

Comparison of extracardiac conduit and lateral tunnel for functional single-ventricle patients: A meta-analysis

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Abstract

Objective: This study aims to assess and compare the early and long-term effects of extracardiac conduit (EC) and lateral tunnel (LT) in patients with a functional single ventricle through meta-analysis.

Design: A systematic search was performed in PubMed, Embase, Cochrane Library, CNKI, VIP, CBM, and WanFang databases for papers that were published until August 1, 2016. Cochrane systematic review method was used for paper screening and information retrieve, and RevMan 5.3 software was applied for the meta-analysis.

Results: Data for 10 studies with a total of 3814 patients were retrieved. The advantages of EC comparing to LT include: lower 30 day postsurgery supraventricular arrhythmia incidence (Relative Risk [RR] = 0.31 [0.17, 0.55], $P < .001$), lower protein loss enteropathy incidence (RR = 0.33 [0.11, 0.96], $P = .04$), and requiring no cardiopulmonary bypass. However, the chest drainage time was longer (mean difference [MD] = 1.99 [1.83, 2.15], $P < .001$) in EC. There were no significant differences in early postoperative mortality, long-term mortality, long-term arrhythmia, Fontan takedown, ventilator-assisted ventilation, ICU stay, thrombosis, pleural effusion, and pericardial effusion between EC and LT.

Conclusions: EC had a lower incidence of supraventricular arrhythmia (30 days after operation) and the rate of protein losing enteropathy than LT, and requiring no cardiopulmonary bypass. These show that EC has an advantage over the LT in patients with a functional single ventricle.

KEYWORDS

extracardiac conduit, Fontan procedure, functional single ventricle, lateral tunnel

1 | INTRODUCTION

Fontan procedure is a palliative surgical procedure first used in the treatment of tricuspid atresia in 1968.¹ Today, the Fontan procedure and its modifications are standard palliation in patients with single ventricle physiology. Extracardiac conduit (EC) and lateral tunnel (LT) are the 2 mostly used Fontan procedures for total cavopulmonary connection (TCPC).² EC directly connects the inferior vena cava and the pulmonary artery through an external canal; while LT uses artificial blood vessels or pericardial flap to drain the blood from inferior vena cava to the superior vena cava, along the longitudinal ridge in the atrium.³ The EC approach is relatively easy to perform and it can be performed in

constrained anatomical conditions even during heart beating; and it requires less atrial suture lines, shorter aortic occlusion time, and shorter extracorporeal circulation time.^{4–6} However, EC operation has the disadvantages of poor fenestration condition, poor matching of tube graft after patient has grown up that caused by lack of growing potential of artificial blood vessels or allogeneic blood vessels, and may require reoperation in some cases.⁷ In the LT approach, the advantages are the growing potential and the simple fenestration procedure, which can be clinically difficult on EC (especially for the patency).⁸ Fenestration on the LT barrier is suggested to reduce postoperative complications, such as postoperative low cardiac output, pleural effusion, pericardial effusion, ascites, and protein loss enteropathy (PLE).^{9,10}

However, the atrial incision and excessive suture lines in the atrium may increase the incidence of postoperative arrhythmia.^{11,12} The thin layer of atrial tissue may lead to atrial bulging and deterioration of hemodynamics in the context of high pressure blood flow.¹³ The EC and LT Fontan operations are different in their advantages and disadvantages.^{14,15} In this study, we aimed to systematically analyze and evaluate the effect of EC and LT on patient with a functional single ventricle, in terms of early postoperative mortality, long-term mortality, and complications.

2 | METHODS

2.1 | Searching strategy

A systematic search was performed in PubMed, Embase, Cochrane library, CNKI (China national knowledge infrastructure), VIP (China Science and Technology Journal Database), WanFang database for papers that were published until August 1, 2016. "Fontan," "modified Fontan," "total cavopulmonary connection," "intracardiac lateral tunnel," "intra-atrial tunnel," "lateral tunnel," "extracardiac conduit" were used as search terms.

Search strategy of combined text and MeSH terms was performed depending on the requirement of databases. Corresponding authors were contacted by telephone or emails for supplemental information when necessary.

2.2 | Inclusion and exclusion criteria

All cohort studies or case-control studies were included. Patients with complex congenital heart diseases in need of surgical intervention were included, without restrictions on the age, race, nationality, or sex. EC was considered as experiment group and LT as control group regardless of intraoperative fenestration or surgery staging. The outcomes included: (1) mortality rate: early mortality, long-term mortality, and Fontan takedown; (2) surgical-related events: extracorporeal circulation time, aortic occlusion time, mechanical ventilation time, chest tube drainage time, intensive care unit (ICU) time, total hospital stay; (3) surgical complications, such as arrhythmia, PLE, thrombosis, pleural effusion, and pericardial effusion. Studies were excluded if they: (1) used unclear surgical intervention; (2) performed a secondary surgery after Fontan; (3) were written in languages other than English or Chinese; (4) had no control group; (5) significantly differed between important features and baseline data; and (6) had no outcome measures.

2.3 | Information extraction and evaluation

All articles were reviewed by 2 independent reviewers to screen titles and abstracts on the basis of predefined inclusion criteria. The full-texts of the eligible articles were reviewed.

The information extraction form were designed, including (1) general information, including the title, author, year, source, and study design; (2) detailed information on the sample, including the number of patients in each group, characteristics, and baseline information of

patients; (3) interventions, including surgical window and staging; (4) outcome measures.

The Newcastle-Ottawa Scale (NOS) was used for quality evaluation.¹⁶ The studies were scaled from 0 to 9, including 4 points (4 items) for target population, 2 points (1 item) for group comparison, and 3 points (3 items) for outcome measures. Studies of more than 6 points were considered as high quality.

Two reviewers extracted and compared information of all included articles and evaluated all the studies. When they disagreed with each other, disagreements were either discussed to reach a consensus between the 2 reviewers or decided by a third reviewer.

2.4 | Statistical analysis

Meta-analysis was performed using RevMan5.3 (Cochrane Collaboration). Odds ratios (OR) and relative risk (RR) with 95% confidence interval (CI) were used to present dichotomous data for case study and cohort study, respectively. If outcome measure was 0, risk difference (RD) was used. Continuous data were presented in mean difference (MD) or standard mean difference (SMD) with 95% CI. The chi-square test was used for heterogeneity analysis between groups, and heterogeneity was assessed by I^2 .¹⁷ If $P > .1$ and $I^2 < 50\%$, the fixed effects model was used; otherwise, the heterogeneity was assessed to determine whether random effects model can be used. If there was obvious heterogeneity, descriptive analysis was used. $I^2 < 25\%$ was considered as of low heterogeneity, 25%-70% was of mediate heterogeneity and $>70\%$ was of high heterogeneity. $P < .05$ was considered as statistically significant.

