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Hyperlipidemia is the Best Predictor of the Need for Routine Coronary Angiography in the Preoperative Evaluation of Chinese Patients Undergoing Valve or Congenital Heart Surgery

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Hyperlipidemia is the Best Predictor of the Need for Routine Coronary Angiography in the Preoperative Evaluation of Chinese Patients Undergoing Valve or Congenital Heart Surgery

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FUNG and SANDERSON: ***Hyperlipidemia is the Best Predictor of the Need for Routine Coronary Angiography in the Preoperative Evaluation of Chinese Patients Undergoing Valve or Congenital Heart Surgery.*** *Background: Coronary angiography is commonly performed before cardiac surgery for patients with valvular and congenital heart disease. However, the yield is not high. We hypothesized that risk factors analysis before angiography could effectively select those patients who may have higher likelihood of coronary artery disease (CAD). Methods: Coronary angiography was performed routinely in 243 patients with valvular or congenital heart disease prior to cardiac surgery. Standard risk factors for coronary artery disease, age, sex, smoking history, chest pain, hypertension, diabetes mellitus and hyperlipidemia (TC >5.2 mmol/l), and the results of angiography were analyzed retrospectively. Results: The age range was 37 to 82 (mean 55 ± 11) and 120 were male. 23 patients (9.5%) had coronary artery diseases, defined as > 50% stenosis detected angiographically in any of the epicardial arteries. Smokers (p=0.044), patients with hypertension (p=0.004) or hyperlipidemia (p<0.001) had significantly higher incidence of CAD than those without these risk factors. Sex, history of chest pain or diabetes mellitus were not significant risk factors. By multivariate analysis, hyperlipidemia was a highly significant independent predictor for CAD (p<0.001). Correlation coefficient between number of risk factors and presence of CAD was 0.418 (p<0.001). No patient who had none of these risk factors had CAD. Only 11 patients had CABG done in addition to planned cardiac operation. By comparing patients with or without CABG, hyperlipidemia was the only significant predictor for CAD (p<0.001). Conclusion: In this pilot study we have found that in Chinese patients hyperlipidemia is the best predictor of CAD that requires CABG, irrespective of age, sex, history of smoking, chest pain, hypertension or diabetes mellitus. Routine preoperative coronary angiography is unnecessary in Chinese patients without risk factors for coronary artery disease. (J HK Coll Cardiol 2000;8:122-128)*

Arterial, Chinese, coronary, hyperlipidemia, risk factors

摘要

背景：對於患有心瓣膜病，先天性心臟病患者，一般都在心臟手術前施行心血管造影術，然而在檢查後發現患有冠心病的數字並不高。本研究的假設是：在做心血管造影術前，分析各危險因素，能有效地助於抉擇那些病人有較高機會傾向患上冠心病。方法：在243個患有心瓣膜病或先天性心臟病的病人中，在心臟手術前，作常規性的心血管造影術檢查會，分析冠心病的標準危險因素：年齡、性別、吸煙歷史、胸痛、血壓高、糖尿病及高血脂(總膽固醇>5.2mmol/L)，

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將心血管造影術的結果作回顧性分析。結果：年齡由37至82歲(平均歲55± 11)，男性120人，23個病人(佔9.5%)是患有冠心病，其確診是任何一條心外膜的動脈在造影術中測得>50%狹窄。吸煙者(p=0.044)，高血壓者(p=0.004)或高血脂(p<0.001)，這些病人發生冠心病的機率顯著高於那些沒有這些危險因素的病人。性別、胸痛歷史或糖尿病的危險因素在統計上均未呈顯著性差異。從多變量分析，高血脂對冠心病是最有統計意義的獨立預測指標(p<0.001)。危險因素數目與冠心病嚴重情度之相關系數是0.418(p<0.001)，而沒有這些危險因素　均沒有患上冠心病。在計劃的心臟手術中，只有1 1 個需附加冠脈搭橋手術。比較施行冠脈搭橋術與否，高血脂對冠心病而言，是唯一最具有統計意義的預測指標(p<0.001)。總結：在這試驗性研究中，中國病患者需接受冠脈搭橋術，高血脂是最佳預測冠心病，而不需顧及其它因素，如年齡、性別、吸煙歷史、胸痛、高血壓或糖尿病。如沒有這些因素，心臟手術前為冠心病者作的常規檢驗—心血管造影術是一種不必要的檢驗。

