Prevalence of Blood Transfusion in Non-Syndromic Craniosynostosis Repairs: Open Versus Minimally Invasive Techniques: A Proportion Meta-analysis of Multiple Centers

Mirnasari Amirsyah[1], Muhammad Ikhlas Abdian Putra[1], Shakira Amirah[2], Seba Talat Al-Gunaid[3], Khalillullah Khalillullah[3], Artha Maressa Theodora Simanjuntak[4], Puan Faiza Nurianada[5], I Nyoman Windiana[6] and Roy Novri Ramadhan[7]*

[1]Plastic Reconstructive and Aesthetic Surgeon, Plastic Surgery Subdivision, Department of Surgery, Medical Faculty of Universitas Syiah Kuala / Zainoel Abidin General Hospital

[2]Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

[3]Faculty of Medicine, Universitas Syiah Kuala, Banda Aceh, Indonesia

[4]Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta, Indonesia

[5]Faculty of Medicine, Universitas Jenderal Soedirman, Banyumas, Indonesia

[6]Faculty of Medicine, Universitas Pendidikan Ganesha, Buleleng, Indonesia

[7]Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

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*Correspondence: roynofri28@gmail.com

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Abstract

Background: Craniosynostosis, a congenital cranial deformity due to premature suture fusion, is managed primarily through surgical intervention to allow normal brain growth. Blood transfusion is a common necessity in these surgeries, especially in open surgery (OS) techniques, given their invasiveness. Minimally invasive surgery (MIS) has been proposed as a less traumatic alternative with potentially lower transfusion requirements.

Aim: The aim of this study was to determine the pooled prevalence of blood transfusion requirements in non-syndromic craniosynostosis surgeries, comparing OS and MIS across multiple centers.

Methods: A systematic review and proportion meta-analysis were conducted, adhering to PRISMA guidelines. A comprehensive search across PubMed, Scilit, Scopus, and Web of Science identified studies reporting blood transfusion rates in non-syndromic craniosynostosis repairs as of March 7, 2024. Pooled prevalence estimates were calculated using the Freeman-Tukey double arcsine transformation.

Results: The analysis included data from nine studies with a total of 619 patients enrolled. The pooled prevalence of blood transfusion in OS was 52% (95% CI: 32% to 72%), while it was significantly lower in MIS at 10% (95% CI: 1% to 20%). Among OS techniques, cranial vault remodeling exhibited the highest transfusion prevalence of 58.1% (95%CI: 37.5% to 78.7%). Among those minimally invasive, strip-assisted surgery had a lower prevalence (3.9% [95%CI: -0.5% to 8.2%]) as compared to endoscopic strip craniectomy (13.1% [95%CI: -0.4% to 26.6%]). OS on metopic craniosynostosis yielded a blood transfusion prevalence of 76.2% (95%CI: 62.9% to 89.5%), which was the highest among other affected sutures. Sagittal craniosynostosis repairs showed a prevalence of 22.5% (95%CI: 9.6% to 35.3%) in OS, contrasting with be 2.6% (95%CI: 1.7% to 11.9%) in MIS.

Conclusion: The prevalence of blood transfusion in craniosynostosis repair is significantly lower in MIS compared to OS, suggesting that MIS may be a safer alternative in terms of transfusion risks.

Keywords: Craniosynostosis, cranial deformity, blood transfusion, cranial vault remodeling, endoscopic surgery

Introduction

Craniosynostosis is a congenital condition resulting from the premature fusion of one or more cranial sutures, leading to an abnormal head shape and potential complications, such as Increased Intracranial Pressure (ICP) and disturbance on respiratory and neurologic systems.[1] Among the patients who are non-syndromic, the majority of craniosynostosis cases, occurs independently and is not associated with other congenital anomalies.[1,2] Common types include sagittal synostosis, coronal synostosis, metopic synostosis, and lambdoid synostosis.[3] The primary treatment for craniosynostosis is surgical intervention, aimed at correcting the shape of the skull and allowing for normal brain growth.[4] Open Surgery (OS) involves a large incision in the body to access the area of interest directly, which allows surgeons to see the organs and tissues clearly.[5] OS comprises of several techniques, such as Cranial Valt remodeling (CVR), cranial distraction osteogenesis (CDO), Fronto-orbital advancement (FOA), and strip craniectomy (SC).[6] Despite being advantageous of offering comprehensive skull reshaping, the large incisions possess high risk of requiring blood transfusion, thus leading to long hospital stay and various complications.[7]