3 | RESULTS

3.1 | Characteristics of patients

There were two hundred thirty-nine English articles and three hundred eighty-eight Chinese articles were initially identified (Figure 1). All of the 10 articles¹⁸⁻²⁷ that were finally included in the systematic review were retrospective cohort studies written in English languages. All the references of included studies were reviewed, however, none met the inclusion criteria. There were 3814 cases, including 2277 EC cases and 1537 LT cases. The characteristics of included studies were shown in Table 1. The NOS score of included studies ranged from 5 to 8 points, with an average score of 6.8 points.

Early death was defined as surgical death or death within 30 days after surgery. Long-term death was defined as death after discharge. Sinus dysfunction included sinus bradycardia, sick sinus node dysfunction, or II°/III° atrioventricular block. Supraventricular tachycardia was defined as nonsinus tachycardia shown on 12-lead electrocardiogram (ECG) or 24-hour ambulatory ECG, including atrial flutter, atrial fibrillation, paroxysmal atrial tachycardia, or junctional ectopic tachycardia.

3.2 | Mortality rate

To determine the survival rate and Fontan failure between EC and LT, the early postoperative mortality, long-term mortality, and Fontan

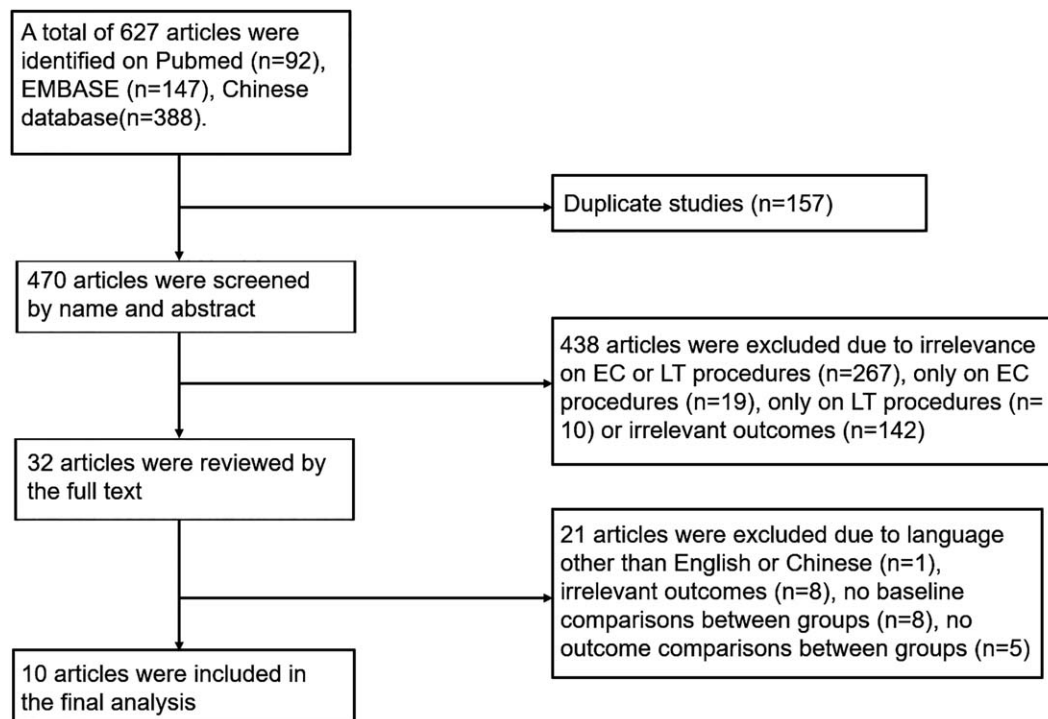


FIGURE 1 Flowchart of study selection process

takedown were compared. All the 10 studies reported detailed information on early mortality. It showed that there were no significant heterogeneity among groups ($P = .48$, $I^2 = 0\%$) and no significant difference in early mortality between EC and LT (RD = 0.01, 95% CI $[-0.00, 0.02]$, $P = .18$) (Figure 2A).

Eight studies reported detailed information on long-term mortality. It showed that there were no significant heterogeneity among groups ($P = .34$, $I^2 = 12\%$) and no significant difference in long-term mortality between EC and LT (RD = -0.02 , 95% CI $[-0.05, 0.02]$, $P = .32$) (Figure 2B).

Nine studies reported detailed information on Fontan takedown. It showed that there were no significant heterogeneity among groups ($P = .02$, $I^2 = 56\%$) and no significant difference in Fontan takedown between EC and LT (RD = 0.01, 95% CI $[-0.02, 0.04]$, $P = .56$) (Figure 2C).

3.3 | Surgical-related events

To determine the differences of surgical-related events between EC and LT, the CPB (cardiopulmonary bypass), ACC (Aortic clamp), ICU, and drainage time were compared. Eight studies recorded detailed information on CPB and ACC. Kuroczynski's study²⁷ did not record operation time for CBP and Fu's study²⁵ did not report operation time for ACC. Nakano's study²² did not report the exact number of people underwent ACC. Some studies^{19,20,23,25} used median (quartile) approach while other studies^{18,21-24,26} used mean \pm standard deviation to report the time of CBP and ACC (Table 2). It showed that the heterogeneity of CBP ($P = .02$, $I^2 = 64\%$) and ACC ($P < .001$, $I^2 = 97\%$) was large among groups. Descriptive analysis showed that

the time and number of ACC in EC group were smaller than that in LT group.

The ventilatory time was converted from median (quartile) into mean \pm standard deviation using the method described by Wan X.²⁸ There was no significant heterogeneity among the groups ($P = .78$, $I^2 = 0\%$), and there was no significant difference in ventilatory time between EC and LT (MD = 5.93 $[-0.08, 11.94]$, $P = .05$). ICU time showed moderate heterogeneity ($P = .02$, $I^2 = 68\%$). Random effects model showed no significant difference in ICU time between EC and LT (MD = -0.97 $[-2.56, 0.63]$, $P = .23$). Thoracic drainage time showed mild heterogeneity ($P = .16$, $I^2 = 39\%$). The thoracic drainage time was shorter in LT group than that in EC group (MD = 1.99 $[1.83, 2.15]$, $P < .001$), as shown in Table 3.

