Brain and Spine 6 (2026) 106275

Contents lists available at ScienceDirect

Brain and Spine

journal homepage: www.journals.elsevier.com/brain-and-spine

Venous dominance and systemic hemodynamic divergence in a coupled craniopagus circulation

Carlo Giussani [a,b,l,*], Giorgio Carrabba [a,b,l], Ilaria Rivolta [b,c], Robert Lober [d], Paolo Remida [e], Fabio Mazzoleni [f,l], Christopher Gordon [g], Andrea Marchesi [h], Akil Patel [i], Alessandra Moretto [j], Alberto Ramponi [a,b], Andrea Trezza [a,l], Giuseppe Citerio [b,k]

[a] Neurosurgery, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy
[b] School of Medicine and Surgery, University of Milan Bicocca, Milano, Italy
[c] Institute of Molecular and Translational Cardiology, IRCCS Policlinico San Donato, San Donato Milanese, Italy
[d] Division of Neurosurgery, Dayton Children's Hospital, Dayton, OH, United States
[e] Neuroradiology, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy
[f] Pediatric Craniofacial Malformations, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy
[g] Department of Plastic and Reconstructive Surgery, Dayton Children's Hospital, World Craniofacial Foundation, Dayton, OH, United States
[h] Plastic Surgery, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy
[i] Department of Brain and Spine, Kettering Health Main Campus, Kettering, Ohio, United States
[j] Department of Emergency and Intensive Care, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy
[k] Neurointensive Care Unit, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy
[l] Smile House Foundation ETS Monza Craniofacial Center, Italy

ARTICLE INFO

Keywords:
Craniopagus twins
Intracranial venous dominance
Systemic hemodynamic divergence
Staged separation

ABSTRACT

Introduction: Total vertical craniopagus twins provide a unique physiological model of two largely independent cardiovascular systems coupled through a shared intracranial venous compartment.
Research question: We investigated whether asymmetric venous drainage could provide a physiologically plausible explanation for persistent inter-twin differences in arterial pressure, central venous pressure, and renal output during staged surgical separation.
Materials and methods: We performed a descriptive, longitudinal physiological analysis of systemic hemodynamics, renal output, biochemical variables, transthoracic echocardiography, and angiographic anatomy in female total vertical craniopagus twins undergoing staged neurosurgical separation. Cardiac structure and systolic function were preserved in both twins. Angiography demonstrated largely independent cerebral arterial inflow without clinically significant arterio-arterial cross-circulation and revealed marked asymmetry of the shared intracranial venous drainage system.
Results: One of the twins (Twin A) had dominant venous drainage, persistently higher arterial and central venous pressures, and greater urine output, whereas her sister (Twin B) had relative hypotension, tachycardia, and intermittent oliguria. The inter-twin blood pressure gradient changed dynamically during staged surgical modification of shared venous pathways, before subsequent reappearance of the original asymmetric dominance. Ultimately, Twin B died following the final stage of separation.
Discussion and conclusions: These observations are consistent with the physiological plausibility that asymmetric venous drainage contributed to the divergent systemic hemodynamic phenotypes observed in the two twins. Within a conceptual Guyton-based physiological framework, progressive modification of the shared venous compartment may have altered venous return conditions and thereby influenced systemic arterial pressure. Although causal inference cannot be established from a single observational case, this study suggests that shared venous architecture may represent an underrecognized contributor to systemic hemodynamic behavior in rare human circulatory systems involving shared venous drainage.

* Corresponding author. University of Milan Bicocca, School of Medicine and Surgery, Milano, Italy.
E-mail address: carlo.giussani@unimib.it (C. Giussani).

https://doi.org/10.1016/j.bas.2026.106275
Received 11 June 2026; Received in revised form 29 July 2026; Accepted 7 August 2026
Available online 7 August 2026

Abbreviations

ADH	antidiuretic hormone
BOT	balloon occlusion test
CO	cardiac output
CPP	cerebral perfusion pressure
CSF	cerebrospinal fluid
CT	computed tomography
CTA	computed tomography angiography
CVP	central venous pressure
DSA	digital subtraction angiography
HR	heart rate
ICU	intensive care unit
MAP	mean arterial pressure
MRV	magnetic resonance venography
Peff	effective downstream pressure
Pms	mean systemic filling pressure
Pra	right atrial pressure
Psinus	pressure within the shared intracranial venous sinus
RPP	renal perfusion pressure
Rvr	resistance to venous return
SBP	systolic blood pressure
SVR	systemic vascular resistance
TTE	transthoracic echocardiography
UO	urine output
VR	venous return

