Clinical Outcome of Right Ventricular Outflow Tract Stenting Versus Blalock-Taussig Shunt in Tetralogy of Fallot: A systematic Review and Meta-Analysis

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Abstract: Aim: Several studies assessed the effectiveness of different therapeutic procedures for repairing right ventricular outflow tract (RVOT) in tetralogy of Fallot (TOF) patients reporting contradictory results. What has been systematically summarized in the present study was to assess the outcome of RVOT stenting in TOF patients and also to compare its outcome with Blalock-Taussig (BT) shunt procedure. Methods and Results: This study was performed according to established methods and in compliance with Preferred Reporting Items for Systematic review and Meta-Analysis Protocols. Two investigators searched the manuscript databases including Medline, Web of knowledge, Google scholar, Scopus, and Cochrane Central Register of Controlled Trials in the Cochrane Library for all eligible studies in accordance with the considered keywords. In final, 10 articles were eligible for the final analysis.

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The pooled success rate of RVOT stenting was found to be 93.6% (95% confidence interval [CI]: 89.6% to 96.2%). The overall improvement in arterial oxygen saturation following RVOT stenting was also shown to be 20.1%% (95% CI: 15.8% to 25.3%). The procedural-related death was also 3.7% (95% CI: 1.9% to 7.3%). The assessment of the outcome of RVOT stenting and BT shunt showed no significant difference in improvement rate of arterial O2 saturation (Odds ratio = 1.419, 95% CI: 0.645 to 3.123, *P*= 0.384) and death rate (risk ratios = 0.341, 95% CI: 0.057 to 2.024, *P*= 0.236). Conclusion: RVOT stenting leads to appropriate clinical outcome in children suffering TOF Comparing RVOT stenting and BT shunt shows comparable results with respect to clinical sequels. Classifications: Right Ventricular Outflow Tract (RVOT), Tetralogy Of Fallot (TOF), BT shunt.

Condensed Abstract:

Aim: Present study was to assess the outcome of right ventricular outflow tract (RVOT) stenting in tetralogy of Fallot (TOF) patients and also to compare its outcome with Blalock-Taussig (BT) shunt procedure.

Methods and Results: This study was performed according to established methods and in compliance with Preferred Reporting Items for Systematic review and Meta-Analysis Protocols. In final, 10 articles were eligible for the final analysis. The assessment of the outcome of RVOT stenting and BT shunt showed no significant difference in improvement rate of arterial O2 saturation and death rate.

Conclusion: RVOT stenting leads to appropriate clinical outcome in children suffering TOF Comparing RVOT stenting and BT shunt shows comparable results with respect to clinical sequels. (Curr Probl Cardiol 2021;46:100643.)

Introduction

Some patients suffering tetralogy of Fallot (TOF) have appropriate size of pulmonary arteries and in this regard can be candidate for primary surgical repairing within the first year of life with an

excellent post-procedural outcome.[1,2] This proper consequence can be achieved mainly when procedures is performed beyond the neonatal period. Against such patients, severely cyanosed patients with improper pulmonary blood flow due to abnormality in right ventricular outflow tract (RVOT) or with valvar stenosis may face with poor prognosis.[3,4] These bad sequels may be deteriorated when neonatal comorbidities such as prematurity, neurological defects, low birth weight or postnatal infections exist.[5] For such patients, different therapeutic options have been employed to improve procedural outcome including the insertion of aortopulmonary shunt, arterial duct stenting, or percutaneous RVOT augmentation.[6] Especially in patients with major comorbidities such as severe cyanotic condition, small pulmonary arteries, Atrio Ventricular Septal Defect, or complex anatomical variants of TOF, these options are significantly limited. In this high risk group, some palliative options such as a surgical systemic to pulmonary shunt (Blalock-Taussig or BT shunt) is frequently employed, however, this procedure may be accompanied with some potential complications such as pulmonary over-circulation or even pulmonary artery stenosis.[7,8] Another recent option has been introduced in these patients is RVOT stenting that has emerged as the main bridging procedure. Although such technique is very effective and low risk for most affected patients, it may also actually result in some complications including pulmonary artery deformation or stent restenosis.[9,10] Several studies assessed the effectiveness of different therapeutic procedures for repairing RVOT in TOF patients reporting contradictory results. What has been systematically summarized in the present study was to assess the outcome of RVOT stenting in TOF patients and also to compare its outcome with BT shunt procedure.