3.4 | Surgical complications

To determine the incidences of complications between EC and LT, postoperative complications and pacemaker installation were compared. As shown in Figure 3A, there was no significant heterogeneity ($P = .71$, $I^2 = 0$) for postoperative supraventricular tachycardia, and the incidence of postoperative supraventricular tachycardia was higher in LT group compared with that in EC group (RR = 0.31 $[0.17, 0.55]$, $P < .001$). Heterogeneity was large for postoperative sinus node dysfunctions ($P < .001$, $I^2 = 84\%$) (Figure 3B). After sensitivity analysis, Azakie's study was excluded due to large heterogeneity. Then the heterogeneity of remaining studies was significantly decreased (RD = -0.02 $[-0.06, 0.03]$, $P = .44$) (Figure 4). There was no significant difference in postoperative sinus node dysfunctions between EC and LT groups ($P = .13$, $I^2 = 41\%$). There was no significant difference in

TABLE 1 Characteristics of included studies

Study	Period	Methods	Number of patients			Mean age (y)		Staging (%)			Fenestration (%)			Matching ^a	Quality score	Outcome
			EC	LT	Total	EC	LT	EC	LT	EC	EC	LT	EC			
Fiore (2007) ¹⁸	1990–2004	Retrospective cohort	49	113	162	5.6 ± 3.8	3.6 ± 2.0	100	100	32.7	73.4	2.5, 6, 7, 9, 10, 11, 12, 13, 15	7	NS		
Azakié (2001) ¹⁹	1994–1998	Retrospective cohort	60	47	60	0.75 (0.25–4)	0.83 (0.25–13)	98	93	77	85	1, 2, 3, 6, 7, 8, 9, 10, 11, 13, 18	8	EC		
Robbers-Visser (2010) ²⁰	1988–2008	Retrospective cohort	107	102	209	3.2 (2.5–4.1)	3.0 (2.5–3.9)	100	100	14	18.6	1, 3, 5, 6, 7, 10, 11, 15	7	EC		
Lee (2007) ²¹	1995–2006	Retrospective cohort	98	67	165	4.3 ± 5.5	3.95 ± 4.21	0	0	37.8	86.5	1, 2, 3, 4, 6, 8, 9, 14, 15	7	EC		
Nakano (2004) ²²	1991–1999	Retrospective cohort	79	88	167	6.2 ± 4.1	6.2 ± 3.9	100	100	1.3	1.1	1, 2, 3, 7, 8, 10, 11, 12, 14, 18	8	EC		
Stewart (2012) ²³	2000–2009	Retrospective cohort	1730	1017	2747	3.2 (2.6–3.9)	2.4 (2.0–3.1)	38	40.2	52	87	1, 2, 3, 5, 6, 16, 17, 18	5	LT		
Kumar (2003) ²⁴	1995–2002	Retrospective cohort	33	37	70	3.9 ± 2.5	2.7 ± 1.1	94	97	100	100	2, 3, 5, 7, 9, 10, 11, 14	7	LT		
Fu (2009) ²⁵	1996–2007	Retrospective cohort	95	19	114	4.23 ± 2.6	5.13 ± 3.43	100	100	61	52.6	1, 2, 3, 4, 5, 6, 7, 11, 15	7	NS		
Attanavanich (2007) ²⁶	1995–2005	Retrospective cohort	13	14	27	8.8 ± 1.8	8.1 ± 6	85	29	84.6	28.6	2, 3, 5, 7, 8, 9, 12, 15	7	NS		
Kuroczynski (2003) ²⁷	1995–2002	Retrospective cohort	13	33	46	3.2 (2.0–20)	3.1 (1.5–8)	0	0	7.7	100	3, 7, 8, 10, 11, 15	5	EC		

^a 1. Age. 2. Sex. 3. Weight. 4. Body surface area. 5. Diagnosis. 6. Preoperative arrhythmia. 7. Preoperative pulmonary artery pressure. 8. Mean pulmonary arterial resistance. 9. Transpulmonary gradient. 10. Ventricle end-diastolic pressure. 11. Oxygen saturation. 12. McGoon index. 13. Ejection fraction. 14. Lung–body blood flow ratio. 15. Atrioventricular valve regurgitation. 16. Preoperative neurologic deficits. 17. Preoperative pacemaker installation. 18. Primary surgery.

the incidence of arrhythmia between the 2 groups (RR = 0.56 [0.25, 1.23], $P = .15$) (Figure 3C).

Eight studies reported pacemaker installation, except for Stewart²³ and Azakié's.¹⁹ It showed minimal homogeneity ($P = .73$, $I^2 = 0\%$) and there was no significant difference in pacemaker installation between the 2 groups (RD = 0.01 [−0.02, 0.03], $P = .70$) (Figure 3D).

For postoperative complications, the EC group had a lower incidence of PLE compared with LT group (RR = 0.33 [0.11, 0.96], $P = .04$). However, there were no significant differences in rates of thrombosis, pleural effusion, and pericardial effusion between groups (Table 4). The funnel plot for the 10 studies for EC and LT was in symmetric distribution, as shown in Figure 5.

4 | DISCUSSION

The present systematic review shows that (1) there are no significant differences of early postoperative mortality, long-term mortality, and Fontan takedown between EC and LT; (2) in terms of surgical-related events, EC group has shorter CPB and ACC time and could be performed without CPB; however EC group has longer drainage time than that of LT group with no differences on ventilatory time or ICU time; (3) as for the surgical complications, EC group has lower incidences of postoperative supraventricular arrhythmias within 30 days and PLE in the follow-up time compared with those of LT group.

Fontan procedure has been constantly improving. The third-generation Fontan procedures of EC and LT have been used as primary approach in the treatment of patient with a functional single ventricle, with benefits of higher surgical survival and lower incidence of postoperative arrhythmia.²⁹ They improve the early and long-term prognosis of tricuspid atresia, major artery transposition, left ventricular dysplasia syndrome.^{30–32}

EC and LT have advantages and disadvantages. EC uses non-growth tube, and the tube with small diameter cannot improve hemodynamics, therefore, EC is often performed in children older than 3 years.^{33,34} LT incorporates part of atrial tissue that is considered to be potentially growing³⁵; however, LT may theoretically increase the incidence of postoperative arrhythmia due to increased atrial operation hemodynamic effects. Clinically, the postoperative mortality of EC and LT as well as incidence of complications was controversial. Backer et al.³⁶ reported 180 cases of Fontan operation, including 67 cases of LT and 113 cases of EC. It showed that EC was advantageous over LT in terms of circulation time, ascending aortic occlusion time, and surgical mortality. Robert D²⁰ showed that in a multicenter review involving 2747 cases, LT had a higher early prognosis rate. Fiore AC¹⁸ reported that EC and LT had similar early and long-term mortality as well as postoperative arrhythmia.

