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Outcomes after surgical coronary revascularization in children with congenital heart disease

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Abstract

Objective—Surgical coronary revascularisation in children with congenital heart disease (CHD) is a rare event for which limited information is available. In this study, we review the indications

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Contributors

KT and JMV were critical to the development of this research question and together wrote the majority of the original draft for this manuscript. BH served a major role in the collection and quality control of data, and he provided review of and edits to the manuscript based on this knowledge. JSM, MSK and AST conducted the data analyses and formulated the presentation of these results. Each of these three also contributed to the writing of the Methods section and provided critical review of the rest of the manuscript. A-MK collected data through extraction of information from PDF files for patients involved in this study and provided important insight into the interpretation of results. JHM, JDSL and LKK were instrumental in the PCCC study design, maintenance and linkage with other datasets. They each provided expertise in database knowledge as well as clinical perspectives in the formulation of this research question, interpretation of findings and the final presentation of results.

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and outcomes of surgical coronary revascularisation from the Pediatric Cardiac Care Consortium, a large US-based multicentre registry of interventions for CHD.

Methods—This is a retrospective cohort study of children (<18 years old) with CHD who underwent surgical coronary revascularisation between 1982 and 2011. In-hospital mortality and graft patency data were obtained from the registry. Long-term transplant-free survival through 2014 was achieved for patients with adequate identifiers via linkage with the US National Death Index and the Organ Procurement and Transplantation Network.

Results—Coronary revascularisation was accomplished by bypass grafting (n=72, median age 6.8 years, range 3 days–17.4 years) or other operations (n=65, median age 2.6 years, range 5 days–16.7 years) in 137 patients. Most revascularisations were related to the aortic root (61.3%) or coronary anomalies (27.7%), but 10.9% of them were unrelated to either of them. Twenty in-hospital deaths occurred, 70% of them after urgent ‘rescue’ revascularisation in association with another operation. Long-term outcomes were available by external linkage for 54 patients surviving to hospital discharge (median follow-up time 15.0 years, max follow-up 29.8 years) with a 15-year transplant-free survival of 91% (95% CI 83% to 99%).

Conclusions—Surgical coronary revascularisation can be performed in children with CHD with acceptable immediate and long-term survival. Outcomes are dependent on indication, with the highest mortality in rescue procedures.

INTRODUCTION

Surgical coronary artery revascularisation procedures are performed in infants and children for a range of conditions including congenital coronary artery anomalies (CCAA) with or without structural congenital heart disease (CHD)^{1–6} and iatrogenic coronary artery injury during other cardiac procedures.^{7–11} The latter is particularly common in the presence of anomalous pattern of coronary arteries.¹² In addition, late coronary abnormalities have been reported in about 5% of patients who underwent arterial switch operation (ASO).¹⁰

Paediatric coronary revascularisation can be accomplished with low early mortality using coronary artery bypass grafting (CABG) or other forms of surgical coronary arterioplasty.^{8,9,13–19} Mid-term and long-term results of the different revascularisation modalities are, however, limited.¹⁶ This is particularly true for younger patients undergoing coronary revascularisation for a surgical indication associated with CHD (rather than secondary to Kawasaki disease or post-transplant coronary vasculopathy).

We, therefore, evaluated the indications, procedure types, in-hospital mortality and long-term outcomes for paediatric coronary artery revascularisation procedures reported in the Pediatric Cardiac Care Consortium, a large, multi-institutional US-based registry²⁰ using linkage with national registries to identify late mortality or cardiac transplantation.

METHODS

Study population

This is a retrospective, cohort study of patients undergoing coronary revascularisation surgery (CABG or non-CABG) in paediatric cardiac centres reporting their outcomes in the

Pediatric Cardiac Care Consortium. The Pediatric Cardiac Care Consortium was formed in 1982 and contains information on all cardiac procedures—including operations and cardiac catheterisations—performed at 47 centres in the USA. The patient-specific longitudinal follow-up within the registry is invaluable when assessing long-term outcomes after operative interventions for rare conditions. Characteristics of the Pediatric Cardiac Care Consortium have been previously reported.²⁰ We restricted our analysis to only the first coronary revascularisation procedure reported for each patient. We disqualified patients with first revascularisation outside the Pediatric Cardiac Care Consortium, operations in adulthood (>18 years) or patients with non-congenital causes of coronary disease (vasculitis including Kawasaki disease, allograft vasculopathy after cardiac transplantation, primary metabolic/lipid disorders). We also excluded percutaneous coronary intervention, as this was predominately used for non-congenital indications in the registry.