1. Introduction

Total vertical craniopagus twins represent one of the rarest forms of human conjoined twinning, accounting for only two to six percent of conjoined twins, and occurring in approximately one in 2.5 million live births (Stone and Goodrich, 2006; Goldman-Yassen et al., 2020; Gupta et al., 2022; Shafarenko and Zuker, 2022; Frawley, 2020; Browd et al., 2008; Goodrich and Staffenberg, 2004; Walker and Browd, 2004; O'Connell, 1976). Skulls are fused in a vertical orientation at the vertices, sharing dural venous sinuses, whereas systemic cardiovascular structures and cerebral arterial inflow generally remain anatomically independent.

This anatomy creates a physiological configuration rarely encountered in human biology: two independent cardiovascular systems operating in parallel but partially coupled through a shared intracranial venous drainage compartment (Shafarenko and Zuker, 2022; Parameswari et al., 2010; Kulhari et al., 2016). Each twin supplies an independent systemic vascular circuit and has largely independent cerebral arterial inflow, while venous outflow from both intracranial compartments partially converges within a common dural sinus system (Walker and Browd, 2004; O'Connell, 1976; Lasjaunias et al., 2004). The resulting interface creates a unique form of intercirculatory interaction that is predominantly mediated through the shared venous compartment.

Therefore, the central question in this setting is not whether the two circulations interact, but rather through which mechanism this interaction occurs and how it propagates to systemic hemodynamics.

Explanations focused on arterial cross-circulation are inadequate when arterial inflow is largely independent and the shared anatomical structure lies within the venous compartment. In this configuration, the system behaves as two circulations coupled downstream rather than upstream.

Venous circulation plays a central role in determining cardiac output. According to the Guytonian model of circulatory equilibrium, the pressure gradient driving venous return may constrain cardiac output independent of intrinsic cardiac pumping capacity. Although pressure within intracranial venous sinuses does not determine right atrial pressure, changes in sinus pressure or venous outflow resistance may modify the effective downstream pressure governing cerebral venous outflow. Craniopagus twins therefore represent a unique opportunity to examine the systemic consequences of venous hemodynamic coupling in humans.

We analyzed the longitudinal hemodynamic evolution of two total vertical craniopagus twins undergoing staged neurosurgical separation. The shared venous anatomy was progressively modified through sequentially staged venous sinus disconnection, while progressive cranial soft tissue expansion was performed during the pre-separation period to facilitate scalp reconstruction. This strategy of gradual separation altered venous outflow conditions over time and provided an exceptional clinical model to examine how changes in venous architecture were associated with systemic arterial pressure, central venous pressure, heart rate, and renal output.

Previous studies have described venous sharing and donor-recipient physiology in craniopagus twins. However, they have not integrated these observations into a physiological framework explaining the longitudinal hemodynamic changes observed during staged separation (Gupta et al., 2020; Edun et al., 2025). Accordingly, we interpret these findings within a Guyton-based physiological in which asymmetric venous return may contribute to persistent systemic hemodynamic divergence.

2. Materials and Methods

2.1. Case material and study design

Female total vertical craniopagus twins were born at term by Cesarean section without prenatal diagnosis and were transferred at 22 months of age to our center for evaluation of possible surgical separation. At admission, both twins were awake and interactive, with preserved brainstem reflexes and symmetric pupillary reactivity. Twin A showed greater neurodevelopmental engagement and better axial control, whereas Twin B showed global psychomotor delay, hypotonia, nutritional fragility, iron deficiency, and hypoalbuminemia. No congenital heart disease was present.

During the observation period, Twin B's body weight remained approximately 9 kg, whereas Twin A increased from approximately eight to nine kg over 10 months. Cardiovascular assessment did not identify structural heart disease, and serial transthoracic echocardiography showed normal biventricular systolic function in both twins. Throughout the staged procedures, routine anesthetic and physiological monitoring provided continuous clinical assessment for evidence of functionally significant systemic cross-circulation. No dedicated pharmacokinetic, tracer, or dye-dilution studies were performed.

