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Effect of Fenestration on Fontan Procedure Outcomes: A Meta-Analysis and Review

Ismail Bouhout, MD, MSc,* Walid Ben-Ali, MD,* Dori Khalaf, BS, Marie Josée Raboisson, MD, and Nancy Poirier, MD

Division of Cardiac Surgery, CHU-ME Sainte Justine, University of Montréal, Montréal, Quebec, Canada; and Montréal Heart Institute, University of Montréal, Montréal, Quebec, Canada

Background. **Many studies investigating fenestration in the context of Fontan procedure have been showing controversial results when it comes to whether this procedure truly improves the Surgical outcomes. The aim of this meta-analysis was to compare the early outcomes of a fenestrated (F) vs a nonfenestrated (NF) Fontan procedure.**

Methods. **The PubMed, EMBASE, and Cochrane Library databases were searched for articles measuring the outcomes of an F vs an NF Fontan.**

Results. **A total of 19 studies were selected with a total of 4806 patients (F. 2727; NF. 2079). There was no difference in the risk of Fontan failure between both groups (odds ratio [OR], 0.95 [95% confidence interval [CI], 0.57, 1.56]; $P = .83$). The F group had a significantly lower need for pleural drainage (OR, 0.59 [95% CI, 0.37, 0.94]; $P = .03$), a lower pulmonary artery pressure (mean difference, −0.99 mm Hg [95% CI, −1.68, 0.30 mm Hg]; $P = .005$), and a lower oxygen saturation (mean difference, −3.07% [95% CI, −4.30%, −1.85%]; $P < .001$) than the NF group. There was no significant difference in the stroke occurrence between the 2 groups (OR, 1.32 [95% CI, 0.40, 4.36]; $P = .65$).**

Conclusions. **The Fontan fenestration effectively reduced the pulmonary pressure and the need for prolonged pleural drainage. However, the risks of Fontan failure, early death, and longer hospital stay were not modified.**

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The procedure described by Dr Francis Fontan in 1971[1] introduced a palliative treatment for tricuspid atresia that would revolutionize the way we treat patients with this condition. It paved the way toward surgical procedures that would include other univentricular congenital defects. Indeed, several modifications to the procedure have been introduced, chiefly the lateral tunnel Fontan, described by De Leval and colleagues[2] in 1983 and the extracardiac conduit Fontan, described by Marcelletti and associates[3] in 1988. These modifications have greatly improved the outcomes of the original Fontan, which is less commonly used nowadays.[4] Furthermore, surgical fenestration of the atrial baffle was introduced in 1989[5] in an attempt to improve outcomes. It relieves the Fontan circuit of hemodynamic burdens and increases cardiac output by increasing preload into the functioning ventricle.[6] However, this is done with the major drawback of increasing systemic desaturation and exposing the patient to thromboembolic risks such as strokes. Because of the negative consequences associated with this procedure, there has been no general consensus on the use of routine fenestration, which is often reserved for patients deemed at high risk of Fontan failure and is also performed at the surgeons' discretion.[7-9] This meta-analysis aimed to explore this issue further by measuring the postoperative outcomes of fenestration among several modified Fontan procedures.

Material and Methods

Study Design and Eligibility Criteria

This study was conducted in accordance with the Meta-Analysis of Observational Studies in Epidemiology guidelines.[10] This manuscript was structured using the

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*Drs Bouhout and Ben-Ali contributed equally to this work and are co-first authors.

Address correspondence to Dr Poirier, Division of Cardiac Surgery, CHU-ME Ste-Justine, University of Montréal, 3175 Côte Ste-Catherine, Montréal, Quebec H3T 1C5, Canada; email: ncpoirier@videotron.ca.

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Table 1. Characteristics of the Studies

