratter reliability test (to test agreement between New Zealand and the new angiography scoring system)

Correlation between clinical variables and angiography score

Prior to coronary angiography, the most reliable indicators of the likelihood of coronary artery disease are clinical characteristics. Some criteria may be more powerful predictors of the angiography score than others Distinguishing those, which are helpful from those which are not can be achieved using uni-variate analysis. Available characteristics were tested to identify those variables that were most closely correlated with the degree of stenosis estimated by both the New Zealand and the new angiography scoring systems.

Using uni-variate analysis on all 372 consecutive patients, several variables were identified as good predictors of the severity of coronary artery disease; these were similar for both the new and the New Zealand angiographic scoring systems (Table 29).

However, by using multivariate analysis and stepwise logistic regression, the following variables were found to be significant for both the new and the New Zealand angiography scoring system: age, sex, hypercholesterolaemia, previous bypass surgery and previous myocardial infarction.

Clinical characteristic	New Zealand angiographic scoring system	New angiographic scoring system
Gender	+	+
Previous myocardial infarction	+	+
Previous bypass surgery	+	+
Hypercholesterolaemia	+	+
Age	+	+
Unstable angina	-	-
Smoking	-	-
Diabetes	+	+
Hypertension	-	-

Table 25: Characteristics identified by uni-variate analysis as poor or good predictors of the severity of coronary lesions *(+ = Good predictor; - = Poor predictor)*

Discussion:

Patients with chest pain can be notoriously difficult to diagnose. Symptoms may be atypical; there may be an excess of cardiovascular risk factors in some patients and poverty in others. If coronary angiography were an entirely safe procedure, it would become a routine part of the investigation of all patients with suspected coronary artery disease. Angiography, however, is not without risk of mortality and morbidity and so it should be reserved for those patients in whom the likelihood of the test being 'positive', that is significant coronary artery disease is confirmed and as a consequence the decision-making process enhanced and patient care improved.

Clinicians tend to use their instincts and experience to guide their thought processes in deciding how to manage each patient. This intuitive approach may be suitable for senior clinicians but the process is more implicit than explicit and is of use to neither juniors in training nor general practitioners. Using clinical parameters to devise a predictive model makes patient selection for coronary angiography more transparent and equitable. There are benefits for both clinical and research purposes.

The most important clinical benefit relates to the ability of a relatively simple model (providing there is access to a programmed computer) to predict the severity of coronary disease and so of the subsequent decision to offer or withhold revascularisation. The new angiography scoring system successfully predicted the outcome of coronary angiography in the majority of patients referred for coronary angioplasty and bypass surgery. 66-76% of patients who were referred for coronary angioplasty were assigned scores of 12 to 21; 85-95% who were referred to coronary bypass surgery were assigned an angiography score between 24 and 45. In the simplest terms, as the score increases, the more likely is angioplasty the recommendation until the highest scores coincide with those for whom bypass surgery is the preferred option.

In clinical practice, surgery is offered to patients with severe disease in single or multiple vessels; if the risk of surgery is high (perhaps because of co-morbidity, a previous bypass operation or severely impaired left ventricular function), patients may still be considered for coronary angioplasty to control symptoms. Inevitably, some patients may be denied revascularisation, either because of co-morbidity or because the distal vessels are too small to graft.

Why use the system described in this chapter when there is already an *off the shelf* solution – the New Zealand project? The new system has particular benefits for clinicians. It can be applied to any angiography result as long as the clinician can apply a few simple scoring rules; on the other hand, the New Zealand angiography scores apply to a very limited number of angiographic findings (just 19) and the scoring system is very complex and difficult to recall. In addition, the repeatability of the new angio- scoring system was better with no loss of sensitivity or specificity.

Clinicians may feel it is straightforward to estimate the risk of coronary artery disease in an individual patient. Even so, a scoring system is objective and lends itself to clinical audit (because it is easy to monitor calculated numbers than clinical variables), explicit (rather than implicit) rationing and improved selection of patients for expensive cardiac procedures.

Chapter 7

Application of non-invasive clinical scoring system in patients with previous coronary bypass surgery

Chapter 7

Application of non-invasive clinical scoring system in patients with previous coronary bypass surgery

INTRODUCTION

Increasingly patients who have undergone coronary bypass surgery are referred for coronary angiography in order to investigate the return of angina symptoms. Those patients most likely had coronary bypass surgery based on the principle that surgery would improve their survival rate, especially in those with multi-vessel disease with impaired left ventricular function and left main coronary artery disease (Conti CR et al *1979*, Emond M et al *1994*, Proudfit WJ et al *1983*); or to control symptoms in patients refractory to medical therapy in whom coronary angioplasty had failed or was unsuitable.

Question marks remain regarding the necessity of performing coronary angiography in this group of patients. It is (reasonably) assumed that a recurrence of symptoms similar to those existing before surgery is most likely to be a critical coronary restenosis. Such patients are at high risk because of severe coronary artery disease before coronary bypass surgery, with either a critical stenosis in a coronary graft or relentless progression of atherosclerotic disease in a native coronary artery.

The aim of this study was to investigate whether a non-invasive angiography scoring system could be developed that would evaluate the progression of coronary artery disease in patients with previous coronary bypass surgery so well that the decision regarding future management could be predicted with sufficient accuracy to make the scoring system approach clinically worthwhile.

METHOD

Patient Population

The clinical findings and test results of patients placed on a waiting list for coronary angiography were collected as described in Chapter 2.

A group of 372 consecutive patients on the waiting list for coronary angiography was used to validate a non-invasive clinical scoring system. One group comprised 40 consecutive patients who had previous coronary bypass surgery and the other 332 consecutive patients who had never had surgery (*Figure 6*).

Clinical data were collected prospectively using a standard form and non-invasive clinical scores based on a modified scoring system were assigned to each patient. Angiographic data were collected as described in Chapter 2 Methods. Angiography scores based on the new scoring system (described in Chapter 6) were assigned to each patient.

The first part of the study was designed to test the power of non-invasive clinical scores to identify group of patients who were referred for intervention (coronary angioplasty, coronary bypass surgery) after the result of coronary angiography were available. The second part was designed to validate the power of angiography scores to identify groups of patients who were referred to PTCA or CABG or who were denied revascularisation and advised to continue with medical treatment.

Statistical methods

The SPSS statistical package was used throughout. The Receiver Operating Curve (ROC) was plotted and the area under the curve and Pearson's Chi-Square were used to test the power of non-invasive clinical scores and angiography scores to predict the recommended management post-angiography.

RESULTS

The power of the non-invasive score to discriminate between intervention and medical treatment

As shown in a previous chapter, a score of greater than 40 proved to be a predictive threshold, identifying patients who were selected for intervention after coronary angiography. This value was applied in this study.

Previous bypass surgery- score of 40 or more

25 of 40 patients who had previously had coronary bypass surgery had a clinical score equal to or more than 40; 7 of these were referred for intervention and 18 patients were recommended to continue with medical treatment (Table 30).

Previous bypass surgery- score of less than 40

15 of 40 patients who had previous coronary bypass surgery had a clinical score of less than 40; 6 of these were referred for intervention and 9 were recommended to continue with medical treatment (Table 30).

Non-invasive score * post-angiogram management * Previous CABG Crosstabulation

Previous CABG				Post-angiogram management		Total
				Medical	PTCA & CABG	
NO	Non-invasive score	< 40	Count	96	90	186
			Expected Count	81.2(24.5%)	104.8(31.5%)	186(56%)
			% Non-invasive score	51.6%	48.4%	100.0%
			% Management	66.2%	48.1%	56.0%
			% of Total	28.9%	27.1%	56.0%
		>= 40	Count	49	97	146
			Expected Count	63.8(19.2%)	82.2(24.8%)	146(44%)
			% Non-invasive score	33.6%	66.4%	100.0%
			% Management	33.8%	51.9%	44.0%
			% of Total	14.8%	29.2%	44.0%
	Total		Count	145	187	332
			Expected Count	145(43.7%)	187(56.3%)	332.0
			% Non-invasive score	43.7%	56.3%	100.0%
			% Management	100.0%	100.0%	100.0%
			% of Total	43.7%	56.3%	100.0%
Yes	Non-invasive score	< 40	Count	9	6	15
			Expected Count	10.1(25.3%)	4.9(12.25%)	15(37.5%)
			% Non-invasive score	60.0%	40.0%	100.0%
			% Management	33.3%	46.2%	37.5%
			% of Total	22.5%	15.0%	37.5%
		>= 40	Count	18	7	25
			Expected Count	16.9(42.25%)	8.1(20.25%)	25(62.5%)
			% Non-invasive score	72.0%	28.0%	100.0%
			% Management	66.7%	53.8%	62.5%
			% of Total	45.0%	17.5%	62.5%
	Total		Count	27	13	40
			Expected Count	27(67.5%)	13(32.5%)	40(40%)
			% Non-invasive score	67.5%	32.5%	100.0%
			% Management	100.0%	100.0%	100.0%
			% of Total	67.5%	32.5%	100.0%

Table 30: The power of the non-invasive score to discriminate between intervention and medical treatment following angiography

Pearson's Chi- Square tests:

Of 40 patients who had coronary bypass surgery, non-invasive clinical scores and referral for intervention were independent and not associated (Chi-Square test value = 0.615; P=0.433 (Table 31)).

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-si
Pearson Chi-Square	.615 (b)	1	.433		
Continuity Correction (a)	.190	1	.663		
Likelihood Ratio	.608	1	.435		
Fisher's Exact Test				.498	.329
Linear-by-Linear Association	.600	1	.439		
N of Valid Cases	40				

a Computed only for a 2x2 table
b 1 cells (25.0%) have expected count less than 5. The minimum expected count is 4.88.

Table 31: Relationship between the non-invasive score and post-angiography management in patients who had previous coronary bypass surgery

ROC

Discrimination power between intervention group and medical group by using under curve area was insignificant 0.377, p=0.21(Table 32).

Area Under the Curve
Test Result Variable(s): non-invasive clinical scores

Area	Std. Error (a)	Asymptotic Sig. (b)	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.377	.091	.214	.200	.555

The test result variable(s): non-invasive clinical scores have at least one tie between the positive actual state group and the negative actual state group.
a Under the nonparametric assumption, b Null hypothesis: true area = 0.5

Table 32: The ability of non-invasive clinical scores to discriminate between intervention and medical management in patients who had previous coronary bypass surgery.

No previous bypass surgery – score of 40 or more

Of the 332 patients who had not had coronary bypass surgery, 146 patients (44% of all study patients) had a non-invasive score of 40 or more. 97 of these (66.4% of this group) were referred for an intervention while 49 patients (33.6%) were recommended to continue with medical treatment (Table 30).

There was a significant association between the non-invasive score and post-angiography management in this group but this result was not clinically significant Chi-Square test value = 10.8; P=0.001 (Table 33).

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig.
Pearson Chi-Square	10.8(b)	1	.001		
Continuity Correction (a)	10.113	1	.001		
Likelihood Ratio	10.944	1	.001		
Fisher's Exact Test				.001	.00
Linear-by-Linear Association	10.802	1	.001		
N of Valid Cases	332				

a Computed only for a 2x2 table
b 0 cells (.0%) have expected count less than 5. The minimum expected count is 63.77.

Table 33: Relationship between the non-invasive score and post-angiography management in patients who had not had coronary bypass surgery.

The area under the ROC findings support other results that, in patients who had not had coronary bypass surgery, the non-invasive score was able to discriminate between those who were referred for an intervention and those in whom continued medical treatment was recommended. (Table 34)

Area Under the Curve				
Test Result Variable(s): Non-invasive clinical scores				
Area	Std. Error (a)	Asymptotic Sig. (b)	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.630	.031	.000	.570	.689

The test result variable(s): Non-invasive clinical scores have at least one tie between the positive actual state group and the negative actual state group.
a Under the nonparametric assumption, b Null hypothesis: true area = 0.5

Table 34: The ability of non-invasive clinical scores to discriminate between intervention and medical management in patients who did not have previous coronary bypass surgery.