Baseline renal function was normal, with serum creatinine 0.2 mg/dL. Systemic osmotic and electrolyte parameters were normal, including plasma osmolality 279 mOsm/kg, urinary osmolality 312 mOsm/kg, serum sodium 136 mmol/L, serum potassium 4.5 mmol/L, and plasma antidiuretic hormone 11.0 pmol/L, within the reported reference range of 1.9 to 13 pmol/L.

Early ICU monitoring showed a reproducible inter-twin hemodynamic asymmetry: Twin A had higher systemic arterial pressure, with mean arterial pressure (MAP) approximately 85 to 95 mm Hg, polyuria at four to seven mL/kg/h, and higher urine osmolarity, whereas Twin B had borderline hypotension, with MAP approximately 55 to 65 mm Hg, lower urine output, and intermittent metabolic acidosis during intercurrent illness. After progressive venous disconnections, Twin B suffered systemic complications from poor perfusion that were ultimately fatal and described herein. Median SBP and MAP values for each window are reported in Table 1.

Major perioperative events potentially influencing systemic hemodynamics, including vasoactive therapy, fluid balance, anesthetic management, metabolic disturbances, and intercurrent illness, were recorded chronologically and integrated into the descriptive analysis (Fig. 1).

These factors were considered potential confounding variables during interpretation of the longitudinal physiological findings.

Complete central venous pressure and urine output measurements

Table 1
Hemodynamic evolution during staged venous separation in craniopagus twins.

Stage	Twin A SBP, mmHg	Twin A MAP, mmHg	Twin B SBP, mmHg	Twin B MAP, mmHg	CVP pattern	Renal/clinical pattern	Physiological pattern
Baseline	116	84.5	94	68.8	Twin A higher, approximately 8–10 mmHg; Twin B lower, approximately 0–5 mmHg	Twin A higher urine output; Twin B lower output	Stable asymmetry: Twin A dominant/higher-pressure phenotype, Twin B lower-pressure phenotype
After Stage I	118	90.6	88	64.4	Persistent A > B CVP difference	Persistent renal output divergence	Persistent divergence after initial venous modification
Pre-Stage II	118	93.0	97.5	71.8	Persistent A > B CVP difference	Stable asymmetry	Stable asymmetry before major venous modification
Post-Stage II	146.1	117.1	89.1	70.9	A > B, with higher-pressure A phenotype	Twin A hypertension/ polyuria; Twin B relative hypotension/oliguria	Marked divergence after major venous modification
Stage III period	123.3	94.6	99.8	75.9	Partial persistence of asymmetry	Persistent dominance of Twin A circulation	Persistent but attenuated A dominance
Pre-Stage III intervention	114.1	84.6	116.0	89.4	Relative convergence	Relative convergence of systemic phenotype	Temporary hemodynamic convergence
Post-Stage III	148.4	116.9	90.2	67.9	Re-emergence of A > B pattern	Twin A higher-pressure phenotype; Twin B relative hypotension	Re-establishment of dominant Twin A phenotype
Pre-final separation	143.4	112.5	86.4	66.8	A > B pattern likely persistent but converging with reduced coupling	Twin A remains hypertensive relative to Twin B	Persistent hypertension in Twin A before final separation

Complete stage-specific median values for HR, urine output, vasoactive exposure, diuretic use, fluid balance, and ventilatory/anesthetic conditions were not available for all periods; these variables were therefore interpreted descriptively. Additional baseline physiological observation: during early ICU monitoring, Twin A showed MAP approximately 85–95 mmHg with polyuria approximately 4–7 mL/kg/h, whereas Twin B showed MAP approximately 55–65 mmHg with consistently lower urinary output, frequently meeting the clinical definition of oliguria (<1 mL/kg/h), and intermittent metabolic acidosis during intercurrent illness.
Complete central venous pressure and urine output measurements were not available for all predefined observation windows because these variables were not recorded consistently throughout the perioperative course. Consequently, median values are reported only for time windows with sufficient available observations. Due to the retrospective nature of the study and the incomplete availability of continuous recordings, the values reported are intended as descriptive median summaries rather than inferential statistical estimates.

