A literature review of the cardiovascular risk-assessment tools: applicability among Asian population

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ABSTRACT

Background Cardiovascular diseases, the main causes of hospitalisations and death globally, have put an enormous economic burden on the healthcare system. Several risk factors are associated with the occurrence of cardiovascular events. At the heart of efficient prevention of cardiovascular disease is the concept of risk assessment. This paper aims to review the available cardiovascular risk-assessment tools and its applicability in predicting cardiovascular risk among Asian populations.
Methods A systematic search was performed using keywords as MeSH and Boolean terms.
Results A total of 25 risk-assessment tools were identified. Of these, only two risk-assessment tools (8%) were derived from an Asian population. These risk-assessment tools differ in various ways, including characteristics of the derivation sample, type of study, time frame of follow-up, end points, statistical analysis and risk factors included.
Conclusions Very few cardiovascular risk-assessment tools were developed in Asian populations. In order to accurately predict the cardiovascular risk of our population, there is a need to develop a risk-assessment tool based on local epidemiological data.

INTRODUCTION

One of the key public issues identified by the WHO was the rising trend in chronic disease globally with an estimated one-third of all deaths attributed to cardiovascular (CV) diseases. The burden of these CV diseases was particularly high, especially in middle- and high-income-group countries.[1] This high incidence of CV diseases normally incurred substantial financial consequences in terms of cost for managing the disease as well as loss of income as a result of CV disease.[2]

RISK ASSESSMENT

In order to halt this epidemic, there is an immediate need to deliver wellness-oriented healthcare whereby prevention of the occurrence of the first CV event is the priority. At the heart of efficient prevention lies the concept of risk-assessment to allow for matching of the intensity of risk interventions to baseline total CV risk.[3] A wealth of epidemiological research has demonstrated that a number of risk factors (RFs) were associated with significant increases in the risk of developing CV events. Within this context, one of the recent published studies (INTERHEART), which had included a significant number of Asian population in their cohort, reported that a total of nine RFs

accounted for more than 90% of the population attributable risk of myocardial infarction in almost 30 000 population.[4]

As a result of the multiplicative and clustering effect of RF, we cannot simply perform RF counting to assess population cardiovascular risk. Instead, there is a need to move towards a more comprehensive and multifactorial approach that focuses on the total risk of an individual.[5] This has led to the development of various risk-assessment tools with the objective of summarising the impact of various RFs into a single statement of absolute CV risk which can be used to guide management strategies.

Currently, there are over 100 CV risk-assessment tools being developed and used. These risk-assessment tools differ in more than one way, and there is still no reliable, comprehensive and universal CV risk-assessment tool for medical professionals to accurately predict CV risk in a given population. Due to the numerous ethnic groups with unique genetic characteristics among the Asian population, the weighting of the RFs used in existing CV risk-assessment tools may not be applicable to this population.[3]

It was reported that a risk-assessment tool can be used interchangeably between populations if three elements are similar between the populations. These are the nature and strength of association between each RF, risk of CV events, prevalence of RFs and incidence of CV events.[3 6]

At a glance, most clinical practice guidelines on primary prevention of CV disease have incorporated different risk-assessment tools for risk stratification. Thus, clinicians are faced with the uncertainties of the applicability and accuracy of these tools for the local population. The aim of this paper is to review the widely used CV risk-assessment tools and its applicability among the Asian population.

LITERATURE SEARCH

Studies were identified by a systematic search strategy. Literature searches were performed for English articles from 1995 to June 2008 using Pubmed, Scopus, Ebsco Host, Ovid, Springerlink and Science Direct. Furthermore, an internet search was also performed using the popular search engine, Google. The strategy used a series of terms to identify the topic of interest using the keywords search. Primary Medical Subject Headings and Boolean terms were used to combine keywords. This was supplemented by examining the reference lists of each of the studies identified. The corresponding author of each study was contacted to request relevant data which were not included in

the published report and also to obtain the full research paper. Reference lists of articles were searched to identify additional relevant reports, and key journals were hand-searched. The keywords used included the following: heart disease risk assessment, coronary disease risk assessment, cardiovascular disease risk assessment, cardiovascular risk assessment, coronary risk score, cardiovascular risk score, cardiovascular disease risk score, cardiovascular risk, coronary risk, risk equation, risk table, risk scoring method, and risk prediction and algorithms.