VALIDATION

The validation process of the power of angio-scores to discriminate between intervention and medical treatment was conducted on 40 patients who had previous CABG and 332 consecutive patients who did not have previous coronary bypass surgery.

Previous coronary bypass surgery – angiography score of 21or less.

Below this score, coronary arteries tended to be described as 'normal' or show 'mild to moderate' coronary disease. Only 6 of 40 (15%) patients in this group had such scores and all were denied an intervention and instead recommended to continue with medical management (Table 35).

Previous coronary bypass surgery- angiography score 24-45

34 of 40 patients (85%) had a score within this range. 21 of these (61.8%) were denied an intervention and instead recommended to continue with medical management. The remaining 13 patients (38.2%) were referred for a further procedure (Table 35).

On review of the angiography scores (Figure 18), a score of 24 appeared to be an important point because it appeared to identify those whose coronary artery disease was severe enough to warrant further revascularisation.

			Severity of coronary artery disease (new angio-scores)		
			0 - 21	24 - 45	Total
Post angiography management	Medical	n	6	21	27
		% within Outcome	22.2%	77.8%	100.0%
		% within angio-scores	100.0%	61.8%	67.5%
		% of Total	15.0%	52.5%	67.5%
	PTCA	n		6	6
		% within Outcome		100.0%	100.0%
		% within angio-scores		17.6%	15.0%
		% of Total		15.0%	15.0%
	CABG	n		7	7
		% within Outcome		100.0%	100.0%
		% within angio-scores		20.6%	17.5%
		% of Total		17.5%	17.5%
Total		n	6	34	40
		% within Outcome	15.0%	85.0%	100.0%
		% within angio-scores	100.0%	100.0%	100.0%
		% of Total	15.0%	85.0%	100.0%

Table 35: The ability of the angio-score to predict post-angiography management in patients with a history of coronary artery bypass surgery *(n=40)*.

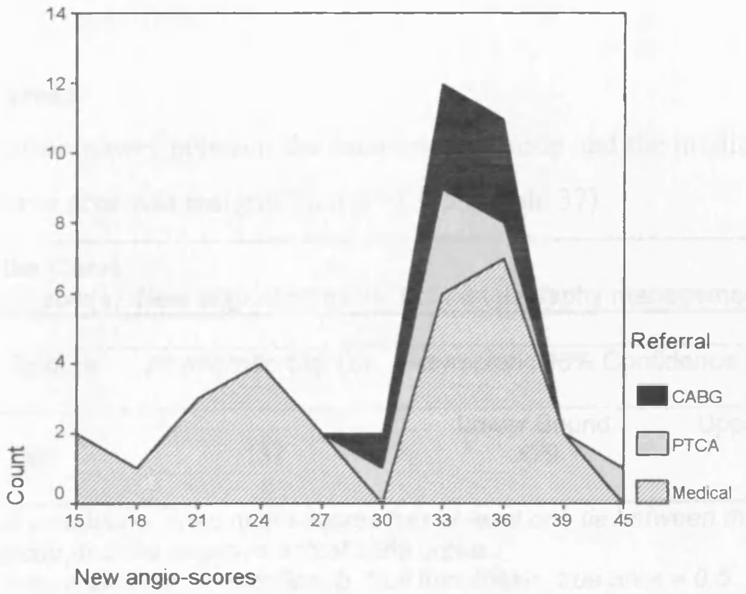


Figure 18: The predictive value of the new angiography scoring system for post angiography management of patients with previous CABG *(n=40)*.

Pearson Chi-Square Test:

Pearson's Chi-Square test was applied to total 40 patients who had previous coronary bypass surgery. It showed severity of coronary artery disease (angio-scores) and referral for intervention was independent and not associated. P=0.065 (Table 36).

Association Phi test was used as cross table had only 2x2 variables it was V=0.29. P=0.065

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	3.399[b]	1	.065		
Continuity Correction[a]	1.879	1	.170		
Likelihood Ratio	5.213	1	.022		
Fisher's Exact Test				.152	.077
Linear-by-Linear Association	3.314	1	.069		
N of Valid Cases	40				

a. Computed only for a 2x2 table

b. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 1.95.

Table 36: Pearson's Chi-Square test shows the relation between angio-score and post-angiogram management in sub-group of patients who had previous coronary bypass surgery

Under ROC area:

The discrimination power between the intervention group and the medical group by using under curve area was insignificant p=0.137 (Table 37).

Area Under the Curve

Test Result Variable(s): New angio-scores vs. Post-angiography management

Area	Std. Error (a)	Asymptotic Sig. (b)	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.647	.086	.137	.479	.815

The test result variable(s): New angio-scores has at least one tie between the positive actual state group and the negative actual state group..

a Under the nonparametric assumption, b Null hypothesis: true area = 0.5

Table 37: Under curve area was applied to test the ability of angio-scores to discriminate between intervention and medical management *(n=40)*.

No previous bypass surgery- angiography score less 24

Patients with angiography scores of less than 21 had no or mild to moderate coronary disease. 216 of 332 patients had an angiography score of less than 21. 124 of these (57.6%) were denied an intervention and instead recommended to continue with medical management. 92 (43%) were referred for further intervention (Table 38, Figure 19).

No previous bypass surgery- angiography score 24 or more than

116 patients (35%) had an angiography score of more than 24. 21 (18%) were denied an intervention and instead recommended to continue with medical management. 95 (82%), and 73(82%) were referred for further intervention (Table 38, Figure 19)

			severity of coronary artery disease (new angio-scores)		
			0 - 21	24 - 45	Total
Post angiography management	Medical	n	124	21	145
		% within Outcome	85.5%	14.5%	100.0%
		% within angio-scores	57.4%	18.1%	43.7%
		% of Total	37.3%	6.3%	43.7%
	PTCA	n	79	22	101
		% within Outcome	78.2%	21.8%	100.0%
		% within angio-scores	36.6%	19.0%	30.4%
		% of Total	23.8%	6.6%	30.4%
	CABG	n	13	73	86
		% within Outcome	15.1%	84.9%	100.0%
		% within angio-scores	6.0%	62.9%	25.9%
		% of Total	3.9%	22.0%	25.9%
Total		n	216	116	332
		% within Outcome	65.1%	34.9%	100.0%
		% within angio-scores	100.0%	100.0%	100.0%
		% of Total	65.1%	34.9%	100.0%

Table 38: The ability of the angio-scores to predict post angiography management in patients with no history of coronary artery bypass surgery *(n=332).*

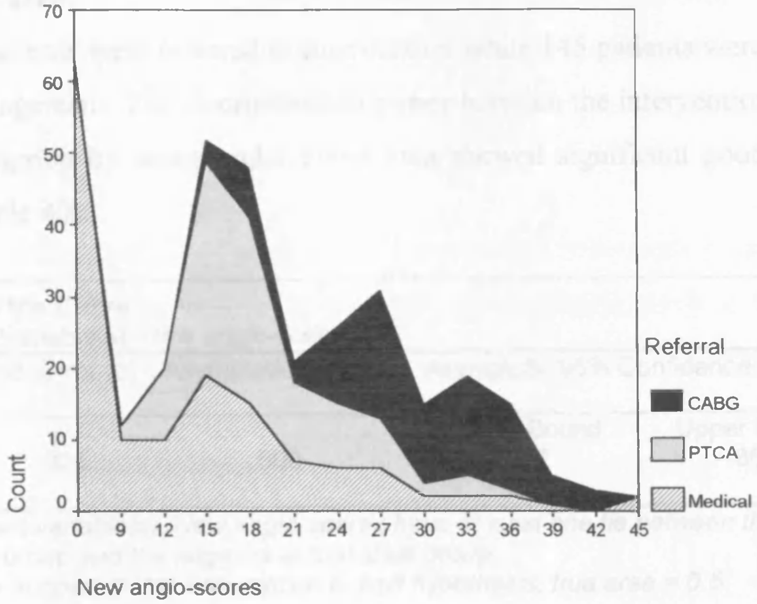


Figure 19: The power of angio-scores to predict the clinical decision following coronary angiography in patients who did not have previous coronary artery surgery *(n=332).*

Pearson's Chi- Square tests:

There was a significant association between the severity of coronary artery disease (angiography score) and post-angiogram management in patients who did not have previous coronary bypass surgery; Chi- Square value = 128; p=0.000 (Table 39).

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	128.75	2	.000
Likelihood Ratio	130.776	2	.000
Linear-by-Linear Association	104.873	1	.000
N of Valid Cases	332		

0 cells (.0%) have expected count less than 5. The minimum expected count is 30.05.

Table 39: Pearson's Chi-Square test shows the relation between angio-scores post-angiogram management in sub-group of patients who did not have previous coronary bypass surgery.

Under ROC area:

187 (56%) patients were referred to intervention while 145 patients were referred to medical management. The discrimination power between the intervention group and the medical group by using under curve area showed significant good area 0.81, p=0.000 (Table 40).

Area Under the Curve

Test Result Variable(s): New angio-scores

Area	Std. Error (a)	Asymptotic Sig. (b)	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.815	.025	.000	.767	.864

The test result variable(s): New angio-scores have at least one tie between the positive actual state group and the negative actual state group.
a under the nonparametric assumption b Null hypothesis: true area = 0.5

Table 40: Under curve area was applied to test the ability of angio-scores to discriminate between intervention and medical management (n=332).

Sample size and their effects on the strength of the tests.

Correlation between non-invasive clinical scores and post-angiography management in 40 consecutive patients who had previous CABG:

The effect of size was tested by using Cohen equation (Denis A 1999):

$$w = \sqrt{\frac{\sum(P_{1i} - P_{0i})^2}{P_{0i}}}$$

w is effect of size

Pi is the proportion of cells expected,

Poi is the proportion of cells observed.

The effect of size was that it was w = 0.56 (calculations based on Table 30).

Cohen (1977) defines the effect of size w = 0.1 to be small, w = 0.3 medium, and w = 0.5 to have a large effect.

The value of w = 0.56 is considered as a large effect, thus for the value of $\alpha = 0.05$ and one degree of freedom for the effect of the size observed, a sample between 25-50 gives power of 0.70-0.94 thus the sample used of 40 was appropriate (appendixes 8, and 9).

Correlation between non-invasive clinical scores and post-angiography management in 332 consecutive patients who did not have previous CABG
The effect of size was calculated as above and it was w = 0.88 (Table 26) According to Cohen's definition, this is a large effect. Thus for value for $\alpha = 0.05$ and one degree of freedom, a sample size of 25 give power of 0.98 in the study sample size was 332 patients (Appendix 8, and 9).

Discussion

There are several reasons for performing coronary angiography. In patients with symptoms of angina, this is generally to establish the presence of coronary atheroma, its extent and severity and suitability for coronary revascularisation. When a patient has had coronary surgery or angioplasty in the past, the goals of investigation are different – the patient is already known to have coronary atheroma (and the extent and severity of the disease having warranted revascularisation) and repeat angiography is intended to ascertain to what extent this has progressed in the native coronary arteries and whether it has developed in the coronary grafts.

Can a non-invasive score assist the clinician to decide whether a patient with recurrent angina symptoms after coronary surgery has to be re-investigated? The argument that the likelihood of coronary disease is so high that the question is irrelevant is not completely true for two reasons. First, the quality of pain that a patient who has had bypass surgery experiences can be very different from that felt before the operation. Second, symptoms from the upper gastrointestinal tract that can so easily mimic angina are very common. Hence, any tool that could identify those who need angiography ought to be fairly evaluated and introduced into routine clinical practice.

Among those patients who had never had a bypass operation, the non-invasive clinical score successfully identified those who would be referred for revascularisation on the basis of the findings at coronary angiography but did not identify those who would be offered a second revascularisation procedure. Consequently, the non-invasive scoring system appears to have a role in the care of patients who have never had coronary bypass surgery.

The non-invasive score does not seem reliable for patients being investigated for a second time. What is the most likely explanation for this? Angiography evaluates the extent of coronary artery disease in native coronary vessels that attract fairly high scores using the system described here. Unsurprisingly, clinicians will be influenced by extensive disease and so will tend to refer for intervention. After bypass surgery, the influential factors are more complicated- to what extent has the atheromatous lesions, both known and new, progressed in native vessels? How have the grafted vessels fared? Is it still technically possible to perform a second procedure? Is left ventricular performance adequate to support another bypass operation? Thus, the selection of patients for a further operation is subject to many more variables than at first review.

