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Comparison of Outcomes of Repair of Complete Atrioventricular Canal Defects before and After 3 Months of Age: A Meta-Analysis

Awori Mark[1]*, Awori Jonathan[2], Mwachanya Edmond[1] and Awori Isaiah[1]

[1]*Department of Surgery, School of Medicine, University of Nairobi, P.O. Box 19676-00202, Nairobi, Kenya.*

[2]*Texas Children's Hospital, Baylor College of Medicine, 6621 Fannin St, Houston, Texas 77030, USA.*

***Correspondence:**
Mark N Awori, Department of Surgery, School of Medicine, University of Nairobi, P.O. Box 76996-00620, Nairobi, Kenya, Mobile No: +254707366336.

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ABSTRACT

Objectives: *It is generally accepted that the ideal age for repair of a complete atrioventricular canal defect (CAVCD) is between 3 to 4 months of age. Patients presenting at younger than 3 months of age, with heart failure despite optimal medical therapy, are generally offered repair too. However, there remains a concern that the outcomes are inferior to repair in patients older than 3 months of age. We aimed to determine if repair before 3 months of age results in inferior outcomes to repair after 3 months of age.*

Method: *Google Scholar and PUBMED were searched between January 1st 2000 and February 10th 2025. A meta-analysis was conducted after pragmatically minimising patient and method heterogeneity: operative mortality and a composite outcome of 'more than' moderate post-operative left atrioventricular valve (LAVV) regurgitation or re-operation for LAVV regurgitation were analysed.*

Results: *Four studies representing 2741 patients were included for the operative mortality analysis: 405 were 3 months old or less; 2336 were older than 3 months. The operative mortalities were 7.9% and 2.0% for repair at less than 3 months of age and more than 3 months of age respectively. Odds Ratio for operative mortality at a younger age was 4.63 (2.93; 7.31). Three studies representing 285 patients were included for the LAVV outcome analysis: 71 were 3 months old or less; 214 were older than 3 months. Odds ratio for 'more than' moderate LAVV regurgitation or re-operation for LAVV regurgitation after repair at a younger age was 1.78 (0.83; 3.78).*

Conclusions: *There was a significantly greater operative mortality in patients repaired prior to 3 months of age; however, the quality of LAVV function was not significantly different.*

Keywords

Complete atrioventricular canal defect, AV canal defect repair, Early vs late surgical repair, Pediatric cardiac surgery, Congenital heart defects.

Introduction

Atrioventricular canal defects (AVCDs) have a prevalence of 0.3 per 1000 live births [1]. They represent 3% of all congenital heart disease (CHD) and are complete (CAVCD) in 50 to 70% of patients. The first repair of a CAVCD was conducted by Lillehei in 1955 [2]. The operative mortality has fallen from 17.6% in the 1970's to 5% in the 1990's [3]. A large database study in 2014 reported an operative mortality of 3% [4]; a large single centre study in 2021 reported an operative mortality of 1% [5]. CAVCDs are usually repaired between 3 to 4 months of age. There have been reports of higher operative morbidity/mortality and more frequent significant ('more-than-moderate') left atrioventricular valve regurgitation (LAVVR) in patients repaired earlier than 3 months of age [4,5]. Despite this, repair of patients who require surgical intervention prior to 3 months of age (because of heart failure and failure to thrive, while on optimum medical treatment), is preferred to pulmonary artery banding and delayed repair [6]. It remains unclear whether repair before 3 months of age is associated with inferior outcomes; we aimed to clarify this.