Study	Study Type	Fenestrated, n	Nonfenestrated, n	Fenestration Size, mm	Fenestration Method	Follow-up Length, mo (range)	Antithrombotic Regimen
Bridges 1992[17]	ROS	91	56	4	Coronary punch	F: (6-30); NF: (6-48)	N/A
Snir 1994[21]	ROS	14	26	4	N/A	17 (1-32)	Aspirin to all patients, warfarin after major pulmonary artery reconstruction
Knez 1999[25]	ROS	21	26	4	N/A	36.5 ± 26.5 (3-84)	ASA
Thompson 1999[6]	ROS	32	49	4-8	Expanded PTFE or side-to-side anastomosis with partial occlusion vascular clamps	40.8 (6-66)	N/A
Airan 2000[14]	ROS	126	222	4-5	Coronary punch	46 ± 18 (6-120)	Low-dose oral AC for 6 mo followed by AP therapy
Atz 2011[16]	ROS	361	175	N/A	N/A	F: 85, NF:104.4	N/A
Fan 2015[24]	ROS	49	41	4-6	Coronary punch	N/A	N/A
Atik 2002[15]	ROS	41	21	N/A	N/A	(8.86-17.66)	Antithrombotic
Lemler 2002[27]	RCT	25	24	3-6	N/A	N/A	Aspirin
Kavarana 2005[26]	ROS	6	48	4	1-2 cm patch of Gore-Tex	33.6 ± 24 (2.4-84)	Warfarin (INR 2-3), discontinued after 1 y; rule out TE or obstruction; then use aspirin
Ono 2006[22]	ROS	91	121	4	Coronary punch	240	N/A
Kim 2008[19]	ROS	85	200	4 (3.5-8)	PTFE tube graft	52.4 ± 32.2 (0.58-120)	Low- dose aspirin except high-risk patients
Fu 2009[18]	ROS	71	24	4-5	Coronary punch	N/A	N/A
Sfyridis 2010[20]	ROS	26	32	N/A	N/A	65.28 (4.32-138)	Lifelong treatment of warfarin OR low-dose warfarin and low-dose aspirin OR aspirin alone
Salazar 2010[23]	ROS	95	131	2.5-4	Coronary punch	24 ± 20.4	Aspirin
Naja 2010[31]	ROS	25	27	N/A	N/A	N/A	N/A
Backer 2011[32]	ROS	67	113	N/A	N/A	N/A	N/A
Stewart 2012[33]	ROS	1788	959	N/A	N/A	N/A	N/A
Fiore 2014[9]	ROS	61	54	5 <15 kg, 6 >15 kg; some patients with 4 mm	Ringed Gore-Tex or direct ECC-RA connection for the 4-mm group	F: 60 ± 39.6; NF: 85.2 ± 48	F: Warfarin (Coumadin) until fenestration closure; then aspirin for life NF: aspirin for life
Fan 2017[8]	ROS	105	78	4-5	Side-to-side anastomosis between conduit and RA free wall	N/A	Aspirin
Januszewska 2017[7]	ROS	56	94	3	Created in the PTFE patch used to make LT	N/A	N/A

AC, anticoagulant; AP, antiplatelet; ECC, extracardiac conduit; F, fenestrated; LT, lateral tunnel; N/A, not available; NF, nonfenestrated; PTFE, polytetrafluoroethylene; RA, right atrial; RCT, randomized controlled trial; ROS, retrospective observational study.

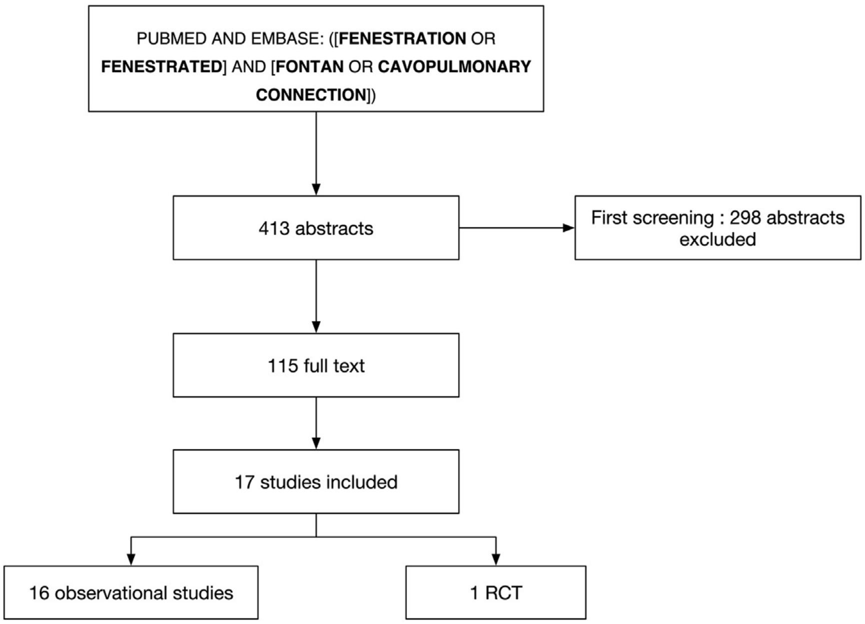

Figure 1. Study flow chart. (RCT, randomized controlled trial.)

