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Addressing surgical challenges in craniopagus twin separation surgery: A systematic review

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This manuscript is a review of the existing literature. Therefore, ethics committee approval and written informed consent were not required. Original studies included in this review obtained written informed consent and ethical clearance from their respective hospital or institutional ethics committees, where applicable.

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Abstract

Craniopagus twins (CPTs) are conjoined twins fused at homologous regions of the crania in either vertical or angular orientations, with the face and foramen magnum spared. They account for approximately 6% of conjoined twins and occur in 0.6 per million births worldwide. The degree of circulatory interconnection is a central consideration when planning separation surgery, particularly when deciding between a single-stage and a multistage approach. In craniopagus twins with fused dural venous sinuses, the superior sagittal sinus is replaced by a circumferential venous sinus (CVS); these cases are classified as total CPTs. Surgical challenges become increasingly complex in the presence of a CVS, prolonged anesthetic exposure, substantial cross-circulation, and the unique anatomical position of the twins. This review compiles data on the surgical management of these challenges and their outcomes, contributing to the continued development and refinement of surgical planning in CPT separation surgery. A Google Scholar search restricted to English-language articles published from 2020 to 2024 identified 329 articles. After detailed review, 19 open-access articles were selected for this manuscript. The reviewed literature showed that the degree of cross-circulation can be assessed through laboratory and physiologic measurements after pharmacologic challenges and can be mapped using multiple imaging modalities. The data also showed that a multistage surgical approach is preferentially selected for total CPTs because it reduces the high risks of hemorrhage, ischemic brain injury, and neurotoxicity associated with a CVS and extensively connected circulatory systems. In addition, staged surgery limits anesthetic exposure, decreasing the risk of anesthesia-induced cerebrospinal fluid stasis and hypotension. It also allows cerebral vasculature to redevelop between operations, thereby supporting adequate venous drainage. During surgery, each twin, their equipment, and their care team should be labeled with a number, letter, and color to provide safe and efficient patient care. This literature review maintains the clinical relevance of craniopagus twin separation surgery by presenting an up-to-date summary of methods and protocols designed to ensure surgical precision and safety when unique preoperative and perioperative challenges arise.

Keywords: conjoined twins, cross circulation, collateral circulation, anesthesia, pharmacokinetics, superior sagittal sinus

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Introduction

Craniopagus twins (CPTs) account for 6% of conjoined twins, with an incidence of 0.6 per million births worldwide [1-3]. This congenital anomaly is characterized by fusion of the twins' crania at homologous regions, in either vertical or angular orientations, while sparing the face and foramen magnum [1]. CPTs are classified as total, when shared dural venous sinuses are present, or partial, when venous structures are separate (Figure 1) [1, 4]. The superior sagittal sinus (SSS), which is involved in venous clearance through the glymphatic system, is the most commonly conjoined venous sinus [3, 5]. In a longitudinal, or vertical, arrangement, the SSS is replaced by a circumferential venous sinus (CVS), which runs along at least half of the circumference of the conjoined region (Figure 2) [1]. The degree to which the twins share circulatory systems, termed cross-circulation, varies by case [2].

Two theories have been proposed to explain the pathophysiology of conjoined twins. The fission theory suggests incomplete cleavage of embryos at the primitive streak stage, whereas the fusion theory proposes rejoining of embryos after their separation [1, 6]. The fission theory is supported by the high incidence of situs inversus in conjoined twins, as dividing cell masses maintain a mirror image; the fusion theory is supported by the various angles of fusion along both the dorsoventral and rostrocaudal axes [1]. Craniopagi are monochorionic and monoamniotic and share both a placenta and an amniotic sac [6, 7]. Early pregnancy symptoms may mimic those of uncomplicated twin pregnancies, most commonly increased uterine size, underscoring the importance of routine prenatal ultrasonographic imaging for diagnosis [7].