Materials and Methods

This study was performed according to established methods and in compliance with Preferred Reporting Items for Systematic review and Meta-Analysis Protocols. Two investigators searched the manuscript databases including Medline, Web of knowledge, Google scholar, Scopus, and Cochrane Central Register of Controlled Trials in the Cochrane Library for all eligible studies in accordance with the considered keywords including: "Right Ventricular Outflow Tract", "Blalock-Taussig Shunt," and "Tetralogy of Fallot." The studies were restricted to English language. We included all randomized controlled trials (RCTs), including individually randomized and cluster randomized trials. We also included the studies reported as full-text and those published as abstracts. The inclusion

criterion for retrieved the studies were children or adult patients who underwent RVOT stenting or BT shunting for TOF repair. The exclusion criteria were thus as follows: (1) a lack of clear and reproducible results, (2) non-English studies, (3) lack of access to the manuscripts full texts, and (4) case reports, case series, and review papers.

Data abstraction was independently performed by 2 un-blinded reviewers on structure collection forms without divergences in data collection. We resolved disagreements by consensus or by involving a third person. We doubled-check that data was entered correctly by comparing the data presented in the systematic review with the data extraction form.

The risk of bias for each study was assessed using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions and also according to QUADAS-2 tool. Any disagreement was resolved by discussion in the whole study team. We assessed the risk of bias according to the following domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective outcome reporting. We judged each potential source of bias as high, low, or unclear and provide a quote from the study report together with a justification for our judgment in the "Risk of bias" table. Binary outcomes from individual studies were to be combined with both the Mantel-Hansel fixed effect model. The risk ratios (RRs) and 95% confidence interval (CI) for RR were used as summary statistics for the comparison of dichotomous variables and for determining the likelihood of each adverse event after interventions. Cochran's Q test was used to determine the statistical heterogeneity of this study. This test was complemented with the I2 statistic, which quantifies the proportion of total variation across studies that is due to heterogeneity rather than chance. A value of I^2 of 0-25% indicates insignificant heterogeneity, 26-50% low heterogeneity, 51-75% moderate heterogeneity, and 76-100% high heterogeneity. Publication bias was assessed by the rank correlation test and also confirmed by the funnel plot analysis. Reported values were two-tailed, and hypothesis testing results were considered statistically significant at P= 0.05. Statistical analysis was performed using the Stata software (version 13.1, Stata Corp, College Station, TX).

Results

Study Selection and Characteristics of Included Studies

The flow diagram of the study selection is presented in Figure 1. Initially, 28 articles were collected by database searching and other sources. After