recommendations of the Systematic Reviews and Meta-Analyses (PRISMA) statement.[11] We included only studies with a Newcastle-Ottawa Scale score of 7 or higher.[12] The Newcastle-Ottawa Scale score was created to evaluate the quality of nonrandomized studies that would be used in meta-analyses by looking at the design, content, and ease of use. Furthermore, randomized trials were assessed using the Cochrane tools, which cover 6 domains of bias: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias.[13] Noncomparative series, case reports, small case series (<30 patients), review articles, letters to the editor, and articles written in languages other than English or French were excluded.

Search Strategy

A PubMed and EMBASE search was conducted with the following key words: ([“Fenestration” OR “Fenestrated”] AND [“Fontan” OR “cavopulmonary connection”’) limited to publications between 1990 and 2018 conducted in humans. The entire Cochrane Library was screened for “Fontan” and “fenestration.” Moreover, to avoid losing major related publications, a second search was made on the 4 major cardiothoracic surgery journals: *The Annals of Thoracic Surgery, The European Journal of Cardiothoracic Surgery, The Journal of Thoracic and Cardiovascular Surgery,* and *the Journal of the American College of Cardiology*. Related journals and references list of selected articles were also cross-checked for other relevant studies.

Study Records

Two reviewers (W.B.A., I.B.) screened the titles and abstracts of all the identified studies. In case of multiple publications with sample overlap, the most recent report was included. Three independent reviewers (N.P., I.B., and W.B.A.) assessed whether inclusion and exclusion were performed correctly and evaluated the degree of bias of each paper. In case of disagreement, a consensus was negotiated. This occurred in 1 instance, in which case a third reviewer (N.P.) was asked to settle the disagreement. The first author and the corresponding author of all included studies were contacted to retrieve additional unpublished data.

Meta-Analysis Outcomes

The primary outcome was Fontan failure, which was defined as death after a Fontan procedure or a take-down of the Fontan circuit (in hospital or <30 days). Secondary outcomes included intrahospital mortality, length of stay in the intensive care unit (ICU) and the hospital, prolonged pleural drainage, pulmonary pressure reduction, postoperative saturation, and stroke occurrence. We have also sought to report late outcomes such as protein-losing enteropathy, catheter interventions, and arrhythmic events (bradyarrhythmia or tachyarrhythmia, as specified in the studies), as well as late cardiac transplantations.

Data Analysis

Data for this study were extracted and analyzed with RevMan 5 (RevMan 5.3, Cochrane Collaboration, Oxford, United Kingdom). Statistics included odds ratio (OR) and weighted mean difference (MD) with the respective 95% confidence interval (CI). Heterogeneity was examined using Cochran’s Q test, as well as the I^2 statistic. When the latter was superior to 25%, we used random effects models to calculate the OR and their 95% CI. Funnel plots were used to study publication bias. Statistical significance was set at a *P* value of .05 or less.

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Table 2. Demographic Data

Preoperative Data	Estimate	*P* Value
Pulmonary pressure	MD 0.58 [95% CI, 0.19-0.97]	<.001
Age, y	MD −8.86 [95% CI, −17.37 to −0.35]	.04
Pulmonary resistance	MD 0.40 [95% CI, 0.23-0.57]	<.001
Heterotaxy	OR 0.70 [95% CI, 0.35-1.41]	.32
Hypoplastic left heart	OR 0.95 [95% CI, 0.52-1.76]	.88
Tricuspid atresia	OR 1.29 [95% CI, 0.53-3.15]	.58
Pulmonary artery distortion	OR 3.42 [95% CI, 1.90-6.17]	<.001

CI, confidence interval; MD, mean difference; OR, odds ratio.

Results

Literature Search Results

The key words used for the search revealed 431 articles. After conducting a first-level screen on titles and abstracts, we excluded 298 articles. Of the 115 articles remaining we included only 21 studies, which were used for our meta-analysis. These include 20 observational studies[6-9,14-26] and 1 randomized controlled trial (RCT) (Table 1).[27] Inspection of the funnel plot for Fontan failure reveals a symmetrical aspect and therefore shows no evidence of possible publication bias. The study flow chart is summarized in Figure 1.

