

Modified Blalock-Taussig-Thomas shunt blockage and mortality: A systematic review and meta-analysis

*Modified Blalock-Taussig-Thomas şant tıkanıklığı ve mortalite:
Sistemik derleme ve meta-analiz*

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ABSTRACT

Background: In this systematic review and meta-analysis, we discuss the estimated of global incidence, shunt related-mortality risk and factors associated with shunt blockage after modified Blalock-Taussig-Thomas (mBTT) procedure.

Methods: A systematic review and meta-analysis were conducted using PubMed, ScienceDirect, and EMBASE up to February 2024. The primary outcomes were the incidence and mortality risk associated with shunt blockage. Additional outcomes included study characteristics, surgical factors, and coagulation profiles. Single and two-group proportional meta-analyses were performed.

Results: A total of 25 studies involving 2,677 patients were included. The global incidence of shunt blockage was 7% (95% confidence interval [CI]: 0.05 to 0.10) with high heterogeneity ($I^2=81\%$; $p<0.01$). In 15 studies eligible for mortality analysis, patients with shunt blockage had significantly higher odds of death (odds ratio [OR]=5.04; 95% CI: 2.69 to 9.44) with low heterogeneity ($I^2=3\%$; $p=0.41$). Shunt size alone was not a significant predictor of blockage. However, patients with shunt blockage exhibited significantly lower partial thromboplastin time and activated partial thromboplastin time values, suggesting coagulation abnormalities. No significant difference was found in platelet counts.

Conclusion: Shunt blockage is a critical complication following mBTT shunt, significantly increasing mortality risk. While shunt size is not independently predictive, multiple factors, including patient weight, underlying pathology, coagulation profile, surgical factors, and shunt size-to-weight ratio, may contribute to thrombosis risk and warrant further investigation.

Keywords: Congenital heart disease, modified Blalock-Taussig-Thomas shunt, mortality, shunt blockage.

ÖZ

Amaç: Bu sistemik derleme ve meta-analizde, modifiye Blalock-Taussig-Thomas (mBTT) şant prosedürü sonrasında küresel şant tıkanıklığı insidansı, şanta bağlı mortalite riski ve şant tıkanıklığı ile ilişkili faktörler incelendi.

Çalışma planı: PubMed, ScienceDirect ve EMBASE veri tabanları kullanılarak Şubat 2024'e kadar yayımlanmış çalışmalar esas alınarak sistemik bir derleme ve meta-analiz yapıldı. Primer sonuçlar, şant tıkanıklığına bağlı insidans ve mortalite riski idi. İlave sonuçlar arasında çalışma özellikleri, cerrahi faktörler ve koagülasyon profilleri yer aldı. Tekli ve ikili grup oransal meta-analizler yapıldı.

Bulgular: Toplamda 2,677 hastayı içeren 25 çalışma dahil edildi. Tüm dünyada şant tıkanıklığı insidansı %7 olarak bulundu (95% güven aralığı [GA]: 0.05-0.10) ve heterojenlik yüksekti ($I^2=81\%$; $p<0.01$). Mortalite analizine uygun 15 çalışmada, şant tıkanıklığı olan hastalarda ölüm olasılığı anlamlı şekilde daha yüksek bulundu (olasılık oranı [OR]=5.04; 95% GA: 2.69-9.44) ve heterojenlik düşüktü ($I^2=3\%$; $p=0.41$). Şant boyutu tek başına tıkanıklık için anlamlı bir öngörücü değildi. Ancak, şant tıkanıklığı gelişen hastalarda kısmi tromboplastin zamanı ve aktive parsiyel tromboplastin zamanı değerlerinin anlamlı şekilde düşük olduğu gözlenmiş ve bu da koagülasyon bozukluklarını işaret etmekteydi. Trombosit sayılarında anlamlı bir fark bulunamadı.

Sonuç: Modifiye Blalock-Taussig-Thomas şant sonrasında şant tıkanıklığı, mortalite riskini anlamlı düzeyde artıran ciddi bir komplikasyondur. Şant boyutu tek başına belirleyici olmasa da, hastanın kilosu, altta yatan patoloji, koagülasyon profili, cerrahi faktörler ve şant boyutu/ağırlık oranı gibi birden fazla faktör tromboz riskine katkıda bulunabilir ve ileri çalışmalarda araştırılmalıdır.

Anahtar sözcükler: Konjenital kalp hastalığı, modifiye Blalock-Taussig-Thomas şanti, mortalite, şant tıkanıklığı.

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Modified Blalock-Taussig-Thomas (mBTT) shunt palliative operations were first reported in 1977 by Elliott et al.^[1] using the polytetrafluorethylene (PTFE) graft as an aortopulmonary shunt as a substitute for a subclavian artery graft in the original Blalock-Taussig-Thomas (BT) shunt. The main goal of this procedure is to help the supply of pulmonary arteries and reducing cyanosis in cases of cyanotic congenital heart disease. The main indication of mBTT is to increase blood flow to the lungs in severe congenital heart disease with the help of grafts, which help heart maturity and pulmonary arteries before definitive reconstruction surgery.^[2,3]

Common complication post-mBTT surgery other than mortality is shunt blockage, obstruction or thrombosis. Treatment options include surgical revision/replacement, endovascular procedures (balloon angioplasty and/or stent placement), and combination of local and systemic thrombolytics.^[3,4] Although the treatment is available, both blockage and mortality post operation still exist up until now and the number vary around the world.

