Ischaemic Heart Disease Risk Scores and their Applications: A Systematic Review

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Received date: Jan 21, 2017; Accepted date: Feb 10, 2017; Published date: Feb 15, 2017

Introduction

Numerous diagnostic strategies can be used on patients suspected of suffering from coronary artery disease (CAD), also referred to as ischaemic heart disease (IHD) [1]. Coronary angiography is currently still considered as the gold standard for diagnosing arterial plaques causing obstructive IHD, yet coronary angiography is invasive and costly, and may still not be able to demonstrate non-atheromatous CAD, which, although rare, may still occur in the younger age group [2]. Since the overall risk of IHD is made up of a number of multiple risk factors several risk assessment tools may be used to try and estimate the risk of this pathology within the different age groups [1].

Methods

Evidence acquisition

PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [3,4] aided the performance of this systematic review. A search of titles and abstracts was initially conducted on PubMed, Science Direct, Google Scholar, CINAHL and Cochrane databases to identify the articles that fitted the inclusion criteria. The following search terms were used: cardiac risk (+/- prediction) model, cardiac risk (+/- prediction) factor and cardiac risk (+/- prediction) index in combination with the term ischaemic heart disease were cross-searched using the following algorithm: cardiac risk (+/- prediction) model AND ischaemic heart disease; cardiac risk (+/- prediction) factor AND ischaemic heart disease; cardiac risk (+/- prediction) factor AND ischaemic heart disease; ischaemic heart disease AND cardiac risk (+/- prediction) index. An additional search term, Ischaemic heart disease and risk scores, was used for Science Direct database, to cover more potential search probabilities for this site which had overall a higher number of ‘hits’. After duplicates were removed, the titles and abstracts of the search results were screened by one of the authors to determine their eligibility (Figure 1 Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow chart (February 2017)).

Exclusion criteria

Commentaries or editorials; and articles that reported only abstracts, pilot data or descriptions of the design of a study were excluded from this systematic review due to the lack of detailed information on the tool used and results obtained.

Articles that discussed cardiac risk factors but did not involve a risk score prediction model were also excluded since the aim of this review was to compare and discuss cardiac risk score models.

Literature that involved cardiac pathologies other than ischaemic heart disease was excluded as this was beyond the scope of this article.

Results

Evidence synthesis

A summary table (Table 1) of the search conducted for each database was prepared. The abstracted studies that met the inclusion and exclusion criteria were then evaluated and discussed. As shown in Figure 1, after conducting an initial search with the terms indicated in...
Table 1, for all databases listed, 240 studies were found. Filters were applied to remove commentaries or editorials, or studies that included only the abstract, with no indication of the type of methodology followed. Duplicated articles were also removed, leaving a total of 224 articles that required further screening for eligibility. Additional filtering (Figure 1) resulted in a total of 43 studies that focused on cardiac risk scoring models used for the assessment of IHD.

<table>
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<th>Date of search</th>
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Table 1: Results of databases search conducted (original, July 2016).

Publication bias
As in all systematic reviews the authors’ own background knowledge does create a risk of bias that may hinder the interpretation of studies being discussed. In order to reduce this bias the research for this study and write up were carried out separately by one of the authors whilst the evaluation and correction of the research paper were performed individually by the other two authors. Corrections were then made to the article based on the comments and suggestions of the reviewing authors.

Discussion
Ischaemic heart disease has been indicated by several authors as being a major cause of premature death in both developed and developing countries [5,6]. This pathology may easily have its onset in early childhood with the various risk factors indicated in literature,
such as an unhealthy diet and lack of physical activity, leading to its clinical manifestation in adulthood [6]. The major risk factors, such as cigarette smoking, have been linked qualitatively with IHD episodes in a diverse set of populations, yet quantitatively the magnitudes of each risk factor and the estimation of absolute risk may vary between different ethnic groups. This indicates clearly the need for risk scoring systems (Table 2: A summary of the identified risk scores) that are more population based, to improve their prognostic ability [7]. Furthermore the use of aggressive preventive treatment and coronary interventions is only justified if the patient's absolute risk of IHD surpasses a known cut-off point [7].