Preoperative Patient Characteristics

Analysis of the patient population used in this study revealed that patients who were undergoing fenestration were younger (weighted MD, −8.86 years [95% CI, −17.37 to −0.35 years]; $P = .04$), had a higher mean preoperative pulmonary artery pressure (0.58 [95% CI, 0.19-0.97]; $P < .001$), a higher preoperative pulmonary resistance (weighted MD, 0.40 [95% CI, 0.23-0.57]; $P < .001$), and finally, a more distorted pulmonary artery (OR, 3.42 [95% CI, 1.90-6.17]; $P < .001$) than the nonfenestrated group (Table 2). Furthermore, there was no significant difference for the presence of heterotaxy syndrome, hypoplastic left heart syndrome, and tricuspid atresia between the fenestrated and the nonfenestrated group.

Primary Outcome: Fontan Failure

Outcomes for the 2 groups are shown in Figure 2. A total of 4919 patients were included for the analysis of this outcome[6-9,15-17,19-30]: 2735 underwent fenestration, and 2184 did not. Overall, the analysis demonstrated that the risk of Fontan failure was similar in both groups (OR, .95 [95% CI, 0.57-1.56]; $P = .83$).

Secondary Outcomes

PROLONGED PLEURAL DRAINAGE. A total of 1556 patients from studies[6-8,14-17,27] were included for this analysis: 837 patients in the fenestrated group and 719 in the nonfenestrated group. Bridges and colleagues,[5] Fan and associates,[8] and Thompson and associates[6] defined prolonged drainage as occurring for more than 14 days after the procedure. Airan and colleagues[14] defined prolonged drainage as happening for more than 10 days or occurring after removal of chest tubes. Finally, Januszewska and associates[7] defined prolonged drainage as lasting longer than 10 days or having a total amount of effusion in at least 1 system (right pleural, left pleural, or pericardial drainage) that was more than 1000 mL.[7] Prolonged drainage occurred less in the patients who underwent fenestration after Fontan procedure (OR, 0.59 [95% CI, 0.37-0.94]; $P = .03$) (Figure 3).

PULMONARY PRESSURE REDUCTION. A total of 791 patients from 5 studies[6,8,17-19] were included in the analysis of this

Study or Subgroup	Fenestrated Events	Fenestrated Total	None fenestrated Events	None fenestrated Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Bridges 1992	6	91	6	56	11.5%	0.62 [0.21, 1.81]	1992
Snir 1994	3	14	0	26	2.7%	12.60 [0.70, 227.89]	1994
Knez 1999	3	21	6	26	9.6%	0.62 [0.18, 2.18]	1999
Thompson 1999	2	32	0	49	2.5%	7.58 [0.38, 152.83]	1999
Airan 2000	9	126	41	222	16.9%	0.39 [0.19, 0.77]	2000
Atik 2002	2	41	0	21	2.5%	2.62 [0.13, 52.20]	2002
Lemler 2002	0	25	0	24		Not estimable	2002
Kavarana 2005	0	6	1	48	2.4%	2.33 [0.11, 51.85]	2005
Kim 2008	4	85	2	200	6.5%	4.71 [0.88, 25.21]	2008
Fu 2009	0	71	2	24	2.5%	0.07 [0.00, 1.40]	2009
Sfyridis 2010	0	26	0	32		Not estimable	2010
Salazar 2010	2	95	1	131	3.7%	2.76 [0.25, 29.97]	2010
Naja 2010	0	25	0	27		Not estimable	2010
Backer 2011	4	67	5	113	9.5%	1.35 [0.38, 4.85]	2011
Stewart 2012	47	1788	26	959	20.3%	0.97 [0.60, 1.56]	2012
Fiore 2014	0	61	1	54	2.3%	0.30 [0.01, 7.11]	2014
Fan 2017	3	105	3	78	7.2%	0.74 [0.15, 3.58]	2015
Januszewska 2017	0	56	0	94		Not estimable	2017
Total (95% CI)		**2735**		**2184**	**100.0%**	**0.95 [0.57, 1.56]**	
Total events	85		94				

Heterogeneity: $Tau^2 = 0.26$; $Chi^2 = 20.79$, df = 13 (P = 0.08); $I^2 = 37\%$
Test for overall effect: Z = 0.21 (P = 0.83)