關鍵詞：動脈的　中國人　冠狀的　高血脂　危險因素

Introduction

It is a common practice to have preoperative coronary angiography as part of routine work-up for patients undergoing valvular or congenital heart surgery. As recommended by the ACC/AHA Task Force, coronary angiography is indicated in patients with valvular heart disease, who have chest discomfort, evidence of ischemia and are of substantial age with multiple risk factors.[1] It is well known that the incidence of coronary artery disease increases with age[2] and varies widely among different ethnic groups. Therefore, the incidence of coronary artery disease in patients with valvular or congenital heart disease will also be expected to vary widely between different ethnic groups. In Western populations, the incidence of coronary artery disease in patients with or without valvular heart disease is about the same frequency, about 30%[3-6] and the prediction of coronary artery disease in patients with valvular heart disease by risk factor analysis is feasible.[3,5] However, the prevalence of coronary artery disease in Chinese population is different roughly one-quarter, that of Western counterparts.[7,8] Moreover, the impact of the traditional risk factors for atherogenesis in Chinese population seems to be less when compared with that of Caucasians.[9]

Information about risk factor analysis in predicting the incidence of coronary artery disease in Chinese patients with valvular or congenital heart diseases is scarce. Therefore, we have analysed the risk factor profiles in a cohort of Chinese patients who had coronary angiography performed as part of preoperative evaluation. The purpose of this study was to evaluate whether risk factor analysis could predict the presence of coronary artery disease in Chinese patients with valvular or congenital heart diseases preparing for cardiac surgery.

Methods

Patients

This is a retrospective analysis of 275 consecutive patients with either valvular or congenital heart diseases who had coronary angiography performed in our cardiac catheterization laboratory as part of their preoperative evaluation. The decision to perform coronary angiography in these patients was made jointly by cardiologists and cardiac surgeons. Patients with known history of coronary artery disease e.g. old myocardial infarction or previously angiographically diagnosed coronary stenosis were excluded from analysis. Patients were also excluded if the purpose of the coronary angiography was to assess the severity of valvular or congenital lesions or look for associated coronary anomalies. A total of 243 patients were available for analysis.

Cardiac Catheterization

Standard cardiac catheterization was performed using femoral artery cannulation Coronary artery disease was defined as any lesion in left main stem artery, left anterior descending artery, left circumflex artery and right coronary artery greater than 50% stenosis by diameter. A simplified scoring system for assessing severity of coronary artery disease was adopted with 1 point for each diseased major epicardial artery. The lowest score was 0 for patients without coronary artery disease and maximum of 4 for patients with coronary artery disease.

Risk Factors Analysis

The risk factors for coronary artery diseases used for analysis in these patients with either valvular or congenital heart diseases were: age, sex, hypertension,

diabetes mellitus, and history of chest pain and hyperlipidemia.

Hypertension was defined as blood pressure measured on two different occasions with systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg. Diabetes mellitus was defined as fasting blood glucose >7.0 mmol/L. Hyperlipidemia was defined as fasting total cholesterol >5.2 mmol/L or LDL cholesterol >3.2 mmol/L. Chest pain was defined as any recurrent retrosternal pain present before coronary angiogram, either typical or atypical for angina.

Risk factor profiles were compared between patients with or without coronary artery diseases and patients with or without CABG performed. The correlation between number of risk factors and the severity of coronary artery disease was also assessed.

Statistics

Statistical analysis was performed by SYSTAT 7.0 for Windows software (SPSS Inc., Chicago). Results were expressed as mean ± SD unless otherwise stated. Predicting factors for co-existing coronary artery disease and requirement of subsequent coronary arterial bypass graft were determined by univariate analysis by Student's t test and Chi-square test whenever appropriate. Regression analysis for independent factors was performed by backward stepwise elimination of identified variables. All probabilities were two-tailed.

Results

There were 243 patients recruited for risk factor analysis. 120 patients were male and 123 patients were female. 33 out of 243 patients had congenital heart disease. Most had an atrial septal defect or patent ductus arteriosus. The remainder had valvular heart disease. The distribution of various valvular or congenital heart diseases is shown in Table 1.