Craniopagi may experience complications such as patent ductus arteriosus, aortic coarctation, hypertension, hypotension, and developmental delay [1]. These physical manifestations, combined with the psychological and social challenges of living as conjoined twins, often lead to consideration of surgical separation [1]. However, only approximately 25% of live-born twins are candidates for surgery, largely depending on the anatomical relationship of shared vital organs [8, 9]. As of July 2022, 62 CPT separation attempts had been reported worldwide; 55% used a single-stage approach and 45% used a multistage approach [8]. Total versus partial classification remains the main determinant of the selected surgical approach [1, 4]. Regardless of approach, these operations are highly complex, multifaceted, and extensive, and are often considered among the most complex neurosurgical procedures [4]. Surgical risks, including blood pressure alterations, disrupted cerebral perfusion, cerebral hemorrhage, and stroke, combined with the prolonged anesthetic exposure required for these lengthy procedures, may have detrimental effects on the developing brain [10]. Advances in medical research and practice have increased long-term survival and quality of life among craniopagi who undergo separation surgery, emphasizing the importance of continued research [1, 3].

The four main challenges of CPT separation surgery arise from the presence of a CVS, extensive anesthetic exposure, the degree of cross-circulation, and the unique anatomical position of the twins. Substantial cross-circulation alters the volume of distribution (Vd) and, therefore, drug pharmacokinetics [11]. Uneven drug distribution, fluid shifts, and blood loss must be carefully managed to maintain hemodynamic control and prevent perioperative complications [9]. In addition, the twins' anatomical position and the need to care for two patients simultaneously create challenges in airway management and patient positioning [12]. Despite the low incidence of CPTs, several case reports describing surgical procedures were published throughout the 1900s and early 2000s [4]. This review aims to compile and analyze data on the surgical management of these challenges and their outcomes, thereby contributing to the continuing development of circulatory understanding, anesthetic management, and refinement of surgical planning, simulation, and execution.

Materials and methods

This review analyzes the surgical challenges of CPT separation surgery related to shared dural venous sinuses, anesthetic exposure, cross-circulation, and unique anatomical position. References were selected from Google Scholar and PubMed using searches limited to 2020-2024. Search terms included craniopagus anesthesia; conjoined twins; craniopagus twins separation surgery; anesthesia effects on craniopagus twins; sagittal sinus in anesthesia; craniopagus twins by a multidisciplinary team; and cross-circulation. References were restricted to English-language publications, and only open-access articles were selected. Both original manuscripts and review articles were reviewed. Initially, 23 articles were selected based on their abstracts. After detailed review of each article, 19 articles were selected for discussion in this paper. Original studies included in this review received ethical clearance from their respective hospital or institutional ethics committees and were conducted in accordance with recognized ethical standards, including the principles outlined in the Declaration of Helsinki. Where applicable, written informed consent was obtained from patients or, in the case of neonatal surgical interventions and case reports, from parents or legal guardians. Images were used with preserved patient anonymity and appropriate permissions and licensing.

Discussion

Evolution of surgical approaches over the years

The first recorded successful separation of CPTs was performed in 1953 by Grossman and colleagues in five surgical stages on 14-month-old male twins with a parietal connection [4, 13]. However, one twin died 34 days postoperatively because of hemorrhage, and the second died 11.5 years postoperatively because of hydrocephalus [4]. These outcomes were attributed to limited anatomical understanding caused by poor imaging modalities, as well as the absence of a robust surgical strategy and technique [4].

In contrast, the first successful separation with long-term survival of both twins was performed by Voris and colleagues in 1957 on 7-month-old female twins with a limited parietal connection [3, 4, 13]. Both girls survived for more than 28 years, although one was severely disabled; their deaths were attributed to complications such as hemorrhage and neurological injury [3, 4, 13].

Successful separations were achieved from the 1960s through the 1970s by Oscar Sugar, who used stepwise venous vasculature clipping and ligation and placed polyethylene sheets to delineate the separation plane [4]. Improvements in surgical outcomes were attributed to advances in neuroanesthesia, intensive care, neuroradiology, and surgical instrumentation [4]. However, perioperative complications limited the possibility of long-term survival until the 1980s, when Dr. Robbers successfully performed a multistage separation of total vertical CPTs with record long-term survival [4].

In 1987, Winston et al. reported 31 CPT separation attempts in which only 27 of 62 twins survived; survival of both twins was reported in only 7 cases [13].