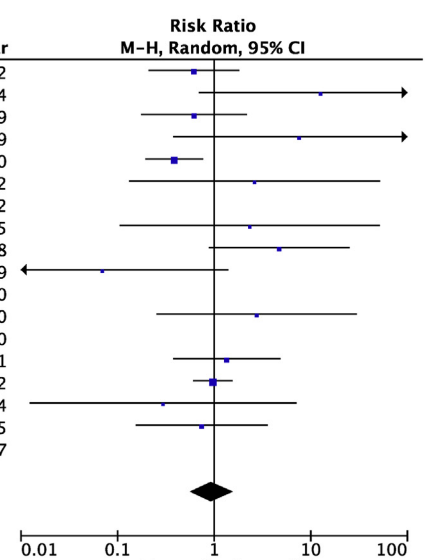

Figure 2. Forest plot for Fontan failure. (CI, confidence interval; F, fenestrated; M-H, Mantel-Haenszel method; NF, nonfenestrated.)

Study or Subgroup	Fenestrated Events	Fenestrated Total	None fenestrated Events	None fenestrated Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Bridges 1992	11	91	20	56	12.8%	0.34 [0.18, 0.65]	1992
Thompson 1999	8	32	5	49	9.4%	2.45 [0.88, 6.83]	1999
Airan 2000	16	126	78	222	14.4%	0.36 [0.22, 0.59]	2000
Atik 2002	17	41	5	21	10.9%	1.74 [0.75, 4.06]	2002
Lemler 2002	7	25	14	24	12.2%	0.48 [0.24, 0.98]	2002
Atz 2011	21	361	35	175	14.2%	0.29 [0.17, 0.48]	2011
Fan 2017	24	105	22	78	14.3%	0.81 [0.49, 1.33]	2015
Januszewska 2017	7	56	26	94	11.7%	0.45 [0.21, 0.97]	2017
Total (95% CI)		**837**		**719**	**100.0%**	**0.59 [0.37, 0.94]**	
Total events	111		205				

Heterogeneity: Tau² = 0.33; Chi² = 28.59, df = 7 (P = 0.0002); I² = 76%
Test for overall effect: Z = 2.24 (P = 0.03)

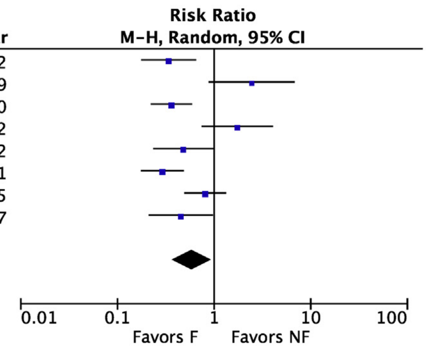

Figure 3. Forest plot for prolonged chest tube drainage. (CI, confidence interval; F, fenestrated; M-H, Mantel-Haenszel method; NF, nonfenestrated.)

outcome: 384 in the fenestrated group and 407 in the nonfenestrated group. The analysis favored the fenestrated group, who showed a significantly lower weighted MD for pulmonary pressure after Fontan procedure than the nonfenestrated group (MD = −0.99 mm Hg [95% CI, −1.68 to 0.30 mm Hg]; *P* = .005), Figure 4. The preoperative and postoperative pulmonary pressures measured in the studies for fenestrated and nonfenestrated groups are displayed in Supplemental Table 1.

STROKE OCCURRENCE. A total of 778 patients from 5 studies[16,18,20,21,27] were included for this analysis: 497 patients in the fenestrated group and 208 patients in the nonfenestrated group. No significant differences were found between the fenestrated group and the nonfenestrated group (OR, 1.32 [95% CI, 0.4-4.36], *P* = .65) (Figure 5). The antithrombotic regimen used for each study investigating strokes is displayed in Table 3.

POSTOPERATIVE SATURATION. A total of 898 patients from 6 studies[9,18,19,22,23,27] were included for this analysis: 367 patients in the fenestrated group and 524 in the nonfenestrated group. We found that the patients in the fenestration group had a significant lower weighted MD for saturation than the nonfenestration group (MD = −3.09% [95% CI, −4.30% to −1.85%]; *P* < .001) (Figure 6).

OTHER OUTCOMES. There was no significant difference between the fenestrated and the nonfenestrated group for intrahospital mortality (OR, 1.10 [95% CI, 0.57, 2.12]; *P* = .78), length of hospital stay (−0.84 days [95% CI, −5.04 to 3.36 days]; *P* = .70), and length of stay in the ICU (0.69 [95% CI, −0.24 to 1.62]; *P* = .14). Late outcomes are displayed in Table 4.

