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Original Article

Evaluation of SERENE-CAG score for assessing suitability for coronary angiography preoperatively in patients undergoing valve replacement surgery

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ABSTRACT

Aims: The aim of this study was to identify better selection criteria for subjecting patients of rheumatic heart disease (RHD) to preoperative coronary angiography (CAG) based on indigenous scoring system (SERENE-CAG [Selecting Patients Of Rheumatic Heart Disease Undergoing Valve Surgery For Presurgical Coronary Angiography]).

Methods: This prospective study included all consecutive 798 patients of RHD patients undergoing preoperative CAG from January 2016 to December 2017 over a duration of 2 years. Multivariate logistic regression analysis was performed with the presence of significant CAD [coronary artery disease] as the dependent variable with traditional risk factors of CAD. An additive score was developed using coefficient derived logistic regression for those variables that were significant. Receiver-operator curve analysis was performed to assess the ability of this score to predict diseased vs normal CAG.

Results: A total of 798 patients had a mean age of 51.7 ± 12.5 years. Significant CAD requiring revascularization along with valve surgery was identified in 50 (6.26%) patients. Male gender was found as significant predictors of CAD with odds ratio 2.6. A SERENE CAG SCORE of >2.8 resulted in sensitivity of 80% and specificity of 36.9% of predicting CAD in RHD patients with positive and negative predictive value of 7.8% and 96.5%, respectively.

Conclusion: The prevalence of CAD in RHD patients is low. Patient risk can be minimized by exploring noninvasive modalities for screening of CAD and by more appropriate selection of patients for invasive coronary angiogram. Using threshold SERENE-CAG score of >2.8 would result in deferring 34.6% of normal angiograms.

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1. Introduction

Coronary artery disease (CAD) has a detrimental effect on long-term survival in patients undergoing valve surgery. Both American College of Cardiology (ACC)/American Heart Association (AHA) and European Society of Cardiology (ESC)/European Association for Cardio thoracic Surgery (EACTS) recommend that coronary angiography (CAG) should be performed before valve surgery in men aged > 40 years, postmenopausal women, patients with risk factors for CAD, left ventricular (LV) dysfunction, and secondary mitral regurgitation.[1,2]

The prevalence of CAD in patients undergoing valve surgery is reported to be 20%–40% in developed countries. It is important to consider that spectrum of valve disease in developing world is different from developed world; the predominant etiology leading to valve surgery in developing world is rheumatic valvular disease (RHD).[3] In India, CAG is usually performed in RHD patients before valve replacement surgery, if there is any suspicion of CAD or the patient is aged >40 years.[3–6] A majority of these CAGs are normal. In addition, CAG in these patients carries higher risk of complication and is technically more challenging especially in the presence of dilated aortic root. Current practice trends expose these patients to risk of invasive procedure with relatively low yield. Thus, the appropriate selection criteria for screening CAG in patients with RHD undergoing valve replacement surgery are unclear and need to be refined. The present study aims to evaluate and frame appropriate criteria for these “screening CAGs” and develop a predictive

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model (SERENE-CAG [Selecting Patients Of Rheumatic Heart Disease Undergoing Valve Surgery For Presurgical Coronary Angiography]) score for the same. The benefits for such an approach were then calculated for the present study population.

2. Methods

The study involved prospective analysis of all-comer patients of RHD undergoing preoperative CAG at a tertiary care center in western India over a period of 2 years (from 1st January 2016 to 31st December 2017). Only patients with confirmed diagnosis of RHD by clinical examination and echocardiography who were planned for surgery were included. Patients having known CAD or presenting with acute coronary syndromes were excluded. CAG was performed and reported by experienced qualified cardiologists with experience ranging from 2 years to 10 years after a doctoral qualification (DM/DNB) with all operators being designate faculty at the institute (Asst. professor and above). Significant CAD was defined as the presence of more than 70% luminal stenosis in any major epicardial coronary artery or more than 50% stenosis of the left main coronary artery. LV systolic dysfunction was defined as an ejection fraction (EF) less than 50%. The case files, procedure records, and CAGs were reviewed for all the patients. Information pertaining to demographic details, traditional risk factors for CAD, predominant valvular lesions, LV function, procedure time, radiation dose, contrast volume, route of CAG, extent and nature of CAD if present, and procedural complications and their outcomes were recorded.