New vascular techniques were reported in 1991, when Dr. Drummond and colleagues performed multistage separation using screw clamps to slowly close the connecting veins [4]. However, long-term survival is unknown because of the absence of updates to the case study [4].

In 2004, 4-month-old female twins conjoined in a left-to-left frontotemporal and orbital fashion were successfully separated by Di Rocco and colleagues in Greece [13]. A single-stage approach was planned and consisted of two phases: separation and subsequent reconstruction [13]. The twins shared a unique thin layer of dura mater that was kept nearly intact in one twin during cortical separation, whereas preservation of the arachnoidal covering was prioritized in the other twin [13]. Favorable defect location, good clinical condition in both twins, and the absence of significant vascular and neural anomalies facilitated this separation [13].

Data collection and analysis allowed the development of practice-based surgical protocols. Surgical staging for separation soon began to be determined based on one of the most critical anatomical structures shared by craniopagi: the SSS, one of the dural venous sinuses [4, 14].

CPTs' conjoined dural venous sinuses and their influence on surgical approach

During the early stages of embryonic and fetal life, the SSS plexus aids cerebral venous drainage [14]. The portion of the plexus closest to the cranial adhesion zone may conjoin if the skull boundary and falx cerebri, which separates the cerebral hemispheres, coincide [14]. The SSS is therefore replaced in CPTs by a CVS, which traverses at least half of the circumference of the conjoined region [1]. O'Connell devised a classification in 1976 to estimate prognosis: partial classification refers to craniopagi with separate venous sinuses, in which the dura mater or leptomeninges of both twins separate the twin brains, whereas total classification refers to craniopagi with a CVS, in which a single transverse dural septum separates the twins' cerebrums (Figure 3) [1, 4, 13]. Digital subtraction angiography can be used to determine sinus anatomy and possible hemodynamic changes after separation by inflating a balloon in the communication defect (Figure 4) [4].

Two theories have been proposed to predict postoperative survival in relation to the CVS. The first suggests that survival is associated with the axial orientation of the junction; the second suggests an association with the anatomical classification of dural venous sinuses as total or partial [4]. Total classification had the worst survival rate, with a 48% mortality rate (P = 0.004) [4, 15]. Several years later, Dr. Kenneth Winston proposed a classification based on the deepest shared structure: A, scalp and subcutaneous tissues only; B, dura mater; C, leptomeninges; and D, brain structures [13]. However, even this classification did not accurately predict surgical difficulties or postoperative survival rates [13].

Initially, total CPT separation surgery was performed with a single-stage approach, averaging 22 to 100 hours, in which the CVS was donated to one twin and reconstructed for the second twin [1, 4, 8]. This approach did not allow collateral circulation to develop and resulted in high morbidity and mortality rates (47%; P = 0.030) [4, 15]. These rates decreased by 26% (P = 0.030) with a multistage approach, as shown across 41 cases in which subsequent surgeries were not planned in advance but were instead determined according to postoperative recovery criteria, including improved vital signs and decreased swelling [4, 15]. These favorable outcomes were attributed to the ability of the second twin to develop a deep venous drainage system through serial ligation of draining veins [1, 3]. Therefore, the multistage approach is specifically beneficial for total CPTs. In contrast, partial CPTs may be successfully separated at an earlier age with a single-stage approach [1]. The most recent reports from July 2022 indicated that a single-stage approach had been performed in 55% of cases and a multistage approach in 45% across 62 cases [8].

In support of these findings, the renowned surgeon Dr. Goodrich, considered a leading expert in CPT separation surgery, performed a successful separation of 2-year-old total vertical CPTs in a 4-stage operation over 9.5 months in 2016 [4]. Staged separation allowed time for cerebral vasculature to redevelop and form adequate venous collaterals through dilation of communicating veins, ultimately achieving venous drainage and avoiding serious complications such as cerebral edema, cerebrospinal fluid (CSF) leaks, venous stasis, ischemic injury, and infarction [1, 4]. He used silicone sheets to separate dissection planes between stages (Figure 5) [4]. Essentially, this approach allowed recovery between operations and provided the medical team with an opportunity to carefully plan, time, and design tissue expansion [1, 4].