Comment

Since being introduced by Bridges and colleagues in 1989,[5] fenestration has been commonly used in the Fontan procedure, particularly among high-risk patients. To this day, there has been no general consensus on the routine use of fenestration, with certain studies arguing against it because it was seen to lead to more negative than positive outcomes.[6,15,24] There were several theoretical benefits to the introduction of fenestration. A right-to-left shunt should increase preload to the functioning ventricle, thus increasing stroke volume and cardiac output through the Frank-Starling mechanism. This would, however, be done at the expense of desaturation, potentially leading to mild cyanosis. Furthermore, it should limit the central venous pressure increase in the Fontan circulation after the procedure, with a resulting impediment of blood flow and congestion.[4,17,27] This was confirmed in the present meta-analysis, with a higher reduction in pulmonary pressure after fenestration rather than no fenestration. However, this did not translate into a reduction in early mortality and Fontan takedown despite the inclusion of a large number of patients. Although this finding could be explained by the selection bias, the net hemodynamic effect of Fontan fenestration is perhaps insufficient to influence these outcomes.

The present meta-analysis pooled the available data on Fontan fenestration on early postoperative outcomes.

Study or Subgroup	Fenestrated Mean	Fenestrated SD	Fenestrated Total	None fenestrated Mean	None fenestrated SD	None fenestrated Total	Weight	Mean Difference IV, Random, 95% CI	Year
Bridges 1992	3	0.3	91	3.3	0.1	56	23.3%	−0.30 [−0.37, −0.23]	1992
Thompson 1999	6.4	1.89	32	7.9	0.44	49	16.5%	−1.50 [−2.17, −0.83]	1999
Kim 2008	1.1	0.3	85	2	0.6	200	23.2%	−0.90 [−1.00, −0.80]	2008
Fu 2009	3	0.42	71	4.6	0.57	24	22.1%	−1.60 [−1.85, −1.35]	2009
Fan 2017	−0.47	3.97	105	−0.3	0.9	78	14.8%	−0.17 [−0.96, 0.62]	2015
Total (95% CI)			**384**			**407**	**100.0%**	**−0.91 [−1.40, −0.41]**	

Heterogeneity: Tau² = 0.28; Chi² = 173.58, df = 4 (P < 0.00001); I² = 98%
Test for overall effect: Z = 3.56 (P = 0.0004)

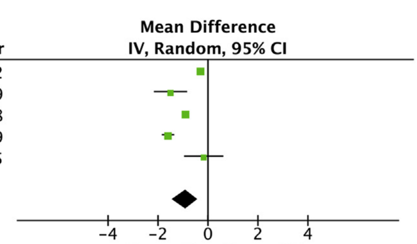

Figure 4. Forest plot for pulmonary pressure reduction. (CI, confidence interval; F, fenestrated; M-H, Mantel-Haenszel method; NF, nonfenestrated.)

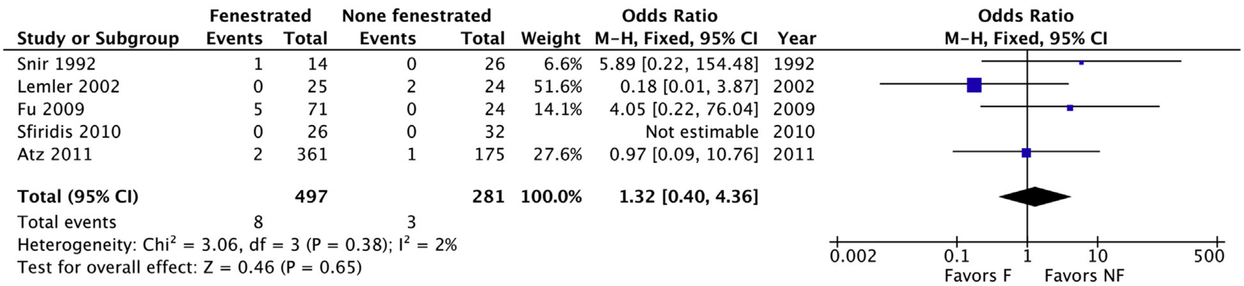

Figure 5. Forest plot for postoperative stroke occurrence. (CI, confidence interval; F, fenestrated; M-H, Mantel-Haenszel method; NF, nonfenestrated.)