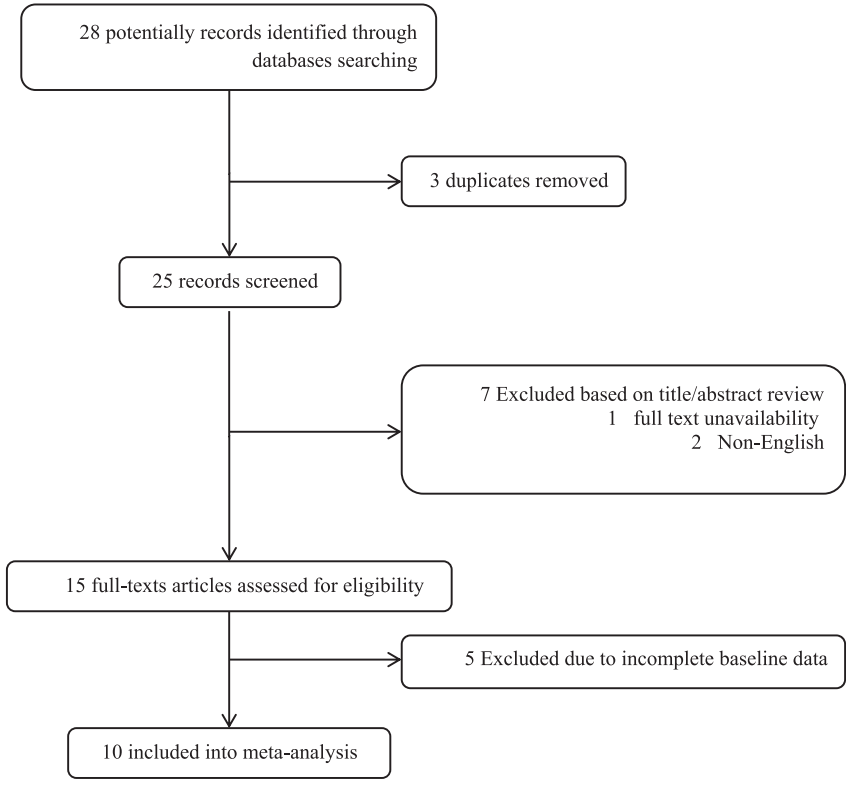

FIG 1. The flowchart of screening the eligible studies.

removing 3 articles due to evidences of duplication, 25 records were primarily under-screened. Based on the titles and abstracts, 10 records were excluded and the remaining 15 citations were assessed for further eligibility. Of those, 5 were also excluded due to incompleteness of the data and contents. In final, 10 articles were eligible for the final analysis (Table 1).[11-20]

Methodological Quality of the Included Studies

The studies included were assessed qualitatively by the QUADAS-2 tool. According to our risk of bias assessment, 5 studies yielded good quality and five of the citation was determined to have moderate to high risk of bias and therefore the pooled results were partially persuasive (Figure 2).

Overall study characteristics

In total, 10 studies (including 354 patients with TOF undergoing RVOT stenting or BT shunt) were finally evaluated in terms of procedural

Table 1. The details of studies included into the meta-analysis

Author, year	Procedure	Number	M/F	Mean age (day)	Mean weight (kg)	RPA size (mm)	RPA Z-score	O2 saturation
Barron, 2013	RVOT stenting	32		60	3.9	3.2	−1.3	72%
Bigdelian, 2018	RVOT stenting	7	2/5	48	3.3	4.60	−3.0	66%
	BT shunt	8	5/3	84	5.1	2.90	−2.9	74%
Castleberry, 2013	RVOT stenting	6		19	2.6	4.60	−3.3	71%
	BT shunt	4		15	2.6	5.60	−3.3	70%
Dohlen, 2009	RVOT stenting	11	7/44	27	2.8	4.9	−4.9	73%
McGovern, 2016	RVOT stenting	9	4/5	40	3.7	3.3	−3.8	60%
Quandt, 2017	RVOT stenting	39	24/15	63	3.9	4.2	−2.3	75%
	BT shunt	28	19/9	60	3.3	2.7	−2.2	75%
Quandt, 2018 [17]	RVOT stenting	60	35/25	61	3.9			75%
	BT shunt	41	29/12	46	3.5			77%
Sandoval, 2016	RVOT stenting	42		21	2.8		−4.0	75%
Stumper, 2013	RVOT stenting	57	30/27	63	3.8		−2.6	71%
Valderrama, 2020	RVOT stenting	12	3/9	20	2.1	1.8	−4.0	74%