Existing research of the factors associated with the shunt blockage-related mortality risk to minimize the number still have limitations. Those limitations mostly are due to the small size of the total patients single-center study, and difference in study design.^[5,6] In addition, there is no systematic review in the literature. To address this gap, in this systematic review and meta-analysis, we discuss the estimated of global incidence, shunt related-mortality risk and factors associated with shunt blockage after mBTT procedure.

PATIENTS AND METHODS

This systematic review is registered in PROSPERO with the registration number CRD42024509795, submitted in February 2024. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guided the search and the development of the flowchart.

Eligibility criteria

The primary outcomes of interest were the incidence of shunt blockage and shunt blockage-related mortality. Only original research articles that reported both shunt obstruction, blockage, occlusion, or thrombosis and shunt blockage-related mortality following the mBTT procedure were included. Mortality was defined as death occurring during hospitalization or postoperatively. Studies that did not specify the timing of death were still included,

but those explicitly reporting late-onset mortality were excluded. Similarly, shunt blockage was defined as shunt malfunction occurring during hospitalization or postoperatively. Studies which did not specify the timing of blockage were included, whereas those reporting late-onset shunt blockage were excluded. In addition, exclusion criteria included the unavailability of a full-text version, irrelevant topics, unrelated outcomes, and data from articles that could not be further examined.

Information sources and search strategy

We searched EMBASE, MEDLINE, PubMed, ScienceDirect, and Web of Science for related publications from January 2004 to February 2024 using four main keywords: “mBTT OR BT shunt,” “Risk factors OR factors associated,” “mortality OR death,” and “shunt obstruction OR occlusion OR blockage.” The search was limited to English-language studies. Duplicates were manually eliminated after the initial examination, and titles/abstracts were screened for relevance. The full texts of potentially relevant articles were, then, assessed using the eligibility criteria. Additionally, the reference lists of relevant articles were reviewed for potential studies.

Study selection

Three authors independently screened the titles and abstracts of potentially eligible articles. They also retrieved and evaluated the full texts for eligibility using predetermined inclusion and exclusion criteria. Mortality and shunt blockage post-mBTT were assessed in each study. Any disputes during the selection process were resolved through discussion and consultation among the main authors and co-authors. The number of articles which passed each screening stage was recorded, and a comprehensive overview of the study selection process is provided in the PRISMA flow chart.

Data collection process and quality of assessment

The characteristics of the eligible articles were organized into a table, and the full text of all studies was examined to collect the following information: author, publication year, study design, sample size, related outcomes, and reported shunt blockage incidence and shunt blockage-related mortality. We divided the total participants into two groups: patients with shunt blockage and patients without shunt blockage post-mBTT. Detailed information about the study characteristics are shown in Table 1. We also

Table 1. Study characteristics

No	Study	Study design and time	Location and population		Mortality and shunt blockage outcome		
			Country	n	Mortality	n	%
1	Abdelmoneim et al. ^[8] 2017	Cohort Prospective March 2014 and February 2015	Egypt	40	Mortality First postoperative day mortality First three day postoperative day mortality Shunt occlusion	20 of 40 10 of 40 5 of 40 11 of 40	50 25 12.5 27.5
2	Ahmad et al. ^[17] 2008	Retrospective cohort from 1999 - 2005	Pakistan	22	≤3 months mortality >3 months mortality ≤3 months shunt malfunction/occlusion/failure >3 months shunt malfunction/occlusion/failure One hour of surgery shunt failure	3 of 22 3 of 22 2 of 22 2 of 22 1 of 22	15 15 9.1 9.1 4.5
3	Alsoufi et al. ^[13] 2016	Cohort Retrospective between 2002 and 2012	USA	341	Hospital mortality Shunt thrombosis	31 of 341 2 of 341	9.1 0.005
4	Bigdelian et al. ^[26] 2018	Retrospective study between May 2015 and October 2016	Iran	8	Mortality Shunt occlusion	1 of 8 0 of 8	12.5 0
5	Bove et al. ^[14] 2015	Cohort Retrospective from August 1995 to December 2013	Belgium	150	In-hospital mortality Interstage mortality Acute shunt thrombosis Late shunt thrombosis	13 of 150 7 of 150 6 of 150 1 of 150	8.6 4.6 4 0.6
6	Chittithavorn et al. ^[7] 2017	Cohort Retrospective from January 2006 and February 2016	Thailand	85	In-hospital shunt thrombosis In-hospital mortality	12 of 85 15 of 85	14.1 17.6
7	Dirks et al. ^[12] 2013	Cohort Retrospective since 2004 until 2011	Switzerland	32	Postoperative mortality Late mortality Shunt thrombosis Late shunt obstruction/thrombosis	3 of 32 0 of 32 3 of 32 0 of 32	9.3 0 9.3 0
8	El-Awady ^[6] 2018	Study design is not stated explicitly. Study conducted since January 2013 to December 2016	Egypt	28	Mortality Shunt occlusion	0 of 28 0 of 28	0 0
9	El Midany and Doghish ^[24] 2019	Prospective study between March 2011 and December 2016	Egypt	50	In-hospital mortality In-hospital shunt thrombosis	3 of 50 2 of 50	6 4
10	Gedicke et al. ^[9] 2010 ^[9]	Cohort Retrospective from January 2002 to December 2006	UK	76	30-day mortality In-hospital mortality 24 h acute shunt blockage 1.5, 5- and 20-months late shunt blockage	3 of 76 3 of 76 9 of 76 4 of 76	3.9 3.9 11.8 5.2
11	Guzzetta et al. ^[27] 2013	Retrospective cohort March 1, 2005 - December 31, 2011	USA	207	In-hospital mortality Shunt occlusion	15 of 207 14 of 207	7.2 6.7
12	Hanet al. ^[18] 2023	Retrospective case review between January 2012 and December 2019	China	52	Death Shunt thrombosis	2 of 52 5 of 52	3.8 9.6
13	Headrick et al. ^[6] 2022	Retrospective cohort study between December 2008 and December 2018	USA	155	In-hospital mortality Early shunt malfunction	11 of 155 10 of 155	7.1 6.4