RESULTS

A total of 25 CV risk-assessment tools were identified from 41 articles. This list was not exhaustive but represented the more commonly used tools. At a glance, these algorithms were developed from different countries and included different variables. Even if the same RFs were included in the equations, they often differed in how they quantify the RF.

A summary of the currently reviewed risk-assessment tools and their characteristics is given in Appendix 1.

Sample

A review of the available risk-assessment tools showed that most of these tools were derived from American or European populations. There were very few tools (8%) that originated from an Asian population. Among these are the USA-PRC Collaborative Study of Cardiovascular and Cardiopulmonary Epidemiology cohort and the Japanese Nippon Data 80 cohort.[7][8]

The range of the sample size recruited for the derivation of these tools varied widely. It ranged from a few hundred to a few million. Most of the cohorts recruited both men and women.

The inclusion age range for most of the derivation cohort was 30–74 years old.

Type of study

Most of the risk-assessment tools were derived from longitudinal prospective cohort study. However, a few of the tools utilised data from an existing cohort, most commonly the Framingham Heart Study.

Time frame

The Framingham Risk Score was developed from a cohort which was enrolled in 1948.[9] Since then, other risk-assessment tools have been developed, and the most recent tool being developed was the risk score using the QRESEARCH Database which completed their follow-up in 2007.[10] Most of the derivation cohorts were followed through from 5 to 15 years, except the original and offspring Framingham cohort which were still ongoing from its inception.[9][11]

End points

Most of the risk-assessment tools adopted general CV disease or CHD risk as their end points. Framingham Heart Study defined CV disease as a composite of CHD, cerebrovascular events, peripheral artery disease and heart failure.[12]

Other end points included fatal CV disease risk, risk of acute coronary event (defined as fatal and non-fatal myocardial infarction and coronary death) and risk of ischaemic cardiovascular disease (defined as CHD events and ischaemic stroke).

Most of the risk-assessment tools gave with a 5- or 10-year risk of CV end points.

Statistical analysis

Almost all the longitudinal studies derived risk-assessment tools utilised one of these three statistical methods: Cox proportional hazards regression models, multiple logistic functions or Weibull proportional hazards model.

Risk factors included

A wide range of RFs commonly known to contribute to the incidence of CV events were studied and included in these risk-assessment tools. Three non-modifiable cardiovascular risk factors commonly included were age, sex and family history of premature CV diseases. Four more common physiological modifiable RFs were constantly implicated in the occurrence of CV events. These included body mass index, blood pressure, cholesterol level and diabetes status. Except for body mass index, the other three physiological RFs were constant features of the existing risk-assessment tools.

Smoking status was almost always included in the available risk-assessment tools. However, other lifestyle RFs such as sedentary lifestyle, dietary consumption and alcohol consumption were seldom featured. Other RFs such as deprivation scores (socio-economic status), left ventricular hypertrophy and past medical history of CHD or chest pain on exertion were included in some risk tools.

The quantification of RFs was also not standardised. Even for the same RF such as blood pressure, several methods of measurement were used. In most cases, systolic blood pressure was used except in the Cardiovascular Event Reduction Tool, whereby diastolic blood pressure measurement was used.[13] Similarly, for cholesterol, various subtypes of cholesterol were used. These included total cholesterol, low-density-lipoprotein cholesterol, high-density-lipoprotein cholesterol, triglyceride and even the total cholesterol:high-density-lipoprotein cholesterol ratio. As for diabetes status, the Reynolds risk score used glycated haemoglobin instead of fasting glucose status to measure the diabetes status.[14]

Apart from the difference in the types of RF being included in these tools, the level of measurement of the data for these RFs also differs between the risk-assessment tools. Some risk-assessment tools used a dichotomised scoring system for anti-hypertensive treatment and blood pressure measurement. This means that the score will be given on whether a treatment has been given or not or whether the disease is present or not.