Clinical variables and follow-up data

Data available within the Pediatric Cardiac Care Consortium included age at operation, sex, type of procedure, cardiac diagnosis, previous cardiac operations, presence of major non-cardiac malformations or conditions, vital status at hospital discharge and target vessel patency information if follow-up catheterisation or reoperation was performed within the Pediatric Cardiac Care Consortium. We defined obstruction as reported by the individual centres, using a cut-off of greater than 50% stenosis. Although a cut-off of 80% is more common in adult atherosclerotic coronary disease, we believe a lower threshold is reasonable for children, as moderate stenosis is more likely to be haemodynamically significant in smaller vessels. For US residents with adequate available identifiers, transplant-free survival through 2014 was ascertained by linkage to the US National Death Index (NDI)^{21,22} and the Organ Procurement and Transplantation Network (OPTN) registry.^{22–24} The OPTN data system includes data on all donor, wait-listed candidates and transplant recipients in the USA, submitted by its members. The Health Resources and Services Administration, US Department of Health and Human Services, provides oversight to the activities of the OPTN contractor. Race and ethnicity data were not consistently available across datasets.

Indications were classified broadly as: (1) CCAA, (2) CHD involving aortic root surgery and (3) other. Procedures were divided into three categories by the relative timing of coronary revascularisation: (1) *primary* coronary revascularisation when the coronary revascularisation was performed as part of the planned surgical strategy for patients with congenital structural coronary anomaly (such as anomalous coronary artery origin or congenital ostial stenosis), (2) *rescue* when the revascularisation was unplanned, performed during or within the same hospitalisation as another surgical procedure and (3) *late* when performed on a background of a previous procedure (other than coronary revascularisation) but with the two procedures occurring in separate hospitalisations independent of time between the operations.

Normality of continuous variables was assessed using histograms, normal probability plots and the Anderson-Darling test for normality. Descriptive statistics are presented as counts and percentages for categorical variables and median with IQR or total range for continuous

data with skewed distribution. Relative risks (RRs) with associated 95% CIs were calculated using a log-binomial model (PROC GENMOD) for each separate exposure. Comparisons between categorical variables were performed using the χ^2 test or Fisher's exact test when expected cell counts were <5. Kaplan-Meier survival plots were constructed to display long-term survival data, with statistical comparisons performed using the log-rank test. Statistical significance was assessed at the 0.05 level. Statistical analyses were performed using SAS V. 9.4.

RESULTS

Patient characteristics

Between 1982 and 2011, a total of 132 048 cardiac surgical operations were reported in 94 690 paediatric patients (<18 years) within the Pediatric Cardiac Care Consortium. Among them, 137 children were identified with CHD and first coronary revascularisation performed surgically within the Pediatric Cardiac Care Consortium per inclusion criteria (figure 1). These patients comprise the study cohort (median age at time of coronary revascularisation: 4.4 years, range: 3 days to 17.4 years). Of these, 39 patients had revascularisation within the first year of life including 12 neonates. The detailed patient characteristics by procedure type (CABG or non-CABG surgery) are displayed in tables 1 and 2.

Indications and timing of coronary revascularisation

Most of the coronary revascularisation procedures were performed in association with operations involving the aortic root (61.3%) (table 1, figure 2A). These included ASOs, aortic valve surgery, supraaortic stenosis (often with Williams syndrome) and proximal aortopulmonary anastomosis (Dams-Kaye-Stansel (DKS) anastomosis or Norwood procedure). Other common indications were various forms of CCAA (27.7%), including anomalous coronary origin from the pulmonary artery or from the aorta. A minority (10.9%) of revascularisation procedures were associated with procedures not directly involving the aortic root or the coronary arteries (online supplementary table 1). Primary revascularisation was performed in 38.9% of patients, while all others were performed due to sequelae of congenital heart surgery, either early (ie, rescue procedures) or late (figure 2B).

The crude incidence of surgical coronary revascularisation was 0.80% (30/3727) among patients undergoing ASO, 0.75% (29/3869) among patients with aortic valve replacements/valvoplasty, 0.08% (3/3805) for DKS/Norwood procedures and 0.02% (19/82 772) among all other paediatric cardiac operations in the Pediatric Cardiac Care Consortium. The operative reports for patients with prior CHD surgery variably reported usage of antegrade and/or retrograde cardioplegia, however no association was found between the coronary complications and the type of cardioplegia (data not shown).