In this meta-analysis, it showed that there were no significant differences in early mortality, long-term mortality, and the incidence of Fontan takedown/revision between EC and LT groups, in accordance with other reports.^{37,38} The Fontan takedown was mostly performed early after Fontan surgery with high mortality rate.³⁹ The postoperative elevated ventricular end-diastolic pressure and prolonged

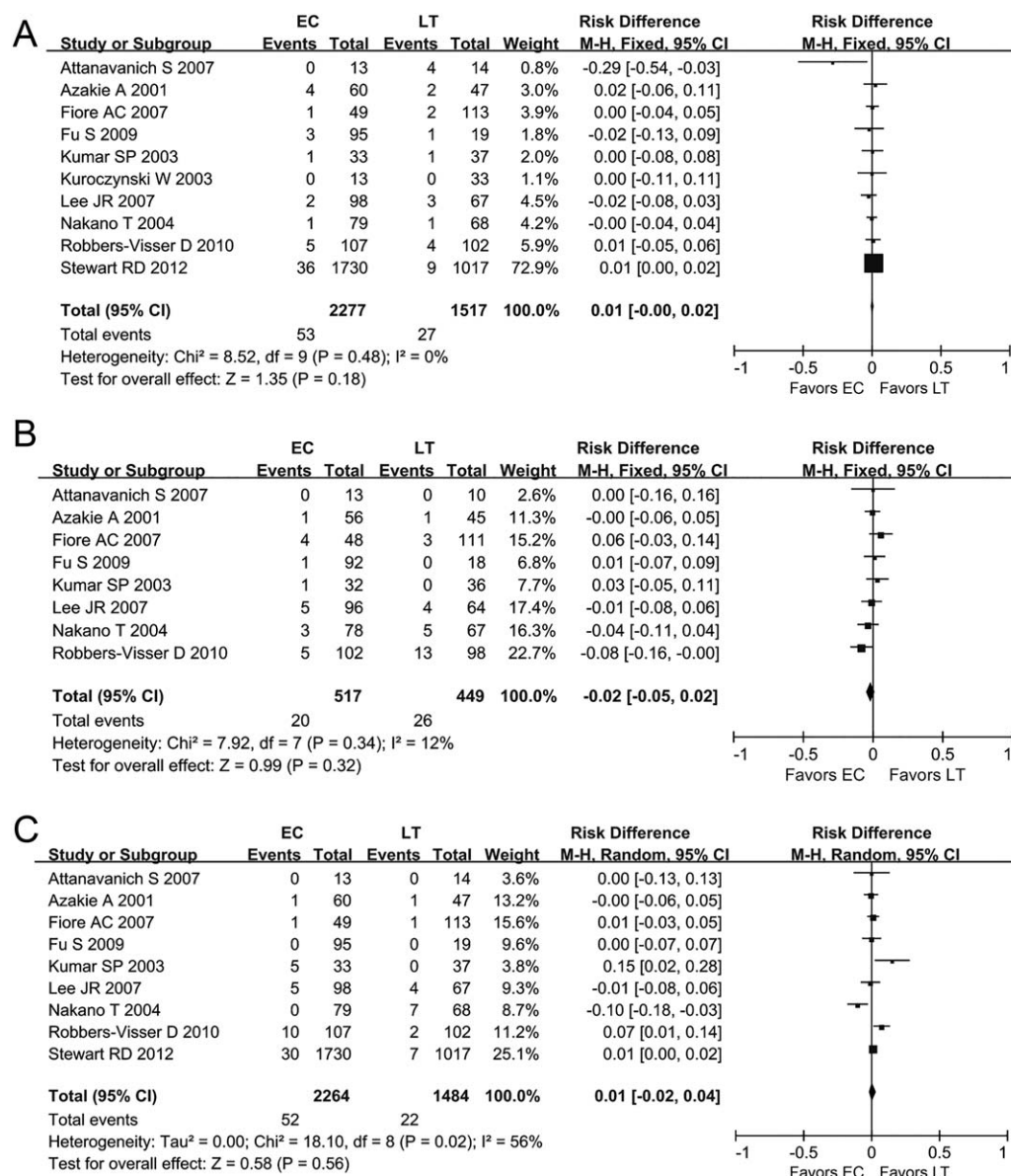


FIGURE 2 Forest plot of mortality for EC and LT. (A) Early mortality; (B) Long-term mortality; (C) Fontan takedown. Abbreviations: df, degrees of freedom; I^2 , heterogeneity among studies; MH, Mantel-Haenszel test; Z, test of overall treatment effect. The 95% confidence interval (CI) for the risk difference of each study is represented on the horizontal line and the point estimate is represented as squares. The size of the square corresponds to the weight of the study in the meta-analysis. The 95% CI for pooled estimates is represented as diamond. There were no significant difference of heterogeneity among early mortality ($P = .48$, $I^2 = 0\%$), long-term mortality ($P = .34$, $I^2 = 0\%$), and Fontan takedown ($P = .02$, $I^2 = 56\%$) between EC and LT

cardiopulmonary bypass time are considered as risk factors for Fontan takedown.⁴⁰ However, no difference of the above risk factors was found between EC and LT in this study.

EC can be performed in the absence of extracorporeal circulation to decrease the generation of pro-inflammatory cytokines and vasoactive substances, in order to protect the myocardial, coagulation, and pulmonary vascular systems.⁴¹ It is reported^{42–44} that prolonged cardiac arrest time and CBP time are risk factors for surgical failure and early mortality of Fontan's procedure. Kawahira showed the inflammation reactions were lower in EC patients without extracorporeal circulation, compared with those with extracorporeal circulation.⁴⁵ Ovrutski

also showed a better early prognosis in Fontan patients without extracorporeal circulation.⁴⁶ In this study, it showed that EC may be more beneficial to patients with a functional single ventricle because of its shorter ACC time and non-stop heart beating procedures, especially for patients with left ventricular dysplasia.⁴⁷ The postoperative chest lead time was shorter in LT group, compared with that of EC. Fu S⁴⁸ found that chest lead time was 3 days shorter in EC patients with window compared those without, which may be resulted from the safety valve created by window to reduce the central venous pressure and improve the blood flow. From the basic characteristics of included studies, EC windowing rate was less than LT. Thus, the chest lead time was shorter in LT group.

