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Coronary risk stratification of patients undergoing surgery for valvular heart disease

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ABSTRACT

Background: Multislice computed tomography (MSCT) is a non-invasive, less expensive, low-radiation alternative to coronary angiography (CAG) prior to valvular heart surgery. MSCT has a high negative predictive value for coronary artery disease (CAD) but previous studies of patients with valvular disease have shown that MSCT, as the primary evaluation technique, lead to re-evaluation with CAG in about a third of cases and it is therefore not recommended. If a subgroup of patients with low- to intermediate risk of CAD could be identified and examined with MSCT, it could be cost-effective, reduce radiation and the risk of complications associated with CAG.

Methods: The study cohort was derived from a national registry of patients undergoing CAG prior to valvular heart surgery. Using logistic regression, we identified significant risk factors for CAD and developed a risk score (CT-valve score). The score was validated on a similar cohort of patients from another registry.

Results: The study cohort consisted of 2221 patients, 521 (23.5%) had CAD. The validation cohort consisted of 2575 patients, 771 (29.9%) had CAD. The identified risk factors were male sex, age, smoking, hyperlipidemia, hypertension, aortic valve disease, extracardiac arteriopathy, ejection fraction <30% and diabetes mellitus. CT-valve score could identify a third of the population with a risk about 10%.

Conclusion: A score based on risk factors of CAD can identify patients that might benefit from using MSCT as a gatekeeper to CAG prior to heart valve surgery.

1. Introduction

Prior to surgery for valvular heart disease (VHD), guidelines recommend evaluation of possible coronary artery disease (CAD) for all patients with symptoms of angina or coronary risk factors, including men aged >40 years and postmenopausal women (1c) [1,2]. As the mean age of patients undergoing surgery for VHD is 65 years and only about 17% are <50 years [3], most patients are evaluated for CAD before surgery. The gold standard for evaluating CAD is invasive coronary angiography (CAG). CAG is associated with a risk of serious complications, and about 5–10 mSv of radiation [4,5]. In addition, the investigation is costly and can only be performed at an invasive center.

Multislice computed tomography (MSCT) is an alternative to CAG. The procedure is non-invasive, less expensive [6–12], and MSCT only exposes the patients to about 1–3 mSv of radiation [4]. Current AHA/ACC guidelines recommend MSCT for evaluation of CAD as an alternative approach in patients with low-to-intermediate risk of CAD prior to surgery for VHD, but there is no established method for selecting this group of patients [1]. Previous studies of MSCT for evaluation of CAD in patients undergoing surgery for VHD are in unselected populations and have shown too high a percentage of patients needing re-evaluations with CAG for this approach to be reasonable [13–16].

The objective of this study was to develop a risk score able to identify VHD patients with a low risk of CAD, who would benefit from a strategy with MSCT as the primary tool for evaluation of the presence of CAD.

2. Methods

Every patient undergoing CAG in the Capital Region and the Region of Zealand are registered in a database (the Web-PATS database). Patients from the remaining part of the country are registered in a similar database (The Western Denmark Heart Registry). From these registries we obtained data from patients who received a CAG with primary indication of surgery for VHD from 2010 to 2013 (Web-PATS) and 2010 to 2014 (The

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Western Denmark Heart Registry). The initial analysis was performed in 2014 and data from Web-PATS from that same year were thus not available at the time.

The databases include information on valvular pathology and known risk factors of CAD such as age, sex, body mass index (BMI), left ventricular ejection fraction (LVEF), diabetes mellitus (DM), family history of ischemic heart disease, prior stroke, smoking, hypertension, hyperlipidemia, extracardiac arteriopathy (e.g. claudicatio intermittens, aortic aneurism or dissection, confirmed >50% carotid stenosis), and prior ischemic heart disease (IHD), percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG). Significant CAD was defined as a stenosis >70% (>50% for the left main coronary artery) or with a fractional flow reserve <0.80.

Data from Web-PATS were used to develop a risk score which was validated in The Western Denmark Heart Registry. The goal was to identify as large a group of patients as possible with a risk of significant CAD at about 10%.

To estimate how much money and radiation that could be saved using MSCT as a gatekeeper for CAG, we searched the literature and national agencies and found prices for MSCT and CAG in 7 countries—the United States [6], the United Kingdom (UK) [12], Germany [7], Australia [8], Korea [9] Denmark [8] and Sweden [12]. Using these, we calculated differences in expenses and radiation [4] if MSCT was used as a gatekeeper for CAG as compared to the routine use of CAG.

The specificity of MSCT can be a challenge and patients with significant calcification of the coronary arteries or borderline stenosis has to be re-evaluated with CAG to determine whether they have significant CAD. Based on a previous study [17], we estimated that 2.5 times the patients with significant CAD would need re-evaluation with CAG if MSCT was used as initial examination for CAD. To avoid groups based on small sample sizes we divided patients into groups according to their score for each 2 points or above 12 points. We calculated the cost-effectiveness of the score by calculating how much money and radiation could be saved per 100 patients in each group factoring in the cost and the expected number of re-evaluations. We also calculated the expected cost–benefit of different cutoff values in a cumulative graph showing the combined savings of different cutoff values factoring in expected re-evaluations, the number of patients in each group and the costs of the procedures.