<table>
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<tr>
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<th>Risk Scores</th>
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<td>Dripps Index by ASA</td>
<td>Vernick and Fleisher,</td>
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<td>Goldman Risk Score</td>
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<td>Revised Cardiac Risk Index or Lee Index</td>
<td>Gilbert et al.,</td>
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<td>Muñoz et al.,</td>
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<td>Patients with chest pain, presenting at a casualty department</td>
<td>HEART score</td>
<td>Backus et al.,</td>
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<td>HEARTS3 score</td>
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<td>The Framingham score</td>
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<td>Systematic COronary Risk Evaluation (SCORE) score</td>
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<td>Coronary artery calcium (CAC) score</td>
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<td>QRISK2 score, an updated version of the QRISK score</td>
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New Risk Stratification score (NERS) Palmerini et al.,
Clinical SYNTAX score (CSS) Wang et al.,
STS-PROM Ad et al.,
EuroSCORE II Farrokhyar et al.,
Ambler score Sullivan et al.,
Providence score Siontis et al.,
Veterans Administration score
ASSIGN score
Prospective cardiovascular munster (PROCAM) score
Reynolds risk score

| Patients undergoing stress testing, as part of a diagnostic procedure | Hubbard-Ho score Kwok et al.,
Morise score Lai et al.,
The Duke’s score Morise and Jalisi,
Pretest and exercise ECG scores |

Table 2: A summary of the identified risk scores (original, October 2016).

The use of risk scores in ischaemic patients about to undergo major surgery

Risk scoring systems such as those proposed by the American Society of Anaesthesia (ASA), Goldman et al., Detsky et al., Eagle et al. and Lee et al. [8], all use multivariate analysis to identify preoperative clinical factors that may predict cardiac morbidity and mortality in patients about to undergo major surgery. The Dripps Index published in 1961 by ASA was the original risk assessment system used for preoperative assessments, but as such it has not been found through research to be predictive of cardiac complications [8]. The Goldman Risk Score [9] studied a cohort of 1001 patients for the presence or absence of over 50 different cardiac risk factors for each patient. This risk score though having been well constructed offered a statistically weak model as it provided just over six risk factors per complication, and studied a large number of risk factors that were dependent on each other in some cases. Lee et al. published the Revised Cardiac Risk Index or Lee Index, which is the most widely used. It assigns a point each for the presence of 6 independent risk factors for major cardiac complications in patients undergoing major surgery [10]. The Lee Index is more robust than the Goldman Cardiac Risk Score as initial studies involved a larger cohort of patients with a larger incidence of cardiac events per associated risk [10]. The Lee Index also takes a broader approach to the definition of cardiac risk factors, although it may still require to be further updated to improve its predictive accuracy [11].

The Goldman, Detsky and Lee cardiac indices were compared for sensitivity, specificity and predictive values, in a sample of 88 cardiac patients. Results of this analytical study indicated that the sensitivity values for the Goldman, Detsky and Lee indices were of 75%, 73.2% and 44.6% respectively while the specificity values were of 84.3% for the Goldman cardiac risk score and 71.8% for the Detsky index in comparison to 93.7% for the Lee score. The Lee index also showed a higher positive predictive value overall (92.5% when compared to 89.3% for the Goldman score and 82% for the Detsky index) [12]. The authors in this case suggested using all three predictive scores in order to optimize risk stratification in patients about to undergo major non-cardiac surgery.

The use of risk scores in ischaemic patients presenting at an Accident and Emergency department

Risk models may also be used to triage patients with chest pain, with the intention to predict acute coronary syndromes (ACS) in patients presenting at the Accident and Emergency department. Such models include the History, Electrocardiogram (ECG), Age, Risk Factors and Troponin (HEART) score developed by Six et al. [13]. The Troponin (HEART) model uses a score from 0 to 10 for predicting ACS. This score may provide the clinician with a fast and reliable way of assessing the emergency patient [14]. Limitations of the HEART score system [15], include the exclusion of gender as a risk factor of IHD and also the lack of appropriate weighting given in this scoring system to certain criteria, such as the presence of ischaemic changes seen on the initial ECG, hence the development of the more complex HEARTS3 score [15].