Data were managed on an Excel spreadsheet and analyzed systematically using MATLAB, version 2016a, and SPSS, v.22. All data were presented as frequency distribution and simple percentages. Descriptive statistics were presented in the form of mean ± SD for all continuous variables. Categorical variables were expressed as percentages and analyzed using the chi-square test. A p-value <0.05 was considered to be statistically significant. A multivariate logistic regression analysis was performed with the presence of significant CAD as the dependent variable, and age, gender, and presence of LV dysfunction as the predictor variables. A simple additive score was developed using the coefficient derived from logistic regression.

$$\text{Score} = \text{coefficient}_1 \text{X variable}_1 + \text{coefficient}_2 \text{X variable}_2 + \text{coefficient}_i \text{X variable}_i$$

Receiver-operating curve (ROC) analysis[7] was performed to assess the ability of this score to predict diseased or normal CAG. The optimal threshold for score was defined at the highest Youden index. The clinical benefits were then calculated from the study population considering if the population above the threshold value underwent CAG and below threshold value underwent computed tomography coronary angiogram (CTCA). The procedural duration and radiation doses for CAG were as calculated from the study. Radiation doses and contrast used for CTCA were calculated from institutional averages during the same time period.

3. Results

A total of 798 patients, 337 (42.23%) men and 461 (57.76%) women, were included in the study. Mean age of the patients was 51.7 ± 12.5 years (52.4 years in men and 51.0 years in women). Mean EF was 54.3 ± 17.8%. Severe mitral stenosis was the most common lesion seen in 56.07% patients (Table 1). The odds of various risk factors are presented in Table 2.

Mean procedure time in and out of cath lab was 20.6 ± 11.4 min. Femoral access was used in 735 (92.10%) cases, and radial, in 63 (7.89%) cases; one patient required conversion from femoral to radial access because of the tortuous aorta. The route of CAG was left to the operators comfort and discretion as in the real world scenario. Because the radial access was used for very few patients in the study, the study was neither powered nor equipped to evaluate the difference between complication rates based on the access site (femoral and radial access). Mean contrast volume used was 53.8 ± 9.8 ml. Data on radiation exposure were available only for 106 patients; mean exposure dose was 4.1 ± 2.1 mSv. Serious adverse events that resulted in death of two patients were first being death resulting from the refractory ventricular tachycardia (VT) and ventricular fibrillation (VF) that the patient developed 2 h after angiography, whereas the other patient died of acute kidney injury and multiorgan dysfunction 5 days after angiography. There were 29 access site complications including 21 hematomas and eight pseudoaneurysm. Blood transfusion was required in two patients. The hospital stay was prolonged in all eight patients of pseudoaneurysm and 13 patients of hematoma. Three patients required CTCA, two for defining anomalous coronary origin which could not be selectively cannulated and one for defining the interarterial course of the anomalous right coronary from the left aortic sinus.

Significant CAD as defined above requiring revascularization with valve surgery was identified in 50 (6.26%) patients, of which 33 (66%) were men. Nonobstructive lesions identified during angiogram not warranting revascularization were also documented during the study but did not influence or contribute to the score evaluated. Because incidence of CAD was low in the study population, the study was not powered to evaluate single vessel vs multivessel disease and did not influence the score. Proportion of men in the CAD group was significantly higher than those without

Table 1
Baseline characteristics of the study population.

Variables	Mean (SD)/N(%)
Total population	798
Cases (RHD patients with CAD)	50 (6.26%)
Control (RHD patients without CAD)	748 (93.73%)
Age	51.65 ± 7.48
Male	337 (42.23%)
Diabetes	3 (0.37%)
Hypertension	4 (0.5%)
Contrast volume	53.77 ± 9.8
Fluoroscopic time	2.39 ± 0.12
Aortic systolic pressure	132.54 ± 34.5
Aortic diastolic pressure	73.94 ± 19.34
Heart rate	86.94 ± 12.8
Ejection fraction	52.49 ± 17.8
LV dysfunction	104 (13.03)

SD, standard deviation; RHD, rheumatic heart disease; CAD, coronary artery disease; LV, left ventricular.

Table 2
Comparison of subjects with and without CAD.