On the other hand, Minimally Invasive Surgery (MIS) approaches do not require large incisions, particularly with the assistance of endoscopic methods.[8-10] Smaller incisions may minimize trauma to surrounding tissues with shorter procedure time, leading to quick recovery and relative safety. In both OS and MIS, if the blood loss exceeds 100 mL (or about 10% of the patient's blood volume, depending on age and weight), blood transfusion should be administered intraoperatively.[11] Measuring the prevalence of blood transfusion is crucial to better anticipate the need for blood products, ensuring they are readily available when needed and minimizing the risk of intraoperative complications.[11] blood transfusions involve significant resources such as collection and storage of the blood, hospitals can allocate these resources more efficiently, reducing the risk of blood shortages.[12] Unfortunately, studies on the prevalence of blood transfusion in craniosynostosis surgeries are limited to a single isolated center.[12-15] A systematic review and meta-analysis can be conducted to estimate prevalence rates when data gaps persist.[16-19] To increase its generalizability, considering the lack of related published studies, it is imperative to perform a meta-analysis on the prevalence data.

Methods

The study employed a proportion meta-analysis design, in which its reporting followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis protocol (PRISMA) statements.[20] The research question was, "what is the prevalence of blood transfusion in OS and MOS for the management of non-syndromic craniosynostosis?". The study was officially recorded in PROSPERO with the registration number CRD42024604632 as of November 01, 2024.

The systematic literature review was performed on March 7, 2024, and involved searching across four databases: PubMed, Scilit, Scopus, and Web of Science. The literature search was carried out with keywords using Boolean operators ‘AND’ and ‘OR’ to combine keywords related to "craniosynostosis surgeries". Details of the search terms have been published elsewhere.[21]

Studies eligible for inclusion focused on patients with non-syndromic craniosynostosis undergoing either OS or MIS, including cranial vault remodeling (CVR), endoscopic strip craniectomy (ES), spring-assisted surgery (SAS), strip craniectomy (SC), remodeling with helmet therapy (RH), and posterior vault distraction (PiP). These studies reported on the prevalence or incidence of blood transfusion as an outcome measure. Accepted study designs included cross-sectional, case-control, and cohort studies that offered primary patient data relevant to surgical outcomes. Studies with non-comparative or incomplete data, including case series without distinct outcome reporting, were excluded. Additionally, review articles, commentaries, editorials, and conference abstracts were excluded.

Following automatic duplicate removal in EndNote 19, screening was carried out in two phases: first by evaluating titles and abstracts, and then by reviewing full texts. Two independent review authors conducted each stage, resolving disagreements through consensus; if consensus was not reached, a third reviewer was consulted for clarification.

Two independent review authors valuated the quality of the included studies. The Newcastle-Ottawa Scale (NOS) was employed for the critical appraisal of observational studies, with a detailed description of this tool provided earlier.[22,23] The maximum scores for cohort and cross-sectional studies are nine and seven, respectively. Any discrepancies were addressed through consensus or by consulting a third reviewer.

We extracted the following data from each included study: first author's name, year publication, country, study design, and sample size. Demographic data of the research subjects was extracted, including age (in months) and gender (male/female). Additionally, clinical characteristics such as affected sutures (sagittal, coronal, metopic, lambdoid, or mixed), surgical technique, and blood transfusion rates were collected. Continuous data were reported as mean ± standard deviation (SD), while other data were converted using methods recommended in previous studies.[24-26] Data extraction was carried out by one review author, and further confirmed by the another review author.