The age of the patients ranged from 37 to 82 with mean age 55.7 ± 10.4. Symptom of chest pain, either typical or atypical for coronary ischemia, was present in 51 (21.0%) patients. 23 (9.5%) patients had hypertension and 14 (5.8%) had diabetes mellitus. 81 (33.3%) patients had history of smoking, either ex-smoker or current smoker. Hyperlipidemia, as previously defined, was present in 55 (22.6%) patients. The risk factor profiles among the study group is shown in Table 2.

Twenty-three (9.7%) out of 243 patients had CAD as demonstrated by coronary angiography. Fourteen of them were male and nine were female patients. Risk factors comparisons between patients with or without coronary artery disease are shown in Table 3. There was no preponderance of either sex for coronary artery disease. The mean age of patients with coronary artery disease was slightly but significantly older than that of patients without coronary artery disease (60.0 ± 9.3 vs 55.3 ± 10.5 respectively, p=0.029). Hypertension (p=0.004), smoking (p=0.044) and hyperlipidemia (p<0.001) were significant predictors for coronary artery disease but neither history of chest pain nor diabetes mellitus were significant predictors. After excluding patients with aortic valve disease, both chest pain and diabetes mellitus were not significant predictors for CAD. Using multivariate analysis, hyperlipidemia (p<0.001) was the only independent significant risk factor to predict the presence of coronary artery disease.

Among those patients with coronary artery disease, defined as more than 50% stenosis in any one of epicardial coronary arteries, 11 patients underwent CABG. By comparing the risk factor profiles between patients with or without CABG done, hyperlipidemia

Table 1. Distributions of various valvular or congenital heart disease

Diseases	No. of patients (%)
Total	243
Mitral valve	90 (37.0)
Aortic valve	86 (35.4)
Mixed mitral and aortic valves	32 (13.2)
Atrial septal defect	21 (8.6)
Patent ductus arteriosus	9 (3.7)
Others	5 (2.1)

Table 2. Risk factor profiles of the study group

Risk factor	
Sex (M:F)	120:123
Chest pain, no. of case (%)	51 (21.0)
Hypertension, no. of case (%)	23 (9.5)
Diabetes mellitus, no. of case (%)	14 (5.8)
Smoking, no. of case (%)	81 (33.3)
Hyperlipidemia, no. of case (%)	55 (22.6)

($p<0.001$) was the only significant predictor of patients requiring CABG, as shown in Table 3.

By using CABG and coronary artery disease as two different outcome measures, the correlation between number of risk factors and these two outcomes is shown in Table 4. No patient with none of these risk factors had coronary artery disease or had CABG done. The Pearson correlation coefficient between number of risk factors and proportion of patients having CAD is 0.42 ($p<0.001$), i.e. patients with more risk factors had higher probability of CAD or CABG. The mean number of risk factors in patients without CAD was significantly less than that of in patients with CAD (0.79 ± 0.88 vs 2.17 ± 0.89, $p<0.001$). By means of the simplified coronary scoring system, the number of cardiovascular risk factors was significantly correlated with the severity of coronary artery disease (Spearman's $r = 0.386$, $p<0.001$).

The incidence of CAD or CABG in different age groups is shown in Table 5. No patient with CAD was younger than the age of 40 and no patient less than age 50 required CABG. The incidences of CAD and CABG were higher in the more elderly group of patients. The proportion of patients with CAD rose from 5.6% in the age <50 group to 9.6% in the age <70 group and that of CABG rose from 2.7% in the age <60 to 3.5% in the age <70 group.