Variables	Cases ($n = 50$)	Control ($n = 748$)	p-value
Age	54.94 ± 5.9	51.43 ± 9.36	0.99
Male	33 (66%)	304 (40.64%)	<0.001
Diabetes	0	3 (0.37%)	1
Hypertension	0	4 (0.5%)	1
Contrast volume	62.6 ± 12.9	53.18 ± 5.5	1
Fluoro time	2.9 ± 0.12	2.36 ± 0.11	1
AO systolic pressure	133.8 ± 38.9	132.45 ± 32.1	0.618
AO diastolic pressure	74.24 ± 12.7	73.92 ± 23.4	0.561
Heart rate	83.27 ± 14.5	87.2 ± 9.2	0.032
Ejection fraction	53.4 ± 13.4	54.35 ± 19.3	0.3199
LV dysfunction	8 (16%)	96 (12.83%)	0.519

CAD, coronary artery disease; LV, left ventricular

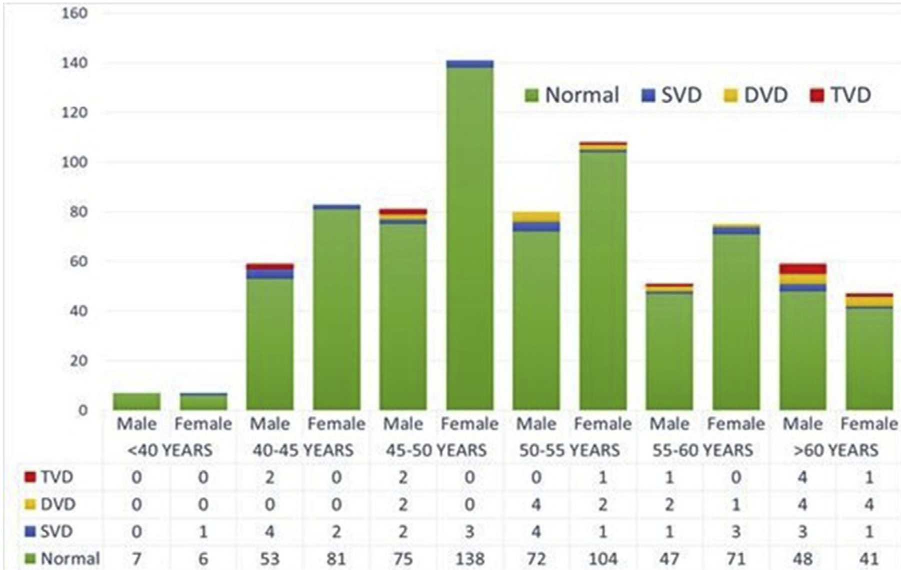

Fig. 1. Distribution of CAD in various age groups in men and women. TVD, triple vessel disease; DVD, double vessel disease; SVD, single vessel disease.

CAD with *a p* value 0.0001. Mean EF in the CAD group was 53.4% which was not significantly different from those without CAD with mean of 54.35%. Distribution of CAD in various age groups in men and women is shown in Fig. 1.

Although the presence and severity of regurgitation such as MR and AR would influence the LVEF in the presence or absence of LV dysfunction, for the study purpose LVEF as measured using Simpson's method was taken as the continuous variable to derive the equation. LVEF as the presence of LV dysfunction was not found to be a significant predictor of CAD in our study (Table 3).

Based on the coefficient derived, simple additive score was developed using coefficients of age and male gender, resting heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP), and presence of diabetes mellitus (DM) as predictor variables. The other traditional risk factors that were nonsignificant on analysis did not form the part of the score. Smoking, dietary pattern, dyslipidemia, and tobacco consumption history were not contributory in this study but in larger population may influence the outcome. The presence of atrial fibrillation also did not contribute to the equation in the sample. By adding and multiplying by common factors, the following formula was derived.

$$\text{SERENE-CAG score} = 0.665 - 0.00237 \times \text{SBP} - 0.000118 \times \text{DBP} - 0.8582 \times \text{diabetes status} - 0.00307 \times \text{HR} + 0.0567 \times \text{AGE (yrs.)}$$

Where DM status was scored as 0 for nondiabetics and 1 for diabetics, SBP (mmHg), DBP (mmHg), HR = heart rate/min, and age is chronological age in completed years.