Meta-analysis was performed on Rstudio version 2024.04.2. The analysis focused on both open surgeries (such as cranial vault remodeling and strip craniectomy) and minimally invasive procedures (including spring-assisted and spring-endoscope surgeries). The pooled proportion was estimated by Freeman-Tukey double arcsine transformation (FTT) method. Back-transformation was performed based on the inverse of the variance of the pooled FTT proportion. The prevalence was calculated by multiplying 100% with the back-transformed value. Heterogeneity among the studies was evaluated using the I^2 statistic, with cut-off criteria of 50% and p-Het<0.1 corresponding to high heterogeneity, respectively. The subgroup analysis was performed based on the surgical techniques, namely CVR, SC, SAS, and ES.

Results

We identified a total of 1473 records from four different databases and found 904 duplicates, which were subsequently removed afterward. The abstract and title screening resulted in 569 records being likely relevant to the review's objectives. Among which 102 articles were retrievable for their full-text and further subjected to a selection process based on the eligibility criteria. We further found six records being duplicated documents, hence removed. Eight, sixty-four, and six other studies were then excluded because of the wrong study design, reporting none of the outcomes of interest, and having ineligible study designs. There are four studies that were likely eligible, but were then excluded because they did not exclude syndromic patients.[27-30] Finally, nine studies were identified as eligible for the data synthesis in the systematic review and meta-analysis.[7,14,15,31-36] The flow-diagram illustrating the screening and selection process involved in the review is presented in Figure 1.

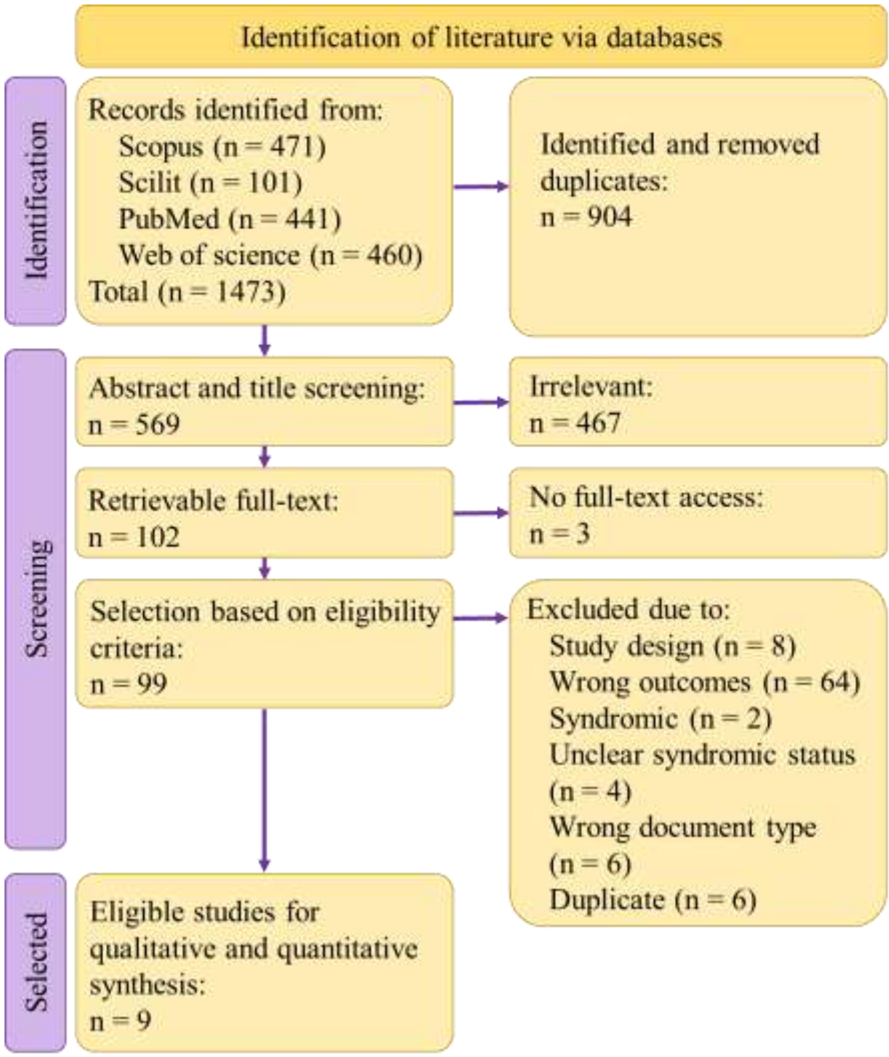


Figure 1: Flow-diagram for the screening and selection of studies eligible for the estimation of blood transfusion prevalence in craniosynostosis repairs.