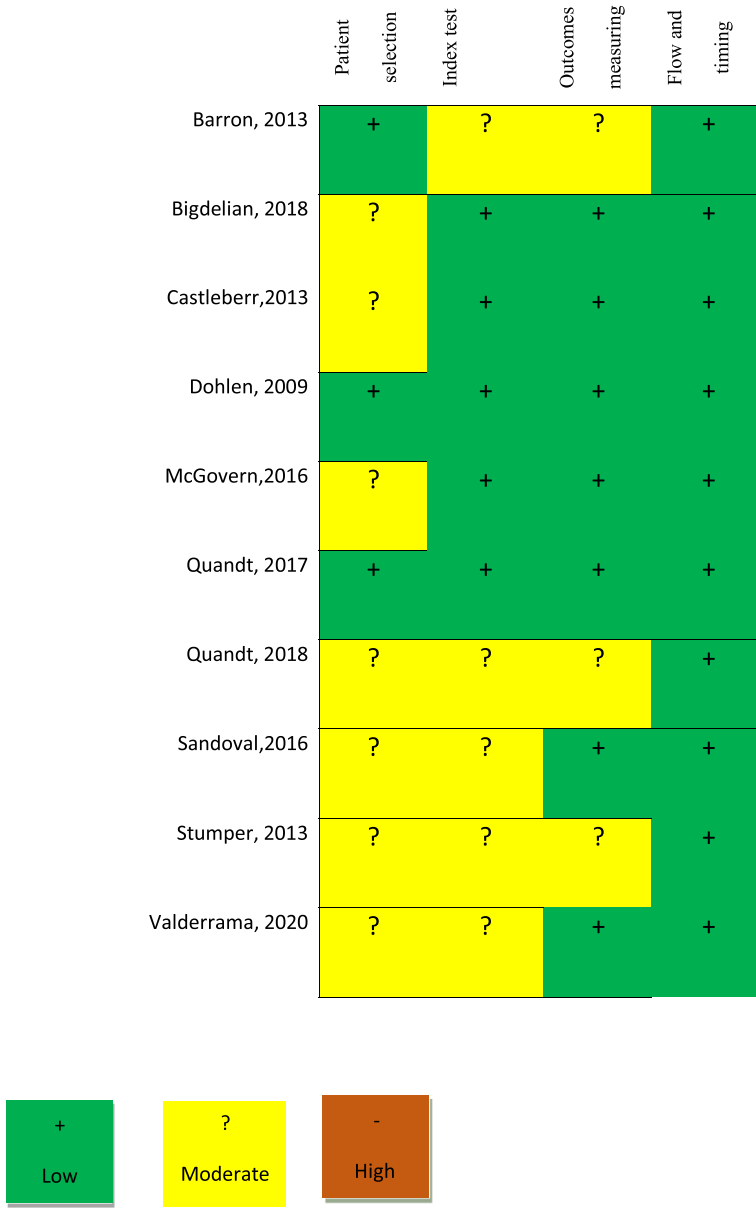

FIG 2. The Assessment of the risk of bias.

outcome and complications. Overall, 6 studies with cross-sectional pattern assessed the outcome of RVOT stenting, while residual 4 studies could compare the outcome of RVOT stenting and BT shunt procedures. The mean age of patients ranged from 20 to 84 days and mean weight

Table 2. outcome of procedure RVOT stenting within the follow-up time

Author, year	Procedure	RVOT success	Improved saturation	Death	ICU stay	ACC time	Final RPA Z-score change	CPB time	transannular patch
Barron, 2013	RVOT stenting	31/32	20%	1/32	48	68	+0.1	109	14/32
Bigdelian, 2018	RVOT stenting BT shunt	7/7	19% 19%	1/7 1/8	94.4 94.3	111.8 89.3	−0.8 −1.1	165.5 129.2	4/7 5/8
Castleberr, 2013	RVOT stenting BT shunt	5/6	23% 20%	0/6 0/4		99 92	−1.8 −1.0	142 169	4/4 4/4
Dohlen, 2009	RVOT stenting	11/11	21%	0/11	120	51	−1.5	99	5/11
McGovern, 2016	RVOT stenting	7/9	36%	0/9			−0.9		
Quandt, 2017	RVOT stenting BT shunt	39/39	20% 15%	0/39 1/28			−0.7 −0.9		22/39 17/28
Quandt, 2018	RVOT stenting BT shunt	57/60	20% 13%	0/60 2/41	72.0 192	65 71		95 108	8/12
Sandoval, 2016	RVOT stenting	39/42	19%	2/42	60		−1.5		
Stumper, 2013	RVOT stenting	55/57	21%	1/57	24		−0.7		
Valderrama, 2020	RVOT stenting	11/12	14%	0/12			+0.5		12/12