Method

In accordance with the PRISMA-P checklist [7], PUBMED (PM) and Google Scholar (GS) were searched between January 1st 2000 and February 10th 2025. The search protocol is shown in Table 1. This search era was chosen as by 2000, contemporary CAVCD repair outcomes were likely achievable [3]. PM searches employed the "title/abstract" option; GS searches employed the "all in title" option; all searches used the "AND" function. Titles and abstracts were reviewed; full-text papers were read when an abstract suggested that a paper might contain data comparing outcomes of repair before and after 3 months of age. Only Human studies written in English were included. Figure 1 represents the search flow. Patients were considered to have had repair before 3 months of age if they were part of a group designated repair 'at' or 'before' 3 months of age (+/- 0.5 months). The meta-analysis was conducted using 'Meta-Mar' free online meta-analyser [8]. To avoid the introduction of arbitrary bias, studies with 'zero-events' in any arm were not included. The I2 statistic was used to assess heterogeneity [9].

Table 1: Search strategy.

Search	Strategy
1.	GS: allintitle; complete, atrioventricular, septal
2.	GS: allintitle; complete, atrioventricular, canal
3.	PM: title/abstract; complete, atrioventricular, three, months

Key: GS=Google Scholar; PM= Pubmed.

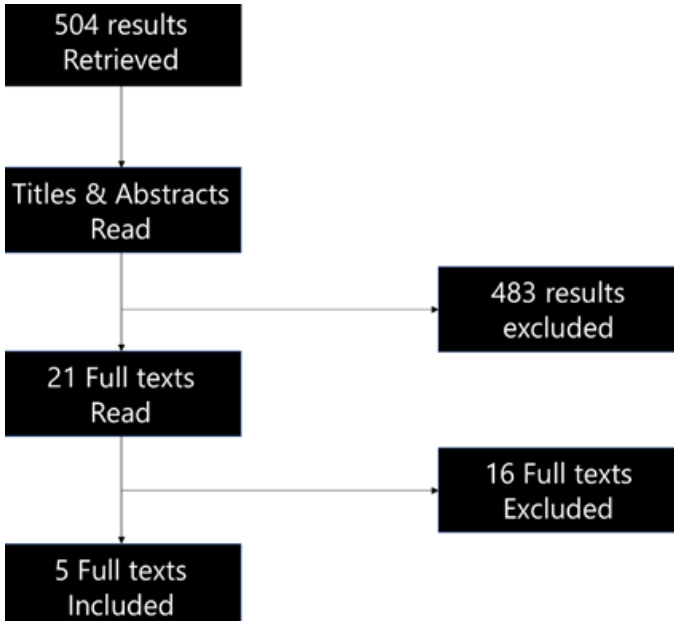

Figure 1: Search flow diagram.

Results

Our search returned 504 results; 21 full-text papers were reviewed. Five papers, representing 3,045 patients, were included in our meta-analysis; the key details of the studies included are summarised in table 2. The results of the operative mortality and LAVVR/LAVV re- operation meta-analysis are shown in Figures 2 and 3 respectively.

Table 2: Full-text papers included in the meta-analysis.

Author	Year	Study Type	Age < 3 months N(OM)	Age > 3 Months N(OM)	Age < 3 Months N (LAVVR/RO)	Age > 3 Months N (LAVVR/RO)	LAVV variable assessed in study
Ramgren (5)	2020	NRCT	-	-	7(1)	74(4)	Re-operation
Stephens (10)	2015	NRCT	38(3)	101(1)	38(4)	101(7)	Re-operation
St. Louis (4)	2014	NRCT	284(26)	2115(44)	-	-	-
Xie (11)	2014	NRCT	57(1)	81(1)	-	-	-
Singh (12)	2006	NRCT	26(2)	39(1)	26(1)	39(1)	Regurgitation

Key: LAVV= left atrioventricular valve; LAVVR/RO = left atrioventricular valve regurgitation or re-operation for regurgitation; NRCT=not randomised controlled trial; OM=operative mortality.

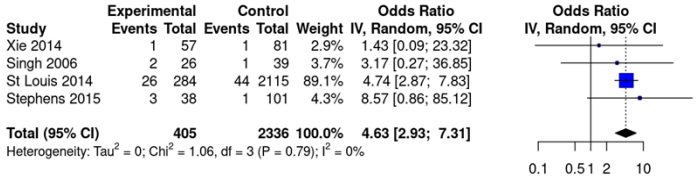

Figure 2: Forest plot for mortality meta-analysis.