3. Statistics

All registered risk factors of coronary artery disease collected in the Web-PATS database were tested with univariate logistic regression for a significant association with the risk of having significant CAD as identified by CAG. Angina was excluded as a risk factor from the analysis because of inconsistent reporting and a lack of data both in the original database and in the electronic records. When added to the risk score as constructed, it slightly weakened the model.

Following univariate regressions, all significant risk factors were entered into a multiple logistic regression with backwards elimination. Risk factors that were non-significant were removed from the regression and the risk estimates were derived from the odds ratios of each factor in the analysis rounded to the nearest integer. All regressions were done with bootstrapping of 1000 to secure the significance of the results. Age was further separated into four groups after a visual reading of a ROC curve of age as a factor for significant CAD. We used a double-sided level of significance of 5%. The calculations were done using SPSS statistics 22 for Windows.

The subsequently developed score was then re-calculated for the patients of The Western Denmark Heart Registry to determine its effectiveness. The effectiveness of the score was judged by the percentage of patients classified as low- to intermediate risk by our score who upon examination turned out to have significant CAD.

4. Ethics

The study complied with the Helsinki Declaration II and was approved by the Danish Data Protection Agency (jr.nr. 2014-41-3261) and The Danish Medicines Authority (3-3013-987/1).

5. Results

Web-PATS held information on 2840 patients with VHD and all risk factors registered or available through electronic records. After excluding patients with prior ischemic heart disease (PCI, CABG or IHD) and examinations on patients already registered in the database the population of this study included 2221 patients. Of these, 521 (23.5%) had significant CAD on their CAG.

In The Western Denmark Heart Registry, we identified patients with all risk factors registered receiving CAG because of planned surgery for VHD. There was no information on extracardiac arteriopathy in the database. This registry included 2575 patients. Of these, 771 (29.9%) had significant CAD (Fig. 1).

The baseline characteristics of both databases are shown in Table 1. The significant differences among the two databases were a slightly higher average age, lower frequency of hyperlipidemia and LVEF <30% and a higher risk of hypertension and aortic valve disease (all $P < 0.01$) in The Western Denmark Heart Registry.

The regressions to determine risk factors are displayed in Table 2. In the univariate regressions all pre-defined risk factors except BMI > 30 and a family history of ischemic heart disease were significantly correlated with CAD. In the multiple logistic regression all factors proved significant except previous stroke ($P = 0.3$) and diabetes mellitus (DM) ($P = 0.073$). Because of the strong association between CAD and DM in the previous literature [18,19], we decided to keep DM as a factor in the score. The resulting CT-valve score can be seen in Table 3. A ROC curve of the score can be seen in Supplementary Fig. 1 and gives an area under the curve of 0.73 (95% confidence interval 0.71–0.75) and 0.67 (0.65–0.69) on the primary and validation cohort.

Using CT-valve score to evaluate patients from the primary and validation cohorts to calculate the percentage of patients with significant CAD gave results as shown in Table 4. If a cutoff value of 7 points was applied, we identified about a third of the total patients with a risk of CAD of 8%–10%. An alternative cutoff of 6 points would identify 20%–25% of the population with a risk of CAD at 6%–10%. A cutoff of 8 points would identify about half of the population with a risk of CAD at 12%–19%.

The cost of a CAG ranged from 1973€ in Australia [8] to 560€ in Korea [9] (mean 1129€), while costs for MSCT ranged from 663€ in Australia to 99€ in Germany [7] (mean 396€). In all countries, the cost of a CAG was at least double the cost of a MSCT, with the highest price difference in the UK [12], where the cost of a CAG amounted to around 6 times the price of a MSCT.

Dividing the patients into groups according to their CT-valve score and estimating the re-evaluation frequency to be 2.5 times the number of patients with significant CAD, we calculated the potential reduction in cost and radiation dosage per 100 patients for each group for 7 countries in Fig. 2. A cumulative graph showing the combined savings of different cutoff values factoring the number of patients in each group as well as the mean costs of the procedures (1129.3€ for CAG and 395.74 € for MSCT) and the number of expected re-evaluations can be seen in Fig. 3. From these graphs, potential cutoff values can be assessed according to their cost-effectiveness.

In all countries, a MSCT first approach would be cost-effective for patients with a score below 8. Likewise, from 10 points and up, the risk of CAD and therefore the expected re-evaluation rate is too high for the approach to be worthwhile.

The same graphs can be seen for radiation in Figs. 2b and 3b. The relatively high radiation dose of a CAG (around 8 mSv) compared with a MSCT (around 2 mSv) [4] results in an optimal cutoff of 9 points. For patients with a score of 8–9, the radiation dosage would be reduced by about 85 mSv per 100 patients. With a cutoff of 7 the estimated total radiation would be reduced by 470 mSv (55%).

6. Discussion

Using known risk factors of CAD, it is possible to construct a score able to identify about one-third of patients undergoing surgery for VHD with a risk of significant CAD of about 10%. These patients might benefit from using MSCT as a gatekeeper for CAG, in terms of lowering radiation exposure, reducing potential complications and provide better cost–benefit.

Large systematic reviews of MSCT have shown conclusive results in predicting CAD. In two meta-analyses of more than 4500 patients