Discussion

In this retrospective analysis, we have demonstrated clinically that traditional risk factors for coronary artery disease including age, hypertension, smoking and hyperlipidemia can predict the presence of significant coronary artery disease in patients with

Table 3. Comparison of risk factors profiles between patient with or without coronary artery disease, and with or without CABG

Risk factor	CAD	No CAD	P value	CABG	No CABG	P value
Sex (M:F)	14:9	111:109	NS	3:8	117:115	NS
Age (years)	60.0 ± 9.3	55.3 ± 10.5	0.029	58.8 ± 10.8	55.6 ± 10.4	NS
Chest pain, no. of case (%)	8 (34.8)	43 (19.5)	NS	4 (36.4)	47 (20.3)	NS
Hypertension, no. of case (%)	6 (26.1)	17 (7.7)	0.004	2 (18.2)	21 (9.1)	NS
Diabetes mellitus, no. of case (%)	3 (13.0)	11 (5.0)	NS	1 (9.1)	13 (5.6)	NS
Smoking, no. of case (%)	12 (52.2)	69 (31.3)	0.044	5 (45.5)	76 (32.8)	NS
Hyperlipidemia, no. of case (%)	21 (91.3)	34 (18.1)	< 0.001	11 (100)	44 (19.0)	< 0.001

Table 4. Correlation between number of risk factors and proportion of patients had CAD or CABG

No. of risk factor	No. of patients	No. of patients with CAD (%)	No. of patients with CABG (%)
0	100	0 (0)	0 (0)
1	81	5 (6.2)	2 (2.5)
2	47	11 (23.4)	6 (12.8)
> or = 3	15	7 (46.7)	3 (20.0)

Risk factors include Age >65, Smoker, DM, HT, Chest Pain and Hyperlipidemia.

Table 5. Proportion of patients with CAD in different age group

Age	No. of patients	No. of patients with CAD (%)	No. of patients with CABG (%)
<40	15	0 (0)	0 (0)
<50	72	4 (5.6)	0 (0)
<60	147	11 (7.5)	4 (2.7)
<70	198	19 (9.6)	7 (3.5)

either congenital or valvular heart disease awaiting cardiac surgery. Moreover, with more risk factors, the chance of having co-existing coronary artery disease was higher, consistent with the additive properties of these common risk factors. However, neither a history of chest pain nor diabetes mellitus was significant predictor for coronary artery disease in our cohort of patients. We have confirmed that the overall prevalence of coronary artery disease in our patient group was 9.6%, which was much lower than that seen in western countries, generally reported to be 20-30%.[3]

Chest pain is a well known to be a poor predictor of the presence of coronary artery disease in patients with valvular heart disease. Conversely, the lack of pain does not predict the absence of disease. For example, one study suggested that coronary artery disease was very rare in patients with aortic stenosis who did not have chest pain,[10] but others had found significant coronary stenosis in as many as 25% of such patients who were free of chest pain.[11,12] Our results also suggest that symptom of chest pain is not a reliable predictor of coronary artery disease. It is surprising to note that diabetes mellitus is not one of the reliable predictors for coronary artery disease. The prevalence of non-insulin dependent diabetes mellitus is high in China, as high as 20% in those aged >70 years.[13] On the other hand, the traditional cardiovascular risk factors including diabetes mellitus are only present in 50% of patients with coronary artery disease in China.[9] New coronary risk factors like hyperhomocysteinaemia may be important in improving the predictability of these traditional risk factors.[17]

Hyperlipidemia is the only reliable predictor for coronary artery disease that required coronary artery bypass grafting in patients with congenital or valvular heart disease requiring cardiac surgery in our study. In western countries, the reported prevalence of hyperlipidemia in patients with co-existing coronary and valvular heart disease was 33%.[20] In those who had no CAD, the prevalence was 6%. The importance of hyperlipidemia in the development of atherosclerosis is well proven. There is concern about the rising mean cholesterol level in the developed areas of Asia like Hong Kong, Taiwan and Singapore as the incidence of coronary artery disease rises almost linearly with the cholesterol level.[13] In our study, 22% of patients had hyperlipidemia.

Using CABG as one of the outcome measurements is much more clinically meaningful as revascularization may not be necessary in patient with borderline coronary artery lesion, e.g. a 50% lesion in a distal artery. The purpose of coronary angiography in patients with valvular or congenital heart disease is to detect co-existing coronary artery lesions that may not be clinically obvious but that may require revascularization. It is logical to bypass the significant lesions detected at the same time as performing valve replacement or correction of a congenital defect.