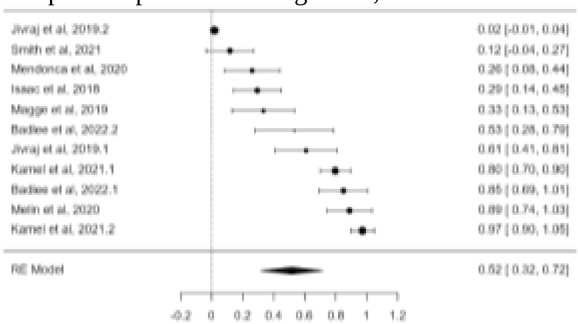
The characteristics of the included studies along with their quality as appraised by NOS tool are presented in Table 1. Most of the studies were reported from the United States,[7,14,31,32,34-36] with one study reported from the United Kingdom[33] and another from India.[15] The overall included studies enroll 619 patients aged from 3 to 18.5 years. The qualities of the included studies were mostly good[7,15,31-36]., with the one study receiving moderate quality due to small sample size (n<20 in one group).[14] Another concern, was found in a study that compared their cohort to the medical records from a different center.[33]

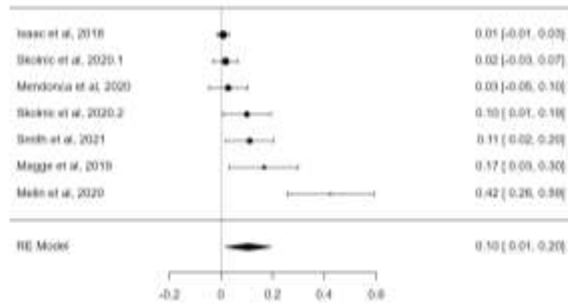
Table 1: Characteristics and qualities of studies eligible for the estimation of blood transfusion prevalence in craniosynostosis repairs.

Study	Location	Study design	Affected suture(s)	Group		Demographic characteristics			Blood transfusion (%)	Quality	Proffesionals
				Technique	Category	Total, n	Age (months)	M/F			
Badiee et al., 2022[14]	United States	Cross-sectional	Metopic	SC	OS	15	5.5±1.7	14/1	53.3	★★★★★★	1 neurosurgeon
				CVR	OS	20	9.8±0.8	14/6	85		4 craniofacial surgeon + 1 neurosurgeon
Kamel et al., 2021[31]	United States	Cross-sectional	Coronal	FOA	OS	64	11.6±10.8	19/45	80	★★★★★★★	2 neurosurgeons + 2 craniofacial surgeons
				CDO	OS	17	9±1.6	3/14	100		1 craniofacial surgeon + 2 neurosurgeons
Magge et al., 2019[32]	United States	Cross-sectional	Sagittal	CVR	OS	21	5.1±2.7	NR	33.3	★★★★★★★	Multiple surgeons
				ES	MIS	30	3.1±1.2	NR	16.7		Multiple surgeons
Jivraj et al., 2019[33]	United Kingdom	Cohort	Unicoronal	FO-CVR	OS	23	18.5±4.2	10/13	60.86	★★★★★★★★	NA
				SC	OS	115	3.3±2.0	50/65	1.73		
Isaac et al., 2018[34]	United States	Cross-sectional	Coronal	FOA	OS	34	10.4±2.3	NR	30	★★★★★★★	1 neurosurgeon + 2 plastic surgeon
				ES	MIS	60	3.0±1.1	NR	0		1 neurosurgeon
Melin et al., 2020[7]	United States	Cohort	Mix	CVR	OS	18	<6	NR	90	★★★★★★★★★	1 neurosurgeon + 1 craniofacial plastic surgeon
				ES	MIS	33	<6	NR	42		1 neurosurgeon + 1 craniofacial plastic surgeon
Mendonca et al., 2020[15]	India	Cohort	Sagittal	ES	MIS	17	3.8±0.6	4/13	0	★★★★★★★★★	NA
				CVR	OS	23	11.9±2.6	10/13	27		
Smith et al., 2021[35]	United States	Cohort	Sagittal	SC	OS	17	12.6±3.2	14/3	11.8	★★★★★★★★★	5 neurosurgeon + 1 plastic surgeon
				SAS	MIS	45	19.9±3.1	33/12	11.1		5 neurosurgeon
Skolnic et al., 2020[36]	United States	Cross-sectional	Sagittal	SAS	MIS	27	4.5±1.3	23/4	0	★★★★★★★	1 neurosurgeon
				ES-HM	MIS	40	3±0.9	29/11	11.1		NA