There are various ways of quantifying smoking status. The Dundee Risk Score differentiates between never smoker, ex-smoker, pipes, cigars, number of cigarettes smoked per day and also 'number of years smoked.'[15] The other risk-assessment tools simply quantified individuals as current smoker or non-smoker, irrespective of their smoking history and the number of cigarettes smoked.

Tool characteristics

These risk-assessment tools come in various forms, including risk charts, risk calculators and computer programs.

Applicability among Asian population

Among all the risk-assessment tools, the Framingham Risk Score remained the most widely used and studied among Asians. Studies conducted among Chinese, Indians and as well as Japanese concluded that the Framingham Risk Score over-estimates the risk for CHD.[16–18]

DISCUSSIONS

A reasonably large sample is needed in order to ensure a representative sample of the population being studied, and at the same time the sample size should be sufficient enough to allow

individual observation during follow-up. If possible, these samples should be stratified according to age, sex and ethnicity due to the differences in the risk for CV disease.

Generally, the risk of CV disease increases steeply with advancing age in both men and women. Lloyd-Jones and colleagues found out that the cut-off age for increased lifetime CV risk in the presence of cardiovascular risk factors was 50 years.[19] However, controversies arise on the applicability of these tools for the prediction of risks in young adults (30—40 years) or older people (70—80 years). These younger adults as well as older people were not commonly included in the derivative sample of most of these tools, and so the incidence of CV or CHD events might not be applicable for these group of population.[20] Therefore, it is important that the age range of the cohort does not unnecessarily increase or blunt the incidence of CV events.

As men and women have different RF characteristics, there is a need for a representative sample from both sexes to accurately estimate the risk for a given population.

A longitudinal prospective cohort of the population to which the model is to be applied will provide information on the actual incidence of the outcome of the cohort, based on the existing lifestyle and RF. This will provide an accurate estimate of CV disease/CHD risk. Moreover, this is subjected to less selection bias and has now become the basis for prevention medicine research.[21]

The fact that most of these risk-assessment tools were derived from studies done in the 1970s and 1980s has limited the generalisability of the tools in this new era. This is because there was a high incidence of CV event and diabetes during 1970s—1980s, and this tends to overpredict the risk at this current time.

A 5- or 10-year follow-up is deemed to be clinically relevant to determine the management strategies for an individual. This is because our aim is to improve the quality and quantity of life in the foreseeable future.

Questions arise as to whether CHD and CV disease risk can be used interchangeably in guidelines. CHD and CV disease risks are said to be correlated but not equivalent. A comparison between risk-estimation tables that estimated CHD and CV disease risk over 10 years found that the ratio of CHD:CV disease risk is close to 3:4.[22]

The Cox proportional hazards model is the preferred statistical method in the derivation of risk scores because it incorporates the time of an event to occur, unlike logistic regression which lacks this function.[23]

Selection of RFs to be included in the risk-assessment tool is controversial and mainly depends on the availability of methods and resources to measure the RFs as well as its effect on the accuracy in predicting risk.[24] The inclusion of other anthropometric measures such as waist circumference or waist—hip ratio is rarely used despite being shown to be more robust and a better predictor of obesity and CV risk.[25] [26] This could be due to the difficulty in obtaining reliable measurement in a large sample.

The inclusion of lifestyle RFs (such as sedentary lifestyle, dietary consumption and alcohol consumption) in risk-assessment tools is rare except for smoking status, despite its role in the risk of CV disease.[27] This may be due to the difficulty in assessment of the RF. Assessment of these RFs is normally based upon self report, and this will affect the validity of these results. In addition, these lifestyle RFs also failed to demonstrate independent significance in multivariate models.