In addition, Dr. Goodrich strongly advocated appropriate physical and occupational therapy, hypothesizing that it supported vascular supply equilibrium, improved venous drainage stasis, facilitated scalp reconstruction, and reduced medical complications and neurological deficits associated with surgery [4]. With these interventions in the twins' care plan, brain damage was avoided, especially in the twin with the minority blood supply [4].

Anesthesia's role in neurotoxicity and brain injury

The CVS shared by total CPTs can easily become occluded under anesthesia, leading to various neurological complications [16]. Anesthesia itself poses a high risk of hemodynamic instability in neonates and infants, which can subsequently lead to infarction, neurotoxicity, and neurodevelopmental defects [10]. More specifically, neonatal brain development is at risk because of fragile and immature structures, including underdeveloped vascular autoregulation and incomplete vessel growth with weak vessel walls [10].

Figure 1: Representation of the Stone and Goodrich classification for total versus partial CPTs, demonstrating different orientations. Illustrated by Aileen Alexandria Treviño.
CAD/CAM: computer-assisted design/modeling, CPT: craniopagus twins, CSF: cerebrospinal fluid, CT: computed tomography, CVS: circumferential venous sinus, DSA: digital subtraction angiography, MR: magnetic resonance, MRI: magnetic resonance imaging, SSS: superior sagittal sinus, Vd: volume of distribution, VSP: virtual surgical planning, VR/AR: virtual reality/augmented reality.

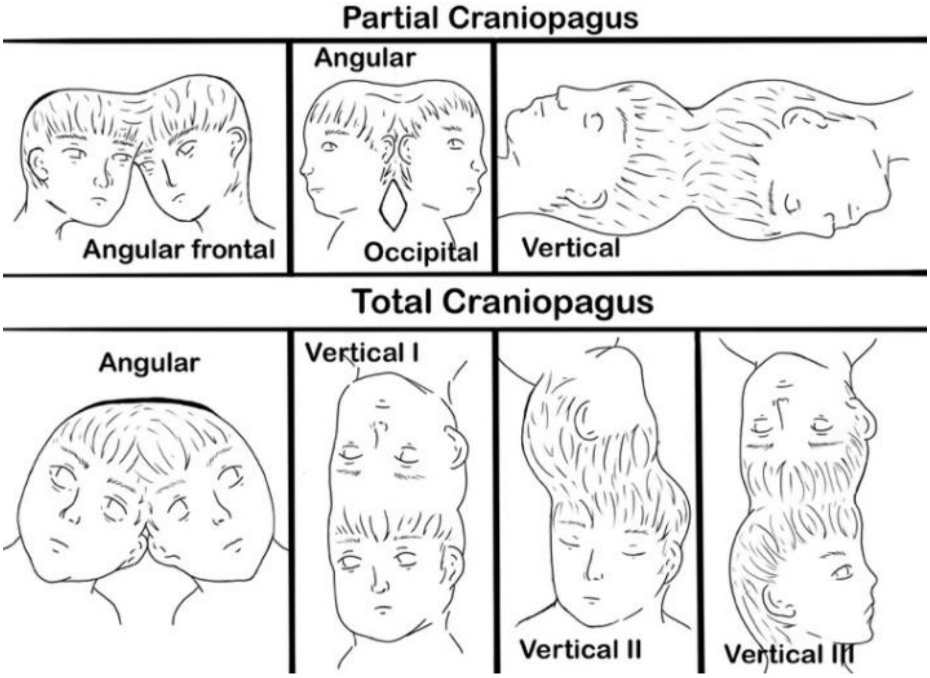

Figure 2 (A, B): Representations of CVS in different orientations. Subunit A demonstrates the anatomical predisposition of the dominant twin to retain the CVS (black arrow) compared with the nondominant twin (dashed line) when fused in a vertical orientation. Illustrated by Aileen Alexandria Treviño. Subunit B is a coronal MRI venography image of a CVS. Reproduced with permission from Mohammad et al. [6].

