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ORIGINAL ARTICLE

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Coronary artery disease screening in adults with congenital heart disease prior to cardiac surgery

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Abstract

Objective: As adults with congenital heart disease (CHD) grow older, preoperative screening for coronary artery disease (CAD) may be indicated prior to CHD surgery. Data regarding the indications for preoperative CAD screening in this population are limited. Current practice is to follow guidelines for patients with valvular heart disease; however, the risk for CAD in certain congenital heart diagnoses may be higher than the general population. This study aimed to assess the results of preoperative CAD screening in patients prior to CHD surgery.

Design: Retrospective study.

Setting: Single tertiary center.

Patients: Patients ≥35 years that had CHD surgery from 1/1/2007 to 5/1/2017.

Outcome Measures: Data regarding CAD risk factors and preoperative CAD screening results were obtained. Prevalence and risk factors for CAD were analyzed, along with their relationship to perioperative outcomes.

Results: A total of 73 patients underwent CAD screening with either cardiac catheterization (56%) or computed tomography angiography (34%) prior to CHD surgery. Overall 16 (22%) patients were found to have CAD. Only two patients had severe coronary stenosis and underwent coronary bypass grafting at time of CHD surgery. Patients with CAD were more likely to be older and have history of hypertension, dyslipidemia, and tobacco smoking. CHD diagnosis was not significantly associated with presence of CAD.

Conclusion: CAD is common in asymptomatic older patients referred for screening prior to CHD surgery; however, severe CAD requiring concomitant coronary intervention is uncommon. Preoperative CAD screening should be based on age and traditional CAD risk factors, rather than underlying CHD.

KEYWORDS

adult congenital heart disease, cardiac surgery, computed tomography angiography, coronary artery disease

1 | INTRODUCTION

Cardiac reoperation to address residual cardiac defects or complications is the most frequent intervention for adults with congenital heart disease (CHD).[1] However, as the population of adults with CHD ages, they are also at risk for coronary artery disease (CAD),[2-7] which may increase surgical risk and/or may need to be addressed at the time of the CHD surgery with concomitant coronary artery bypass grafting.[8,9]

There are no formal recommendations for when to refer adults with CHD for preoperative screening for CAD prior to cardiac surgery.

Current practice is to extrapolate from the American College of Cardiology and American Heart Association guidelines for intervention on valvular heart disease, which recommends preoperative invasive coronary angiogram for asymptomatic men >40 years old, women who are postmenopausal, and any patient with several risk factors for coronary artery disease.[10] In addition, the guidelines state that noninvasive computed tomography coronary angiogram (CTA) may be used as substitute for cardiac catheterization in patients that are felt to be low-to-intermediate risk for CAD.[10] However, these guidelines were published primarily for adults with acquired heart disease. The risk for CAD may differ in adults with congenital heart disease compared to the general population, in particular in patients that have long-standing secondary hypertension after aortic arch surgery, or in those that require coronary artery reimplantation at the time of cardiac repair.[2,3,5,11]

Furthermore, the optimal imaging modality for CAD screening in congenital heart disease patients is not clear.[12] Cardiac catheterization with coronary angiography is considered the gold standard. Whether noninvasive assessment with CTA may serve as a substitute for cardiac catheterization in low or intermediate risk CHD patients is unknown. Therefore, our study aim was to assess the results and outcomes of preoperative CAD screening in adults with CHD prior to cardiac surgery at our institution.

2 | METHODS

We identified all patients ≥35 years of age with congenital heart disease that underwent nonemergent cardiac surgery requiring cardiopulmonary bypass from the years 2007-2017. Data regarding their preoperative CAD risk and evaluation were collected. Data collected including details about the CHD diagnosis, coronary disease risk factors, preoperative coronary disease screening modality and results, and postoperative outcomes with regards to complications such as myocardial infarction. This study was approved by the Children's Hospital of Wisconsin Human Research Review Board and was conducted in accordance with all human research regulatory.

The decision to obtain preoperative imaging with either coronary angiogram or CTA was made at the discretion of the primary adult congenital cardiologist, and was based on the patient's age and CAD risk factors. CAD risk factors included hypertension, hyperlipidemia, diabetes mellitus, and tobacco-smoking history.

All CAD screening studies were performed within 3 months prior CHD surgery. Cardiac catheterizations with coronary angiograms were performed with standard protocols involving either femoral artery or radial artery access. CTAs were performed with a standard protocol utilizing a 64-Slice Computed Tomography Scanner with prospective cardiac gating and three-dimensional reconstruction. Severe CAD was defined as ≥70% stenosis of the coronary artery identified either on cardiac catheterization or CTA.