TABLE 2 Time and number of patients underwent CPB, cross-clamp, and ACC

Study	CPB time (min)		Cross-clamp (N, %)		ACC time (min)	
	EC	LT	EC	LT	EC	LT
Attanavanich (2007) ²⁶	161 ± 144	158 ± 26	0 (0%)*	14 (100%)	0*	83 ± 25
Fiore (2007) ¹⁸⁹	117 ± 41	107 ± 42	4 (8%)*	113 (100%)	51 ± 34	54 ± 25
Kumar (2003) ²⁴	145 ± 42	134 ± 30	17 (52%)*	37 (100%)	26 ± 15*	55 ± 13
Lee (2007) ²¹	147.3 ± 56.2	154.4 ± 72.5	39 (39.8%)*	67 (100%)	36.1 ± 19.7	49.9 ± 22.5
Nakano (2004) ²²	132.3 ± 46.9*	153.3 ± 50.3	NA	NA	15.4 ± 20.7*	57.5 ± 22.7
Azaki (2001) ¹⁹	102 (59–306)	109 (62–289)	9 (15%)*	47 (100%)	29 (11–105)	50 (22–135)
Fu (2009) ²⁵	102 (0–98)	165 (50–399)	0 (0%)*	33 (100%)	NA	NA
Robbers-Visser (2010) ²⁰	141 (97–204)*	107 (90–138)	26 (24.2%)	102 (100%)	42 (19–62)*	61 (49–74)
Stewart RD (2012) ²³	80 (60–116)	99 (77–125)	436 (25.2%)	713 (70.1%)	36 (22–55)	46 (35–63)

Abbreviations: ACC, aortic clamp; CPB, cardiopulmonary bypass; NA, not applicable.

* $P < .05$.

There was no statistical significance in mechanical ventilation time and length of ICU stay between the 2 groups.

Arrhythmia is the leading cause of death for postoperative Fontan.⁴⁹ Sustained arrhythmia may lead to cardiac insufficiency and thrombosis, which may further result in long-term death, disability, and re-admission.⁵⁰ The cause of supraventricular arrhythmias is multifactorial. The incidence of postoperative atrial arrhythmia of EC was lower than that of LT due to the following reasons: (1) absence of atrial sutures; (2) stable venous pressure of right atrium; (3) less operation around the sinus node; and (4) less impaired ventricular function due to prolonged cardiopulmonary bypass and cardiac arrest.¹⁴ For the sinus node dysfunction, there were no difference between LT and EC group.⁵¹ Many factors may contribute to arrhythmia. Amodeo's study⁵² showed that LT had a higher arrhythmia incidence and multivariate analysis showed that primary surgery might be the main risk factor. The extent of injury of primary surgeries on the sinus node and its blood supply may be different, as in consistent with Rajanbabu's^{53,54} rebuttal against Balaji's⁵⁵ review. This study showed that LT had a higher incidence of postoperative supraventricular tachyarrhythmia, and there were no significant differences of the pacemaker installation, postoperative sinus node dysfunction and postoperative arrhythmia between the 2 groups.

PLE is a rare but serious long-term complication. Multivariate analysis showed that prolonged extracorporeal bypass and right ventricular ventricle were risk factors for PLE.⁵⁶ EC may decrease the duration of bypass to decrease PLE incidence. The mechanism of thrombosis is still unknown. Theoretically, the slow flow of venous blood, increased venous pressure, stasis of venous system and expanded atrial wall of LT all favor thrombosis, which is on the contrary to EC. However, it showed that there were no significant differences in thrombosis incidence among different surgical incisions, and the thrombosis rate was equal between artery and venous thrombosis, indicating that blood stasis alone may not be the main reason.^{57,58} In this study, we found that there were no significant differences in thrombosis, pericardial effusion, and pleural effusion between EC and LT.

This study is limited in the original data that may expose it to potential bias. In one study,¹⁸ EC was only used in patients with weight of 13–16 kg and older than 10 years old, and there was no record of thrombosis due to data limitations. In one study,²³ data was extracted from 68 STS (Society of Thoracic Surgeons Congenital Heart Surgery Database) databases, some indicators were not recorded due to database limitations. These indicators may have an effect on the outcome, especially when detailed surgical operations were not recorded. One study excluded patients older than 6 years.²³ In one study,²⁶ LT was

TABLE 3 Surgical events of EC and LT (CPB time, ACC time, Duration of mechanical ventilation, ICU stay, and chest lead time)

	Number of studies	EC (n)	LT (n)	MD (95% CI)	P value for overall effect	I ²	P value for heterogeneity	Effect model
CPB time (min)	5	272	319	−1.76 (−16.95, 13.44)	.82	64%	.02	Random
ACC time (min)	5	272	319	−33.68 (−53.47, −13.89)	.0009	97%	<.00001	Random
Duration of mechanical ventilation (h)	5	253	297	5.93 (−0.08, 11.94)	.05	0%	.78	Fixed
ICU stay (d)	4	298	253	−0.97 (−2.56, 0.63)	.23	68%	.02	Random
Chest drainage time (d)	5	393	272	1.99 (1.83, 2.15)	<.00001	39%	.16	Fixed

Abbreviations: ACC, aortic clamp; CPB, cardiopulmonary bypass; EC, extracardiac conduit; LT, lateral tunnel; MD, mean difference.