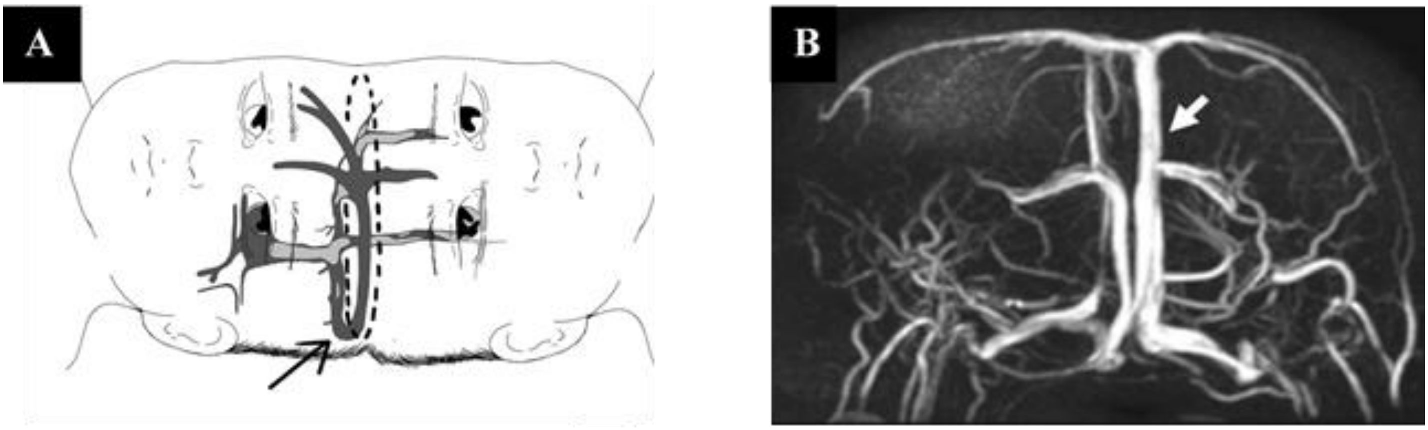

Figure 3: Coronal MRI demonstrating CVS coursing in the periphery of the septum (red arrow) and cerebral tissue separated by a transverse dural septum (black arrow). Reproduced with permission from Goldman-Yassen et al. [1].

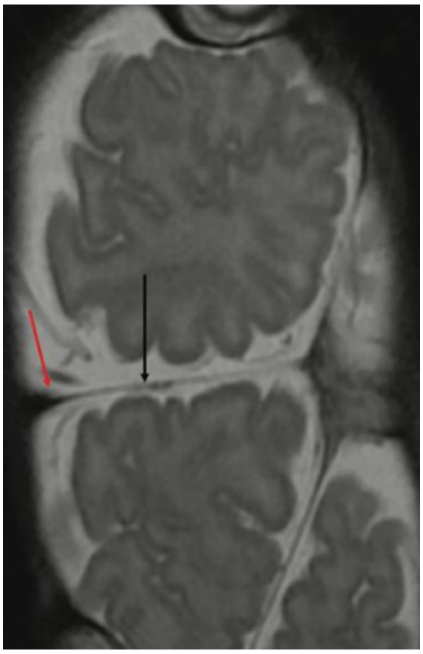

Figure 4: Venography with digital subtraction angiography demonstrates venous flow between twins after balloon inflation in the communication defect, demonstrating expected hemodynamic changes after separation. Reproduced with permission from Goldman-Yassen et al. [1].

Figure 5: Illustration representing silicone sheet placement to separate the dissection plane between surgeries. Reproduced with permission from Lehrich et al. [4].