2.1 | Statistical methods

Data are presented as mean with standard deviation (SD) or number with percent of total. Statistical analysis was performed using Fisher's exact test for categorical outcomes and *t* test for continuous measures. Multivariate logistic regression analysis was performed to assess for risk factors for abnormal CAD screening. Known CAD risk factors, with $P < .2$ from univariate analysis, were entered into the regression as independent variables. The regression was performed with backward elimination. Statistical analyses were performed using SPSS Version 21.0 (Chicago, Illinois) with a $P < .05$ considered significant.

3 | RESULTS

We identified 100 patients ≥35 years old that underwent congenital cardiac surgery at our institution during the study period. Of these 100 patients, 73 underwent preoperative coronary screening with either cardiac catheterization or CTA at the discretion of the patient's primary cardiologist based on their age and presence of coronary disease risk factors. All of the 27 patients that did not undergo preoperative CAD screening were <40 years of age and had no traditional risk factors for CAD.

Table 1 shows the demographic characteristics, including the various congenital heart disease diagnoses, for the 73 patients that underwent preoperative CAD screening prior to their CHD surgery. The most common primary diagnoses were tetralogy of Fallot or pulmonary atresia with ventricular septal defect in 22%, atrial septal defect in 20%, congenital bicuspid aortic valve with a significant valve dysfunction in 14%, congenital pulmonary valve stenosis in 8%, and coarctation of the aorta in 6%. The most common surgery was pulmonary valve replacement in 32%, followed by closure of atrial or ventricular septal defect in 16% and aortic valve replacement and aortic root replacement both in 15%.

The median age at the time of cardiac surgery was 44 years (range = 35-68 years), and 53% were male. The median number of prior cardiac surgeries was 1 with a range from 0 to 6. Prevalence of CAD risk factors included hypertension in 27%, cigarette smoking in 21%, dyslipidemia in 18%, and diabetes mellitus in 5%.

Of the 73 patients that underwent preoperative CAD screening, the majority, 48 (66%), underwent cardiac catheterization with coronary angiography, while 25 patients, who were deemed to be lower risk for CAD, underwent preoperative CTA alone.

Table 2 summarizes the results of preoperative CAD screening. Of the 73 that underwent coronary imaging, 16 (22%) were found to have evidence of coronary artery disease. Of these 16, only 2 had severe CAD, defined as ≥70% stenosis of any coronary artery. These two patients subsequently underwent coronary artery bypass grafting at the time of their CHD operation. One of these two patients was a 62-year-old male patient with history of repaired tetralogy of Fallot and dyslipidemia, who underwent CAD screening with cardiac catheterization prior to an elective pulmonary valve replacement. He had no history of CAD symptoms, and his screening coronary angiogram demonstrated 90% stenosis of the proximal left anterior descending artery and 80% stenosis of the distal right coronary artery. The second patient with severe CAD was a unique case that had unrepaired tetralogy of Fallot who presented late at 59 years old with cyanosis and dyspnea. His

TABLE 1 Patient characteristics for 73 patients that underwent preoperative CAD screening prior to CHD surgery

Characteristic	Median (range) or number (%)
Median age at time of CHD surgery (years)	44 (35-68)
Male	39 (53%)
# prior cardiac surgery	1 (0-6)
Primary CHD diagnosis	
TOF or PA/VSD	16 (22%)
Atrial septal defect	15 (20%)
Bicuspid aortic valve	10 (14%)
Congenital pulmonary valve stenosis	6 (8%)
VSD or DORV	5 (7%)
Coarctation of the aorta ± bicuspid aortic valve	4 (6%)
Genetic aortopathy	4 (6%)
Coronary artery anomaly	3 (4%)
Ebstein anomaly	3 (4%)
Subaortic membrane	3 (4%)
Atrioventricular septal defect	3 (4%)
Transposition of the aorta (s/p arterial switch operation)	1 (1%)
Primary cardiac surgery performed	
Pulmonary valve replacement	23 (32%)
Septal defect closure	12 (16%)
Aortic valve replacement	11 (15%)
Aortic root replacement	11 (15%)
LVOTO repair	7 (10%)
Tricuspid valve repair/replacement	5 (7%)
Other	4 (5%)
CAD risk factors	
Hypertension	20 (27%)
Tobacco smoking	15 (21%)
Dyslipidemia	13 (18%)
Diabetes mellitus	4 (5%)

Abbreviations: CAD, coronary artery disease; CHD, congenital heart disease; DORV, double-outlet right ventricle; LVOTO, left ventricular outflow tract obstruction; PA/VSD, pulmonary atresia with ventricular septal defect; TOF, tetralogy of Fallot; VSD, ventricular septal defect.

baseline oxygen saturations were 88% at time of presentation. He did have a history of hypertension, dyslipidemia, and tobacco smoking, and his preoperative cardiac catheterization demonstrated 80% occlusion of the right main coronary artery.