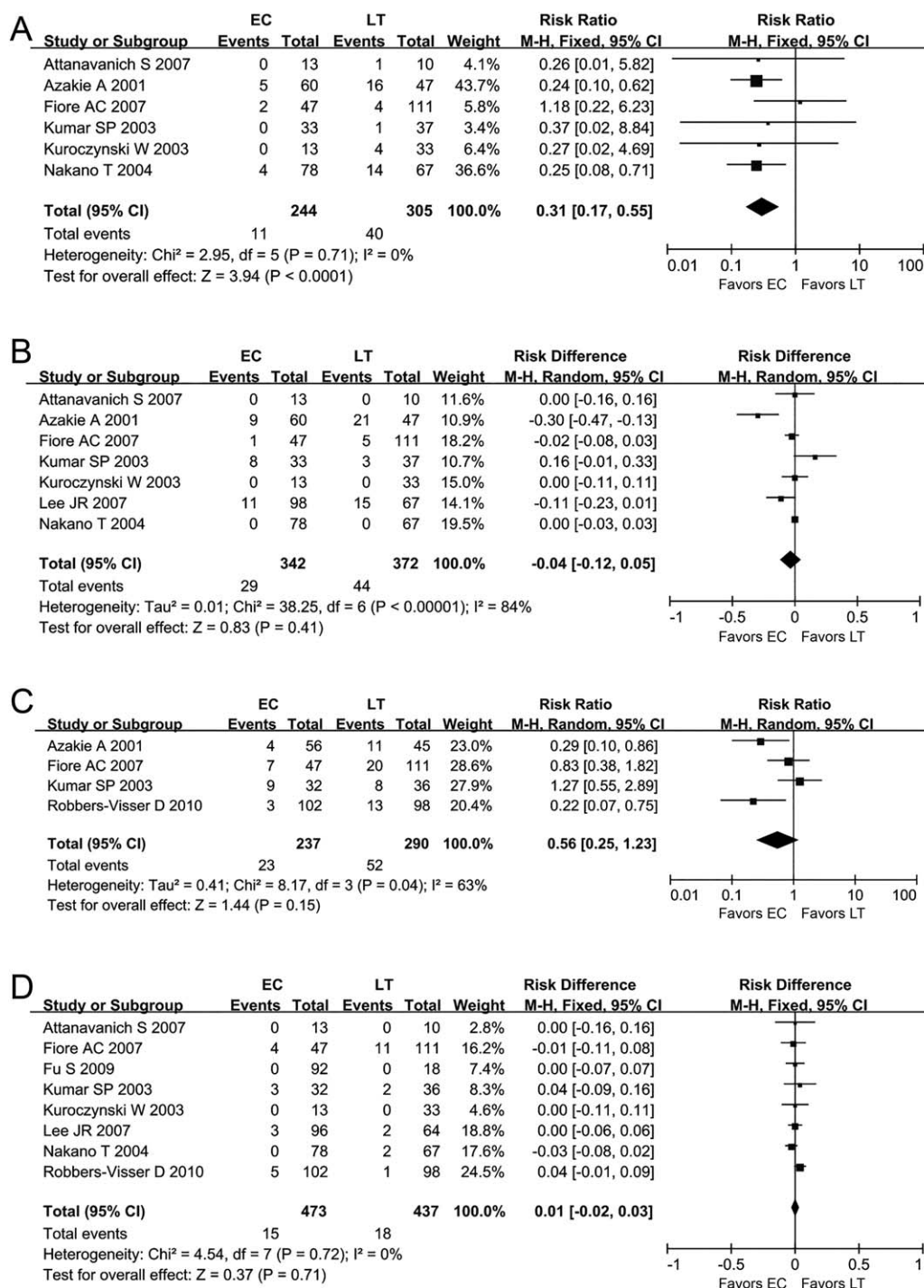


FIGURE 3 Forest plot of arrhythmias for EC and LT. (A) Supraventricular arrhythmia; (B) Sinus node dysfunction; (C) Arrhythmias during follow-up; D, Pacemaker installation. Abbreviations: df, degrees of freedom; I^2 , heterogeneity among studies; MH, Mantel-Haenszel test; Z, test of overall treatment effect. The 95% confidence interval (CI) for the risk difference of each study is represented on the horizontal line and the point estimate is represented as squares. The size of the square corresponds to the weight of the study in the meta-analysis. The 95% CI for pooled estimates is represented as diamond. There were no significant differences of heterogeneity among supraventricular arrhythmia ($P = .71$, $I^2 = 0\%$), sinus node dysfunction ($P < .001$, $I^2 = 84\%$), arrhythmias during follow-up ($P = .04$, $I^2 = 63\%$), and pacemaker installation ($P = .73$, $I^2 = 0\%$) between EC and LT

performed in patients younger than 3 years of age, while EC was performed in patients older than 6 years. Patients' surgical approach was determined by the patients' medical conditions and surgeon's decisions, which were not randomized nor blinded. Though the funnel plot

(Figure 5) showed great consistency, reporting bias cannot be ruled out. All included studies were retrospective cohort studies from 2001 to 2012. The surgery methods may evolve during the research span. Moreover, the follow-up length varied, and no recent studies

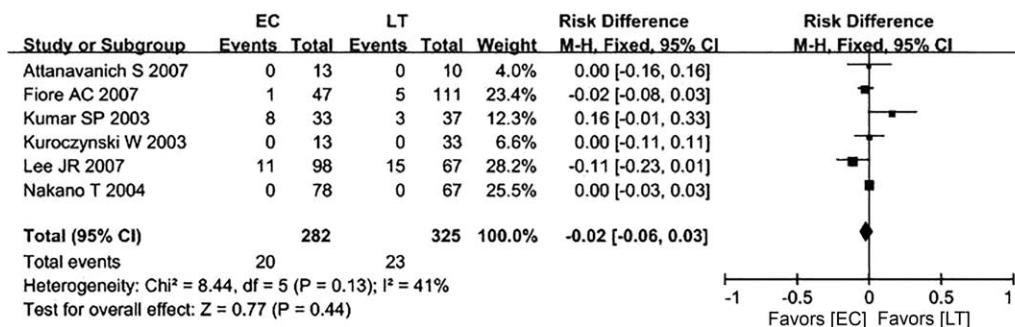


FIGURE 4 Forest plot of sinus node dysfunction for EC and LT. Abbreviations: df, degrees of freedom; I², heterogeneity among studies; MH, Mantel-Haenszel test; Z, test of overall treatment effect. The 95% confidence interval (CI) for the risk difference of each study is represented on the horizontal line and the point estimate is represented as squares. The size of the square corresponds to the weight of the study in the meta-analysis. The 95% CI for pooled estimates is represented as diamond. There were significant differences of heterogeneity for sinus node dysfunction between EC and LT ($P = .13$, $I^2 = 41\%$)

TABLE 4 Surgical complications between 2 groups

	Number of studies	EC (n)	LT (n)	RR (95% CI)	P value for overall effect	I ²	P value for heterogeneity	Effect model
Thrombosis	7	428	389	1.20 (0.70, 2.07)	.5	49%	.07	Fixed
Protein loss enteropathy	5	313	301	0.33 (0.11, 0.96)	.04	0%	.7	Fixed
Pleural effusion	2	73	55	1.10 (0.54, 2.25)	.8	0%	.62	Fixed
Pericardial effusion	2	73	55	0.51 (0.09, 2.88)	.44	0%	.69	Fixed

Abbreviations: EC, extracardiac conduit; LT, lateral tunnel; RR, relative risk.

were identified. Some outcome indicators were of insufficient sample size. Therefore, further investigations involving more studies are needed.

In conclusion, EC and LT are safe and effective in the management of complex congenital heart diseases. There were no significant differences in early mortality, long-term mortality, long-term arrhythmia, Fontan takedown, ventilator-assisted ventilation, ICU stay, thrombosis, pleural effusion, and pericardial effusion between the EC and LT groups. However, EC had lower incidences of supraventricular arrhythmia (30 days after surgery) and PLE compared with LT, showing that

EC may be advantageous over LT in patients with a functional single ventricle.

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CONFLICT OF INTEREST

The authors do not have any conflicts of interest to report.

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REFERENCES

- [1] Fontan F, Baudet E. Surgical repair of tricuspid atresia. *Thorax*. 1971;26:240–248.