More than 4900 patients were included, and this size permitted enough statistical power to compare infrequent outcomes such as death and Fontan failure. The main findings of this study were that there is no association between fenestration and the incidence of Fontan failure. However, the fenestrated group had a significantly lower need for pleural drainage, a lower pulmonary artery pressure, and a lower oxygen saturation than the nonfenestrated group. Strokes, hospital and ICU length of stay, and early mortality were similar between patients who underwent fenestrated and nonfenestrated Fontan procedures. The fenestration group did have a higher risk of postoperative complication because patients had higher preoperative pulmonary resistance, were younger, and had a higher incidence of pulmonary artery distortion.

Interestingly, even though the fenestrated group had a lower need for pleural drainage, it did not translate into a shorter hospital length of stay than in the nonfenestrated group. This may be explained by the finding that the fenestrated group had more comorbidities than the nonfenestrated group. Therefore, the hospital stay could have been driven by the preoperative condition of these patients, rather than by the pleural drainage itself.

Because the presence of fenestration allows communication between venous and arterial circulations, there has been a major concern that this procedure would result in thromboembolic events, leading to strokes. This study did not find a significant number of strokes in the fenestrated group compared with the nonfenestrated group. The presence of thromboembolic events could be limited by the long-term prescription of anticoagulant or antiplatelet medications. There is, however, no clear consensus on which antithrombotic regimen should be used. Many studies in this meta-analysis used aspirin for all patients regardless of fenestration status,[8,19,23,25,27] whereas others used a regimen consisting of warfarin that could be followed with aspirin therapy under certain circumstances[20,26,31-33] (Table 1).

A large meta-analysis including 1200 patients that was conducted by Alsaied and colleagues[28] on thromboprophylaxis after Fontan procedure revealed that thromboembolic events could be lowered with either aspirin or warfarin because no statistical difference was found between these 2 medications. For that matter, it is recommended to use antithrombotic medication in all patients after Fontan procedure because it has been shown that these agents lower the incidence of thrombotic events and are associated with fewer hospitalizations and a lower risk of death.[4,28]

This meta-analysis showed that, as predicted, the fenestrated group had a lower oxygen saturation after Fontan procedure than the nonfenestrated group. Oxygen desaturation could have detrimental long-term sequelae on the development of the nervous system in children.[8] Indeed, the benefits of fenestration seem to come at the cost of oxygen desaturation, which could lead to intolerable cyanosis as fenestration size increases.[29] Moreover, a large shunt created by the fenestration could result in a hypoxemia-induced acid-base disturbance that would lead to vasoconstriction and thus increase pulmonary vascular resistance.[30] This increase could induce a low cardiac output syndrome, which remains a main cause of morbidity after Fontan procedure.[25,30]

Table 3. Stroke Events and Anticoagulation Regimen After Fontan Procedures

Study	Fenestrated (n/N in category)	Nonfenestrated (n/N in category)	Anticoagulation Regimen
Snir 1994[21]	1/14	0/26	Aspirin to all patients; warfarin after major pulmonary artery reconstruction
Lemler 2002[27]	0/25	2/24	Aspirin
Fu 2009[18]	5/71	0/24	Not available
Sfyridis 2010[20]	0/26	0/32	Lifelong treatment of warfarin OR low-dose warfarin and low-dose aspirin OR aspirin alone
Atz 2011[16]	2/361	1/175	Not available

Study or Subgroup	Fenestrated Mean	Fenestrated SD	Fenestrated Total	None fenestrated Mean	None fenestrated SD	None fenestrated Total	Weight	Mean Difference IV, Random, 95% CI
Fiore 2014	89	4	61	94	4	54	18.4%	−5.00 [−6.46, −3.54]
Fu 2009	90.3	4	71	91.7	5.2	24	13.4%	−1.40 [−3.68, 0.88]
Kim 2008	90.8	4.4	85	92.8	4.6	200	20.6%	−2.00 [−3.13, −0.87]
Lemler 2002	90	3	25	96	8	24	8.5%	−6.00 [−9.41, −2.59]
Ono 2006	90.2	3.2	30	93.6	4.1	91	18.7%	−3.40 [−4.82, −1.98]
Salazar 2010	91	4	95	93	5	131	20.3%	−2.00 [−3.17, −0.83]
Total (95% CI)			**367**			**524**	**100.0%**	**−3.07 [−4.30, −1.85]**

Heterogeneity: $Tau^2 = 1.56$; $Chi^2 = 17.86$, df = 5 (P = 0.003); $I^2 = 72\%$
Test for overall effect: Z = 4.92 (P < 0.00001)