A threshold angio-score at which a patient being investigated for the first time might be offered an intervention was observed so any patient who achieved an angio- score of 24 or more is much more likely to be referred for revascularisation.

Conclusion

The rationale for a first coronary angiogram is very different from a repeat investigation post-bypass – investigation of the latter will inevitably show evidence of coronary artery disease. The non-invasive scoring system seems capable of identifying patients with symptoms of angina who have not had bypass surgery but who will be offered revascularisation but the current model is inadequate as a tool for patients who have already had bypass surgery. Consequently, it seems reasonable to calculate a non-invasive score for patients who have not had coronary surgery. Until a better scoring system can be developed, the decision to refer patients who have had surgery before must rely on the skill and experience of the clinician.

Chapter 8

A comparison of non-invasive clinical scoring system and existing appropriateness systems

Chapter 8

A comparison of non-invasive clinical scoring system and existing appropriateness systems

INTRODUCTION

The appropriateness rating is useful to ascertain whether a hypothetical indication is appropriate or not; a major disadvantage is that it cannot deal with the findings of coronary angiography and post-angiography management. In one study, 29% of patients who were considered to have an *inappropriate* indication for coronary angiography had major coronary atheroma (Noonan SJ et al 1995). Gray et al reported that 18% of cases considered *inappropriate* for coronary angiography had no significant disease and over one third underwent coronary artery bypass surgery.

The non-invasive clinical scoring system, however, is able to predict the severity of coronary artery disease and post-angiography management, as reported in previous chapters. A comparison of the appropriateness and non-invasive clinical scoring systems would identify the strengths and weaknesses of each.

METHODS

Population

A group of 372 consecutive patients on the waiting list for coronary angiography was used in order to compare non-invasive clinical scoring system with other appropriateness systems. (The population has been described in an earlier Chapter [2], Figure 7)

The appropriateness system

The appropriateness system developed by RAND and reported by Gray et al (Gray D et al *1993*) was applied to all patients in the following sequence:

Appropriateness ratings for hypothetical clinical scenarios

In the RAND/UCLA study, an expert panel consisting of nine clinicians who represented all geographic regions of the country and both academic and private hospitals were nominated. There were three cardiac surgeons, three interventional cardiologists, one non-interventional cardiologist, and two internists while the Nottingham panel had two cardio-thoracic surgeons, a consultant cardiologist, two physicians, a cardiac radiologist, a general practitioner and two researchers with a clinical interest in cardiology.

The expert panel rated hypothetical clinical scenarios that included a wide range of possible indications for the investigation of chronic stable angina. This list included all conceivable circumstances in which coronary angiography might be contemplated. Panellists were asked on two separate occasions to rate these hypothetical indications on a scale of 1 to 9. On the first occasion this was made individually, but the second was conducted after discussion by all 9 members of the panel. An *extremely inappropriate* indication was rated 1 and an *extremely appropriate* indication was rated as 9.

An indication was defined as *appropriate* when the medical benefit (prolonged life, relief of the pain and improved function) exceeded the mortality and morbidity of the procedures with an acceptable margin to make it worth doing the procedure (Leape LL et al *1991*. Gray D et al *1993*). An indication was defined as *inappropriate* when there was more potential for harm than benefit from undertaking the procedure. An indication was considered as *uncertain* or *equivocal* when potential benefits and risks were the same.

The highest and lowest ratings were discarded and the median of the remaining seven ratings calculated. Based on the median rating, the procedures were considered a) appropriate if the median rating was 7-9, b) equivocal if the median rating was 4-6, and c) inappropriate if the median rating was 1-3. The full list of ratings applied to patients in this study is shown in Appendices 5, 6 and 7.

Panellists were considered to be in agreement if all gave an indication the same rating (whether appropriate, equivocal or inappropriate), once the highest and the lowest scores had been discarded.

Allocation of ratings to patients

The author applied the ratings for hypothetical, clinical scenarios to actual cases. The median scores and agreement status were noted. The allocation process was conducted as follows (Figure 20):

Step I:

The relevant chapter (or main indication for the procedure) was identified for each patient. Patients referred for elective coronary angiography were enrolled in the chapter *'Chronic stable angina'* and subdivided as follows:

1. **Severity of angina**:
   Angina on mild exertion (class III, IV)
   Angina on moderate exertion (class I, II)
2. **Extent of medical treatment**:
   No or less than maximal therapy (>2 anti-angina drugs)
   On maximal therapy (>2 anti-angina drugs)
3. **Result of exercise test**:
   Strongly positive exercise test (positive stage I)
   Positive exercise test (positive stage II, III)
   Negative exercise test
4. **Age**:
   Age > 75 years
   Age <75 years

Some patients had unstable angina (progressive angina) in the preceding three months. Patients were subdivided as follows:

1. **Severity of angina**:
   Angina subsequently recurs during mild exertion (class III, IV)
   Angina subsequently recurs during moderate exertion (class I, II)
2. **Extent of medical treatment**:
   No or less than maximal therapy (>2 anti-angina drugs)
   On maximal therapy (>2 anti-angina drugs)
3. **Age**:
   Age > 75 years
   Age <75 years

Few patients were asymptomatic and only two clinical scenarios of this chapter were applied to the study sample, and scores were allocated as described above.

Step II:

Appropriateness rating were taken from the *hypothetical case scenarios* of RAND/UCLA and assigned as described above. These ratings were applied to the *clinical scenarios.*

Step III:

The ratings, median scores and agreement status were upgraded if an individual patient had more than one indication. For example, some patients had a history of myocardial infarction or coronary artery bypass surgery; some had had an episode of unstable angina.

Worked example 1:

1. A 76-year-old patient was referred for elective coronary angiography. He had a 2-year history of stable angina on mild exertion (class III); his current medication was Beta-blocker and a nitrate spray. Exercise tolerance test was positive in stage II. What would be RAND appropriateness rates for this patient?

   a) ***Severity of symptoms:*** *stable angina class III.*

   b) ***Extent of medical treatment:*** *Less than maximum medical treatment.*

   c) ***Exercise test:*** *Positive stage II.*

   d) ***Age:*** *> 75 years.*

Applying RAND ratings, this patient was assigned an *uncertain rating*. As the median of the rating was 5.

Worked example 2:

If the same patient mentioned above had a history of unstable angina that required hospitalisation during the previous three month of referral, the following would apply:

a) **Severity of symptoms:** stable angina class III.

b) **Extent of medical treatment:** Less than maximum medical treatment.

c) **Exercise test:** Not appropriate

d) **Age:** > 75 years.

By using the RAND ratings this patient had an *appropriate* rating, as the median of rates was 7. In this situation, the higher rating would be allocated

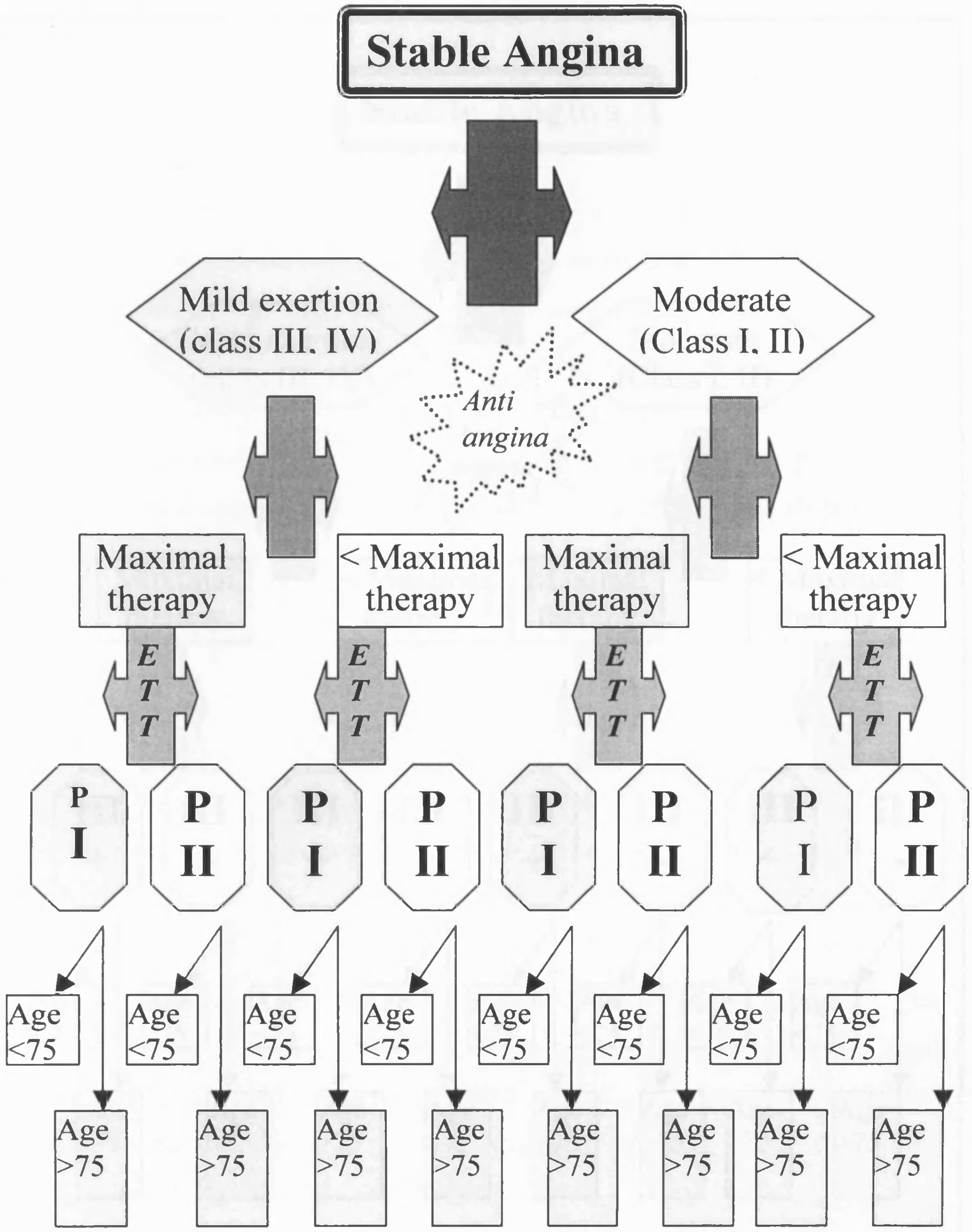


Figure 20: Allocating appropriateness rating- based on exercise test (ETT) (RAND appropriateness system)

P I: positive in stage one. PII: positive in stage two.