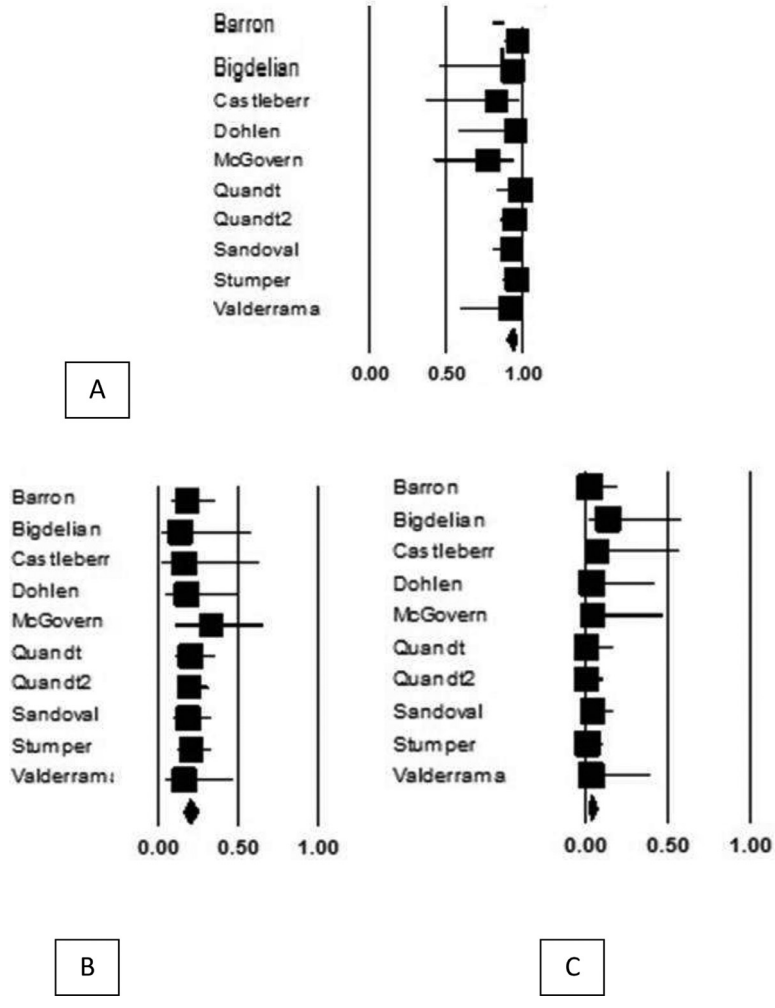

FIG 3. Forest plots of pooled rate of RVOT stenting success rate (A), improvement in O2 saturation (B) and death rate (C).

ranged from 2.1 to 5.1 kg. The initial oxygen saturation was reported in the range of 60 to 77%. The outcome was defined as RVOT and shunt success rate, improvement of arterial oxygen saturation, improvement of right pulmonary artery Z-score, final ACC and CPB times, requiring transannular patch, length of ICU stay and occurring death (Table 2). The studies published between 2009 and 2020.

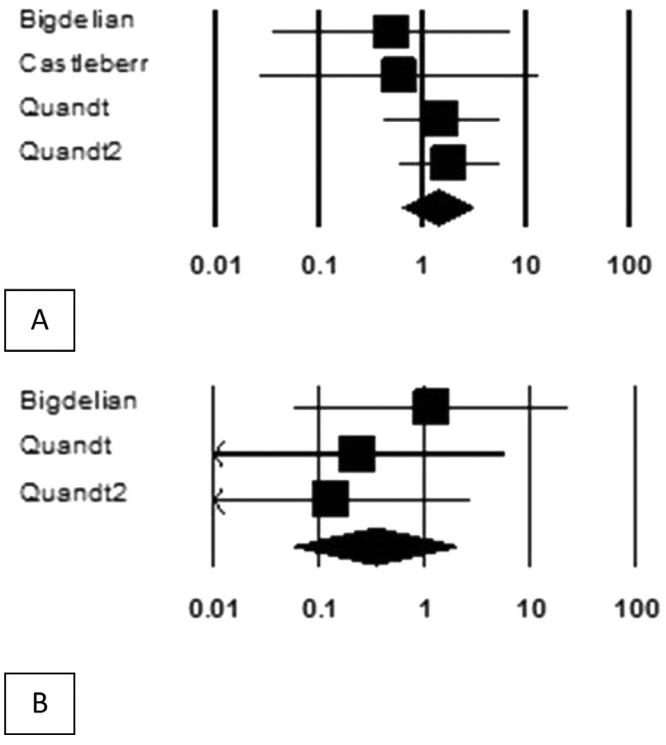

FIG 4. Forest plots of the odds ratio for improvement in O2 saturation (A) and death rate (B).