Table 1. Continued

No	Study	Study design and time	Location and population		Mortality and shunt blockage outcome		
			Country	n	Mortality	n	%
14	Ismail et al. ^[22] 2018	Retrospective cohort study from January 2000 till December 2015	Saudi Arabia	197	Mortality Shunt obstruction	35 of 197 5 of 197	17.25 2.5
15	Lapmahapaisan et al. ^[10] 2017	Cohort Retrospective from January 2009 and December 2015	Thailand	102	6 h acute shunt blockage 24 h acute shunt blockage 24 h postoperative mortality	11 of 102 14 of 102 3 of 102	10.7 13.7 2.9
16	Lenoir et al. ^[28] 2020	Retrospective study between January 1995 and November 2018	France	70	Hospital mortality Thrombosis	3 of 70 6 of 70	4.2 8.5
17	Li et al. ^[21] 2020	Retrospective review from May 2008 to December 2018	China	25	Hospital mortality 1.2 years follow-up graft blockage 1.2 years follow-up death	3 of 25 0 of 25 1 of 25	12 0 4
18	McMullan et al. ^[29] 2014	Retrospective review December 2002 to April 2011	USA	42	Procedure-related deaths First postoperative day mortality Thrombotic occlusion of the shunt	0 of 42 1 of 42 4 of 42	0 2.3 9.5
19	Küçük et al. ^[11] 2016	Observational Study between 2009 and 2013	Türkiye	44	Mortality 48 hours mortality Thrombosis	8 of 44 3 of 44 4 of 44	18.1 6.8 9.1
20	Oofuvong et al. ^[30] 2021	Cohort Retrospective between January 2005 and December 2016	Thailand	380	Death ≤90 days Death >90 days Shunt thrombosis	63 of 380 56 of 380 38 of 380	16.5 14.7 10
21	Sasikumar et al. ^[10] 2017	Cohort Retrospective from January 2004 to December 2014	Canada	95	In-hospital mortality Interval mortality/death after hospital discharge Shunt thrombosis	3 of 95 3 of 95 1 of 95	3.1 3.1 1.05
22	Shaikh et al. ^[31] 2020	Retrospective study from January 2016 to December 2018	Oman	50	Early/in-hospital mortality Interstage/interval mortality Shunt blockade	5 of 50 3 of 50 6 of 50	10 6 12
23	Shibata et al. ^[20] 2015	Cohort retrospective between July 2004 and January 2013	Japan	18	Hospital mortality Shunt occlusion	0 of 18 0 of 18	0 0
24	Ussiri et al. ^[15] 2007	Retrospective study from January 2004 to December 2006	India	20	Mortality Shunt thrombosis	0 of 20 0 of 20	0 0
25	Zhu et al. ^[23] 2019	Cohort Retrospective from January 2008 and December 2014	China	388	Hospital deaths Hospital shunt obstruction	3 of 388 11 of 388	0.7 2.8

collected operative data, including the number of mortalities and shunt blockages, shunt size diameter, pulmonary artery (PA) diameter, inflow shunt location, and surgical technique.

Three authors independently evaluated the quality of the studies using the Critical Review Form for Quantitative Studies. The critical review components included study purpose, literature background, study design, sampling method, validity and reliability of outcomes, intervention or exposure, significance and appropriateness of results, reported drop-out rates, conclusions, and study limitations. Good-quality components were shaded green, while poor-quality components were shaded red.

Statistical analysis

Statistical analysis was performed using the R Studio (R Foundation for Statistical Computing, Vienna, Austria) and Review Manager version 5.4 software (The Cochrane Collaboration, Oxford, UK). We conducted a single-group proportional meta-analysis to estimate global mortality and shunt blockage incidence using a random-effects model. The estimated proportion was calculated as the number of events divided by the total sample size

of patients who underwent the mBTT procedure. The odds ratio (OR) was calculated as the odds of mortality in patients with shunt blockage divided by the odds of mortality in patients without shunt blockage. Meta-analyses were also performed to evaluate additional outcomes, such as shunt size diameter, coagulation factors, and platelet count. The *I*² statistic was used to determine the level of statistical heterogeneity, with 25% indicating low heterogeneity, 25 to 50% indicating moderate heterogeneity, and above 50% indicating high heterogeneity. The results of the meta-analysis are presented in forest plots as proportions (%) and ORs with 95% confidence intervals (CIs). We also assessed publication bias using funnel plots and Egger’s regression test. A random-effects model and to assess potential clinical heterogeneity. A *p* value of <0.05 was considered statistically significant.