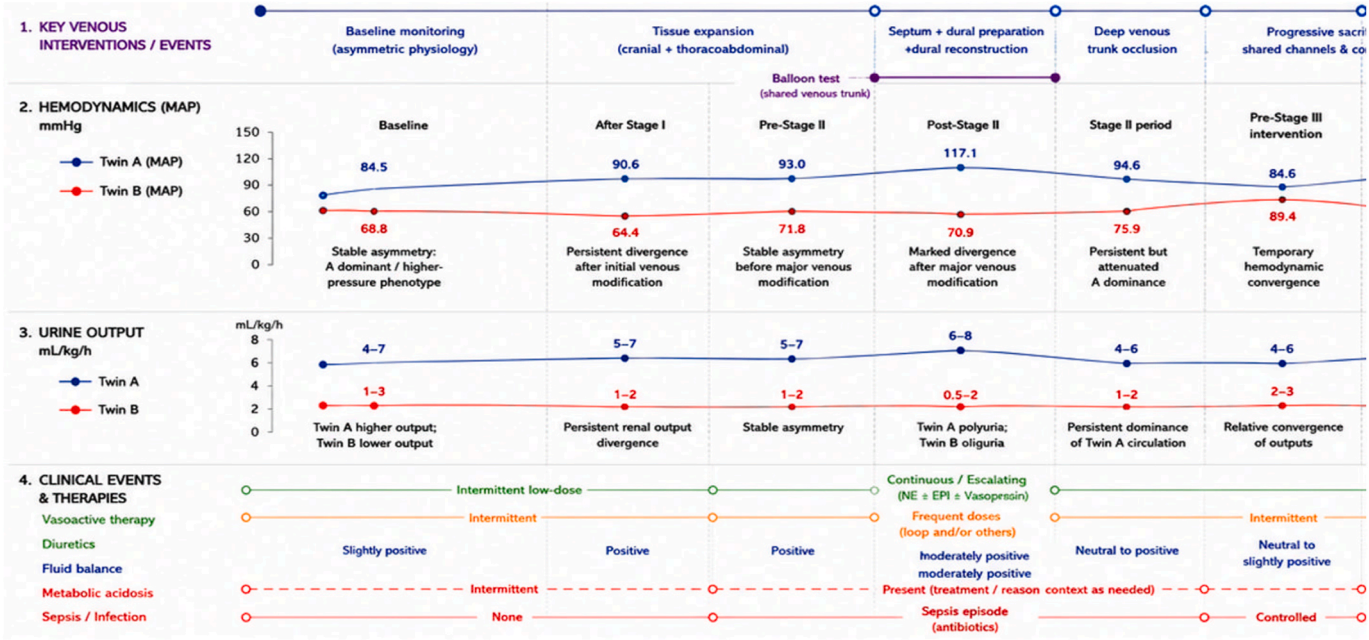

Fig. 1. Chronological timeline of staged separation and hemodynamic evolution throughout the clinical course. To facilitate interpretation of the longitudinal physiological changes, this figure summarizes the chronological relationship between staged venous interventions, systemic hemodynamics, urine output, vasoactive support, metabolic complications, and major clinical events. Values represent stage-specific median observations whenever available. Variables that were not consistently available throughout all stages, including heart rate, fluid balance, ventilatory settings, anesthetic conditions, and diuretic exposure, are summarized descriptively.

were not available for every predefined observation window because continuous invasive monitoring was not maintained throughout the entire treatment course, in part to limit the cumulative procedural burden associated with prolonged intensive monitoring. Consequently, quantitative analyses are presented descriptively using median values where sufficient observations were available.

The staged separation was planned as Stage I: venous disconnection and partial parenchymal division, Stage II: continuation of venous

detachment with greater hemispheric separation, Stage III: scalp tissue expansion with custom distraction devices, and Stage IV: final separation with cranial reconstruction.

The study was designed as a descriptive, observational, hypothesis-generating case study. Owing to the unique anatomical configuration and retrospective design, no formal statistical comparisons or causal inferences were intended. The physiological interpretation based on Guytonian circulatory equilibrium has been developed retrospectively to provide a conceptual framework for integrating the observed longitudinal hemodynamic findings and was not intended as a validated quantitative cardiovascular model.

2.2. Cardiac assessment

Serial transthoracic echocardiography was reviewed to assess whether differences in systemic arterial pressure could be explained by structural heart disease or primary myocardial dysfunction. The hearts were structurally normal, with no evidence of congenital heart disease, relevant intracardiac shunt, ventricular outflow obstruction, or significant valvular abnormality. Serial examinations demonstrated preserved biventricular systolic function in both twins. These findings did not identify any structural cardiac disease or overt systolic dysfunction as plausible explanations for the persistent divergence in systemic arterial pressure, although more subtle differences in cardiovascular physiology cannot be excluded.