The remaining 14 patients had milder degrees of CAD and did not undergo any coronary intervention at the time of their CHD surgery. There were no acute postoperative coronary complications in the cohort, including no postoperative myocardial infarctions or any other coronary events.

Table 2 also details the results of the subset of 25 patients that had only a preoperative CTA as part of their CAD screening. This modality was used in those patients that were considered low risk for CAD based on younger age and presence of no or only one coronary disease risk factor. In this subset, the majority, 84%, had no evidence of CAD, 16% had mild CAD, and no patients had severe CAD.

Table 3 displays the difference in prevalence of various risk factors in those patients that were found preoperatively to have CAD compared to those that did not. Patients who had CAD were significantly older at a mean age of 58.6 years, compared to 46.9 years in the group without CAD ($P < .001$). Patients with CAD were also significantly more likely to have history of hypertension, dyslipidemia, and tobacco smoking. Diabetes mellitus was more common in patients with CAD, but this was not statistically significant, likely due to low numbers of patients with this co-morbidity in our population. There was no relationship between CAD and underlying congenital heart disease, including no association with tetralogy of Fallot, bicuspid aortic valve, or coarctation of the aorta. Greater number of previous surgeries was also not a risk factor for CAD.

Table 4 shows the results of a multivariate logistic regression analysis, assessing for independent risk factors for CAD. Traditional risk factors including age, male gender, dyslipidemia, and smoking were significant risk factors for having abnormal preoperative coronary screening for CAD. There were no characteristics related to the underlying CHD that were risk factors for the presence of CAD in this cohort.

4 | DISCUSSION

We found that CAD was relatively common in our older CHD population undergoing nonemergent cardiac surgery. Preoperative screening identified CAD in 22% of patients in this cohort, but only 2.7% had severe CAD requiring coronary bypass grafting at the time of their cardiac surgery.

The prevalence of CAD in our study is similar to those reported from other single-center studies. Giannakoulas et al identified a prevalence of coronary artery disease in 14% of adults with CHD that underwent coronary angiography, of which 9.2% had "significant CAD" defined as >50% diameter stenosis.[2] However, unlike our study, the majority (71.2%) underwent coronary angiography due to symptoms or other concern for CAD, rather than just as part of preoperative screening. Giamberti et al reported, similar to our study, that only a relatively small percentage (4.3%) of adults with CHD required coronary artery bypass grafting at the time of CHD surgery at their institution; however, their overall results of preoperative CAD screening were not included in this study.[5]

Similar to these previous studies, we found that adults with CHD found to have CAD were more likely to have traditional CAD risk factors, rather than risk factors related to the underlying CHD.[3,6] For example, age, male gender, dyslipidemia, and tobacco smoking were strongly associated with CAD in our study cohort. A history of hypertension was a risk factor in univariate, but not in the multivariate

TABLE 2 Results of preoperative CAD screening with coronary angiogram performed either by cardiac catheterization or computed tomography

	Imaging modality		
CAD severity	Catheterization (*N* = 48)	CTA (*N* = 25)	Total (*N* = 73)
No CAD	40 (83%)	21 (84%)	61 (83.6%)
CAD present	12 (25%)	4 (16%)	16 (22%)
<Severe CAD	10	4	14
Severe CAD	2	0	2

Abbreviations: CAD, coronary artery disease; CTA, computed tomography coronary angiography.

TABLE 3 Comparison of the prevalence of various risk factors in patients with CAD and without CAD identified on preoperative screening

Risk factor	No CAD (*N* = 57)	CAD (*N* = 16)	*P* value
Mean age (years)	46.9 (±8)	58.6 (±6)	<.001
Age >50 years-old	36 (63%)	15 (94%)	.028
Hypertension	14 (25%)	10 (63%)	.007
Dyslipidemia	6 (11%)	11 (69%)	<.001
Tobacco smoking	7 (12%)	8 (50%)	.003
Male gender	26 (46%)	11 (69%)	.087
Diabetes mellitus	3 (5%)	2 (12.5%)	.3
≥1 prior CHD surgery	50 (88%)	12 (75%)	.25
Coarctation of the aorta	4 (7%)	0 (0%)	.57
Tetralogy of Fallot	14 (24.6%)	2 (12.5%)	.25
Septal defects (ASD, VSD, AVSD, DORV)	18 (32%)	5 (31%)	.62
Bicuspid aortic valve	9 (16%)	1 (6%)	.44

Abbreviations: ASD, atrial septal defect; AVSD, atrioventricular septal defect; CAD, coronary artery disease; CHD, congenital heart disease; DORV, double-outlet right ventricle; VSD, ventricular septal defect.