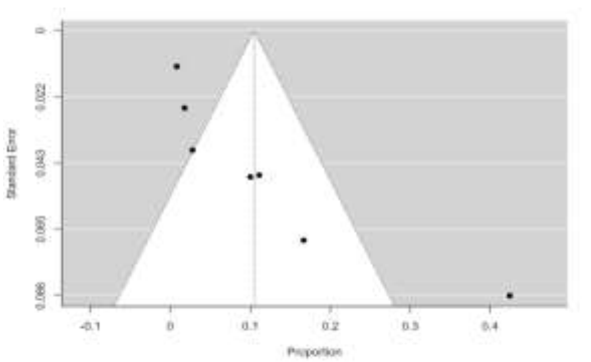
CDO, cranial distraction osteogenesis; FOA, fronto-orbital advancement and cranial vault remodeling; M/F, male-to-female ratio; MIS, minimally invasive surgery; OS, open surgery;

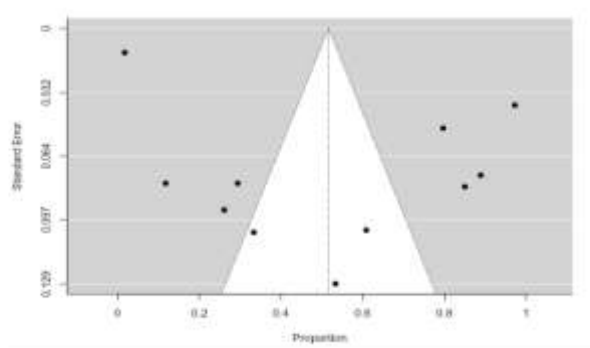
The pooled prevalences of blood transfusion for OS or MIS are presented in Figure 2a,b. The Prevalence for the OS was 52% with 95%CI ranging from 32% to 72%. As for the MIS, the prevalence was 10% (95%CI: 1% to 20%). The heterogeneities were high in both pooled estimates with I^2 values of 92.13% (p<0.001) and 97.53% (p<0.001) for OS and MIS, respectively. Egger's correlation suggested that the presence of publication bias (p<0.001) in the pooled analysis of blood transfusion prevalence among patients undergoing OS. However, the publication bias was negligible for MIS with p-value in the Egger's correlation of 0.955. The symmetry and asymmetry of the data presented in the funnel plot are presented in Figure 2c,d.





(a) (b)





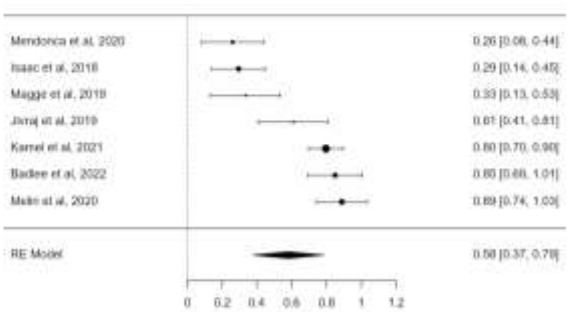
(c) (d)