The Sanchis score and the Vancouver rule were also devised to assess the risk of IHD in casualty patients presenting with chest pain, yet even if these risk stratification systems did show a correlation between the risk of ACS and adverse outcomes, none of them gained widespread acceptance in clinical practice [15]. The Framingham score, developed in a large population cohort to predict the 5 and 10 year risk of developing IHD, is the basis of most of the risk scores in this category [6,15,16]. Asymptomatic patients should be screened in order to identify intermediate or high-risk cardiac patients, aiding to
The Framingham score and also the systematic coronary risk evaluation (SCORE) serve this purpose, but new biomarkers and imaging methods have emerged within the past years (high-sensitivity C-reactive protein (CRP), lipoprotein associated phospholipase A2 and secretory phospholipase A2, coronary artery calcium (CAC) score, carotid intima-media thickness and ankle-brachial index) which can add further value to a patient risk assessment [6].

According to a cohort study by Kavoussi et al. [16], the Framingham risk score (FRS) is, 'the most commonly used CHD risk prediction instrument in clinical setting and constitutes the basis for the Adult Treatment Panel III guidelines for cholesterol lowering therapy' The Framingham risk score was used to evaluate the importance of considering newer risk factors that may be indicative of IHD, such as: levels of N-terminal fragment of prohormone B-type natriuretic peptide (NT-proBNP), von Willebrand factor antigen levels, fibrinogen levels, chronic kidney disease (CKD), leucocyte count, CRP levels, homocysteine levels, uric acid levels CAC scores, carotid intima-media thickness (cIMT), peripheral arterial disease and pulse wave velocity [16]. The participants included 5933 asymptomatic participants, with a mean age of 69.1 years. Individuals with a known history of myocardial infarction (MI), coronary artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA) were not included in this research. A limitation of this study was its lack of applicability to a younger cohort of patients, reducing its potential to be used in diverse ethnic cultures. Out of all the newer risk factors that were studied, the coronary artery calcium (CAC) score appeared to be a good predictor of IHD. This result was confirmed in several other studies [17-19].

It can be argued that the variation of certain risk factors with age, such as NT-proBNP, may be a better predictor of coronary disease in older populations than the use of calcium scoring [16]. The calculation of coronary calcium scoring is recommended in the ACCF/AHA (American College of Cardiology Foundation/American Heart Association) guidelines 2010, and also by the European guidelines, as being useful for risk assessment in adults with intermediate-risk (class IIa) [20]. Another important clinical marker that may be considered is ultrasonographic C-reactive protein (uCRP). Baseline uCRP and low-density lipoprotein cholesterol (LDLc) were seen to be indicative of the presence of cardiovascular events in the ASCOT (Anglo-Scandinavian Cardiac Outcomes Trial) even if the inclusion of uCRP to the Framingham risk prediction model did not improve the results of this score [5].

Moreover the value of the ankle brachial index (ABI) was assessed together with the Framingham risk prediction model in a meta-analysis study [21]. It was concluded that the measurement of this index may significantly improve the accuracy of predicting cardiovascular risk. The authors in this research acknowledged the fact that predicting future IHD episodes based solely on traditional risk factors and scoring systems may prove difficult. The Framingham risk prediction model was seen to give varying results when used across different ethnic groups in comparison to cohort specific risk models [7].

Different population groups were found to have varying cardiovascular risk estimates, indicating the need for population validated risk scores [22,23]. The European Society of Cardiology (ESC) developed a risk score to predict the 10 year risk of fatal cardiovascular disease, stratified by high or low risk regions, called SCORE [24]. The ESC guidelines on cardiovascular disease prevention in clinical practice recommend the use of this score for total risk estimation in asymptomatic adults without evidence of cardiovascular disease [25]. The revised SCORE takes into account high-risk patients including those with chronic kidney disease (glomerular filtration rate<60 mL/min/1.73 m²). It also offers a supplementary chart with risk adjustment based on the level of high-density lipoprotein cholesterol (HDLC), apart from other important concepts [25]. Collins et al. [26] discussed the use of the QRISK2 score, an updated version of the QRISK score within the UK (United Kingdom) population, indicating that this score has a good discrimination capability for estimating the 10-year risk of cardiovascular disease within this population. The performance of risk scores however may vary between high and low risk regions. The SCORE method was found to have a receiver operating curve area of 0.81 (95% CI 0.80-0.82) in high-risk regions and 0.74 (95% CI 0.72-0.76) in low-risk regions.