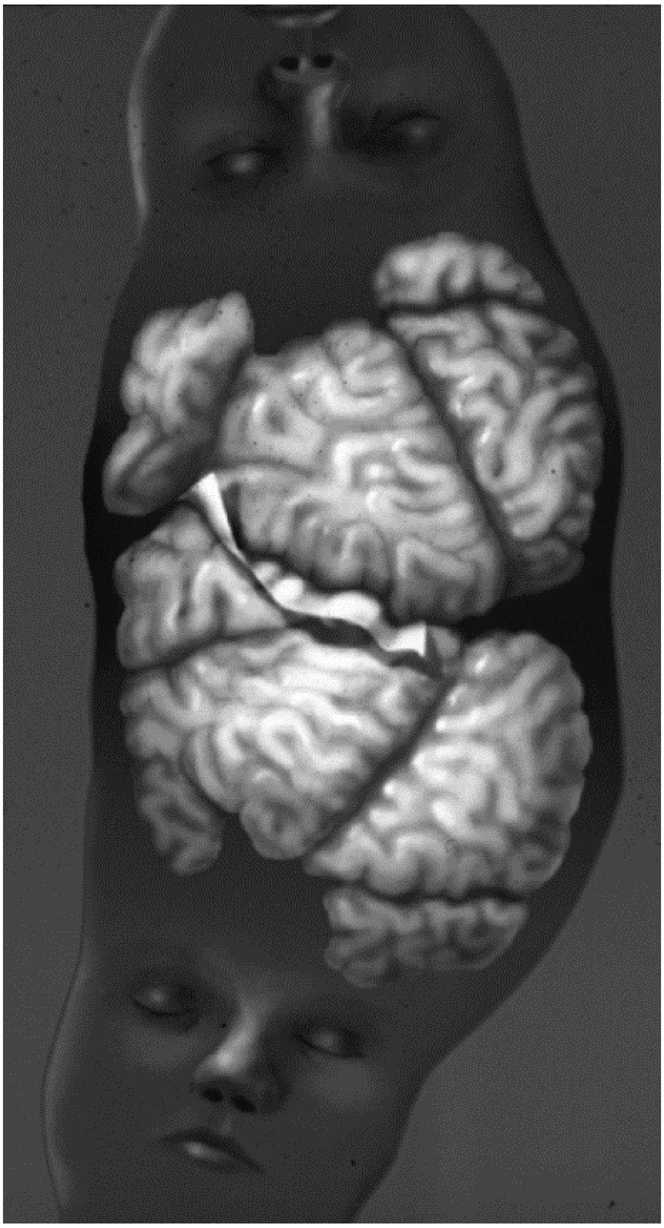

Figure 6: Three-dimensional surface-rendered images. Subunit A demonstrates the site of fusion (arrows). Subunit B demonstrates limited sacral fusion (dashed arrow), crossed fused kidneys in one twin (black arrow), and a single kidney with crossed ectopia in the other twin (white arrow). Subunit C demonstrates continuous thecal sacs (short arrow). Reproduced with permission from Mohammad et al. [6].

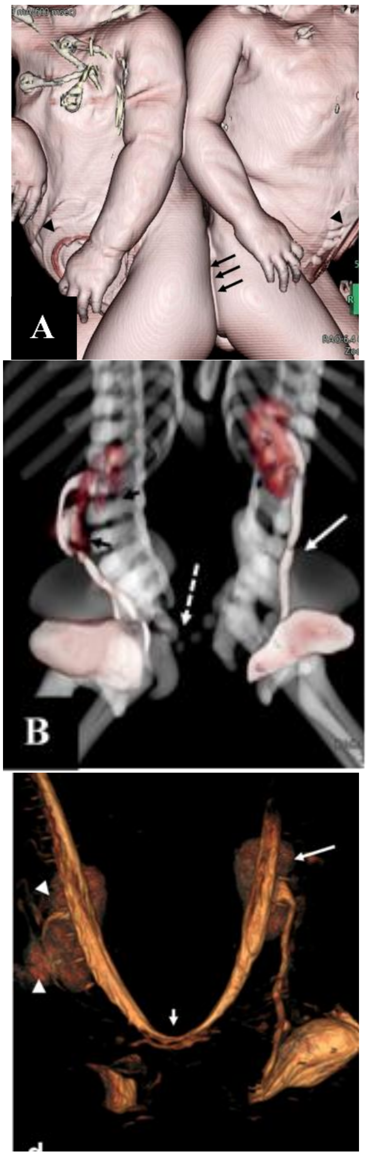

Figure 7: Photograph demonstrating two separate anesthesia teams. Reproduced with permission from Lehrich et al. [4].