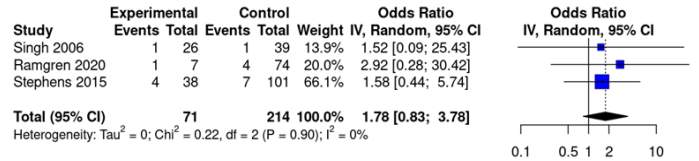

Figure 3: Forest plot for composite end-point of LAVVR (more-than-moderate) or re- operation on the LAVV.

Conclusions

Our meta-analysis found that the operative mortality (OM) was significantly higher in patients who had repair under 3 months of age; the Odds Ratio was 4.63. Based on this: if we assume an OM of about 2% in patients repaired over 3 months of age [4]; the operative mortality in patients repaired under 3 months of age would be 8.6%. To our knowledge, this is the first time that the difference in operative mortality as been quantified by performing a meta-analysis on pragmatically homogenous data. Our results likely represent the current best available evidence with regards to the relationship between OM and age at surgery.

According to natural history data, 30% of patients with CAVCD die before 3 months of age [13]. It is comforting to know that although surgery prior to 3 months of age has a higher operative mortality, it remains significantly lower than the natural history mortality. Patients having repair prior to 3 months of age are generally likely to be sicker (heart failure) than those who have repair older than 3 months. It remains unclear whether this is the main reason for the increased OM or whether other factors such as patient age or increased technical difficulty of operating on 'smaller' hearts is

responsible. A relatively large study that performed a multivariable analysis to examine the effect of patient age at repair (mean age in early repair group; 1.6 months), found that age at surgery was not a risk factor for OM [5]. It seems likely that this increased OM is due to greater preoperative morbidity.

There has been concern that fragility of LAVV tissue in patients under 3 months of age, compromises early repair [4]. The reports in the literature regarding the status of valve function post-repair or re-operation rates for unacceptable LAVVR are equivocal [4,10]. LAVVR that is 'more-than-moderate' is generally considered an indication for re-operation: to obtain as large a population as possible for analysis, without introducing heterogeneity, we choose a composite endpoint of 'more-than-moderate' LAVVR or re-operation for LAVVR. The results of our meta-analysis show that there was no significant difference in this composite endpoint between repair prior to 3 months of age and repair after 3 months of age. These findings are consistent with the results of two large studies that performed a multivariable analysis to examine the relationship between age at surgery and LAVVR or re-operation for LAVVR [10]. This is reassuring and taken together with our OM analysis results strengthens the argument for early repair when this is indicated.

Our study has some limitations. We did not factor in the 'surgical technique' into our analysis. With respect to surgical technique there are two areas of concern: technique for atrial septal defect (ASD)/ventricular septal defect (VSD) closure and whether to close the mitral cleft. There are two common techniques for CAVCD repair (ASD/VSD closure): the 'single-patch' technique and the 'two-patch' technique; available evidence suggests that short-term and long-term outcomes are equivalent [14,15]. In terms of cleft closure, evidence suggests that it does not matter whether the cleft is left open or closed [16]. Based on this evidence, we do not think that failure to account for 'surgical technique' has significantly affected the results our meta-analysis. Conclusions about the longevity of adequate LAVV function, cannot be reached from the results of our meta-analysis. Finally, we did not examine post-operative management protocols; for example, the use of extracorporeal membrane oxygenation (ECMO). However, we do not think that this compromised our analysis.

In conclusion, the results of our meta-analysis suggest that repair of CAVCD prior to 3 months of age is associated with a higher operative mortality but the function of the LAVV is not compromised. Our results support the argument that early CAVCD repair does not lead to inferior LAVV function. Our findings support the safety of early repair when medically necessary, but further research is needed to refine risk stratification.

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