Literature also identifies numerous risk prediction models that may be used to predict mortality and recurrent episodes of myocardial infarction (MI) in patients with past episodes of myocardial ischaemia [27]. The in-hospital Global Registry of Acute Coronary Events (GRACE) risk model is one such model, offering the possibility to assess the mortality risk across a wide range of acute coronary syndromes. Similar scores comprise the Thrombolysis in Myocardial Infarction (TIMI) score and the Platelet Glycoprotein IIb/IIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) score [28]. Although the TIMI and GRACE scores have been used successfully on casualty department patients presenting with chest pain and having past episodes of myocardial ischaemia, these scores were specifically designed to predict the outcome in patients with diagnosed acute coronary syndrome of mortality and recurrent myocardial infarction [15].

In fact at the 2010 Congress of the European Society of Cardiology, investigators reported that the HEART score outperformed the GRACE and TIMI scores for the identification of a 6-week outcome of AMI, PCI and CABG and death in 2150 patients presenting with chest pain in 10 different hospitals during a 6 month period [15].

In contrast to this, in a meta-analysis of 40 derivation studies involving 216,552 patients and of 42 validation studies on 31,625 patients, the results indicated that TIMI and GRACE risk scores appear to be the only ones that have been validated in all types of ACS. For ACS the GRACE score derivation and validation AUC was of 0.83 and 0.82 respectively at short term patient follow up when compared to a TIMI score AUC of 0.66 in derivation studies and of 0.73 for validation cohorts, for the same follow up period [29]. In a more recent study based on 1748 patients the HEART score was seen to outperform the other risk scores with an AUC of 0.86, when compared to 0.73 of the GRACE score and 0.80 of the TIMI score. Moreover the HEART risk score with 98% sensitivity identified the highest amount (n=381) of ‘low risk’ patients [30].

The use of risk scores in ischaemic patients before or after coronary interventions

Other risk score models such as the Texas Heart Institute risk score [31], the Cleveland Clinic model by Ellis et al. [31], the Michigan model [32], together with the model put forward by Singh et al. [33], all try to identify patients at increased risk of morbidity and mortality after percutaneous coronary interventions (PCI) or cardiac surgery.
The AusScore was developed by Reid et al. [34], for an Australian Cohort of patients after the widely used EUROPEAN SYSTEM for cardiac operative risk evaluation (EuroSCORE) validated poorly in this population when used to predict outcomes following CABG. On the other hand the EuroSCORE appears to be the most widely used pre-operative risk prediction model in European cardiac surgery [35]. In Malta the EuroSCORE is the risk score used by cardiac surgeons in patients about to undergo PCI and CABG. Literature has shown pitfalls in this risk score [35] several authors describe a EuroSCORE mortality overestimation in low-risk patients and an underestimation of mortality in high-risk patients.

Other such scoring systems include the Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score, a semi quantitative angiographic score developed to prospectively assess patients undergoing coronary revascularisation by PCI or CABG; the Age, Creatinine and Ejection Fraction (ACEF) score [36] used to predict operative mortality in patients undergoing elective cardiac surgery; the New Risk Stratification score (NERS) and the Clinical SYNTAX score (CSS) [37-39]. All these risk scores were compared in the ACUITY trial [37], and results showed that the Clinical SYNTAX score was the most accurate for risk prediction of 1 year cardiac mortality following cardiac interventions.

The American Society of Thoracic Surgeons (STS) Predicted Risk of Mortality (PROM) is another standard risk prediction algorithm for patients undergoing coronary artery bypass grafting (CABG), isolated valve replacement, and CABG together with a valve replacement, and is based on the STS National Adult Cardiac Surgery Database, one of the largest specialty-specific clinical data registries in the world with periodic updates and revisions [40]. STS-PROM has clearly demonstrated good predictive ability when applied to patients with coronary artery disease [41,42]. Recent studies concerning valve surgery mortality have shown that STS-PROM out performs not only the EuroSCORE but also other cardiac risk prediction models, such as the Ambler score, Providence score, and Veterans Administration score, when applied to aortic valve replacement (AVR). The STS 2008 cardiac risk models performed well when predicting the mortality for Chinese patients who underwent valve surgery [40], even if this study validated only mortality, and 8 of the 9 other endpoints that the STS cardiac surgery risk models provide were not validated. Furthermore combined valve surgery and CABG accounted for approximately 3% of the study’s population, so this group could also not be accurately validated in this research. For the reasons mentioned, the true performance of the STS 2008 cardiac risk models in the Chinese population may have been biased [40].