Types of intervention

CABG was the most common type of revascularisation procedure (n=72; 85 individual grafts) in the Pediatric Cardiac Care Consortium (online supplementary table 2). The left coronary arterial system was targeted in 55 patients (76.4%), the right in 15 (20.8%) and

both coronary arterial systems in 2 patients (2.8%). A single graft was used in 62 patients (86.1%); 10 patients received multiple grafts at the same operation (two grafts each, except one patient with three grafts and one with four grafts). Inclusively, 66 grafts (77.6%) were arterial grafts and 19 (22.4%) were saphenous vein grafts.

Non-CABG surgery was most often some form of arterioplasty with/without patch augmentation involving the ostium, lumen or both (n=51, 78%). Other procedures were coronary reimplantation/transfer (standard reimplantation during ASO is not counted here; n=9), unroofing of an intramural coronary artery (n=4) and intraoperative stent placement (n=1).

Early outcomes

Early outcome is defined as survival to hospital discharge according to Pediatric Cardiac Care Consortium records.

In-hospital mortality after coronary revascularisation was 14.6% (20 of 137 patients), with 18.1% in the CABG group and 10.8% in the non-CABG ($P=0.228$). The most important risk factor for in-hospital mortality was rescue coronary revascularisation (29.8% in-hospital mortality), with an RR of rescue versus primary of 7.9 (95% CI 1.9 to 32.9, $P<0.005$). Univariate models showed duration of cardiopulmonary bypass was also associated with increased risk of in-hospital mortality (data not presented), but likely a marker for an adverse intraoperative course leading to the need for rescue coronary revascularisation, rather than directly causal. Additional variables considered were sex, age at surgery, weight at surgery and surgery type but none were found to be significant. In-hospital mortality did not occur in patients having coronary revascularisation as primary therapy for congenital coronary anomalies (0 of 27 patients), and was very low for late revascularisation procedures of any cause (3 of 27 patients) (figure 3).

Long-term follow-up

Of the 93 patients potentially eligible for linkage to NDI and United Network for Organ Sharing (UNOS), 77 were discharged alive after coronary revascularisation. Of them, a subcohort of 54 (70%) patients had adequate identifiers for submission to the NDI and UNOS. The availability of adequate identifiers was not associated with any significant differences in clinical characteristics between the groups with/without adequate identifiers (online supplementary table 3). Of the patients with NDI/UNOS follow-up data after hospital discharge, three underwent heart transplant and four died without transplant (two from heart failure and two from pneumonia). The 15-year transplant-free survival of this subcohort was 90.7% (95% CI 83.2% to 98.8%) over a median follow-up period of 14.9 years (maximum 29.8 years) (figure 4). The median age of the surviving cohort at the end of the follow-up period was 20.7 years (maximum 43.6 years). Despite initial mortality attrition in rescue procedures, long-term outcomes after discharge were similar to patients with primary and late procedures ($P=0.90$). There were no significant differences in in-hospital or overall survival between patients undergoing CABG or non-CABG surgery ($P=0.28$) (figure 5). Overall long-term follow-up status (figure 4) and on an individual basis for the entire cohort, as a function of age at revascularisation, are shown in online supplementary figure 1.

Targeted vessels patency

Because of the observational study design and nature of the Pediatric Cardiac Care Consortium, angiographic long-term patency follow-up data were available only for 25 patients (17.5%) returning for a subsequent diagnostic catheterisation at a participating centre (online supplementary table 2). Of the patients with available angiographic follow-up, 10 had partial or total occlusion of at least one revascularised vessel. Four of 10 underwent additional revascularisation procedures, four received a heart transplant and one had an internal defibrillator placed. The graft/vessel patency for those with follow-up was 58% for CABG after a median 15.6-year (range 6.8–29.8 years) follow-up and 63% for non-CABG after a median 10.3-year (range 1.4 months–16.9 years) follow-up. However, the patency percentage calculations reflect substantial selection bias as performance of follow-up angiography is targeted at patients with risk factors for, or clinical evidence of, occlusion.

DISCUSSION

Coronary artery revascularisation is a rare surgical procedure in children with CHD, but can be used in select cases either as part of the primary surgical strategy or in cases with coronary artery compromise as a result of another surgical procedure.

Such compromise can occur for various reasons, including narrowing at suture lines, kinking after reimplantation, ostial stenosis and iatrogenic injury to the coronary arteries during surgical manipulations including application of cardioplegia.²⁵

In this study, we linked the Pediatric Cardiac Care Consortium, a long-standing multi-institutional registry for paediatric cardiac interventions, with the NDI and UNOS datasets to study a rare procedure cross-nationally and address challenges of longitudinal follow-up. By integrating data from these sources, we are able to report incidence, indications and early/late outcomes for a large cohort of children with coronary reperfusion procedures associated with operations for CHD.