When arterial blood pressure falls below intracranial pressure, hypoperfusion ensues, increasing the risk of hypoxic-ischemic brain injury [10, 16]. Some studies in nonhuman primates have shown that exposure to volatile anesthetics, including isoflurane and propofol, for more than 5 hours may exacerbate injury through mitochondrial damage and hyperoxia and may induce widespread neuronal and oligodendrocyte apoptosis, particularly in the cerebrum and cerebellum [10]. Furthermore, increasing doses of anesthesia have been associated with an increased risk of perioperative complications [5, 10, 16].

Ischemic injury is also exacerbated by CSF stasis. The glymphatic system is a waste-clearance system mediated by continuous interstitial replacement through CSF bulk flow [5]. Contrary to the previous belief that cerebral CSF circulation was active only during extracellular space dilation, such as under general anesthesia, recent studies show that it is impaired under general anesthesia [5]. As such, the CVS in total CPTs is at higher risk for occlusion, preventing arachnoid granulations, or villi, from draining CSF from the subarachnoid space into the dural sinuses. This aggravates stasis and causes hydrocephalus and increased intracranial pressure, which typically occur simultaneously [16].

Moreover, inflammation-induced vascular rupture activates microglia to release cytokines, free radicals, and glutamate, which then accumulate because of ongoing anesthesia-induced CSF stasis and hypoperfusion [10]. Glutamate accumulation, known as excitotoxicity, is a neurotoxic and neurodegenerative process involving neurons and highly vulnerable oligodendrocyte precursors, leading to hypomyelination and subsequent neurocognitive decline [10].

CPT separation surgery is extensive, takes many hours, and consequently requires large, continuous doses of anesthesia. The triad of inflammation, immature vascularization, and neurotoxicity associated with prolonged exposure to anesthetic drugs may ultimately result in brain injury; these processes are interrelated and may exacerbate one another [10]. Therefore, craniopagi, particularly total CPTs with a shared CVS, further benefit from a multistage approach because it can decrease the duration of anesthetic exposure and help avoid these complications.

Pharmacokinetic alterations due to cross-circulation

The term cross-circulation refers to the exchange of blood between two parts. In conjoined twins, it refers to connection between their circulatory systems, which may vary from poor to extensive [1, 4, 11]. Most commonly, one twin assumes an increased workload and supports the other [11]. From a pathophysiological standpoint, cross-circulation creates challenges because of uncertainty regarding pharmacokinetic distribution of administered agents, Vd in each twin, and maintenance of hemodynamic control [11]. As Rodman et al. stated, “Containing the effect or risk of adverse effects [...] is not possible with a completely shared circulation system” [11]. A thorough understanding of cross-circulation in craniopagi and its direct influence on drug distribution is crucial for developing surgical protocols that ensure safety and efficacy. Various methods have been developed to this end, including pharmaceutical administration followed by easily obtained laboratory values or measurable physiological changes, as well as advanced imaging modalities [11].

Experimental administration of gentamicin has demonstrated incomplete cross-circulation through comparable levels between twins: elevated values in the neonate who received the medication, but not in the other twin [11].

Anticholinergic drugs have also been used to determine the presence of cross-circulation by comparing vital signs. Yadav et al. ruled out cross-circulation between their twins because no heart rate changes were observed in the second twin, whereas a heart rate spike occurred in the twin who received the medication [17]. In a case study of thoraco-omphalopagus twins, Antônio et al. reported cross-circulation through heart rate changes in both twins after administration of 0.10 mg atropine to only one twin [18]. All drugs and intravenous fluids administered during surgery were calculated based on the total weight of the twins, and half was administered to each twin [18]. Because of cross-circulation, a continuous adrenaline infusion was necessary to maintain hemodynamic control [18].

Benzodiazepine administration was used to assess the extent of cross-circulation before surgery in a case study by Rawat et al., who reported no changes in the second twin after administration of midazolam (0.75 mg/kg) to the sibling, demonstrating the absence of cross-circulation between them [9].

Considering these findings, two types of cross-circulation have been described: incompletely shared circulation, in which doses are based on each twin’s individual weight, and completely shared circulation, in which combined weight is considered [9, 11].

Imaging modalities, including prenatal imaging, high-resolution computed tomography (CT), magnetic resonance (MR) imaging, angiography, and other neuroimaging techniques, are necessary to map and identify craniopagus anatomy [1, 4, 13]. This is essential for preoperative management, surgical planning, and surgical execution.