In a recent study the uses of the new EuroScore (EuroSCORE II), the STS score and the ACEF score were discussed in a meta-analysis review [43]. The authors compared 22 articles published between 2012 and 2015 in which these risk scores were used. Results indicated that the EuroSCORE II and STS score performed similarly showing a summary difference in AUC equal to 0.00, but both outperformed the ACEF score with summary AUC differences of 0.10 and 0.08 respectively (p<0.05).

It was argued that in 82% of the reviewed articles limitations included a small or limited sample size, which may have influenced the results obtained with the various scores, limiting the differences between them. Only 3 of the reviewed articles contained more than 200 death events, and over half of the reviewed studies involved European patients.

It is important to outline that assigning patients to risk categories could affect the outcome of risk scores, with potential implication in the patient clinical management [43]. In a unique study [44], eight cardiovascular risk prediction models were compared through a systematic review. The eight risk scores included: two variants of the Framingham risk score, the assessing cardiovascular risk to Scottish Intercollegiate Guidelines Network to assign preventative treatment (ASSIGN) score, the SCORE, Prospective cardiovascular munster (PROCAM) score, QRESEARCH cardiovascular risk (QRISK1 and QRISK2) algorithms and Reynolds risk score. This study further indicated that risk prediction models may have different results in different populations and settings, obtaining statistical inconsistent differences across the studied risk models. Patient risk stratification may help to improve such inconsistencies.

The use of risk scores in ischaemic patients undergoing stress testing

The Hubbard-Ho and Morise scores, together with the Duke's score were developed to predict the risk of IHD in patients referred for or undergoing stress testing. Literature has investigated numerous times the diagnostic and prognostic value of exercise stress testing, with the Duke's treadmill score being even recommended by the American College of Cardiology/ American Heart Association (ACC/AHA) [45]. A study involving this score indicated that the Duke's treadmill score performs less well when using it to risk stratify patients above the age of 75 years. Age appeared to have a major impact on the utility of this score, probably because an older age group has a higher prevalence of severe IHD and poor exercise tolerance overall, although only a small number of elderly in the high risk subgroup were included [45].

The use of the Duke's treadmill score was further investigated in 1,872 patients equal to or above the age of 65 years, with a mean follow-up period of 6 years [46]. Results of this investigation revealed that on the contrary this score may be of aid in the diagnosis of CAD in the elderly. This study had limited survival analysis since patients who underwent cardiovascular procedures during follow-up were not accounted for as no such data was available. Also exercise treadmill data in the recovery period was not included in the overall results, which may have influenced the overall conclusions.

In another research it was further concluded that exercise ECG alone may be of significant use in the diagnosis and clinical management of the symptomatic patient suffering from IHD [47]. This research also collected patient risk factor data before the exercise ECG, and proceeded to risk stratify patients into low, intermediate and high risk subgroups depending on pre-test and exercise ECG scores assigned to patients. It is interesting to note that the pre-test and exercise ECG scores, taking in consideration the patient risk factors, risk-stratified patients better than the Duke treadmill score alone. The findings could also be extended to diabetics, inpatients, postmenopausal women and patients on beta-blockers. This further reinforces the idea that population based risk factors must be accounted for prior to the use of risk scoring systems.

It should also be remembered that risk models 'tend to lose their calibration and predictive ability when they are applied to geographically and temporally different populations' [31].

This would imply that ideally a tried and tested risk model is available for each population, in order to limit sources of errors. Estimated risk based on clinical characteristics alone is difficult and
imprecise, leaving the need for robust risk prediction models that can guide triage of patients and key management decisions [27]. ‘An ideal risk score system requires accuracy for the prediction of prognosis, and simplicity for an early therapeutic plan decision’ [27].

Limitations

With so many risk score models available within the literature it is difficult to discuss the merits and pitfalls of each risk score in relation to others within the same category. The authors of this review had to limit the debate to those risks scores that are more widely used in comparison to other less well known models.

Conclusion

The wide variety of available risk scoring prediction models present within the literature have the potential to impact upon imaging procedures and protocols by which patients with myocardial ischaemia are assessed. The presence of so many cardiac risk factors and different risk scoring tools can introduce confusion [43] amongst staff and referring clinicians regarding the applications of these risk scores, leading to variation and non-standardisation in the delivery of treatment and diagnostic pathways. Patient risk stratification prior to the use of risk scores may aid in this regards [47].

Conflict of Interest

The authors declare that there are no conflicts of interests.

Ethical Approval

Not required.

References