Careful selection of patients with congenital or valvular heart disease to undertake coronary angiography as part of routine preoperative evaluation is vital as this invasive investigation is not free of complication. From the Registry of the Society for Cardiac Angiography and Interventions, the reported mortality of coronary angiography was 0.1%, myocardial infarction 0.06%, cerebral ischemia 0.07%, vascular complication 0.46% and contrast reactions 0.23%.[14] In our study, 2 (0.8%) patients had vascular complications, 1 (0.4%) patient had cerebral ischemia, 1 (0.4%) patient had acute renal failure and 1 (0.4%) patient had a severe allergic reaction to contrast agent and required admission to intensive care unit. No patient died after coronary angiography in our cohort. Unfortunately, none of the above patients who had complications following angiography had coronary artery disease. This indicates how important it is to correctly identify those patients requiring non-coronary surgery who are at risk of coronary artery disease and who need to have coronary angiography done as part of the preoperative evaluation. A variety of non-invasive methods have been investigated over the years as possible substitutes for coronary angiography as a means of detecting coronary artery disease in combination with valve or congenital heart disease. Exercise testing is in general not satisfactory as the ECG changes are often uninterpretable and the exercise tolerance of these patients is often very limited. Myocardial perfusion scanning with thallium has not shown a sufficient degree of diagnostic accuracy to be clinically useful.[15,16] Stress echocardiography may be more useful.[18,19] However, at the present time, coronary arteriography is the most reliable way of demonstrating coronary disease. The other techniques do not seem to be any more accurate than predictions based on risk factors.[3,5]

Useful information can be derived from our study for selecting those patients, especially Chinese patients,

with valvular or congenital heart disease who should undergo coronary angiography prior to cardiac surgery. Coronary angiography should not be obligatory in patients with age <50 or patients who have no known cardiovascular risk factors regardless of age and sex. Patients with hyperlipidemia should have a relatively lower threshold for coronary angiography even though the clinical likelihood is not high, as hyperlipidemia is a strong independent predictor for coronary artery disease that may require CABG. Patients with only 1 risk factor (age >65, smoking, diabetes mellitus, hypertension, chest pain and hyperlipidemia) have a 6.2% chance of having co-existing coronary artery disease while the presence of two risk factors increases the chance to 23.4%. Patients with 3 or more risk factors have a 46.7% chance of having coronary artery disease. Therefore patients with 2 or more risk factors should have coronary angiography done as part of routine preoperative evaluation. For patients with single risk factor, other modality of non-invasive investigation may be able to provide further information to assess the need for coronary angiography.

The current cardiac surgical advice, based on the recommendation from ACC/AHA Task Force, demands coronary angiography in most patients over the age of 40 prior to valve or congenital heart surgery. Such an approach has never been proven to be scientifically or practically sound, and angiography is not without risk. In our study, risk factor analysis seems to be able to select the appropriate patients who may have higher chance of co-existing coronary artery disease and who should have coronary angiography preoperatively. Therefore, the combined risks of investigation and surgery can then be lower in patients who have relatively lower chance of coronary artery disease. In this era of cost-constraints, the strategy of performing coronary angiography as a routine pre-operative investigation to look for coronary artery disease is definitely unacceptable given the low likelihood of detecting disease in this study population. Risk factor analysis as in our study seems to be a more cost-effective method in proper selection of patients for coronary angiography. When considering the cost of various non-invasive investigations e.g. thallium scan or stress echocardiogram, risk factor analysis is again the method of choice. However, in borderline cases, e.g. patients with only one risk factor, these investigations may be helpful. More sensitive and specific non-invasive ways to detect clinically significant coronary disease would solve the above issues. Magnetic resonance angiography may be the best investigation in the future.

Limitation

This is a retrospective analysis. The underlying rationale for deciding which patients need coronary angiography may change with time. A prospective study using predefined rationale will be the best approach to assess how useful is risk factor analysis in detecting coronary lesion in patients with valvular or congenital heart disease. Moreover, the absolute number of patients with coronary artery disease was small making statistical analysis less reliable, especially in analysing those patients who had CABG done.

Conclusion

Hyperlipidemia is the best predictor of coronary artery disease that requires CABG irrespective of age, sex, history of smoking, chest pain, hypertension or diabetes mellitus in patients with either congenital or valvular heart disease undergoing corrective surgery or valvular replacement. Routine preoperative coronary angiography is unnecessary in patients without risk factors for coronary artery disease. Risk factor analysis can effectively select the high-risk patients who really need coronary angiography before surgery.

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