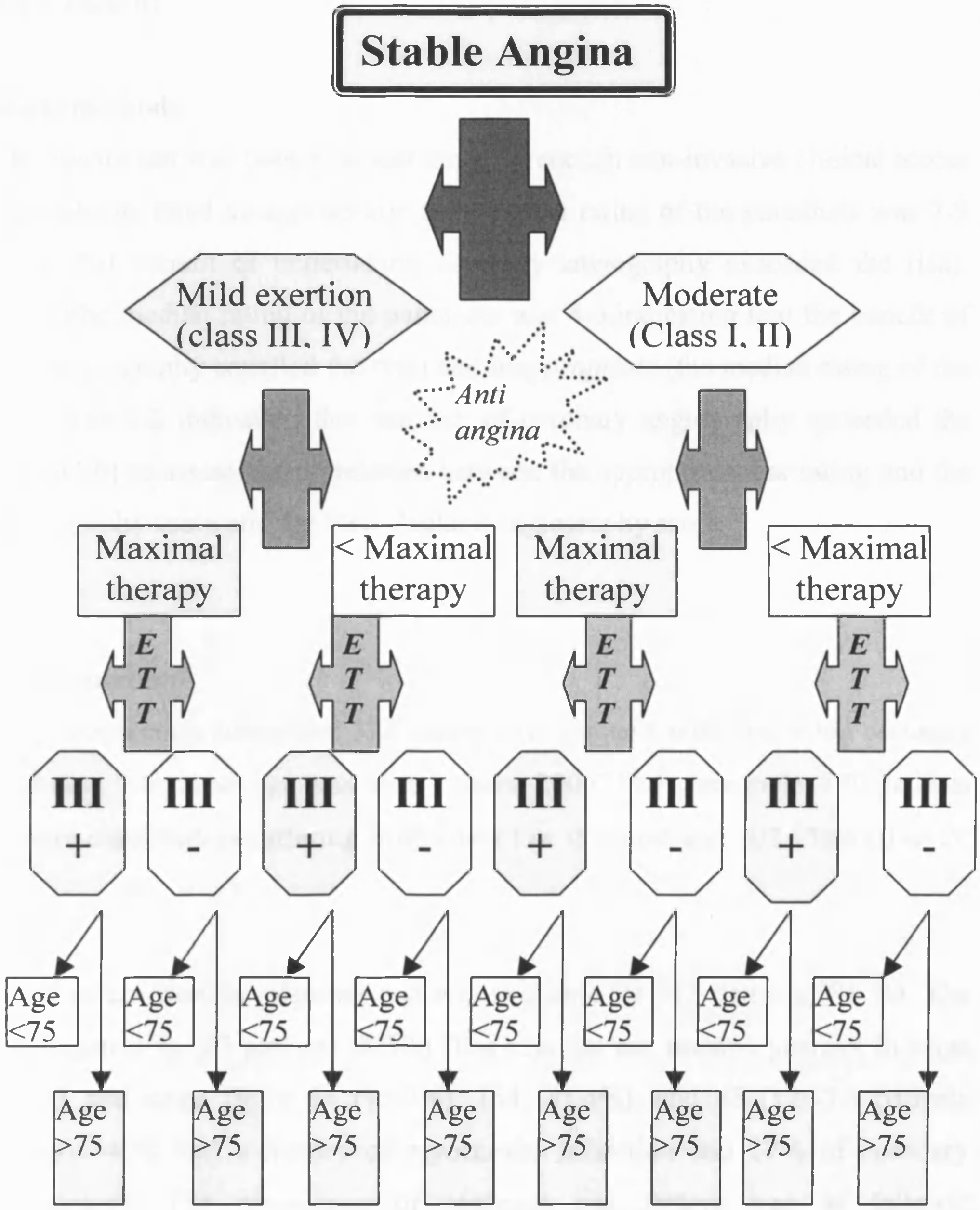


Figure 20 continued: Allocating appropriateness rating- based on exercise test (ETT) (RAND appropriateness system)

III+: ETT positive at stage three. I -: ETT negative at stage III

Non-invasive test scores

Non-invasive clinical scores were allocated as described in a previous chapters (Chapters 3 and 4)

Statistical methods

The Chi-Square test was used a) to test the difference in non-invasive clinical scores between patients rated as *appropriate* (the median rating of the panellists was 7-9 indicating that benefit of undertaking coronary angiography exceeded the risk), *equivocal* (the median rating of the panellists was 4-6 indicating that the benefit of coronary angiography equalled the risk) and *inappropriate* (the median rating of the panellists was 1-3 indicating that the risk of coronary angiography exceeded the benefit); and b) to assess the correlation between the appropriateness rating and the new angiography score and the New Zealand angiography score.

Result:

Patient population

The study population comprised 372 consecutive patients with suspected coronary artery disease. The mean age was 61 ± 9 years. 200 (73%) were male. 170 patients (46%) were classified as suffering from Class I or II angina and 202 Class III or IV angina.

The result of an exercise tolerance test was available for 313 patients (84 %). The test was negative for 27 patients (8.6%). The exercise test became positive in stage I, Stage II and stage III in 84 (15.9%), 154 (41.4%), and 48 (12.9%) patients respectively. 48% had a history of myocardial infarction and 17% of coronary bypass surgery. The prevalence of common risk factors was as follows: hypercholesterolaemia 29%, diabetes mellitus 14 %, and blood hypertension 22% of patients.

Coronary angiography revealed significant disease in the left main coronary artery in 9% of patients and proximal left descending artery in 29%. One, two and three affected vessels were found in 23%, 27%, and 32 % of patients respectively

The appropriateness system

The individual clinical circumstances for each patient were identified for each patient. The hypothetical scenario was identified and the appropriateness rating assigned by the Author in accordance with the panellists' decision. The median rating was calculated and then allocated to each patient. (43, 37 clinical scenarios based on the Nottingham report and RAND appropriateness systems respectively). The panellists in Nottingham's report tend to be more conservative this may be due to differences in the constitution of each panel differences in health care systems in USA, and UK. The UK panellists rated the same clinical scenarios less appropriate (underscored) than RAND's Panellists. This result in lower ratings of an 'appropriate' indication when Nottingham report was applied. Some of the main deferences between both systems were abstracted from appendixes 6, and 7 as the follows:

Nottingham rates :	**RAND rates :**
- Patients with angina on mild exertion, and positive exercise test considered appropriate indication, only if on maximal medical treatment. - Cut off age considered 65 years, older age considered less appropriate for coronary angiograhy. - Patients with acute myocardial infarction during the previous 6 months, considered appropriate indication for coronary angiography, if on maximal medical treatment, but indication considered equivocal if on less than maximal	- Patients with angina on mild exertion, and. positive exercise test considered appropriate indication, weather on maximal or less medical treatment. - Cut off age considered is 75 years; older age, considered less appropriate for coronary angiograhy - Patients with acute myocardial infarction during the previous 6 months, considered appropriate indication for coronary angiography, whatever the status of medical management

Non-invasive clinical scores:

A cut-off 'threshold' of 40 was used to determine whether patients should be referred for coronary angiography, as well as to compare the appropriateness system with the non-invasive clinical scoring system in both groups of patients. 200 and 172 patients were assigned to non-invasive clinical scores of less than 40 and more than 40 respectively (Tables 41, 42)

Validation of the non-invasive clinical scoring system with appropriateness ratings *(Nottingham report)*

Appropriateness rating and non-invasive clinical scores

The median value of the appropriateness rating in the study population patients was 8 – this implies that this group of patients was referred for coronary angiography *appropriately*. The mean of the median (7.26 ± 1.9) fell into the 'appropriate' range but the standard deviation indicates there were some patients within the 'equivocal' range. The mean of the non-invasive clinical scores was 38 ±11. The mean of the median in the group of patients with non-invasive clinical scores less than 40 was 7.21± 2 while in the group of patients with non-invasive clinical scores more than 40 it was 7.31±1.9. Figure 21 shows the relationship between non-invasive clinical scores and median appropriateness rates.

Hypothetical indications

Hypothetical indications that were deemed *appropriate* (ratings of 7, 8 or 9) were allocated to 277 patients (74.5% of the study population), *inappropriate* to 22 patients (6%) and *equivocal* to 73 (19.5%), (Table 41)

Non-invasive clinical scores

200 patients had non-invasive clinical scores of less than 40 and 172 patients had scores of more than 40. Of these, panellists had rated 74.5% as appropriate for investigation, 6.5% inappropriate and 19% equivocal (Table 41).

Of a possible 490 hypothetical indication described by Gray et al, only 43 indications (9%) were relevant to the clinical cases.

	Non-invasive clinical score				
		<40	**%**	**≥ 40**	**%**
Median appropriateness score (Nottingham report)	***Inappropriate***	13	6.5	9	5.2
	Uncertain	38	19	35	20.3
	Appropriate	149	74.5	128	74.5
	Total	200	100	172	100

Table 41: Non-invasive clinical scores and appropriateness rates (Nottingham report).

The mean of non-invasive clinical scores for the group of patients who were rated as appropriate (median ≥ 7) was 37.8 ±11.6 which was less than in the group of patients who were rated inappropriate and uncertain (median <7) 38.6 ±11.

The correlation between non-invasive clinical scores and the appropriateness ratings (adapted from Gray et al) was tested using Chi-Square; this showed no significant correlation between non-invasive clinical scores and appropriateness ratings (P=0. 885; Table 43).

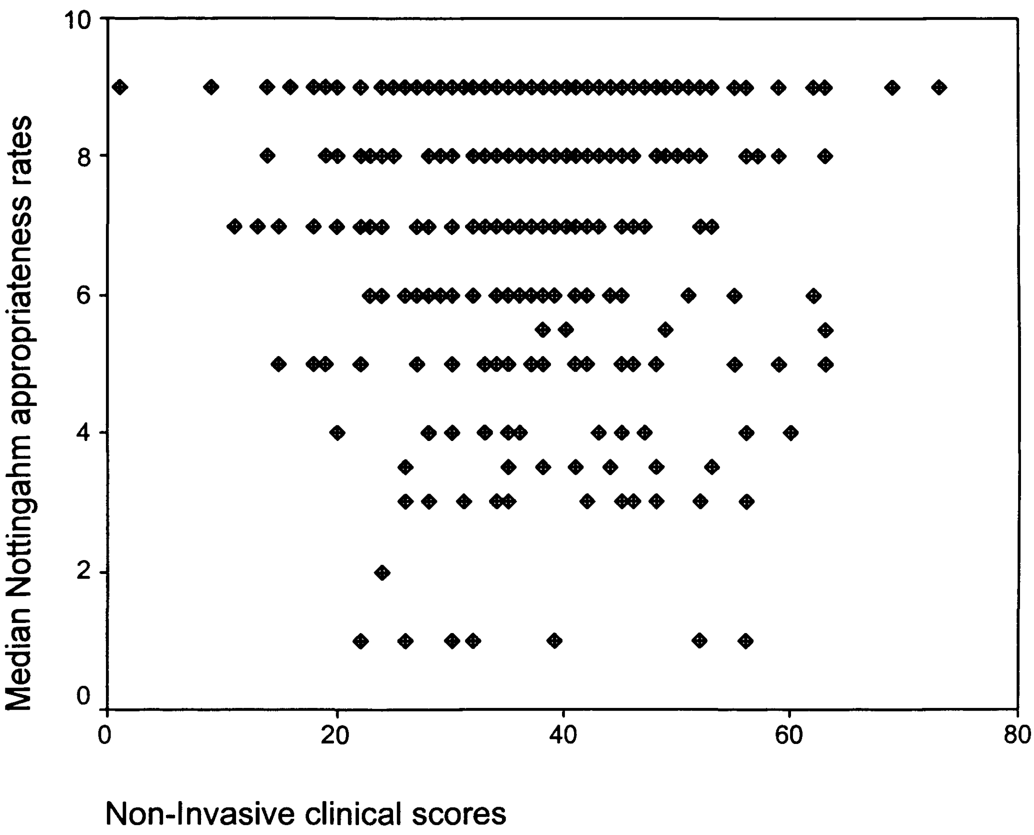


Figure 21:Correlation between non-invasive clinical scores and median appropriateness rates (Nottingham report).

II) Validation of the non-invasive clinical scoring system with RAND/UCLA appropriateness method

The same population of 372 consecutive patients as described above was used to validate the scoring system. The method of assigning appropriateness ratings and non-invasive clinical scores was described above.

Appropriateness rating and non-invasive clinical scores:

The mean of the median RAND rating was used in order to determine *appropriate*, *equivocal* and *inappropriate* indications. The mean of the RAND median was 8.61 ±0.72; this very high score implies that the panellists rated the group of 372 patients as 'highly appropriate'.

Hypothetical indications

An 'appropriate' indication (median 7-9) was allocated to 363 patients (97.6% of total patients) while 'uncertain' was assigned to 9 (2.4% of total patients). No patient was rated as 'inappropriate' for coronary angiography (Table 42).

Non-invasive clinical scores

For patients whose clinical scores were less than a nominal threshold of 40 (who would not be referred for coronary angiography according to a non-invasive clinical scoring system), the mean of the median was 8.60±0.70. For those patients whose score was greater than 40 (who would be referred for coronary angiography), the mean of the median was 8.63±0.70.

Table 42 shows that 200 patients had non-invasive clinical scores of less than 40; 98% of these were rated as appropriate and 2% as 'uncertain'. 172 patients had non-invasive clinical scores of more than 40, 97% appropriate and 3% 'uncertain'.