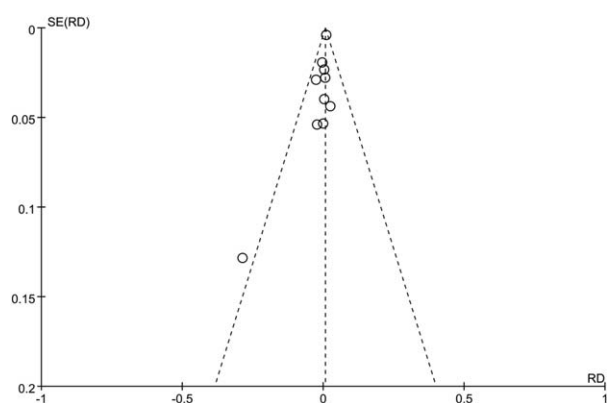


FIGURE 5 Funnel plot of the risk difference (RD) for EC and LT. The dashed line represents 95% confidence intervals. Circles represent individual studies

- [2] Jonas RA. The intra/extracardiac conduit fenestrated Fontan. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu.* 2011;14:11–18.
- [3] Jonas RA, Castaneda AR. Modified Fontan procedure: atrial baffle and systemic venous to pulmonary artery anastomotic techniques. *J Card Surg.* 1988;3:91–96.
- [4] Uemura H, Yagihara T, Yamashita K, Ishizaka T, Yoshizumi K, Kawahira Y. Establishment of total cavopulmonary connection without use of cardiopulmonary bypass. *Eur J Cardiothorac Surg.* 1998;13:504–507.
- [5] Tam VKH, Miller BE, Murphy K. Modified Fontan without use of cardiopulmonary bypass. *Ann Thorac Surg.* 1999;68:1698–1703.
- [6] Yetman AT, Drummond-Webb J, Fiser WP, et al. The extracardiac Fontan procedure without cardiopulmonary bypass: technique and intermediate-term results. *Ann Thorac Surg.* 2002;74:1416–1421.
- [7] Chowdhury UK, Airan B, Kothari SS, et al. Specific issues after extracardiac Fontan operation: ventricular function, growth potential, arrhythmia, and thromboembolism. *Ann Thorac Surg.* 2005;80:665–672.
- [8] Stamm C, Friehs I Jr, JEM, et al. Long-term results of the lateral tunnel Fontan operation. *J Thorac Cardiovasc Surg.* 2001;121:28–41.
- [9] Ono M, Boethig D, Goerler H, Lange M, Westhoff-Bleck M, Breyman T. Clinical outcome of patients 20 years after Fontan operation — effect of fenestration on late morbidity. *Eur J Cardiothorac Surg.* 2006;30:923–929.
- [10] Lemler MS, Scott WA, Leonard SR, Stromberg D, Ramaciotti C. Fenestration improves clinical outcome of the fontan procedure: a prospective randomized study. *ACC Curr J Rev.* 2002;11:207–212.
- [11] Nürnberg JH, Ovroutski S, Alexi V. New onset arrhythmias after the extracardiac conduit Fontan operation compared with the intraatrial lateral tunnel procedure: early and midterm results. *Ann Thorac Surg.* 2004;78:1979–1988.
- [12] Lasa JJ, Glatz AC, Daga A, Shah M. Prevalence of arrhythmias late after the Fontan operation. *Am J Cardiol.* 2014;113:1184–1188.
- [13] Hsia TY, Migliavacca F, Pittaccio S, et al. Computational fluid dynamic study of flow optimization in realistic models of the total cavopulmonary connections. *J Surg Res.* 2004;116:305–313.
- [14] Kogon B. Is the extracardiac conduit the preferred Fontan approach for patients with univentricular hearts? The extracardiac conduit is the preferred Fontan approach for patients with univentricular hearts. *Circulation.* 2012;126:2511–2515.
- [15] Khairy P, Poirier N. Is the extracardiac conduit the preferred Fontan approach for patients with univentricular hearts? The extracardiac conduit is not the preferred Fontan approach for patients with univentricular hearts. *Circulation.* 2012;126:2516–2525.
- [16] Wells G, Shea B, O'Connell J, et al. The Newcastle-Ottawa scale (NOS) for assessing the quality of nonrandomised studies in meta-analysis. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Assessed May 1, 2016.
- [17] Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med.* 2002;21:1539–1558.
- [18] Fiore AC, Turrentine M, Rodefeld M, et al. Fontan operation: a comparison of lateral tunnel with extracardiac conduit. *Ann Thorac Surg.* 2007;83:622–629.
- [19] Azakie A, McCrindle BW, Van Arsdell G, et al. Extracardiac conduit versus lateral tunnel cavopulmonary connections at a single institution: impact on outcomes. *J Thorac Cardiovasc Surg.* 2001;122:1219–1228.
- [20] Robbers-Visser D, Miedema M, Nijveld A, et al. Results of staged total cavopulmonary connection for functionally univentricular hearts; comparison of intra-atrial lateral tunnel and extracardiac conduit. *Eur J Cardiothorac Surg.* 2010;37:934–941.
- [21] Lee JR, Kwak J, Kim KC, et al. Comparison of lateral tunnel and extracardiac conduit Fontan procedure. *Interact Cardiovasc Thorac Surg.* 2007;6:328–330.
- [22] Nakano T, Kado H, Ishikawa S, et al. Midterm surgical results of total cavopulmonary connection: clinical advantages of the extracardiac conduit method. *J Thorac Cardiovasc Surg.* 2004;127:730–737.
- [23] Stewart RD, Pasquali SK, Jacobs JP, et al. Contemporary Fontan operation: association between early outcome and type of cavopulmonary connection. *Ann Thorac Surg.* 2012;93:1254–1260.
- [24] Kumar SP, Rubinstein CS, Simsic JM, Taylor AB, Saul JP, Bradley SM. Lateral tunnel versus extracardiac conduit Fontan procedure: a concurrent comparison. *Ann Thorac Surg.* 2003;76:1389–1397.
- [25] Fu S, Valeske K, Muller M, Schranz D, Akinturk H. Total cavopulmonary connection: lateral tunnel anastomosis or extracardiac conduit? —an analysis of 114 consecutive patients. *Chin Med Sci J.* 2009;24:76–80.
- [26] Attanavanich S, Lertsithichai P. Extracardiac conduit versus lateral tunnel for total cavopulmonary connections. *J Med Assoc Thailand.* 2007;90:2513–2518.
- [27] Kuroczynski W. The Fontan-operation: from intra- to extracardiac procedure. *J Cardiovasc Surg.* 2003;11:70–74.
- [28] Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol.* 2014;14:135.
- [29] d'Udekem Y, Iyengar AJ, Cochrane AD, et al. The Fontan procedure contemporary techniques have improved long-term outcomes. *Circulation.* 2007;116:1157–1164.
- [30] Hirsch JC, Ohye RG, Devaney EJ, Goldberg CS, Bove EL. The lateral tunnel Fontan procedure for hypoplastic left heart syndrome: results of 100 consecutive patients. *Pediatr Cardiol.* 2007;28:426–432.
- [31] Khairy P, Fernandes SM Jr, MJ, et al. Long-term survival, modes of death, and predictors of mortality in patients with Fontan surgery. *Circulation.* 2008;117:85–92.
- [32] Mitchell ME, Ittenbach RF, Gaynor JW, Wernovsky G, Nicolson S, Spray TL. Intermediate outcomes after the Fontan procedure in the current era. *J Thorac Cardiovasc Surg.* 2006;131:172–180.
- [33] Leval MRD. The Fontan circulation: a challenge to William Harvey?. *Nat Clin Pract Cardiovasc Med.* 2005;2:202–208.
- [34] Petrossian E, Thompson LD, Hanley FL. Extracardiac conduit variation of the Fontan procedure. *Adv Card Surg.* 2000;12:175–198.
- [35] Fujii Y, Kotani Y, Takagaki M, et al. Growth of the lateral tunnel in patients who underwent a total cavopulmonary connection at less than 5 years of age. *Eur J Cardiothorac Surg.* 2010;38:66–70.
- [36] Backer CL, Deal BJ, Kaushal S, Russell HM, Tsao S, Mavroudis C. Extracardiac versus intra-atrial lateral tunnel Fontan: extracardiac is better. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu.* 2011;14:4–10.
- [37] Tweddell JS, Nersesian M, Mussatto KA, et al. Fontan palliation in the modern era: factors impacting mortality and morbidity. *Ann Thorac Surg.* 2009;88:1291–1299.
- [38] Chungsomprasong P, Soongswang J, Nana A, et al. Medium and long-term outcomes of Fontan operation. *J Med Assoc Thai.* 2011;94:323–330.
- [39] van Melle JP, Wolff D, Hörer J, et al. Surgical options after Fontan failure. *Heart.* 2016;102:1127–1133.
- [40] Murphy MO, Glatz AC, Goldberg DJ, et al. Management of early Fontan failure: a single-institution experience. *Eur J Cardiothorac Surg.* 2014;46:458–464.