ROC analysis for this score as a predictor of CAD resulted in a threshold value corresponding to a maximum Youden index score >2.8 as the threshold; resulting in sensitivity of 80% (95% CI 65.0–89.5) and specificity of 36.9% (95% CI 33.3–40.6). *p* (score) is calculated as = 1.0434 × (exp (((score- 3.0049) 2/(0.3465))). A threshold score value of >2.8 would result in deferring 34.6% of normal angiograms (Table 4 & Fig. 2). The other cutoffs (>2.5 and > 3) were also assessed for diagnostic potency, and the results are presented in Table 4.

Table 3
Multivariate analysis of different variables as a predictor of CAD.

Predictor	Coefficient	Odds Ratio	95% CI	*p* value
Age	0.054	1.0560	1.0175 to 1.0959	**0.004**
Male sex	0.956	2.6003	1.4135 to 4.7837	**0.002**
LV dysfunction	0.218	1.2442	0.5599 to 2.7651	**0.591**

CAD, coronary artery disease; LV, left ventricular.

4. Discussion

The need for CAD evaluation before valve surgery is now well established.[1,2,8] However, CAG in patients with severe RHD is more complex and riskier than in patients without valve disease.[9,10] Our study also clearly highlights increased complication rates in such patients. Procedure related mortality was 0.25% higher than expected with diagnostic CAG. There were 29 local site complications, 21 hematoma and eight pseudoaneurysm. The higher complication rates probably reflect unstable hemodynamics and rhythm, limited cardiac output, and higher bleeding risk due to anticoagulation. The increased procedure time probably results from altered aorticroot geometry resulting in unstable catheter position and difficult cannulation of the coronary arteries. This results in increased contrast volume and radiation exposure of the patient and operator. Despite increased risk of procedural complication, yield of CAG in these groups of patients is low.[4,5,11–15] The prevalence in our study for obstructive CAD is 6.27% which is comparable with studies by Jadhav et al,[15] Narang et al,[5] Manjunath et al[4], and Shaikh et al.[16]

Given the low incidence of asymptomatic CAD in RHD patients compared with other etiologies seen in the developed world, the existing practice trends expose significant number of patients to risk of procedure with relatively low yield. This mandates need for protocols, improving yield and reducing patient risk. Although CAG remains as a gold standard and safe procedure with good risk–benefit ratio for CAD evaluation in valvular heart disease patients, alternative noninvasive modalities such as CTCA needs to be proposed only for low likelihood patients of CAD.

Patient risk can be minimized by exploring noninvasive modalities for screening of CAD in these patients. Recent guidelines on management of valvular heart disease both by ACC/AHA and ESC/EACTS reflect the recognition of efficiency of noninvasive

Table 4
Cutoff analysis.

Parameters	Score >2.5	Score ≤2.5	Total	Score >2.8	Score ≤2.8	Total	Score >3	Score ≤3	Total
CAD present	49	1	50	40	10	50	27	23	50
CAD absent	691	57	748	472	276	748	344	404	748
Total	740	58	798	512	286	798	371	427	798
Sensitivity	**98.0**			**80.0**			54.0		
Specificity	**7.6**			**36.9**			54.0		
PPV	6.6			7.8			7.3		
NPV	**98.3**			**96.5**			**94.6**		
CAG avoided	**(58/798) 7.26%**			**(286/798) 35.83%**			**(427/798) 53.50%**		

PPV, positive predictive value; NPV, negative predictive value; CAD, coronary artery disease; CAG, coronary angiography.