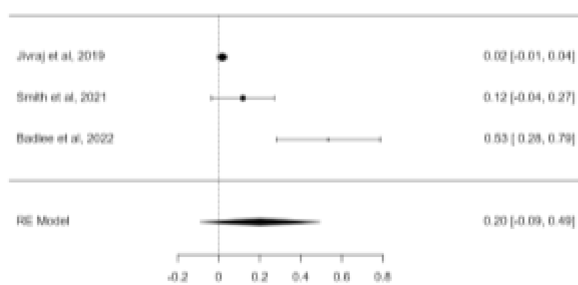
Figure 2: Pooled prevalence of blood transfusion among patients undergoing open (a) and minimally invasive surgeries (b). The funnel plot for publication bias detected in the pooled analysis of the prevalence analysis in open (c) and minimally invasive surgery groups (d).

Results from the pooled estimates based on the surgical techniques and types of sutures are presented in Table 2. The highest blood transfusion prevalence was observed in CDO (100%), though it was only reported in one study. The second highest prevalence was observed in CVR (58.1% [95%CI: 37.5% to 78.7%]), with SC (10.5% [95%CI: 1.4% to 19.5%]) occupied the last position among the OS. The lowest prevalence among MIS was found in SAS (3.9% [95%CI: -0.5% to 8.2%]), followed by ES with a prevalence of 13.1% (95%CI: -0.4% to 26.6%). Among OS, from the highest to the lowest prevalence was observed in metopic (76.2% [95%CI: 62.9% to 89.5%]), coronal (69.2% [95%CI: 29.8% to 10.87%]), sagittal (22.5% [95%CI: 9.6% to 35.3%]), and unicoronal sutures (2.6% [95%CI: 0.2% to 4.9%]). In the case of MIS, we were only able to pool the data for sagittal sutures, where the prevalence was found to be 2.6% (95%CI: 1.7% to 11.9%).

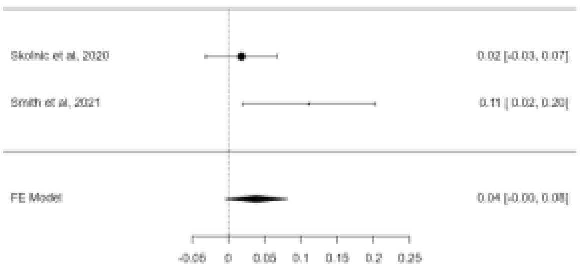
Table 2: Subgroup analysis for the pooled estimates of blood transfusion prevalence in craniosynostosis repairs.

Variable	**Study, n**	**Sample size, n**	**Prevalence (95%CI)**	***I*^{2} (%)**	***p*-Het**
Open surgeries					
Cranial vault remodeling	7	203	58.1% (37.5% to 78.7%)	92.02	<0.001
Strip craniectomy	3	147	10.5% (1.4% to 19.5%)	92.13	<0.001
Osteogenesis	1	17	100% (not applicable)	Not applicable	Not applicable
Minimally invasive surgeries					
Spring-assisted surgery	2	72	3.9% (-0.5% to 8.2%)	67.56	0.079
Spring-endoscope surgery	5	180	13.1% (-0.4% to 26.6%)	93.1	0.057
Suture					
Open surgeries					
Coronal	3	115	69.2% (29.8% to 10.87%)	97.69	<0.001
Sagittal	3	61	22.5% (9.6% to 35.3%)	37.14	0.210
Metopic	2	35	76.2% (62.9% to 89.5%)	77.1	0.037
Unicoronal	2	138	2.6% (0.2% to 4.9%)	97	<0.001
Minimally invasive surgeries					
Sagittal	5	159	2.6% (1.7% to 11.9%)	48.15	0.103

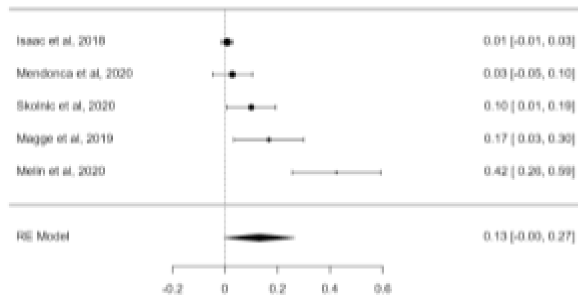




(a) (b)