Preoperative ultrasound evaluated the optimal positioning and size of the internal jugular vein in both twins in a case study by Kaur et al. [19], in which central venous cannulation was needed. By employing preoperative ultrasound scanning and positioning rehearsal for central line cannulation, complications were successfully avoided [19].

Other studies used three-dimensional (3D) depictions and holograms generated from craniofacial CT and MRI/MR venography, which demonstrated clear visualization of the arterial and venous circulations [1]. For instance, in Dr. Goodrich’s 2004 case report, these techniques demonstrated a 2-inch fusion of the posterior parietal lobe before surgery, indicating dominant venous vascular supply in one twin compared with the other [4]. He favored high-resolution CT, MRI, MR venography, angiography, and tractography for bone, brain, and vascular mapping [4]. More recently, computer-assisted design/modeling (CAD/CAM), virtual surgical planning (VSP), and augmented or virtual reality have been used in CPT separation, dramatically improving surgical precision and safety [1, 3]. Goldman-Yassen explains that neuroradiologic imaging data have produced life-sized, 3D, transparent acrylic and ceramic models to better depict surgical anatomy, as well as holograms that demonstrate complex intracranial vascular anatomy in relation to the skull and brain [1].

Three-dimensional techniques were used by Mohammad et al., in whose case study 3D surface-rendered imaging created a roadmap for surgical planning in pygopagus conjoined twins (Figure 6), and by Di Rocco et al., in which trigonocephalic deformation and the left cerebral hemisphere of twin A were reconstructed from CT scans [6, 13].

Intraoperative management of two patients simultaneously

Caring for two patients during one operation presents a challenge for surgical staff, primarily because the unique anatomical position of CPTs impedes airway management and because equipment must be duplicated, which may lead to confusion [1, 4, 12, 13]. Operating room nurses are expected to meet the special positioning and equipment organization needs of extremely rare craniopagi [13].

To accurately distinguish the twins, surgical teams label them with a letter, number, and color [9, 12]. Monitoring cables, intravenous lines, tubing, and all equipment connected to the twins are color-coded with tape [9, 12]. For example, Rawat et al. used red and blue colors for the twins to avoid confusion [9].

A multidisciplinary team consisting of specialists in pediatric surgery, urology, neurosurgery, plastic surgery, anesthesiology, and circulating nursing is crucial in preparation for separation surgery [12, 13]. Two teams are formed, one for each twin (Figure 7), and are then color-coded to ensure that they treat the corresponding twin [9, 12]. Two operating rooms are prepared: one master operating room as the primary operating theater and a second adjacent room for use after separation [20]. This requires two to three anesthesia machines, two multiparameter monitors, two drug trolleys, two airway trolleys, two video laryngoscopes, two ultrasound machines, and two sets of all other required tools and equipment, such as defibrillators and suction devices [18, 20]. Clinical communication is supported by a control table containing patient data, laboratory results, emergency doses, and critical time points [20]. Closed-loop communication is indispensable [13]. These practices ensure patient safety and facilitate transfer to a new operating room once the twins are successfully separated, where further surgical management is needed for closure [18].

Conclusion

Separation surgery for craniopagus twins presents many challenges because of conjoined dural venous sinuses, prolonged anesthetic exposure, cross-circulation, and unique anatomical position. A multistage separation approach supports adequate collateral vasculature development and minimizes anesthetic exposure, thereby reducing potential risks of neurotoxicity and hemorrhagic or ischemic brain injury. Mapping craniopagus anatomy using 3D reconstructions from CT scans and CAD/CAM techniques allows more accurate and precise surgical planning. Surgical rehearsal with VSP and virtual or augmented reality supports successful outcomes with minimal complications. Labeling twins and their respective equipment and healthcare teams supports safe care. Because of the low incidence of CPTs, their preoperative, perioperative, and postoperative challenges remain incompletely evaluated. This literature review presents an up-to-date summary of existing methods and protocols established to address these unique challenges and to maintain the relevance of this condition, encouraging further studies of CPT cases and improvement of long-term surgical outcomes.

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