RESULTS

Study characteristics, operative profiles and quality assessment

There were initially 90 studies found in total after searching through databases as described in the methodology section with the PRISMA flow

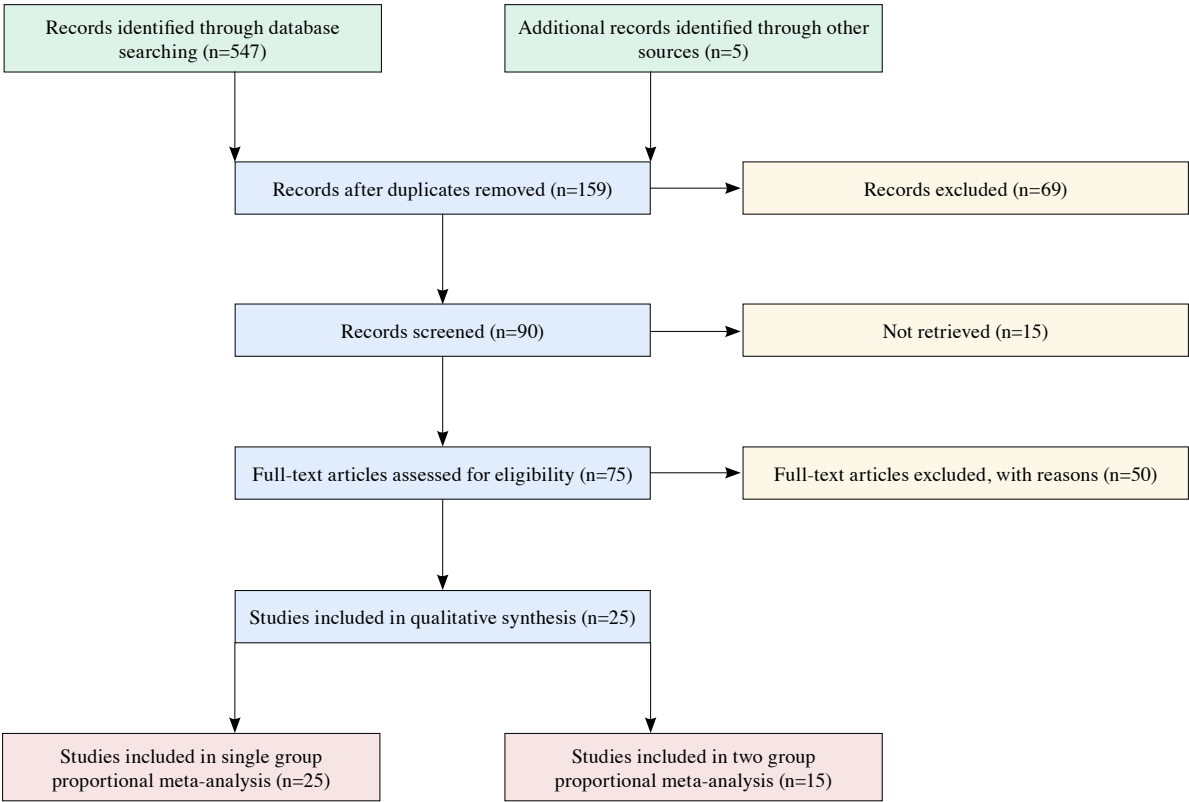


Figure 1. PRISMA chart.

Table 2. Study operative profiles

Study	Population	Shunt blockage	Mortality	Shunt size		Shunt inflow artery location		Mean of PA size		Surgical technique	
				<4 mm	≥4 mm	Innominate	Brachiocephalic/ central	Right	Left	Sternotomy	Thoracotomy
Abdelmoneim et al. ^[18] 2017	40	11	20	22	18	No data	No data	4.23±1.448	4.115±0.796	34	6
Ahmad et al. ^[17] 2008	22	1	6	0	22	No data	No data	3.0±0.2	2.9±0.2	0	22
Alsoufi et al. ^[13] 2016	341	2	31	315	21	No data	No data	No data	No data	No data	No data
Bigdelian et al. ^[26] 2018	8	0	1	No data	No data	No data	No data	3.2±0.32	2.5±0.42	8	0
Bove et al. ^[14] 2015	150	7	20	16	134	No data	No data	No data	No data	24	126
Chittithavorn et al. ^[7] 2017	85	12	15	62	23	No data	No data	No data	No data	33	52
Dirks et al. ^[12] 2013	32	3	3	27	5	12	20	No data	No data	32	0
El-Awady et al. ^[16] 2018	28	0	0	10	18	No data	No data	6.5±5.6	4.5 ±1.4	0	28
El Midany and Doghish ^[24] 2019	50	2	3	50	0	No data	No data	No data	No data	50	0
Gedicke et al. ^[9] 2010	76	9	3	No data	No data	70	6	No data	No data	Majority thoracotomy	
Guzzetta et al. ^[27] 2013	207	14	15	198	9	No data	No data	3.7±1.0	3.1±0.8	No data	No data
Han et al. ^[18] 2023	107	5	2	No data	No data	107	0	No data	No data	0	107
Headrick et al. ^[6] 2022	155	10	11	69	85	139	12	No data	No data	64	91
Ismail et al. ^[22] 2018	197	5	30	19	4	No data	No data	No data	No data	197	0
Lapmahapaisan et al. ^[19] 2017	102	14	3	60	42	No data	No data	No data	No data	1	101
Lenoir et al. ^[28] 2020	70	6	3	No data	No data	No data	No data	7.4	7.9	No data	No data
Li et al. ^[21] 2020	25	0	3	12	13	No data	No data	No data	No data	25	0
McMullan et al. ^[29] 2014	42	4	1	13	29	No data	No data	No data	No data	No data	No data
Küçük et al. ^[11] 2016	44	4	8	No data	No data	No data	No data	No data	No data	26	18
Oofuvong et al. ^[30] 2021	3,804	44	63	No data	No data	No data	No data	No data	No data	No data	No data
Sasikumar et al. ^[10] 2017	95	9	17	80	5	11	84	No data	No data	92	3
Shaikh et al. ^[31] 2021	50	6	13	No data	No data	No data	No data	No data	No data	45	5
Shibata et al. ^[20] 2015	18	0	0	18	0	0	18	No data	No data	18	0
Ussiri et al. ^[15] 2007	20	0	0	No data	No data	No data	No data	No data	No data	0	20
Zhu et al. ^[23] 2019	388	11	3	No data	No data	No data	No data	5.3±2.3	4.8±1.9	388	0