CABG and non-CABG procedures were performed almost equally for initial paediatric coronary revascularisation in our dataset. Most revascularisations in the Pediatric Cardiac Care Consortium were either rescue or late procedures to address iatrogenic sequelae of operations performed for other cardiac anomalies. Expectedly, most of these operations involved the aortic root. Among them, ASO was one of the leading conditions associated with coronary revascularisation, although our incidence of coronary compromise was less than previously reported (3%–11%).¹⁰¹⁶²⁶²⁷ This likely reflected only a subset of patients with coronary compromise (only those who had sufficiently severe compromise yet also viable chance of recovery) who were offered surgical intervention. Interestingly, a substantial minority of coronary revascularisation was prompted by coronary compromise during or after other CHD surgery not expected to involve the proximal aortic root.

In our study, the overall in-hospital mortality was 14.6%, comparable with previous reports,^{16–18} despite our young patients with a potentially more severe case mix (all had CHD, many requiring rescue revascularisation). Poor outcomes of rescue procedures may be related to the severity of the underlying condition, myocardial injury from coronary

compromise or non-cardiac effects of prolonged or repeated cardiopulmonary bypass exposure when revascularisation was required during/soon after the initial CHD operation. This is consistent with a previous report from a European multicentre study.¹² For patients who survived to discharge, long-term survival was similar after rescue and non-rescue procedures.

Since the substrate of coronary ischaemia in children differs from adults, the main question regarding the use of coronary revascularisation (in particular of CABG) in children remains the long-term durability when performed at a young age. Reasons for concern regarding long-term outcomes include technical challenges related to the small size of the targeted vessels and the frequent coexistence of a competitive source of flow in the case of CABG.²⁸ To maximise long-term follow-up, Pediatric Cardiac Care Consortium data were supplemented with linkage to the NDI and UNOS datasets, identifying deaths and heart transplantation beyond the postoperative period. With a median follow-up period of 15 years (double the longest follow-up time in previous studies), our data provide reassurance about the durability of the procedure in young children.

The observed 15-year patency rate of 58% for CABG and 62.5% for non-CABG in the subcohort with angiographic follow-up is similar to the 65% reported in a similar cohort after 7.6 years of follow-up,¹² although the true patency rate in our study may be underestimated (low-risk and asymptomatic patients are less likely to have follow-up angiography). Conversely, it is also possible that some of the long-term survivors have established coronary collaterals bypassing an area of stenosis. In adults, long-term predictors of patency include the use of arterial versus venous grafts and larger size of targeted vessel.²⁹ We also found that the patency of arterial grafts was greater than venous grafts but this difference could not be addressed statistically due to the small number of angiographic follow-up. For the same reason, we cannot reach conclusions about the effect of target vessel size.

Regarding the potential impact of competitive coronary blood flow, we found no disadvantage of CABG compared with non-CABG revascularisation in either the early or late mortality rates, although differences in case mix limit the validity of direct comparison between the two modalities.

Strengths and limitations

The major strength of our study is access to one of the largest available databases for paediatric cardiac operations; even so, coronary revascularisation remains rare enough to preclude detailed multivariable analysis. The observational and procedure-focused nature of the Pediatric Cardiac Care Consortium limits clinical follow-up data to those patients undergoing catheterisation or reoperation within the Pediatric Cardiac Care Consortium. However, linkage with the NDI and UNOS datasets provides us with robust, long-term transplant-free survival data. Despite their limitations, these nationwide registries are the best available sources for determining long-term outcomes in the USA. We previously showed that for Pediatric Cardiac Care Consortium patients with a complete set of identifiers, sensitivity of NDI/UNOS matching reached 88.1% and 89.7% for mortality and transplantation, respectively.²²

Other limitations include the lack of direct information regarding patency of the reperfused coronary arteries in the survivors and the potential for referral bias due to the paediatric orientation of centres (older children needing late coronary revascularisation may be managed at adult centres outside the Pediatric Cardiac Care Consortium).

Despite these limitations, to our knowledge, this study is the largest and longest reported series of coronary revascularization procedures in children with CHD and has more than 15 years of follow-up for these rare but potentially lifesaving procedures.