		Non- Invasive clinical score			
Median appropriateness scores (RAND.)		**<40**	**<40 %**	**≥ 40**	**≥ 40 %**
	In appropriate	0	0 %	0	0 %
	Uncertain	4	2 %	5	3 %
	Appropriate	197	98 %	166	97 %
	Total	200	100%	172	100%

Table 42: Non-invasive clinical scores and RAND appropriateness rates.

Comparison of the two ratings systems

The mean non-invasive clinical score for patients who were rated *appropriate* was 37.9 ±11.4; while for those patients who had an *inappropriate* or *uncertain* rating it was 41.33±11.3. The mean of the median RAND rating for patients who had a non-invasive score of more than 40 was almost the same as for patients who had scores of less than 40 at 8.6 3 ± 0.73 vs. 8.6 0 ± 0.70. Figure 22 shows the relationship between non-invasive clinical scores and median appropriateness rates (RAND/UCLA).

The correlation between non-invasive clinical scores and the RAND Appropriateness ratings was tested using the Chi-Square test which showed no significant correlation between non-invasive clinical scores and RAND appropriateness rates P=. 559 (Table 43).

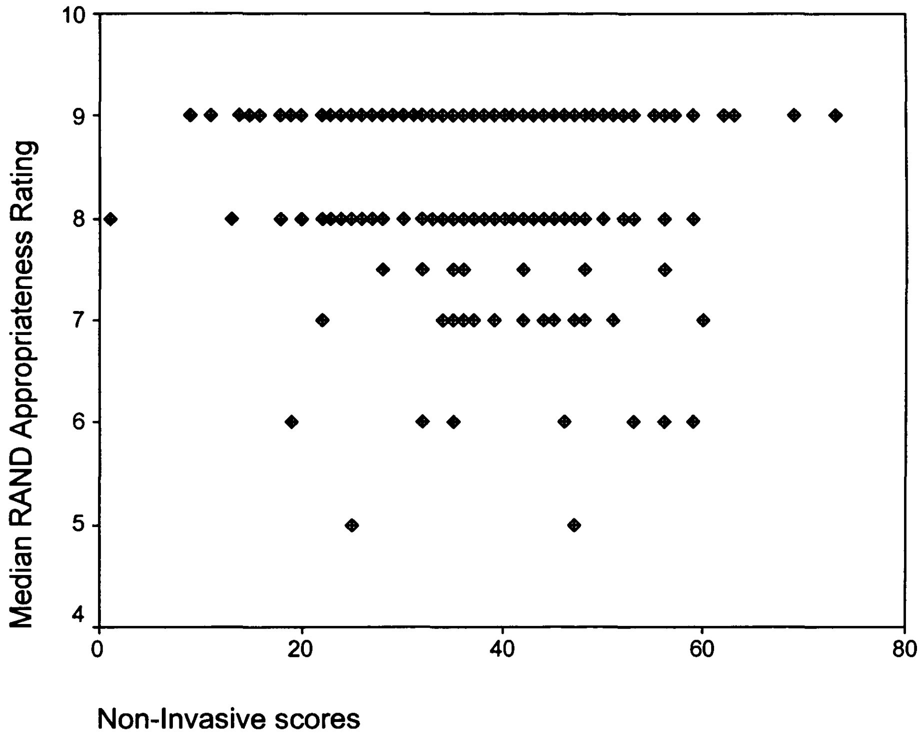


Figure 22:Correlation between non-invasive clinical scores and median appropriateness rates (RAND/UCLA).

		Pearson Chi-Square value	df	Asymp. Sig (2-sided p)	Minimum expected count
Appropriateness rates[1]	Non-invasive clinical scores	.244	2	.885	10.11.
RAND Appropriateness rates	Non-invasive clinical scores	.341	1	.559	4.14

Table 43: Correlation between appropriateness rating and non-invasive clinical scoring system. ***1= as reported in Gray D et al 1989***

III) The correlation between appropriateness rating and angiography score (predicting severity of coronary artery disease):

In order to apply the Chi-Square test to test the correlation between appropriateness rating and angiography scores, angiography scores were combined according to the severity of coronary artery disease. One group consisted of patients with severe coronary disease (a new angiography score greater than 24 or a New Zealand angiography score greater than 19) and the other with mild to moderate coronary artery disease (new angiography score less than 24 or a New Zealand angiography score of less than 19). Appropriateness ratings were applied, as described elsewhere.

There was no significant correlation between appropriateness ratings (Nottingham report) and the severity of coronary artery disease either measured by the New Zealand angiography score (p=0.46) or by the new angiography scoring system (P=0.46). There was no significant correlation between the appropriateness rating (RAND) and the severity of coronary artery disease either measured by the New Zealand angiography score (p=0.6) or by the new angiography scoring system (P=0.34)(Table 44).

		Pearson Chi-Square	df	Asymp. Sig. (2-sided p)	Minimum expected count
Appropriateness rating (Nottingham report)	New angiography scores	1.534	2	.464	8.87.
	New Zealand angiography scores	1.528	2	.466	10.41
RAND Appropriateness rating	New angiography scores	.889	1	.346	3.63
	New Zealand angiography scores	.251	1	.616	4.26

Table 44: Correlation between appropriateness rating and angiography scores measured by New Zealand and New angio-scoring systems.

IV) Correlation between non-invasive clinical scores and severity of coronary disease (Angio-scores)

1. Non-invasive clinical scores versus new angiography scores

Table 45 shows that mean angiography score for the group of patients with clinical score less than 40 was 16.2±11.8 while it was 22.8±10.5 for the group of patients who had clinical scores more or equal to 40. Pearson's Chi-Square test showed a weak but significant correlation (Pearson's Chi-Square 27.3 p=0.001; Cramer's V = 27; Table 46).

2. Non-invasive clinical scores versus New Zealand angiography scores

The mean angiography score for the group of patients who were assigned a non-invasive clinical scores of less than 40 was 13.4 ± 9.35; for those with a non-invasive clinical score of more than 40, it was 18 ± 7.78 (Table 45). Pearson's chi-square test showed a significant but weak correlation (Pearson Chi-Square 16.3 p=0.001; Cramer's V = 21; Table 46).

		New Zealand angiography scores		New Angiography *scores*	
Non-invasive clinical scores		**<40**	**>=40**	**<40**	**>=40**
N	Valid	201	171	201	171
Mean		13.40	18	16.2	22.8
Median		15	19	15	24
Std. Deviation		9.35	7.78	11.86	10.48
Minimum		.00	.00	.00	.00
Maximum		36	36.00	45	45
Percentiles	25	8	15.0000	9	15
	50	15	19.0000	15	24
	75	19	19.0000	24	33

Table 45 Correlation between non-invasive clinical scoring system and angiography scores.

		Pearson Chi-Square	**df**	**Sig. (2-sided) P=**	**minimum expected count**	**Cramer's V**
Non-invasive clinical scores	New angiography scores	27.347	1	.0001	80.90.	27
	New Zealand angiography scores	16.320	1	.0001	68.95	21

Table 46: Correlation between non-invasive clinical scores and angiography scores.

DISCUSSION

Although coronary angiography is effective in selected populations, the overall appropriateness of its use has been questioned. Similarly, the generalisation of the appropriateness ratings is questionable given that the assessment of appropriateness of use of coronary angiography has differed from one study to another in the level of clinical detail used to judge appropriateness and the methods used to generate the appropriateness criteria.

It is clear that, while the appropriateness rating may indicate that an individual should or should not have coronary angiography, it is not a good predictor of whether significant coronary disease will be found. For example, 39% of patients rated as appropriate have normal or mild coronary artery disease; in this circumstance, appropriateness is associated with overuse of the procedure. At the same time, an inappropriate rating is imperfect because many patients will have significant coronary disease. It must be concluded that the RAND system is not a clinically useful method for selecting patients who might warrant revascularisation.

Appropriateness ratings (Nottingham criteria) showed no significant correlation with angiography scores when measured by either the New Zealand or the new angiography scoring system (Chi-Square test p value was 0.46). There was a significant correlation between clinical scores with angio-scores measured by either the New Zealand or the new angiographic scoring system (Chi square p=0.001). There was no significant correlation between the non-invasive clinical scoring system and appropriateness ratings using Nottingham criteria or RAND criteria (p 0.89 for the former and 0.56 for the latter).

The new angiography scoring system described in this chapter is superior to the RAND approach- of patients who were rated as having an inappropriate indication for coronary angiography (who would not have been offered the procedure), 36% were predicted according to the new angiography score to have severe coronary artery disease; and 46% with an uncertain indication (who also would have been denied investigation) also had severe disease.

It may be reasonable to conclude that 1) Non-invasive clinical scoring systems are powerful tools for predicting the severity of coronary artery disease while appropriateness ratings are not; 2) there is no correlation between non-invasive clinical scores and appropriateness rating; 3) there is a considerable difference in the appropriateness ratings adapted from the Gray et al and RAND studies.

These findings are important for policy makers as they contemplate whether to expand resources for cardiovascular care in the UK. Both appropriateness and non-invasive clinical scores have a place in selecting patients for coronary angiography.

Appropriateness criteria (RAND *1991*; Gray, D., et al *1993*) take inadequate account of individual peculiarities and so they are not suitable for clinical decision-making in individuals. Nevertheless, they do have a role as a quality control screening tool and could be used in primary and secondary care as a means of assessing whether to refer patients for coronary angiography. Non-invasive clinical scores can then be calculated to decide whether a patient is eligible for the procedure or not.

Certainly, easily gathered clinical data can be utilized more effectively to assist in the clinical decision-making process- physicians might select patients who are more likely to have significant coronary disease and who warrant revascularisation; and public health physicians might be able to contain an unnecessary growth in expensive and potentially dangerous procedures. A non-invasive score is an important step in refining patient selection for coronary angiography.

Chapter 9

Conclusion

Chapter 9

Conclusion

Clinicians may be distinguished in the way they employ coronary angiography in the management of patients with symptoms of angina. Some do reserve coronary angiography for patients whose symptoms have failed to respond to medical treatment – they wish to establish the *extent* of coronary disease as a prelude to a revascularisation procedure, while others argue that they can only manage patients well if coronary angiography is undertaken – they wish to establish the *existence* of coronary disease to risk stratify patients into those who need urgent revascularisation (those with left main stem disease) from the remainder. There is perhaps one area of agreement – most clinicians would propose coronary angiography to establish *once and for all* whether coronary disease is responsible for patients whose symptoms defy diagnosis using conventional tests.

Such divergent views have important physical, social and economic consequences for the individual and the NHS, irrespective of problems regarding equity of access. What is required is a satisfactory method of establishing the presence and severity of coronary disease without recourse to an invasive procedure that is not without hazard. The development of a reliable non-invasive clinical scoring system would contribute to improved clinical care of patients and would provide a reference system for selecting who should be offered angiography and who should not.

The development of a new scoring system

The prioritisation scoring system has proved to be simple reliable system, which is easily understood by health professionals. This system does not need a special experience to use friendly user can be used with or without computer assistance. Based on just a few clinical and risk factors, a scoring system reliably and statistically predicted the severity of coronary artery disease and the outcome of coronary angiography and revascularisation procedures.

Scores were assigned to each factor according to their significance in predicting outcome, were summed together and used to describe receiver-operator curves and to define a threshold score above which patients ought to be referred for coronary angiography. The recommended threshold can be reviewed periodically and adjusted to achieve highly appropriate referrals for invasive and potentially harmful procedures. Moreover patients with marginal clinical scores that did not achieve the threshold score can be reviewed if the clinical situation changes within a predetermined follow up period selected by the individual physician. Alternatively, the procedure can be funded by a source other than public funds.

Coronary angiography is considered to be the only procedure that determines coronary anatomy sufficiently to allow a recommendation for a subsequent revascularisation procedure but it is not without risk. Thus it is advisable a prerequisite that all patients referred for coronary angiography should have an appropriate indication for the procedure.