PA: Pulmonary artery.

Table 3. Study quality assessment

Study	Purpose	Literature	Design	Sample	Outcomes	Intervention	Results	Drop-out	Conclusion	Limitation
Gedickie et al. ^[9] 2010										
Abdelmoneim et al. ^[8] 2017										
Ahmad et al. ^[17] 2008										
Alsoufi et al. ^[13] 2016										
Bigdelian et al. ^[26] 2018										
Bove et al. ^[14] 2015										
Chittithavorn et al. ^[7] 2017										
Dirks et al. ^[12] 2013										
El Awady et al. ^[6] 2018										
El Midany et al. ^[24] 2019										
Gedickie et al. ^[9] 2010										
Guzzetta et al. ^[27] 2013										
Han et al. ^[18] 2023										
Headrick et al. ^[6] 2022										
Ismail et al. ^[22] 2018										
Lapmahapaisan et al. ^[19] 2017										
Lenoir et al. ^[28] 2020										
Li et al. ^[21] 2020										
McMullan et al. ^[29] 2014										
Küçük et al. ^[11] 2016										
Oofuvong et al. ^[30] 2021										
Sasikumar et al. ^[10] 2017										
Shibata et al. ^[20] 2015										
Shaikh et al. ^[31] 2021										
Ussiri et al. ^[15] 2007										
Zhu et al. ^[23] 2019										
Good-quality components were shaded green, while poor-quality components were shaded red.										

diagram (Figure 1). After screening, 75 papers were matched our aim of study. There were 25 of 75 papers met our inclusion criteria and were consequently included in the meta-analysis while 50 studies were excluded with reasons. Four of the included studies were conducted in the United States, three studies were conducted in Thailand and Egypt, two studies in Australia and China while one study were conducted in United Kingdom, Belgium, Switzerland, Canada, France, Türkiye, Japan, India, and Saudi Arabia. All included studies were designed cohort either prospective or retrospective.

In these 25 studies which were published from 2007 to 2023, a total of 2,677 patients who underwent mBTT procedure were included (Table 1). The sample sizes were ranged from 8 to 388. The included studies reported the frequency of shunt blockage and mortality. Patients with shunt blockage reported in 179 patients. The highest number of shunt blockage reported in a study was 44 events from 380 total patients. There were five study did not experience with shunt blockage. Overall mortality reported in 274 patients with 34 patients identified had a mortality related to shunt blockage. Only 16 of them reported the number each size of the shunt used, six of the included studies reported the number of inflow location of the shunt, seven studies reported

the size of each size of the pulmonary arteries and 19 studies reported the surgical technique (Table 2). The quality of study was received a various quality. There was only one study had six poor qualities from 10 aspects. However, we still included the study for the reason that the data taken was not the result of analysis, but rather the raw data. Overall, the studies had a good quality according to study quality assessment (Table 3).

Meta-analysis

All included studies were analyzed in a single proportional meta-analysis to estimate the global incidence of shunt blockage. The global incidence was found to be 7% (95% CI: 0.05 to 0.10) with 175 events among 2,677 participants. The heterogeneity was high and statistically significant ($I^2=81\%$; $p<0.01$), suggesting considerable variability across the studies. The funnel plot showed an asymmetrical pattern, indicating potential publication bias, and the Egger's regression test revealed a highly significant result ($p<0.0001$), which further supports the presence of bias (Figures 2).

Fifteen studies were included in a two-group proportional meta-analysis. Five studies were excluded, as they reported no shunt blockage events and the data were not estimable, while another five