Conclusion

Coronary revascularisation procedures are rare in children and are mostly performed for iatrogenic sequelae of procedures involving the aortic root. Both CABG and non-CABG revascularization surgeries can be successfully performed throughout the age spectrum and with acceptable immediate and long-term outcomes, although in-hospital mortality after urgent rescue revascularisation is substantial.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key messages**What is already known on this subject?**

Compromise of coronary perfusion is a rare but serious condition in children with congenital heart disease (CHD) and often prompts consideration of surgical revascularisation by coronary artery bypass grafting or other operations. The short-term outcomes from these procedures are reported to be favourable but the long-term outcomes are less well studied.

What might this study add?

Early survival after surgical revascularisation in children with CHD was 100% for primary coronary revascularisation, 88.9% for planned procedures for late complications of other congenital heart surgery, but only 70.2% when revascularisation is done urgently due to acute coronary mishappenings. Regardless of the original circumstances, 15-year survival after discharge is 91% which is promising considering the challenging nature of these cases.

How might this impact on clinical practice?

Detailed preoperative delineation of coronary artery anatomy, heightened awareness of indicators of perioperative coronary malperfusion, planning for coronary reperfusion and back-up strategies in high-risk cases may be helpful to decrease the need for high-risk coronary rescue procedures in patients with CHD.

Figure 1.

Patient flow diagram describing inclusion cohort and long-term cohorts. CABG, coronary artery bypass grafting; HIPAA, Health Insurance Portability and Accountability Act; NDI, National Death Index.

Figure 2.

Distribution of revascularisation procedure indications and timing within age group. (A) Distribution of indications for coronary revascularisation by age group. (B) Distribution of timing of coronary revascularisation by age group. Diagonal lines indicate deaths. CCAA, congenital coronary artery anomalies; yr, years.

Figure 3. Summary of early and late outcomes by timing of revascularisation surgery. (A) Early outcome in the overall cohort. (B) Early, late and overall outcomes in the group eligible for long-term follow-up analysis. Early outcome indicates transplant-free survival to hospital discharge and is completely ascertained. Late outcome indicates 15-year transplant-free survival among those alive at hospital discharge. Overall outcome indicates 15-year transplant-free survival including in-hospital mortality. Teal colour indicates survival >90%, blue 75%–90% and light brown <75%. CHD, congenital heart disease.

Figure 4.

Kaplan-Meier plot of transplant-free survival after surgical coronary revascularisation. Long-term transplant-free survival among those alive at hospital discharge. +Censor, indicates the end of follow-up time for an individual subject at each crosshair ; Tx, heart transplant

Figure 5. Overall transplant-free survival by revascularisation type, including in-hospital mortality. CABG, coronary artery bypass grafting.

Table 1

Indications and therapeutic approaches for coronary revascularisation surgery

Type of intervention	Primary (n=53)		Rescue (n=47)		Late (n=37)		Total (n=137)
	CABG	Non-CABG	CABG	Non-CABG	CABG	Non-CABG	
CCAA	14	13	2	-	8	1	38 (27.7%)
Aortic root procedures	4	22	17	16	17	8	84(61.3%)
Williams/supra-AS	4	10	1	5	1	1	22(16.1%)
Arterial switch	-	2	8	4	11	5	30(21.9%)
Aortic valve surgery *	-	9	6	7	5	2	29(21.2%)
DKS or Norwood	-	1	2	-	-	-	3(2.2%)
Other procedures	-	-	9	3	1	2	15(10.9%)
Total	18	35	28	19	26	11	137

* Aortic valve surgery comprises aortic valve repair or replacement, including pulmonary autograft (Ross procedure).

CABG, coronary artery bypass grafting; CCAA, congenital coronary artery anomalies; DKS, Damus-Kaye-Stansel procedure.; Williams/supra-AS, Williams syndrome/supravalvar aortic stenosis.

Table 2

Patient characteristics by primary procedure type

Patient characteristic	All patients	CABG	Non-CABG
Total (%)	137(100)	72 (52)	65 (48)
Sex (%)			
Male	86 (62.8)	41 (57)	45 (69)
Female	51 (37.2)	31 (43)	20(31)
Median age (range)	4.4 years (3 days–17.4 years)	6.8 years (3 days–17.4 years)	2.6 years (5 days–16.7 years)
Median weight (kg) [*] (range)	13.5(2.3–106.0)	22.5(2.8–106.0)	9.7 (2.3–80.0)
Centres	48	30	28

^{*} One patient was omitted from median calculation due to missing weight data.

CABG, coronary artery bypass grafting.