Using data from morbidity and mortality studies to identify the power of different clinical and risk factors to predict the extent and severity of coronary artery disease, the application of weighting factors makes it easier to quantify coronary lesions and to conduct comparative studies of different scoring systems. Scores based on symptomatology and the result of exercise testing were adapted from the New Zealand project; comparison with the Leicester-based angio-scores showed a weak statistically insignificant correlation. By local (i.e. Leicester cardiologists') consensus, a new score was devised, taking into account the extent of anti-angina medication and previous acute myocardial infarction to which additional weightings were applied. The resulting scores were combined with the scores of exercise test and symptoms to yield a new, non-invasive consensus based, clinical scoring system.

Once again, the scoring system was of limited clinical value. The inclusion of multiple risk factors enhanced the prediction of the severity of coronary artery disease as well as post -angiography management.

In clinical practice, however, the ability to predict the severity of coronary artery disease is probably more important than the power to predict post-angiography management and so it was considered worthwhile trying to refine and improve the predictive model to overcome by taking into account a much wider range of clinical variables.

Based on uni- and multivariate analysis, a model was developed that incorporated the following variables: age, sex diabetes, hypercholesterolaemia and previous myocardial infarction. Weightings – based on statistical analysis and on a consensus of Leicester Cardiologists – were applied to these factors, and they were subsequently included into another model (*Non-invasive clinical scoring system modified version*). Receiver-operator curves were used to assess how successful such a scoring system might be in predicting the severe coronary artery disease. From the ROC curves, a threshold score was identified that corresponded to disease of sufficient severity to warrant intervention (that is revascularisation by coronary angioplasty or bypass surgery) on prognostic grounds.

A threshold score of 40 yielded a sensitivity of 71% and specificity of 60% in predicting the severity of coronary artery disease. A score of less than 40 tended to identify a group of patients in whom, continued medical management was the preferred option, while scores over 40 largely identified those who were referred for revascularisation.

Application of a scoring system approach to patient management

The scoring system described above, using easily obtainable clinical variables, successfully predicted with reasonable accuracy those with severe coronary artery disease and consequently those for whom revascularisation was the most appropriate management. Accepting that no scoring system is ever perfect, the introduction of this non-invasive clinical scoring system into routine clinical practice in the UK could improve the quality of health services in patients with symptoms suggestive of coronary disease; ration access to coronary angiography by establishing a threshold score; and shorten waiting lists immediately and perhaps eliminate waiting time for this procedure in long term.

For a patient with coronary artery disease, the main goals of any cardiac procedure are to control symptoms and to reduce the risk of an avoidable acute cardiac event such as acute myocardial infarction, unstable angina or cardiac death. The question arises whether a non-invasive clinical scoring system can identify a group of patients who are at high risk of sustaining an acute cardiac event. There was a significant difference in non-invasive clinical scores between the group of patients who had cardiac events and those who did not. The non-invasive clinical scoring system identified a group of patients who were vulnerable to a future acute cardiac event. Empirically, a score of 40 distinguished between those who did and did not have an acute cardiac event, with 6% of patients with score of *less than 40* and 21% of those with a score *greater than 40* having a major cardiac event.

Clinical utility of the scoring system

It is important when evaluating any non-invasive clinical scoring system, which might predict the severity of coronary artery disease to establish that it is reliable. The aim of developing a new angio-scoring system was to overcome the difficulties and criticisms of the New Zealand angio-scoring system that were due to the following. First, lesions in branch vessels (such as the obtuse marginal and diagonal arteries) were not scored although the clinical decision-making process usually takes into account all lesions in any vessel. Second, the New Zealand scoring system is very complex, difficult for clinical scorers to remember and difficult to construct formulae for computer application. And third, many patterns of coronary disease achieve the same score.

The New Angio-scoring system resolved these issues and proved to be a relatively simple for users to apply. Most importantly it covers all possible clinical scenarios of coronary artery disease with minimal overlap and does deal with lesions in branch vessels of the main coronary arteries. The greatest successes of the new system is that it predicted the severity of coronary disease and so the subsequent decision to offer or withhold revascularisation; it successfully predicted the outcome of coronary angiography in 66-76% of patients referred for coronary angioplasty and 85-95% referred for bypass surgery. This has a significant impact on individuals as well as on the organisation of coronary artery disease services on a national basis.

Relevance of the scoring system in patients with previous bypass surgery

Increasingly a high percentage of referrals for investigation of recurrent angina will be in patients already known to have coronary artery disease, which has been treated by coronary bypass surgery. This group of patients present problems to clinicians because of the severity of the underlying disease as well as technical difficulties in 'redo' coronary bypass surgery, which increase risk.

Can a non-invasive score assist the clinician to decide whether a patient with recurrent angina symptoms after coronary surgery ought to be re-investigated and whether this system is predictive of the progression of coronary artery disease in native artery or in the grafted vessel? Based on the findings of this study, the non-invasive clinical scoring system did not seem sufficiently reliable for patients being investigated for a second time and it proved necessary to develop an alternative system to facilitate the clinical decision-making process of whether or not to recommend coronary angiography.

Demonstrating superiority over alternative scoring systems

The RAND appropriateness system does not seem to be a clinically useful method for selecting patients who might warrant revascularisation as 36% of patients rated as having an inappropriate indication for angiography and 46 % of patients rated as having an uncertain indication for coronary angiography, who would not have been offered the procedure, were found to have severe coronary artery disease while the non-invasive clinical scoring system was able to predict the severity of coronary artery disease. There was no significant correlation between appropriateness ratings and the severity of coronary artery disease as measured by the New Zealand angiography score or by the new angiography scoring system.

It is clear that, while the appropriateness rating may indicate whether an individual should or should not have coronary angiography, it is not a good predictor of whether significant coronary disease will be found.

It is important to emphasis the following points which make this new scoring system of value. First, scoring was developed on the basis of outcome research in order to reduce uncertainty reflected by wide variation in the utilisation of coronary angiography between different countries and different states in same country. Focussing on outcome increases the understanding of the effectiveness of a referral system for coronary angiography, which can be presented by a simple scoring system.

Second, the scoring system successfully predicted the severity of coronary artery disease, which is usually considered a principal determinant of the management of coronary artery disease- with significant benefits locally and. nationally.

Third, the scoring system is robust and capable of informing the management of patients with suspected coronary disease because it discriminated between patients who had significant coronary artery disease and those who did not; this is a considerable step forward in efforts to identify and eliminate inappropriate use of coronary angiography.

Fourth, the system has the ability to be updated to cover emerging issues and threshold scores can be modified according to the available funds.

Fifth, scoring is simple, flexible and includes a reasonable number of risk factors, which help predict the presence of coronary disease. It can be applied anywhere and at any time and be updated to take account of continuous improvement in the outcome of clinical research.

Sixth, it is easy to formulate both non-invasive clinical scoring system and the new angio-scoring system in the form of a computerised programme which makes the implantation of this system possible in both clinical and research settings.

Finally, the system addresses issues of overuse and under use in referring patients for coronary angiography and establishes the possibility of evaluating the clinical situation for patients with marginal scores that do not reach a predetermined threshold.

Weaknesses of the scoring system

Although the new scoring system appears to be successful, the number of patients in which the scoring system was devised and tested was small and testing on further patient populations is necessary to confirm its applicability and generalization. In addition, the scoring approach has certain limitations.

The system might have underestimated other factors which might be important in clinical practice but which did not seem (at least statistically) to be relevant in the various models developed. The scoring system does not seem particularly relevant to patients with previous coronary bypass surgery nor does it take into account the role of physician in the referral process.

Areas for improvement

The outcome of this research is so promising that it is reasonable to subject the non-invasive scoring system to testing on a much larger group of patients, at several centers within a single country, or preferably in a multi-center international study. It would be clinically useful to develop a means of allocating places on a revascularisation waiting list for patients who have achieved the threshold score which reflected the severity of coronary artery disease and the risk of sustaining a cardiac event as well as the likelihood of improving a patient's symptoms.

Some clinicians might argue that there should be some role for the physician to influence the scoring to indicate physician preference- for example, a patient limited by arthritis may warrant coronary angiography as a prelude to a total hip replacement operation and might precede a patient with simple chronic stable angina.

Within the constraints on health resources, this system would provide an ethical mechanism for balancing the interests of single patients and of society, or autonomy sacrificed to meet broader responsibilities toward society. The price paid by the physician is a loss of clinical autonomy; probably an outmoded concept in an era of evidence-based medicine but the benefit would be freeing the clinician from a role of queue management.

The benefits of adopting non-invasive clinical scoring system

Reduced variation

There is wide variation in the use of coronary angiography between different countries and even among different areas of the same country. This can be explained by the lack of clinical trial data that generally inform and guide clinical practice. Application of this scoring system would go a long way to standardising the selection process and would inevitably reduce the extent of variation.

Equity and improved use of scarce resources

The primary objective of health care policy is "to facilitate reasonable access to health services without financial or other barriers." Many clinicians consider it unethical to have economic considerations forced on them, as is the case today in both primary and secondary care. Even so, most would agree that it is important to mobilise resources for the good of the individual patient according to individual need. Difficulties arise when clinicians are forced to choose one patient over another, or one procedure over another, or one condition over another. Scoring guarantees equity.

Reduced queuing and waiting times and death on a waiting list

Queuing is a form of rationing but increases the risk of death on a waiting list. For those with coronary heart disease, the process of queuing for coronary angiography is accompanied by a risk of increased (and avoidable) cardiovascular mortality and morbidity, irrespective of any impact on a patient's symptomatology or quality of life. Other undesirable consequences of queuing are the mentally debilitating effects of persistent and irreducible symptoms, increasing anxiety while awaiting the procedure and the largely hidden or ignored social and economic costs for the individual patient and family members. Scoring will ensure that queuing is kept to a minimum and is based on genuine demand and need.

Prolonged waiting time for a procedure is common in the NHS. Acute cardiac events such as acute myocardial infarction, unstable angina, and even death may occur on the waiting list- generally, the longer the wait, the greater the number of events. Patients at high risk of an acute cardiac event ought to be referred for coronary angiography and revascularisation procedures with a minimum of delay.

Less implicit and more explicit decision-making

The adoption of clear principles for selecting patients for coronary angiography will improve patient and physician confidence that appropriate patients are being investigated. The need for rationing will be reduced as the decision-making process is seen to be more transparent.

Improved prioritization

The decision of a single clinician may no longer be entrusted to take clinical decisions on health spending when there is immense diversity of competition for health care expenditure. A health care system is at its most effective when those in greatest need receive an acknowledgement of that need through prioritisation for treatment. The essential prerequisite is to restrict access to coronary angiography without adversely affecting the quality of health care. This would ensure that patients have access to coronary angiography according to their medical need and probability of having significant coronary artery disease. All medically deserving patients would then be allocated a place in a much shorter queue according to each patient's risk of having severe coronary artery disease. Adopting a scoring system would improve prioritisation because scores can be ranked to establish a position on a waiting list-those patients with a high probability of having significant coronary artery disease would be accorded a higher ranking than those with a low probability. At some (predetermined) threshold score, angiography would not be offered but a strategy of 'watch and wait and treat medically' would be recommended, which must be better than the current imperfect rule of "first come, first served".

Prioritisation does give some flexibility because coronary angiography is not ruled out completely- if a patient's clinical situation changes, so will the score (and hence priority) change over time.

What remains to be done?

It is unlikely that any clinical evaluation of a routine procedure like coronary angiography could be conducted today as it is exceedingly difficult to reduce or withdraw established services. Strategies which involve consensus or necessity criteria or which assess clinical urgency as the basis for improving patient selection for potentially hazardous procedures like coronary angiography have not led to major changes in medical practice. Consequently, medical uncertainty (evident as clinical variation) regarding who should and who should not have angiography still exists. However, if a rational system that facilitated the decision-making process and focused on clinical outcome could be devised, medical decision-making might improve. Strategies that might improve the effectiveness of referral for coronary angiography could be presented by a simple scoring system. The scoring system proposed in this thesis has all the desired qualities to improve patient selection for coronary angiography- the potential to discriminate, within an acceptable margin, what constitutes under use and what overuse, of coronary angiography; reliable; robust; capable of being updated to take account of new trial data. It is worthy of further large-scale evaluation.