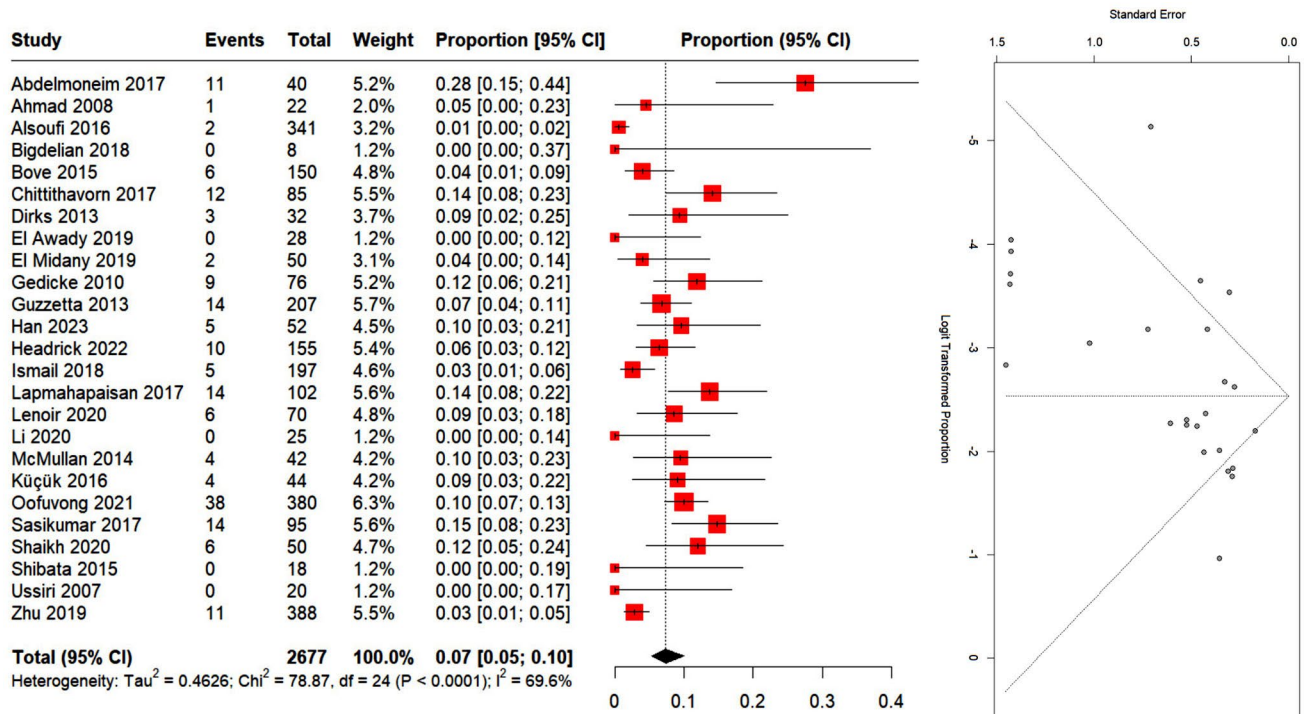


Figure 2. Incidence of shunt blockage forest plot.
CI: Confidence interval.

studies were excluded due to the lack of detailed mortality data related to shunt blockage. Among the 171 deaths included in the analysis, 34 were related to shunt blockage. Additionally, 1,477 surviving patients were included, 75 of whom experienced a shunt blockage event. The odds of mortality in patients with shunt blockage were estimated to be 5.04 times higher than in those without shunt blockage (OR=5.04; 95% CI: 2.69 to 9.44). The heterogeneity for this analysis was low and not statistically significant ($I^2=3\%$; $p=0.41$), and the funnel plot demonstrated a symmetrical pattern across the included studies (Figures 3).

Meta-analysis of shunt size showed no significant association with shunt blockage (OR=0.99; 95%

CI: 0.29 to 3.36) (Figure 4). Conversely, analyses of continuous variables (partial thromboplastin time [PTT], activated partial thromboplastin time [APTT], and platelets) suggested statistically significant and clinically relevant mean differences favoring patients with shunt blockage, with these patients consistently showing lower values for PTT (minimal difference [MD]=-1.67; 95% CI: -2.52 to -0.83) (Figure 5) and APTT (MD=-7.00; 95% CI: -8.68 to -5.32) (Figure 6). However, the analysis of platelet count (MD=7.67; 95% CI: -37.53 to 52.87) (Figure 7) showed no statistically significant difference between patients with and without shunt blockage, as the wide confidence interval crosses zero. These findings indicate

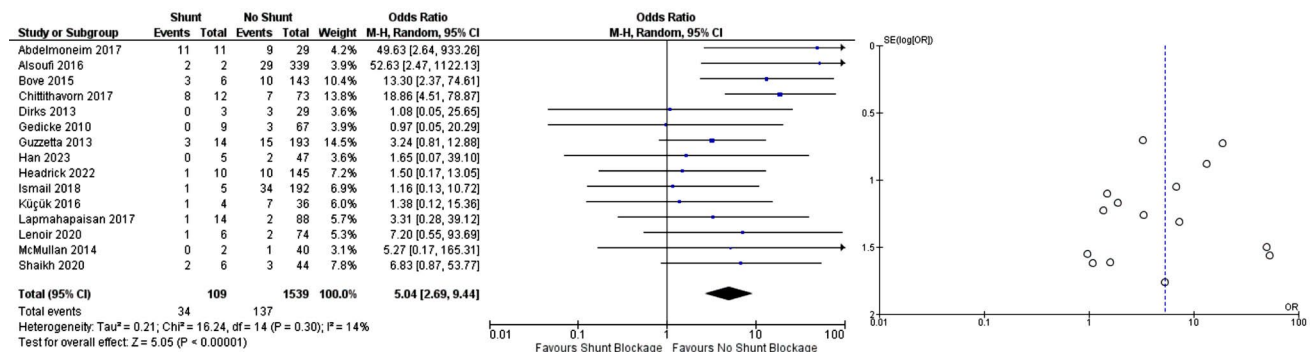


Figure 3. Mortality risk factor of shunt blockage forest plot.