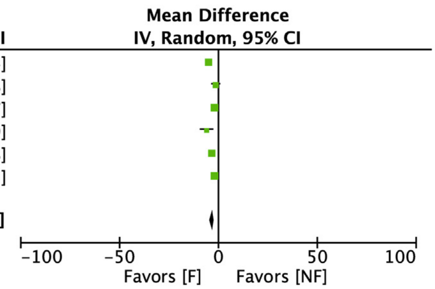

Figure 6. Forest plot for postoperative systemic saturation. (CI, confidence interval; F, fenestrated; M-H, Mantel-Haenszel method; NF, nonfenestrated.)

In a prospective randomized study, Cai and associates[30] found that administering inhaled nitric oxide (NO) in combination with milrinone to patients who had undergone a fenestrated Fontan procedure improved arterial blood oxygenation and reduced pulmonary vascular resistance. A transient increase in pulmonary vascular resistance could result in hemodynamic compromise in patients undergoing a Fontan procedure, and this could, in part, be caused by trauma from cardiopulmonary bypass.[25,34]

Because pulmonary blood flow in Fontan-type hemodynamics is not driven by the heart, it is primordial to control pulmonary vascular resistance and ensure it is low enough not to hinder blood flow. To address this issue, Knez and colleagues[25] administered inhaled NO to patients undergoing a total cavopulmonary connection procedure and who had a transpulmonary gradient of more than 10 mm Hg or a central venous pressure of more than 20 mm Hg in the early postoperative period. There was a significant hemodynamic benefit in the group treated with inhaled NO and a significant survival rate after 72 months of follow-up, compared with the group that did not receive NO treatment.[25]

Study Limitations

This meta-analysis was restricted by the limited number RCTs that sought to test the effect of fenestration on early Fontan outcomes. Indeed, only 1 RCT was included in our study[27]], and this prevents us from drawing any definite conclusions. Because several retrospective observational studies were included in this study, the effect of interstudy variations on the observed outcomes could not be excluded. This is notably the case with measuring the outcome of pleural drainage because the studies used different definitions, which would make the study of this outcome difficult. It is also difficult to account for factors that could influence the stroke rate in a meta-analysis of mostly retrospective studies, such as the use of specific anticoagulation therapies. In fact, given that we did not have access to the original data, an adjusted analysis could unfortunately not be achieved. In addition, the fenestrated group in our study had more preoperative risk factors for Fontan failure because they were younger, with higher pulmonary artery pressure and resistance, as well as more anatomic pulmonary artery distortion. These factors could, as such, potentiate the effects of fenestration on outcome compared with a lower-risk group. There is also a lack of long-term follow-up that was consistent among the different studies that were selected. Finally, late outcomes such as protein-losing enteropathy, plastic bronchitis, or heart transplantation, were not included in this meta-analysis because there were only few events for each outcome. This situation made it difficult to pool and study these data.

Conclusion

The Fontan fenestration seems to reduce the pulmonary pressure and the need for prolonged pleural drainage

Table 4. Long-term Outcomes After Fontan Procedures

Study	PLE	Arrhythmia	Catheter Interventions	Transplantation	Follow-up (mo; range in parentheses)
Atz 2011[16]	F: 3/361 NF: 6/175	F: 19/361 NF: 24/175	F: 0.6 ± 1.0 NF: 0.3 ± 0.9	Not available	F: 85, NF:104.4
Thompson 1999[6]	F: 0/32 NF: 0/49	Not available	Not available	Not available	Median: 40.8 (6-66)
Ono 2006[22]	3/121	Tachyarrhythmia: 40/121 Bradyarrhythmia: 27/121	34/121	1/121	240
Stewart 2012[33]	Not available	Not available	Not available	0	Not available
Salazar 2010[23]	Not available	Not available	F: 28/95 NF: 8/131	F: 1/95 NF:1/131	24 ± 20.4

Values are n ± SD or n/N.

F, fenestrated; NF, nonfenestrated; PLE, protein-losing enteropathy.

effectively. However, the risks of Fontan failure, early death, and longer hospital length of stay were not modified. Therefore, fenestration has limited benefit on postoperative outcomes and should be offered to high-risk patients (high pulmonary resistance, younger age, and with pulmonary distortion). With the broader use of postoperative pulmonary vasodilators in many centers, the role of adding a surgical fenestration must be subject of future study.

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