Publications

DP De Bono, I ELZoubi, B Ravilious, T Dyer, Y Podenovskaya:
A prioritisation system for elective coronary angiography. Heart 1998; 79: 448-453

APPENDICES

APPENDICES

Appendix 1

Severity of coronary artery disease in The New Zealand Project

(Hadron DC et al BMJ 1997).

DEGREE OF CORONARY ARTERY OBSTRUCTION (% DIAMETER OCCLUDED)	SCORE
No coronary artery disease (<50%)	0
1 Vessel disease (50-74%)	8
>1 Vessel disease (50-74%)	9
1 Vessel disease (75%)	9
1 Vessel disease (≥90%)	14
2 Vessel disease (50-89%)	15
2 Vessel disease (both ≥ 90%)	15
1 Vessel disease (≥90%) proximal left anterior descending artery	19
2 Vessel disease (≥90%) left anterior descending artery	19
2 Vessel disease (≥90%) proximal left anterior descending artery	19
3 Vessel disease disease	19
3 Vessel disease (≥90%) in at least one	19
3 Vessel disease (75%) proximal left anterior descending artery	19
3 Vessel disease (≥90%) proximal left anterior descending artery	27
Left main stem disease (50%)	27
Left main stem disease (75%)	32
Left main stem disease (≥90%)	36

Appendix 2

Weights for symptoms, social factors, and exercise test applied in The New Zealand Project

(Hadron DC et al BMJ 1997).

ANGINA CLASS	SCORES
Class I: angina on strenuous exertion	**1**
Class II: angina on walking or climbing stairs rabidly	**2**
Class III: angina on walking one or two blocks	**8**
Class IV A: unstable angina or rest pain	**18**
Class IV B: unstable angina in hospital on oral treatment	**22**
Class IV C: unstable angina in hospital on IV heparin or nitrate	**26**
EXERCISE TEST (BRUCE PROTOCOL)	
Negative	**0**
Mildly positive	**8**
Positive	**12**
Very positive	**22**
ABILITY TO WORK	
Not threatened but more difficult	**1**
Threatened but not immediately	**5**
Threatened immediately	**16**

Appendix 3

Appendix 3: (3A, 3B): The result of student's *t- test* showing the prediction of non-invasive (original version) for referral to intervention

(n=125).

Appendix 3a:

	Referred revascularisation	N	Mean	Std. Deviation
Angio-scores				
	.00	66	11.7121	9.29151.1437
	1.00	59	19.2203	5.0823.6617

Appendix 3b:

		Levene's Test for Equality of Variances		t-test for Equality of Means				
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference
Non-invasive score orginal version	Equal variances assumed	.182	.671	-2.3	123	.022	-4.32	1.86
	Equal variances not assumed			-2.3	122.3	.021	-4.32	1.85

Appendix 4

New angio-scores

(The outcome of sensitivity and specificity)

	Group A (n=169)		Group B (n=203)	
Positive if Greater Than or Equal To	Sensitivity	Specificity	Sensitivity	Specificity
6	1.000	0.41	1.00	0.33
12	1.000	0.44	0.98	0.42
15	0.95	0.50	0.93	0.47
18	0.76	0.65	0.79	0.47
21	0.60	0.76	0.62	0.65
24	0.51	0.81	0.57	0.71
27	0.43	0.87	0.45	0.78
30	0.24	0.88	0.38	0.85
33	0.16	0.88	0.31	0.87
36	0.07	0.93	0.17	0.91
39	0.03	0.97	0.05	0.97
42	0.011	1.00	0.03	0.98
45	0.00	1.00	0.01	0.98
48	0.00	1.00	0.00	1.00

The result of sensitivity and specificity of deferent new angio-scores to identify referral for intervention A: group of 169 consecutive patients B: group of 203 consecutive patients (Chapter 7).

Appendix 5

Detailed explanation of clinical scenario as adapted from RAND appropriateness methodology

Chapter: Stable angina

Anti angina medication

Exercise test result

	Inappropriate			Uncertain			Appropriate			
Panelists	3	1	1	1	1		1	1		
Rates	1	2	3	4	5	6	7	8	9	(2)*
		3						D		
	Median of rates						Agreement Status A: agreement D: disagreement I: indeterminate			

Explanation:

5 members of the panel rated this scenario as inappropriate (rating score 1, 2, and 3 was given by 3, 1, and 1 members of the panel respectively). Two members rated this scenario as uncertain indication; one of them gave a score 4 and the other gave a score 5. The other two members of the panel considered it appropriate and they gave it scores 7 and 8.

Median of rates was score of 3 and this fell within the range of (1-3) thus considered inappropriate.

According to relaxed definition of agreement between panelists, all of rates after excluding two extreme rates thus score 1 and scores 8 were excluded and the rest of rates not included in one main rates appropriate, uncertain, or inappropriate) as a result this was considered as disagreement about rating this clinical scenario (D: disagreement)

(2): This is the series number of scenarios in the original appropriateness system*

APPENDIX 6

Theoretical clinical scenarios allocated to 372 consecutive patients

(Adapted from Nottingham appropriateness report)

III Coronary angiography indicated in patients with stable angina:

A-----

B Patients who are any age, without strong contraindication to CABG, have angina on mild exertion (class III, IV), and have received:

1:No or less than maximal medical management and

a: No exercise ECG and no stress imaging study 3 1 1 1 1   1 1

1 2 3 4 5 6 7 8 9 (2)

(3.0, 2.1, D)

b---

c: Negative exercise test and:

No or negative stress imaging study 4 3   1   1

1 2 3 4 5 6 7 8 9 (5)

(2.0, 1.6, I)

d: Positive exercise ECG and:

No or negative stress imaging study 3   1 1 1   2   1

1 2 3 4 5 6 7 8 9 (7)

(4.0, 2.4, D)

e: Very positive exercise ECG and

No or negative stress imaging study 2   1   1 3 2

1 2 3 4 5 6 7 8 9 (10)

(8.0, 2.2, D)

2- Maximal medical management and:

a: No exercise ECG and no stress imaging study 2   1   1 1 3   1

1 2 3 4 5 6 7 8 9 (13)

(6.0, 2.2, D)

b---

c: Negative exercise test and:

No or negative stress imaging study 3   1 2   1   1

1 2 3 4 5 6 7 8 9 (17)

(3.5, 2.0, I)

d: Positive exercise ECG and:

No stress imaging study 1   1   1 1 2 3

1 2 3 4 5 6 7 8 9 (20)

(8.0, 2.0, D)

e: Very positive exercise ECG and

No stress imaging study 1 1 1 5

1 2 3 4 5 6 7 8 9 (23)

(8.0, 2.2, D)

C: Patients who are under 65 years, without strong contraindication to CABG, have angina on moderate exertion (class I, II), and have received:

1:No or less than maximal medical management and

a: No exercise ECG and no stress imaging study

5 3 1

Ejection fraction not known 1 2 3 4 5 6 7 8 9 (26)

(1.0, 0.7,)

b---

c: No or negative exercise test and:

Ejection fraction not known and 5 1 2 1

No or negative stress imaging study 1 2 3 4 5 6 7 8 9 (30)

(1.0, 1.0,)

d: Positive exercise ECG and:

No stress imaging study and 5 1 1 1 1

Ejection fraction not known. 1 2 3 4 5 6 7 8 9 (46)

(1.0, 1.6, I)

e: Very positive exercise ECG and

No stress imaging study 1 1 1 1 3 1 1

1 2 3 4 5 6 7 8 9 (58)

(7.0, 1.8, D)

2- Maximal medical management and:

a: No exercise ECG and no stress imaging study

2 2 1 1 1 2

Ejection fraction not known 1 2 3 4 5 6 7 8 9 (61)

(5.0, 2.6, D)

b---Indeterminate ECG and

No stress imaging study and 1 1 1 1 1 1 2

Ejection fraction not known 1 2 3 4 5 6 7 8 9 (65)

(5.5, 2.3, D)

d: Positive exercise ECG and:

No stress imaging study 1 1 2 3 2

Ejection fraction not known 1 2 3 4 5 6 7 8 9 (89)

(7.0, 2.0, D)

e: Very positive exercise ECG and

No stress imaging study 1 1 1 2 4

1 2 3 4 5 6 7 8 9 (101)

(8.0, 1.1, I)

D.........

E: Patients who are 65 years or older, without strong contraindication to CABG, have angina on moderate exertion (class I, II), and have received:

1: No or less than maximal medical management and

a: No exercise ECG and no stress imaging study

5 3 1

Ejection fraction not known 1 2 3 4 5 6 7 8 9 (139)

(1.0, 0.7,)

b---

c .....

d: Positive exercise ECG and:

No stress imaging study and 5 1 1 1 1

Ejection fraction not known. 1 2 3 4 5 6 7 8 9 (159)

(1.0, 1.4, I)

e: Very positive exercise ECG and

No stress imaging study 2 2 1 1 3

1 2 3 4 5 6 7 8 9 (171)

(4.0, 2.6, D)

2- Maximal medical management and:

a: No exercise ECG and

No stress imaging study 2 1 1 1 1 1 2

Ejection fraction not known 1 2 3 4 5 6 7 8 9 (174)

(4.0, 2.4, D)

b :Indeterminate ECG and

No stress imaging study and

Ejection fraction not known (178)

1	2	3	4	5	6	7	8	9
2	1	1	1	1	1		1	1

(4.0, 2.3, D)

C.....

d: Positive exercise ECG and:

No stress imaging study

Ejection fraction not known (202)

1	2	3	4	5	6	7	8	9
1	1	2		1	2			2

(5.0, 2.3, D)

e: Very positive exercise ECG and

No stress imaging study (214)

1	2	3	4	5	6	7	8	9
			1	2		1	3	2

(8.0, 1.4, I)

V . Coronary angiography indicated in patients who were hospitalised in the prior 3 months for unstable angina.

A........

B. Who are under 65 years, without strong contraindication to CABG, whose angina responded to inpatients medical management during the period admission and,

1.Angina subsequently recurs during mild exertion (class III, IV) on:

a : No or less than maximal outpatient medical management. (2)

1	2	3	4	5	6	7	8	9
1		1		3		2		2

(5.0, 2.0, D)

b: Maximal outpatient medical management (3)

1	2	3	4	5	6	7	8	9
1								8

(9.0, .9,)

2. Angina subsequently recurs during mild exertion (class III, IV) on:

a: No or less than maximal outpatient medical management. (4)

1	2	3	4	5	6	7	8	9
1	1	2			2	1	1	1

(6.0, 2.3, D)

b: Maximal outpatient medical management (5)

1	2	3	4	5	6	7	8	9
1			1			2	2	3

(8.0, 1.8, I)

C. Who are 65 years or older, without strong contraindication to CABG, whose angina responded to inpatients medical management during the period admission and,

1.Angina subsequently recurs during mild exertion (class III, IV) on:

a: No or less than maximal outpatient medical management. (16)

1		2		4	1			1
1	2	3	4	5	6	7	8	9

(5.0, 1.4, I)

b: Maximal outpatient medical management (17)

							4	5
1	2	3	4	5	6	7	8	9

(9.0, 0.4,)

2. Angina subsequently recurs during mild exertion (class III, IV) on:

a: No or less than maximal outpatient medical management (18)

3	1	1	1	1		1		1
1	2	3	4	5	6	7	8	9

(3.0, 2.2, D)

b: Maximal outpatient medical management (19)

1			1		2	2	1	2
1	2	3	4	5	6	7	8	9

(7.0, 1.8, I)

VII. Coronary angiography indicated in patients within 6 months of an acute MI:

A........

B........