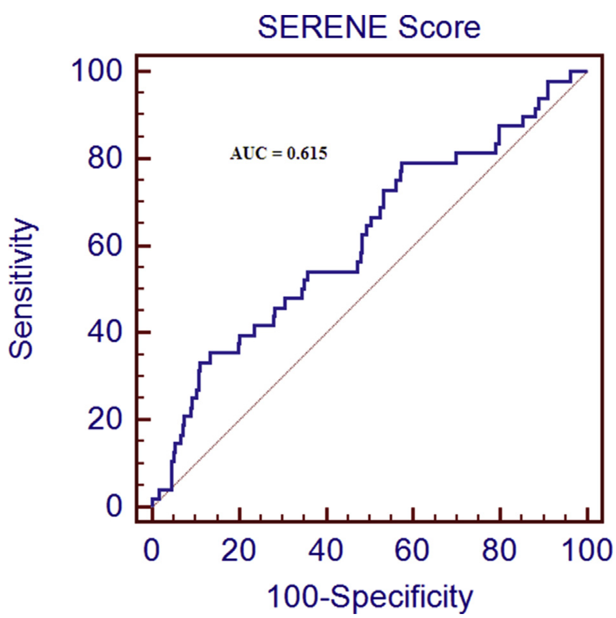

Fig. 2. Area Under Curve (AUC) for SERENE CAG score

modalities for evaluation of CAD in these patients. Bettencourt et al[17], evaluating CTCA for exclusion of CAD in patients undergoing valve surgeries, reported a sensitivity of 95%, specificity of 89%, positive predictive value (PPV) of 66%, and negative predictive value (NPV) of 99% in patient-based analysis. In another study, Joshi et al[10] report that sensitivity and specificity of CTCA technique was 100% (95% CI: 39.76%–100%) and 91.30% (95% CI: 79.21%–97.58%), respectively, in identifying CAD in patients undergoing non-coronary heart surgery. Joshi et al, however, highlighted the fact the CTCA required higher contrast volume to be administered than the CAG. The initial use of calcium score can overcome this problem. As suggested by Bettencourt et al[17], a calcium score of less than 390 correlates consistently with normal coronary artery on CAG. Hence, CAC may be applied in deferring contrast administration in low-risk patients.

Risk prediction models have been developed for prediction of CAD in RHD patients aiming to improve the yield of CAG in these patients.[11,12] Most of these incorporate age, gender, presence of other risk factors and family history of CAD. Age and gender are clearly the most important predictors in most of these models. The simple additive score uses these variables and combines them into an easy clinician friendly derivative. Using a threshold value > 2.8 to subject a patient for CAG results in sensitivity of 80.0%. The initial use of CTCA in patients below threshold value, with CAG reserved for those having abnormal CTCA, further improves sensitivity without compromising on patient safety.

Using a threshold score value of >2.8 and using CTCA on patients having score ≤2.8 would result in deferring 286 (34.6%) negative angiograms in the present study population. The PPV and NPV for the score is 7.8% and 96.5%, respectively. The computed benefits for using above approach amongst study population are summarized in Table 4. Hence, adopting the SERENE-CAG score of <2.8 for CTCA would prevent 9.3 min of cath lab occupancy for invasive angiogram, reduce procedural complications by 52%, and prevent one death but at a cost of 2 mSV of radiation and 12.63 ± 1.8 ml of contrast which was insignificant as depicted in Table 5.

5. Limitations

The main limitation of the study is that it is a single-center study. This study also did not evaluate the presence of novel risk factors such as high sensitivity C reactive protein (hsCRP), coronary artery calcification (CAC), and so forth for CAD and their impact on occurrence of CAD in patients of RHD. Incorporation of CAC alone rather than CTCA for patients with low score could not be separately evaluated. A larger population-based study evaluating the SERENE-CAG score in a prospective manner in an artificial intelligence–based model can improve the score.

6. Conclusion

RHD is a most important cause of valve surgeries in the developing world, mandating a large number of patients undergoing screening for CAD. We recommend the use of the proposed SERENE-CAG score for prediction of CAD, with initial test as CTCA

Table 5
Benefits of using score at the threshold> 2.8 for screening CAG.

Parameter	Current practice	Proposed strategy	Difference
Mean contrast volume	54 ml ± 1.3 ml.	66.63 ml ± 2.8 ml	12.63 ± 1.8 ml
Mean radiation exposure	4.1 mSv	6.1 mSv	2.0 mSv
Mean cath lab occupancy saved	–	9.3 min	- NA-
Access site complication	–		decreased by 52%
Mortality due to procedural complication	2 (0.25%)	1(0.125%)	1 life saved

CAG, coronary angiography.

for score ≤2.8 and invasive CAG for those >2.8. The above strategy is likely to result in significant improvements in cost, patient comfort, and procedural complications and risks without significant difference in radiation exposure or contrast volume used.

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Disclosure

On behalf of all the contributors I herewith declare that all the authors have substantially contributed in the preparation of this manuscript.

Conflict of interest

All authors have none to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ihj.2018.10.033.

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