(c)



(d)

Figure 3: Forest plots for the pooled prevalence of blood transfusion in various craniosynostosis repair techniques such as open cranial vault remodeling (a), strip craniectomy (b), spring-assisted surgery (c), and endoscope-assisted surgery (d)

Discussion

The impact of age on blood transfusion requirements and perioperative outcomes in craniosynostosis surgery is multifaceted, influenced by physiological factors, blood volume dynamics, and surgical complexity. While younger patients (under 24 months) generally experience lower rates of surgical site infections and shorter hospital stays, studies indicate that the overall need for blood transfusion does not significantly differ across age groups (Puthumana et al., 2022; Beethe et al., 2020). However, lower hematocrit levels and smaller circulating blood volume in younger children increase their susceptibility to intraoperative blood loss, often necessitating transfusion (Puthumana et al., 2022; Puente-Espel et al., 2016). Despite this, select cases of transfusion-free hospitalization have been documented after craniofacial reconstruction (Beethe et al., 2020). However, younger patients often require prolonged hospitalization, potentially due to the need for closer postoperative monitoring and recovery considerations (Uitert, 2011).

The timing of surgery significantly influences blood loss and transfusion rates, with optimal intervention within the first year of life, particularly in syndromic cases, to minimize complications and promote neurodevelopmental outcomes. Delayed intervention increases the risk of perioperative complications (OR=2.53 at 3 years vs. <1 year, 95% CI: 1.67–3.82), reinforcing the importance of early surgical correction to mitigate cognitive impairment associated with craniosynostosis (Bruce et al., 2019). Blood loss is also proportional to surgical duration, with prolonged operative time correlating with greater intraoperative hemorrhage and transfusion dependence (Ali et al., 2014). Reported transfusion rates in craniosynostosis surgery vary widely, ranging from 20% to 100%, depending on the study and patient-specific factors (Kumba, 2021). Younger patients are at greater risk of significant blood loss due to lower total blood volume and increased red cell volume loss, necessitating stringent intraoperative hemodynamic management. In severe cases, rapid hemorrhage may require massive transfusion protocols (Park et al., 2017; Kumba, 2021).

Transfusion management in craniosynostosis surgeries requires a patient-specific approach that accounts for surgical technique, intraoperative hemodynamics, and transfusion thresholds. Blood loss varies across procedures, with OS often necessitating early transfusion, while MIS typically require less. Guidelines recommend transfusion when hemoglobin falls below 8 g/dL in stable patients or 10 g/dL in cases of instability, with additional considerations for infants with congenital conditions. To minimize transfusion-related complications such as TRALI (Transfusion-related complications, including transfusion-related acute lung injury) and circulatory overload, restrictive strategies, antifibrinolytics, and intraoperative cell salvage, effective management balances evidence-based guidelines, patient factors, and intraoperative discretion to optimize outcomes while reducing transfusion risks.

Our findings aligns with Smith et al., who reported that age-matched wOS and MIS groups exhibited comparable transfusion rates. This suggests that surgical approach and suture involvement, rather than age alone, are key determinants of transfusion needs. MIS procedures, predominantly performed on sagittal sutures, demonstrated significantly lower transfusion rates, whereas OS cases—often involving metopic and unicoronal sutures—required more extensive interventions, leading to higher transfusion volumes.