C: Patients without strong contraindication to CABG, who had a Q wave infarct with congestive heart failure and

1.Post MI angina occurs with mild exertion (class III, IV) on:

a: No or less than maximal outpatient medical management. (31)

1		1		2	2	2	1	
1	2	3	4	5	6	7	8	9

(6.0, 1.6, D)

b: Maximal outpatient medical Management (32)

						1	2	6
1	2	3	4	5	6	7	8	9

(9.0, 0.4,)

2. Post MI angina occurs with moderate exertion (class I, II) on:

a: No or less than maximal outpatient medical management. (33)

2		1	1	2		3		
1	2	3	4	5	6	7	8	9

(5.0, 1.9, D)

b: Maximal outpatient medical 1 1 1 4 2

management 1 2 3 4 5 6 7 8 9 (34)

(8.0, 1.6, I)

D. Patients without strong contraindication to CABG, who had a Q wave infarct without congestive heart failure and

1.Post MI angina occurs with mild exertion (class III, IV) on:

a: No or less than maximal 1 1 2 4 1

Outpatient medical management 1 2 3 4 5 6 7 8 9 (48)

(7.0, 1.7, D)

b: Maximal medical management 2 7

1 2 3 4 5 6 7 8 9 (49)

(9.0, 0.2,)

2. Post MI angina occurs with moderate exertion (class I, II) on:

a: No or less than maximal outpatient 2 1 2 2 2

medical management 1 2 3 4 5 6 7 8 9 (50)

(5.0, 1.9, D)

b: Maximal medical management 1 1 1 3 3

1 2 3 4 5 6 7 8 9 (5)

(8.0, 1.6, I)

IX. Coronary angiography indicated in patients following CABG:

A.....

B: Patients without strong contraindication to CABG, and angina occurred following CABG with mild exertion (class III, IV) on :

1 : No or less than maximal outpatient 3 1 2 1 2

medical management 1 2 3 4 5 6 7 8 9 (2)

(6.0, 2.7, D)

2 :Maximal medical management 3 6

1 2 3 4 5 6 7 8 9 (3)

(9.0, 0.3,)

C :Patients without strong contraindication to CABG ,and angina occurs following CABG with moderate exertion (class III, IV) on :

1 : No or less than maximal outpatient 3 1 1 2 1 1

medical management 1 2 3 4 5 6 7 8 9 (4)

(3.0, 2.3, D)

2 :Maximal medical management	1 1 2 2 3 1 2 3 4 5 6 7 8 9 (5) (7.0, 1.9, I)

APPENDIX 7

Theoretical indication allocated to 372 consecutive patients (Adapted from RAND appropriateness system)

CHAPTER 1 : A symptomatic :

Note all patients were considered high risk occupation because this factor was not included in our study thus only two theoretical indications for a symptomatic patient were used:

1) Very positive exercise stress test :

d : No stress imaging study — 1 2 2 4 / 1 2 3 4 5 6 7 8 9 (16) / (8.0, 0.9, A)

2) Positive exercise stress test :

d : No stress imaging study and silent ischaemia — 1 2 3 3 / 1 2 3 4 5 6 7 8 9 (46) / (8.0, 0.9, A)

CHAPTER 4: hospitalised in the prior three months with unstable angina, whose angina responded to inpatient medical management during the prior admission and:

1.Angina subsequently recurs during mild exertion (class III,IV)

a : On maximal medical therapy ,

and age ≥75 year — 1 1 2 2 2 / 1 2 3 4 5 6 7 8 9 (1) / (7.5, 1.1, A)

and age <75 year — 1 7 / 1 2 3 4 5 6 7 8 9 (2) / (9.0, 0.1, A)

b : On less than maximal medical therapy ,

and age ≥75 year — 1 2 1 1 2 2 / 1 2 3 4 5 6 7 8 9 (3) / (7.0, 1.7, I)

and age <75 year — 1 3 5 / 1 2 3 4 5 6 7 8 9 (4) / (9.0, 0.7, A)

2.Angina subsequently recurs during moderate exertion (class I,II)

a : On maximal medical therapy ,

and age ≥75 year 1 1 2 4 1

1 2 3 4 5 6 7 8 9 (5)

(7.0, 0.8, I)

and age <75 year 3 5

1 2 3 4 5 6 7 8 9 (6)

(9.0, 0.4, A)

b : On less than maximal medical therapy ,

and age ≥75 year 1 2 1 4 1

1 2 3 4 5 6 7 8 9 (7)

(7.0, 1.6, I)

and age <75 year 1 1 3 4

1 2 3 4 5 6 7 8 9 (8)

(8.0, 0.8, A)

CHAPTER 3 : Chronic stable angina:

A. Angina on mild exertion (class III,IV) and received:

1) No or less than maximal medical therapy and

a)Very positive exercise test and no stress imaging study

2 1 1 3 1 1

and age ≥75 year 1 2 3 4 5 6 7 8 9 (7)

(7.0, 1.6, I)

2 2 2 3

and age <75 year 1 2 3 4 5 6 7 8 9 (8)

(8.0, 1.2, A)

b) Positive exercise test and no stress imaging study

1 3 1 3 1

and age ≥75 year 1 2 3 4 5 6 7 8 9 (15)

(5.0, 2.1, D)

3 1 1 4

and age <75 year 1 2 3 4 5 6 7 8 9 (16)

(8.0, 1.7, I)

c) Indeterminate exercise test and no stress imaging study and age ≥75 year

```
22   2 2 1
123456789   (23)
(5.0, 2.4, D)
```

and age <75 year

```
 111  2  22
123456789   (24)
(6.0, 2.1, I)
```

d) Negative exercise test and no stress imaging study

age ≥75 year

```
  4  1  211
123456789   (31)
(5.0, 2.4, D)
```

and age <75 year

```
2  1  12111
123456789   (32)
(6.0, 2.2, D)
```

2) Maximal medical therapy and

a) Very positive exercise test and no stress imaging study,

and age ≥75 year

```
    122211
123456789   (47)
(6.0, 1.2, I)
```

and age <75 year

```
1     17
123456789   (48)
(9.0, 0.8, A)
```

b) Positive exercise test and no stress imaging study

age ≥75 year

```
    122211
123456789   (55)
(6.0, 1.2, I)
```

age <75 year

```
    1   26
123456789   (56)
(9.0, 0.7, A)
```

c) Indeterminate exercise test and no stress imaging study

1 2 4 1 1

and age ≥75 year 1 2 3 4 5 6 7 8 9 (63)

(5.0, 1.3, I)

1 1 1 2 4

and, age <75 year 1 2 3 4 5 6 7 8 9 (64)

(7.0, 1.6, I)

d) No exercise test and no stress imaging study,

2 2 2 1 1 1

and age ≥75 year 1 2 3 4 5 6 7 8 9 (79)

(5.0, 2.6, D)

1 1 2 2 3

age <75 year 1 2 3 4 5 6 7 8 9 (80)

(8.0, 2.2, I)

B. Under age 75 ,with angina on moderate exertion (class I,II) and have received:

1) No or less than maximal medical therapy and

a) Very positive exercise test and no stress imaging study

2 1 6

unknown ejection fraction 1 2 3 4 5 6 7 8 9 (93)

(9.0, 0.6, A)

b) positive exercise test and no stress imaging study

2 2 2 3

unknown ejection fraction 1 2 3 4 5 6 7 8 9 (109)

(8.0, 1.2, A)

c) Indeterminate exercise test and no stress imaging study

1 2 1 2 1 2

Unknown ejection fraction 1 2 3 4 5 6 7 8 9 (133)

(7.0, 2.2, D)

d.) ....

e) No exercise test and no stress imaging study

	1 2 2 1 2 1	
unknown ejection fraction	1 2 3 4 5 6 7 8 9	(189)
	(6.0, 2.3, D)	

2) Maximal medical therapy and

a) Very positive exercise test and no stress imaging study

	9	
unknown ejection fraction	1 2 3 4 5 6 7 8 9	(209)
	(9.0, 0.0, A)	

b) Positive exercise test and no stress imaging study

	1 1 1 6	
unknown ejection fraction	1 2 3 4 5 6 7 8 9	(225)
	(9.0, 0.7, A)	

c) Indeterminate exercise test and no stress imaging study

	1 1 1 4 2	
unknown ejection fraction	1 2 3 4 5 6 7 8 9	(249)
	(8.0, 0.9, A)	

d.....

e. No exercise test and no stress imaging study

	1 1 2 4 1	
unknown ejection fraction	1 2 3 4 5 6 7 8 9	(305)
	(8.0, 1.8, A)	

C. Age over 75 ,with angina on moderate exertion (class I,III) and have received:

1) No or less than maximal medical therapy and

a) Very positive exercise test and no stress imaging study

	1 2 3 1 2	
unknown ejection fraction	1 2 3 4 5 6 7 8 9	(325)
	(7.0, 1.0, I)	

b) Very positive exercise test and no stress imaging study

	1 1 4 1 1 1	
unknown ejection fraction	1 2 3 4 5 6 7 8 9	(341)
	(6.0, 1.0, I)	

c.......

e) Negative exercise test and no stress imaging study		
	1 1 2 2 2 1	
unknown ejection fraction	1 2 3 4 5 6 7 8 9	(393)
	(6.0, 2.2, D)	
2)Maximal medical therapy (no patients)		

Appendix 8

Power of sample sizes

(Adapted from Anthony D 1999. Understanding advanced statistics; a guide for nurses and health care researchers)

a) Power table for the x² test (one degree of freedom) with sample size (n) for deferent effect of sizes (w) at an ∝ level of 0.01, and with one degree of freedom

					W				
N	**0.10**	**0.20**	**0.30**	**0.40**	**0.50**	**0.60**	**0.70**	**0.80**	**1.00**
25	0.01	0.02	0.03	0.05	0.09	0.16	0.27	0.41	0.57
50	0.01	0.02	0.06	0.13	0.27	0.48	0.70	0.87	0.96
100	0.02	0.05	0.16	0.41	0.72	0.92	0.99		
200	0.02	0.13	0.48	0.87	0.99				
500	0.07	0.56	0.98						

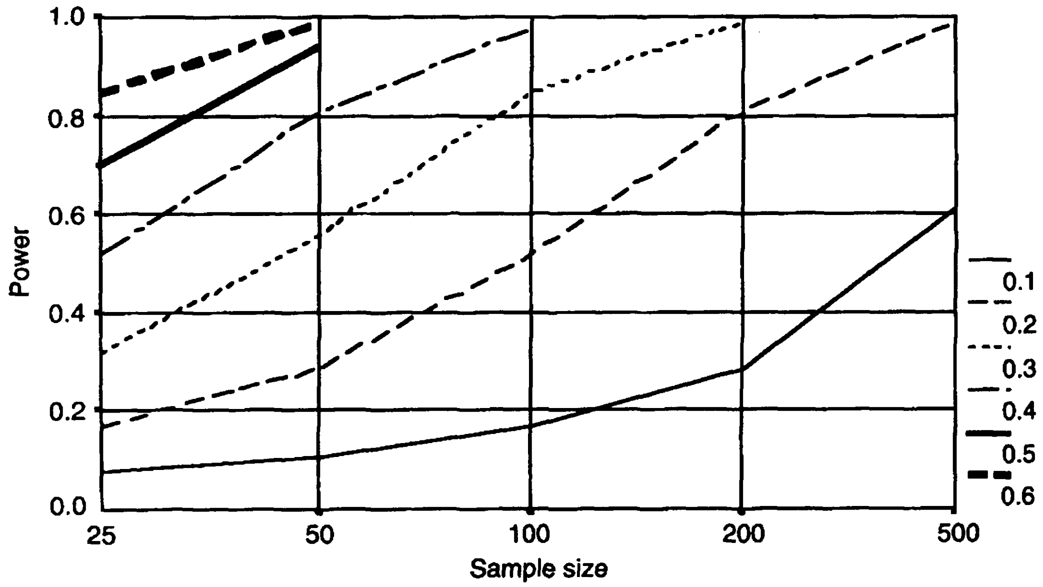
b) Power table for the x² test (one degree of freedom) with sample size(n) for deferent effect of sizes (w) at an ∝ level of 0.05

					W				
n	0.10	0.20	0.30	0.40	0.50	0.60	0.70	0.80	1.00
25	0.08	0.17	0.32	0.52	0.70	0.85	0.94	0.98	0.99
50	0.11	029	0.56	0.81	0.94	0.99			
100	0.17	052	0.85	0.98					
200	0.29	081	0.99						
250	0.35	089							

Appendix 9

Power of sample sizes

(Adapted from Anthony D 1999. Understanding advanced statistics; a guide for nurses and health care researchers)



Chi square: Power for various effect magnitudes and sample sizes, using an alpha value of 0.05 and one degree of freedom.

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