CI: Confidence interval.

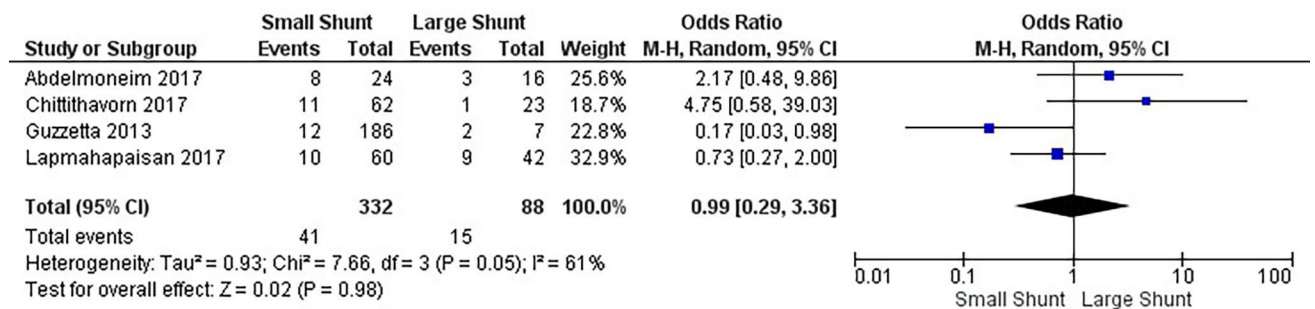


Figure 4. Subgroup meta-analysis of shunt size forest plot.

CI: Confidence interval.

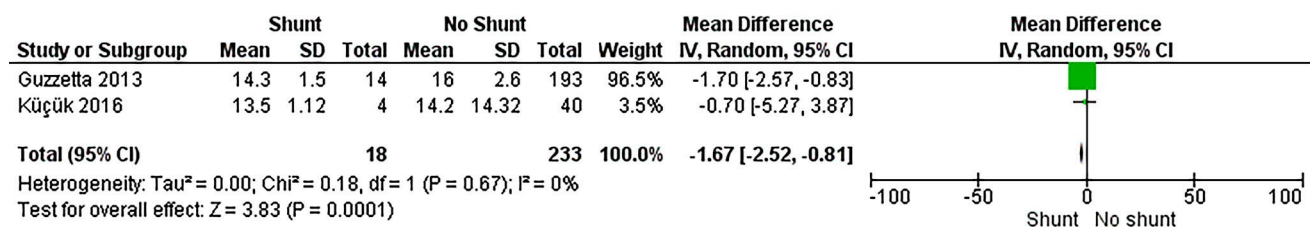


Figure 5. Subgroup meta-analysis of PTT forest plot.

CI: Confidence interval; PTT: Partial thromboplastin time.

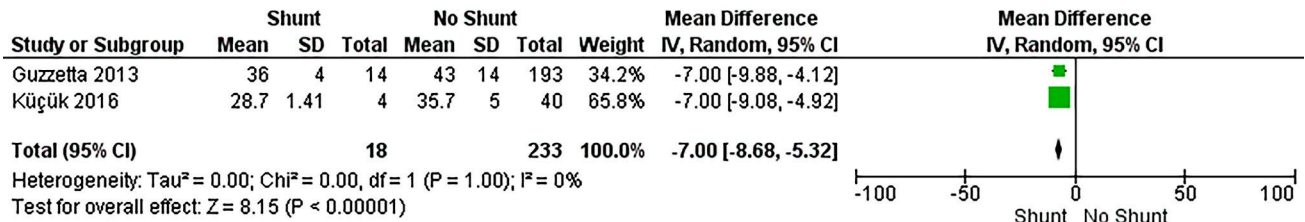


Figure 6. Subgroup meta-analysis of aPTT forest plot.

CI: Confidence interval; PTT: Partial thromboplastin time.

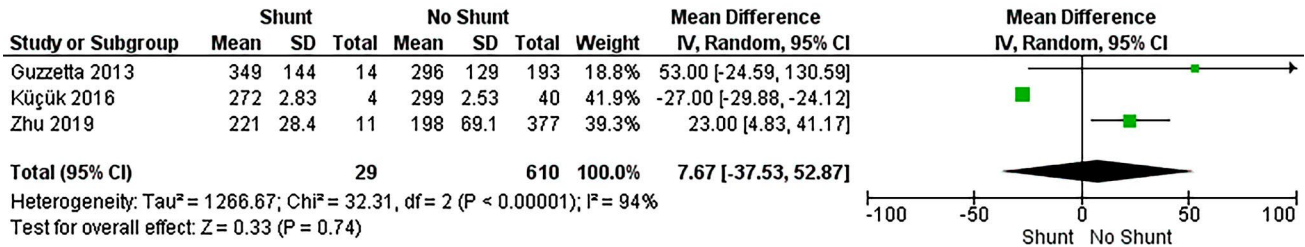


Figure 7. Subgroup meta-analysis of platelet count forest plot.

CI: Confidence interval.

potential coagulation abnormalities, particularly in PTT and APTT, in patients with shunt blockage, which may warrant further investigation.