The outcome of RVOT stenting

In all studies assessed the outcome of RVOT stenting, the pooled success rate was found to be 93.6% (95% CI: 89.6%-96.2%; Figure 3). In this regard, the overall improvement in arterial oxygen saturation was also shown to be 20.1% (95% CI: 15.8% to 25.3%; Figure 4). Regarding mortality, the procedural-related death was calculated to be 3.7% (95% CI: 1.9% to 7.3%). The length of ICU stay after procedure ranged 24 to 120 hours. The mean ACC time was in the range of 65 to 111 minutes and the mean CPB time was also 95 to 165 minutes. The pooled assessment of the studies showed significantly improvement in final RPA Z-score as compared to the baseline values (Table 2). The heterogeneity across the groups was insignificant for assessment of all measurements including success rate (I^2 square of 0.001, P= 0.609), improvement in oxygen saturation (I^2 square of 0.001, P= 0.998), and death rate (I^2 square of 0.001, P = 0.864) with no publication bias in all studies (P values of 0.928, 0.089, and 0.244, respectively).

Comparing the outcome of RVOT stenting versus BT shunt

The assessment of the outcome of RVOT stenting and BT shunt in 4 studies showed no significant difference in improvement rate of arterial O2 saturation (OR = 1.419, 95% CI: 0.645-3.123, *P*= 0.384) and death rate (RR = 0.341, 95% CI: 0.057-2.024, *P*= 0.236). The heterogeneity across the studies remained also insignificant for assessment of arterial O_2 saturation (I^2 square of 0.001, P = 0.784) and death rate (I^2 square of 0.001, *P*= 0.581). No publication bias was also revealed in all studies (*P*values of 0.174 and 0.601, respectively).

Discussion

RVOT stenting is now known as an effective and safe technique in the initial palliation of selected patients with TOF. This procedure has been recently considered as a good alternative for BT shunt with acceptable early and long-term outcome. RVOT stenting can result in improving pulsatile forward flow of systemic venous blood to the pulmonary artery, improving arterial O_2 saturation, as well as improve pulmonary arterial growth. Some studies could demonstrate its superiority as compared to BT shunt with regard to the pointed variables, however some other studies led to contradictory results emphasizing systematically reviewing the literature to obtain an agreement in which procedure can be considered with better clinical outcome. The present systematic review and meta-analysis could first show high clinical effectiveness of RVOT stenting in terms of achieving proper pulmonary arterial growth during palliation along with obtaining proper arterial O_2 saturation. We also showed notably low post-procedural morbidities and death following RVOT stenting. In next phase, comparing the clinical outcome of this procedure and BT shunt indicated no significant difference in procedural outcome. Interestingly, the findings of the studies had a good homogeneity and thus in assessment of clinical consequences of RVOT stenting as well as comparing the outcome of two procedures, the results seems to be reliable. However, deeply reviewing the studies regarding risk of bias led to some limitations. First, some studies failed to assess some clinical outcomes such as the time for aortic cross-clamp time, cardiopulmonary bypass time, or ICU requirement. Furthermore, the time of patients' follow-up widely varied emphasizing the necessity for breaking up early and long-term consequences of the two procedures. Another limitation of the studies was to ignore potential comorbidities of TOF patients such as prematurity, low weight, infection, neurological injury, and other conditions requiring non-cardiac surgeries that might affect the outcome of the

procedures. Hence, it seems that to achieve better evidences on the effectiveness of both procedures, further original researches considering such parameters are necessary.

Limitation: Our analyses were substantially limited in the number and quality of studies available. Non-English and lack of access to the full-text studies were exclusion criteria.

Conclusion

RVOT stenting leads to appropriate clinical outcome in children suffering TOF. Comparing RVOT stenting and BT shunt shows comparable results with respect to clinical sequels. Due to acceptable homogeneity across the studies, the results of the present meta-analysis can be reliable and applicable.

Impact of daily practice

RVOT stenting leads to appropriate clinical outcome in children suffering TOF.

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