In the present study, we found that the pooled prevalence of blood transfusion among OS and MIS were 52% (95%CI: 32% to 72%) and 10% (95%CI: 1% to 20%), respectively. All patients receiving CDO, was reported to require blood transfusion. Among other OS, the CVR was found to have the highest prevalence (58.1% [95%CI: 37.5% to 78.7%]), with SC having the lowest prevalence (10.5% [95%CI: 1.4% to 19.5%]). Moreover, the blood transfusion was more common among those receiving OS to repair the metopic suture (76.2% [95%CI: 62.9% to 89.5%]), while the prevalence was the lowest in cases affecting unicoronal sutures (2.6% [95%CI: 0.2% to 4.9%]). Furthermore, sagittal craniosynostosis repairs had a higher transfusion prevalence in the OS group (22.5% [95% CI: 9.6%-35.3%]) compared to the MIS group (2.6% [95% CI: 1.7%-11.9%]). These findings highlight that suture type plays a critical role in transfusion requirements, as MIS was predominantly used for sagittal craniosynostosis, while OS was necessary for multi-suture involvement, particularly metopic cases, which had the highest transfusion rates.[7,15,33,34]

Herein, the findings suggest that MIS techniques may reduce blood transfusion needs in craniosynostosis surgeries, which could lower risks associated with transfusions, such as infection, immune responses, and prolonged recovery times. This can be associated with the fact that OS typically involves more extensive tissue manipulation and larger incision.[7,15] Prioritizing MIS could be especially beneficial for patients at higher risk of transfusion-related complications or in facilities where blood supply is limited.[37] Data on transfusion prevalence in craniosynostosis repairs informs clinical outcomes and aids in refining transfusion strategies. Moreover, OS in all studies are performed primarily by neurosurgeons and craniofacial plastic surgeons, while MIS are only performed by neurosurgeons. OS is done on older patients or complex cases, typically at around 9-17 months of age compared to MIS which typically is done on 3-5 months of age. Guidelines recommend transfusion when hemoglobin falls below 10 g/dL in stable padiatrics. The data can be used as the basis in preparation of potential blood loss, including the assurance of availably adequate blood products and considering preoperative hemoglobin optimization strategies.[38] In previous studies on the outcomes of non-craniosynostosis surgeries, restrictive transfusion strategies may even reduce mortality.[39] Furthermore, prioritizing procedures with lower transfusion needs supports effective blood allocation and cost reduction, as fewer transfusions decrease healthcare expenses related to transfusion reactions and extended hospitalizations.[40]

However, it is worth-noting that the choice of the repair techniques is not limited to the risk of blood transfusion. In a previous survey-based study, the consideration of surgeons in a choosing a specific repair technique is based on the skull maturation.[4] For example, skull malleability is reduced and bone thickness is increased among those aged older than 12 months, thus more invasive approach is preferable.[41] Previously, the CVR and CDO were among the preferable approach for patients older than 12 months old.[42] The correction of the cranial deformity is more likely achieve when extensive anatomic exposure was provided during the repair, which could not be achieved in endoscopy-assisted techniques. Moreover, concerns on the surgical impacts on the neurodevelopment should also be prioritized.[43,44]

We recommend that hospitals and clinicians should consider implementing MIS techniques, especially in cases where transfusion risks must be minimized. Training and resources for these procedures could be beneficial in reducing patient morbidity. There are limitations in the present that are worth of consideration such as high heterogeneity in prevalence estimates which suggests considerable variability across studies. This variability emphasizes the need for tailored blood management strategies in craniosynostosis repair, as transfusion requirements may differ significantly by setting. Caution is advised in generalizing these findings, as local factors could influence actual transfusion needs. Further research with standardized methods could help refine these estimates for clinical application. More large-scale, multicentre studies comparing long-term outcomes of OS versus MIS are recommended to assess not only transfusion rates but also other clinical outcomes, such as recurrence of craniosynostosis, neurodevelopmental outcomes, and overall patient quality of life. Standardized study designs will be essential to refining surgical guidelines and optimizing perioperative blood management strategies.

Conclusion

There are significant differences in blood transfusion requirements between OS and MIS for craniosynostosis repair. The pooled prevalence of blood transfusion is notably higher in OS (52%) than in MIS (10%). Specific procedures, such as CVR and metopic suture repairs, show particularly high transfusion rates. These findings suggest that adopting MIS techniques, where appropriate, could improve patient safety by minimizing transfusion requirements. Additionally, targeted blood management strategies for high-risk OS cases may further optimize surgical outcomes.

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