DISCUSSION

In this systematic review and meta-analysis, we assessed the global incidence of shunt blockage, evaluate the associated mortality risk, and identify factors contributing to shunt occlusion. The pooled global incidence of shunt blockage following mBTT shunt placement was found to be 7%, with incidence rates varying across different countries. Our meta-analysis revealed a strong association between shunt thrombosis and mortality, consistent with findings from previous studies.^[7,8] Reported causes of mortality other than shunt blockage included cardiac arrest, bradycardia, sepsis, ventilator-associated pneumonia, heart failure, and unknown causes.

Interestingly, our analysis indicated that shunt size was not significantly related to shunt thrombosis, a finding that contrasts with several previous studies. Other factors, such as the shunt size-weight ratio and patient weight, have been suggested as predictors of thrombosis and mortality in earlier research.^[9-12] Blood flow dynamics influenced by shunt size, PA diameter, and initial PA pressure play a crucial role in thrombosis risk. However, the lack of detailed data in the included studies prevented a meta-analysis on these factors. Only

two studies identified PA size as a risk factor for shunt thrombosis and mortality,^[6,8] highlighting a gap in the current literature.

Patient-related factors such as body weight and pre-existing pathology may influence the likelihood of shunt occlusion. Univentricular patients, in particular, experience altered hemodynamics that may predispose them to thrombosis and adverse surgical outcomes compared to those with biventricular physiology. This association has been consistently observed, with significantly higher rates of extracorporeal membrane oxygenation support (12% vs. 4%, $p=0.004$) and unplanned cardiac reoperations (14% vs. 7%, $p=0.051$) among univentricular patients.^[13] Univentricular circulation has also been identified as an independent predictor of poor outcomes (hazard ratio [HR]=4.10; 95% CI: 1.05 to 17.43; $p=0.01$), particularly in those undergoing unifocalization for pulmonary atresia with ventricular septal defect.^[14] The need for cardiac decongestive therapy due to shunt thrombosis has also shown a strong association with univentricular anatomy ($p<0.001$), reinforcing the heightened thrombotic risk in this subgroup.^[12]

Surgical factors, including the choice of incision (sternotomy vs. thoracotomy), the use of cardiopulmonary bypass (CPB), and intraoperative protamine administration, have also been implicated in shunt failure. In our review, 12 studies predominantly

used a single surgical approach (six sternotomy, six thoracotomy), while 13 studies reported varied use of both techniques. Among the thoracotomy-dominant studies, early shunt failure rates ranged from 0 to 13.73%, with most reporting values above 4%.^[9,15-19] In contrast, sternotomy-dominant studies reported lower early failure rates, ranging from 0 to 9.38%, with several below 3%.^[12,20-24] This suggests a potential trend toward improved outcomes with sternotomy, possibly due to reduced pulmonary artery distortion and more effective management of concurrent lesions such as a patent ductus arteriosus (PDA).^[25] However, the sternotomy approach may also increase the risk of over-shunting due to greater proximal arterial inflow, shorter shunt length, and the presence of an additional source of pulmonary blood flow. Chittithavorn *et al.*^[7] reported that, in 78% (18 of 23) of patients with 4-mm shunts, the mBTT shunt was performed through the thoracotomy approach, intentionally avoiding the proximal arterial inflow or central pulmonary arteries to reduce coronary steal and over-shunting. Over-shunting occurred in only two patients and was successfully managed with decongestive therapy.

Furthermore, the shunt characteristics themselves, including graft diameter, artery diameter, and material properties, could impact thrombosis risk. While data on these parameters were often incomplete, further research should aim to explore their contributions.^[11] Moreover, specific shunt characteristics such as graft-to-weight ratio and target artery diameter have been associated with clinical outcomes. An increased shunt size-to-weight ratio was significantly associated with mortality (HR=2.72; 95% CI: 0.80 to 9.18; $p=0.04$).^[14] and has also been identified as a statistically significant risk factor for both thrombosis and mortality ($p=0.004$).^[12] Additionally, the use of antithrombotic strategies, such as dual antiaggregant therapy or prophylactic acetylsalicylic acid, warrants closer evaluation, particularly in relation to PDA closure and shunt patency. The potential interplay between PDA closure, antiplatelet regimens, and thrombotic events remains a critical area for future investigation.

Most studies demonstrated good methodological quality. One study showed poor quality in six out of 10 assessed criteria; however, it was retained in our analysis, as it contributed raw data rather than pre-analyzed results. While the overall quality was acceptable, this assessment highlights potential methodological limitations across the evidence base, such as unclear reporting or lack of standardization

in data collection, which may introduce bias into the findings. Additionally, the funnel plot showed an asymmetrical pattern, and Egger's regression test was highly significant, indicating potential publication bias that may have influenced the pooled estimates. Although most included studies were of acceptable methodological quality, the presence of potential reporting limitations and clear evidence of publication bias reduce the overall strength of evidence. The evidence should be interpreted with moderate caution. It is suggestive but not definitive, and further high-quality, prospective studies are needed to strengthen the conclusions.

In conclusion, the incidence of shunt blockage following Modified Blalock-Taussig-Thomas shunt procedures varies by country, likely influenced by differences in surgical techniques and postoperative management. Our meta-analysis confirms that shunt blockage is strongly associated with increased mortality. While shunt size alone is not a significant predictor of thrombosis, other factors including body weight, pre-existing pathology, coagulation profiles, surgical factors and size-to-weight ratio may collectively influence the risk.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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