TABLE 4 Multivariate logistic regression analysis of associated risk factors for presence of coronary artery disease

Risk factor	Odds ratio	95% CI	*P* value
Dyslipidemia	8.1	1.4-47.7	.02
Tobacco smoking	13.3	1.5-44.7	.03
Male gender	20.8	1.4-310	.03
Age/year	1.27	1.08-1.51	.003

analysis. Hypertension is actually quite prevalent in adult patients with CHD, and is more common than in the general population with similar age and gender.[13,14] This higher prevalence especially in the younger patients in the cohort may have limited its ability to discriminate as a significant risk factor in the relatively older patients with CAD. Diabetes mellitus was surprisingly not a risk factor for CAD in our CHD cohort, but this may have been related to the low number of diabetic patients in our study population.

In our study, there was no association between congenital heart diagnosis and CAD. There is speculation that certain forms of CHD may have a higher predisposition for the development of CAD. For example, many CHD patients have abnormal or surgically reimplanted coronary arteries, such as those after aortic root replacement or arterial switch operation for transposition of great arteries. They are at higher risk for endothelial dysfunction and there is concern that they may develop CAD at a younger age.[15,16] Patients with coarctation of the aorta may develop hypertension at an earlier age than the general population, and potentially are also at risk for premature CAD.[17,18] In our study, history of coarctation of the aorta was not a significant predictor of CAD in our study. Analysis of other congenital heart diagnoses was limited given the small numbers, including only one patient that had transposition of the great arteries and history of arterial switch operation, who ultimately was not found to have CAD during screening prior to their CHD reoperation.

Previous studies have also suggested that cyanotic adult CHD patients have a decreased risk of atherosclerotic disease.[11,19] We only had one patient that was cyanotic at the time of CHD surgery, and thus were not statistically powered to assess for cyanosis as a risk factor. But interestingly, this cyanotic patient had unrepaired tetralogy of Fallot and actually was one of the two patients who had severe CAD that required coronary artery bypass grafting at the time of CHD surgery. However, he also had several traditional risk factors for CAD including older age, hypertension, dyslipidemia, and history of tobacco smoking.

In the subset of low-risk patients that underwent preoperative CTA, mild CAD was discovered in 12%, but no patients were found to have severe CAD that would require coronary intervention at the time of CHD surgery. CTA was performed in patients that were considered lower risk based on younger age and presence of <2 risk

factors for CAD, which is consistent with current ACC/AHA guidelines for valvular heart disease, and also explained the low prevalence of severe CAD in this subset. Unfortunately, there were no patients that obtained both CTA and coronary angiogram in this retrospective study, which would have allowed for an assessment of the predictive value of CTA for assessment of CAD in CHD patients. Future prospective studies that incorporate both CTA and coronary angiogram as part of pre-operative CAD screening may allow for a proper comparison between the two modalities in this population.

Nevertheless, our data support routine CAD screening prior to cardiac surgery in older adults with CHD. We feel it is reasonable to follow current ACC/AHA guidelines for preoperative CAD screening in patients with acquired heart disease. Based on these recommendations, CAD screening should be based on older age and presence of traditional coronary risk factors, including dyslipidemia, hypertension, diabetes mellitus, smoking, being postmenopausal for women, and family history of CAD. In addition, noninvasive CTA may be reasonable as a substitute for cardiac catheterization in low/intermediate-risk CHD patients.

This study is limited by its retrospective study design at a single center with relatively small sample size. As a tertiary care center, we may have a referral bias for complex patients with more comorbidities that may overestimate the prevalence of CAD in adults with CHD. And finally, invasive coronary angiogram is considered the gold standard for preoperative screening for coronary disease, and we did not have enough patients that underwent both CTA and catheterization to make a comparison between the two modalities to assess the predictive value of CTA in the assessment of coronary disease in CHD patients.

In conclusion, preoperative coronary imaging successfully identified a relatively high prevalence of CAD in asymptomatic adults referred for CHD surgery. However, the prevalence of severe CAD requiring concomitant coronary artery bypass grafting at the time of CHD surgery is low. It is reasonable to follow ACC/AHA Valvular Heart Disease Guidelines that recommend preoperative CAD screening based on age and traditional CAD risk factors. Noninvasive CTA may be considered in patients considered low/intermediate risk for CAD.

CONFLICTS OF INTEREST

None.

AUTHOR CONTRIBUTIONS

Research design, data acquisition, data analysis, interpretation of data, drafting the manuscript, and approval of the submitted and final versions of the manuscript: Bradley Johnson, Salil Ginde

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