- [41] Mainwaring RD, Lamberti JJ, Hugli TE. Complement activation and cytokine generation after modified Fontan procedure. *Ann Thorac Surg.* 1998;65:1715–1720.
- [42] Gentles TL Jr, JEM, Gauvreau K, et al. Fontan operation in five hundred consecutive patients: factors influencing early and late outcome. *J Thorac Cardiovasc Surg.* 1997;114:376–391.
- [43] Kaulitz R, Ziemer G, Luhmer I, Kallfelz HC. Modified Fontan operation in functionally univentricular hearts: preoperative risk factors and immediate results. *J Thorac Cardiovasc Surg.* 1996;112:658–664.
- [44] Knott-Craig CJ, Danielson GK, Schaff HV, Puga FJ, Weaver AL, Driscoll DD. The modified Fontan operation: an analysis of risk factors for early postoperative death or takedown in 702 consecutive patients from one institution. *J Thorac Cardiovasc Surg.* 1995;109:1237–1243.
- [45] Kawahira Y, Uemura H, Yagihara T. Impact of the off-pump Fontan procedure on complement activation and cytokine generation. *Ann Thorac Surg.* 2006;81:685–689.
- [46] Ovroutski S, Sohn C, Miera O, et al. Improved early postoperative outcome for extracardiac Fontan operation without cardiopulmonary bypass: a single-centre experience. *Eur J Cardiothorac Surg.* 2013;43:952–957.
- [47] Feinstein JA, Benson DW, Dubin AM, et al. Hypoplastic left heart syndrome: current considerations and expectations. *J Am Coll Cardiol.* 2012;59:1–42.
- [48] Song Z-C, Feng S. Dietmar Factors influencing pleural effusion after Fontan operation: an analysis with 95 patients. *Chin Med Sci J.* 2010;25:38–43.
- [49] Weipert J, Noebauer C, Schreiber C, et al. Occurrence and management of atrial arrhythmia after long-term Fontan circulation. *J Thorac Cardiovasc Surg.* 2004;127:457–464.
- [50] van der Bosch AE, Roos-Hesselink JW, Domburg RV, Bogers AJ, Simoons ML, Meijboom FJ. Long-term outcome and quality of life in adult patients after the Fontan operation. *Am J Cardiol.* 2004;93:1141–1145.
- [51] Nakano T, Kado H, Tatewaki H, et al. Results of extracardiac conduit total cavopulmonary connection in 500 patients. *Eur J Cardiothorac Surg.* 2015;48:825–832.
- [52] Amodeo A, Galletti L, Marianeschi S, et al. Extracardiac Fontan operation for complex cardiac anomalies: seven years' experience. *J Thorac Cardiovasc Surg.* 1997;114:1030–1031.
- [53] Rajanbabu BB. Arrhythmia prevalence after extra cardiac conduit Fontan: a viewpoint. *J Thorac Cardiovasc Surg.* 2015;149:1223–1224.
- [54] Rajanbabu BB, Gangopadhyay D. Sinus node dysfunction after extracardiac conduit and lateral tunnel Fontan operation: the importance of the type of prior superior cavopulmonary anastomosis. *World J Pediatr Congenit Heart Surg.* 2016;7:
- [55] Balaji S, Daga A, Bradley DJ, et al. An international multicenter study comparing arrhythmia prevalence between the intracardiac lateral tunnel and the extracardiac conduit type of Fontan operations. *J Thorac Cardiovasc Surg.* 2014;148:576–581.
- [56] Powell AJ, Gauvreau K, Jenkins KJ, Blume ED, Mayer JE, Lock JE. Perioperative risk factors for development of protein-losing enteropathy following a Fontan procedure. *Am J Cardiol.* 2001;88:1206–1209.
- [57] Coon PD, Rychik J, Novello RT, Ro PS, Gaynor JW, Spray TL. Thrombus formation after the Fontan operation. *Ann Thorac Surg.* 2001;71:1990–1994.
- [58] Rosenthal DN, Friedman AH, Kleinman CS, Kopf GS, Rosenfeld LE, Hellenbrand WE. Thromboembolic complications after Fontan operations. *Circulation.* 1995;92:287–293.

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