There are uncertainties on the relative importance of blood pressure components in predicting CV risk. Systolic blood pressure, diastolic blood pressure and pulse pressure have been used. The evidence thus far supports the use of combination of systolic blood pressure and diastolic blood pressure in determining the CV risk.[28]

Similarly, there is still no consensus as to which cholesterol component should be used in CV risk assessment. In recent years, the superior predictive efficacy of the total cholesterol: high-density-lipoprotein cholesterol ratio as compared with existing cholesterol components has been studied and confirmed.[29]

Diabetics have an increased risk of CV mortality. Both fasting glucose level and glycosylated haemoglobin have been used in determining CV risk-assessment tools. The evidence regarding the use of these components is not conclusive. The association between fasting blood glucose and CV risk is only weakly correlated, as shown in the Cardiovascular Heart Study. Similarly, several studies also confirmed a positive association between glycosylated haemoglobin as well as postprandial glucose level and CV risk.[30] [31]

The other RFs that have been used include deprivation scores and education status. The effect of these RFs on the accuracy of risk estimation needs to be studied further. As for left ventricular hypertrophy, this requires expertise and facilities to perform the echocardiography, and so it is not very practical for screening purpose in general practice.

Some potential novel RFs of interest such as ankle brachial index measurement, intima media thickness, coronary calcium score, exercise stress test, C-reactive protein, lipoprotein (a), homocysteine, LDL particle size and thrombotic markers have not yet been studied for their inclusion in the risk-assessment tools. We are still uncertain whether these novel RFs would improve risk assessment.[32] [33] The future of CV risk estimation will probably involve genotyping the RFs for targeted risk management.[34]

The quantification of RFs used in the risk-assessment tools will affect the accuracy of the estimated risks. As expected, a continuous level of measurement will give a better estimate. On the other hand, dichotomous measurement is easier to use but will yield crude estimates. However, dichotomous measurement tends to overlook the considerable proportion of persons who were at high risk because of multiple marginal abnormalities.[35]

Generally, the available risk-assessment tools are not universal due to our genetic differences, cultures, eating habits, and social and behavioural characteristics.[3] A study on the global burden of CV disease reported a difference in the disease burden as well as key RFs contributing to this burden in different populations.[36] The Asia Pacific Cohort Studies Collaboration, which aimed to compare the Asian and Framingham cohort in terms of RFs and disease incidence, found that systolic blood pressure, total cholesterol and CV events were higher in the Framingham cohort, whereas smoking was higher in the Asian cohort.[6] This is one of the reasons why the Framingham Risk Score has been shown to overestimate the risk in Asian population.[17]

So far, there is no consensus as to which risk-assessment tools to follow and use for risk stratification in Asian populations. This has resulted in confusion among clinicians and consequently a failure to practise risk stratification for prioritising individuals for primary prevention strategy. It is more relevant to derive a predictive equation from data obtained from a representative and contemporary cohort of a population, based on the local genetic characteristics and the current mix of known and unknown RF.[37] Therefore, when any one of these risk-assessment tools is used, we must be aware of its limitations and interpret the results cautiously.

Nevertheless, several researchers have shown that by recalibrating and validating the existing tools with local epidemiology data, it is possible to apply these tools to the local setting.[6 16 38] Furthermore, these tools need to be evaluated and validated continuously to coincide with the temporal trends in population data.[3 39]

CONCLUSIONS

The use of global CV risk scoring is essential for targeted aggressive management of RF management. It is generally used as a population screening tool, and so the cost of measurement of RFs must be balanced with the accuracy of the risk estimation.

Generalisation of different predictive risk models for a specific population has its problems, and several criteria need to be fulfilled for an accurate prediction of risk. Therefore, the development of local epidemiological studies is essential.

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