2.3. Hemodynamic, renal, and biochemical variables

Systemic arterial pressure, mean arterial pressure (MAP), central venous pressure (CVP), heart rate, urine output, and relevant biochemical and hormonal variables were reviewed across the staged separation course. Hemodynamic values were summarized within each study period. Median SBP and MAP values were tabulated. CVP data were analyzed descriptively because complete measurements were not consistently available across all observation windows.

Renal output was interpreted as a complementary physiological indicator of effective systemic perfusion. Urine output was reported qualitatively throughout the longitudinal analysis and quantitatively whenever sufficient source documentation was available.

Biochemical variables included serum electrolytes, plasma osmolality, urinary osmolality, renal function markers, and antidiuretic hormone (ADH) measurements when available.

2.4. Angiographic assessment

Arterial and venous anatomy was characterized using simultaneous inter-twin digital subtraction angiography (DSA). Arterial phases assessed carotid and vertebrobasilar inflow and the presence of functionally significant arterio-arterial cross-circulation. Venous phases evaluated the architecture of the partially shared intracranial venous sinus system, including a “circular sinus” complex, torcular region, transverse sinus drainage, and asymmetry in venous outflow capacity.

During selective arterial injections into one twin, Valsalva maneuvers were performed in the contralateral twin to assess whether minimal cortico-pial communications could sustain functionally significant arterial cross-circulation.

Venous dominance was assessed according to the direction of venous drainage, the caliber and development of superficial, deep, and dural venous collectors, and the venous drainage pattern observed during provocative maneuvers.

2.5. Venous tolerance assessment and staged venous separation

A staged diagnostic and surgical pathway was developed to evaluate the feasibility of achieving anatomical separation while preserving adequate cerebral venous drainage and neurological function in both twins.

Diagnostic DSA under general anesthesia was followed by balloon occlusion testing of the dominant deep venous channel draining Twin A. The aim was to evaluate the capacity of collateral venous pathways to maintain adequate cerebral venous drainage following temporary interruption of the dominant shared venous channel.

The aim was to assess whether venous rerouting through collateral drainage could maintain adequate cerebral venous drainage in case of surgical disconnection.

Tolerance was assessed by cortical venous drainage during temporary balloon occlusion, including evaluation of venous phase delay and collateral venous filling. The staged separation strategy was designed to progressively modify shared venous pathways through selected venous disconnections, in line with previously described staged occlusions in which gradual modification of venous drainage is used to reduce abrupt hemodynamic changes and promote collateral venous adaptation (Goldman-Yassen et al., 2020; Gupta et al., 2022). In parallel, staged cranial soft-tissue expansion was performed for reconstructive planning. Although primarily reconstructive, tissue expansion may have affected extracranial venous drainage by modifying scalp and diploic emissary veins.

2.6. Data handling and physiological analysis

The retrospective physiological interpretation explored whether the observed longitudinal hemodynamic changes were compatible with alterations in venous return.

The conceptual framework used established relationships among MAP, cardiac output, systemic vascular resistance, downstream venous pressure, mean systemic filling pressure, and resistance to venous return. It has been developed as a hypothesis-generating physiological interpretation of the observed longitudinal changes rather than as a validated hemodynamic model. Because intracranial venous pressure, cardiac output, systemic vascular resistance, mean systemic filling pressure and resistance of venous return were not directly measured, the model was considered conceptual, interpretative, and hypothesis-generating rather than a validated quantitative cardiovascular model.

3. Results

Cardiac structure and systemic circulations were independent. Serial transthoracic echocardiography showed structurally normal hearts, with preserved qualitative biventricular systolic function. No congenital heart disease, relevant intracardiac shunt, ventricular outflow obstruction, or major valvular abnormality was identified. These findings did not identify structural cardiac disease or overt myocardial dysfunction as plausible explanations for the persistent inter-twin arterial pressure difference.

Functional independence of the systemic circulations was also supported by perioperative pharmacological observations. Administration of atropine and remifentanil to one twin produced no clinically evident effect in the other. This allowed twin-specific anesthetic and hemodynamic management and were consistent with the absence of clinically significant systemic pharmacological cross-circulation.

Cerebral arterial inflow was largely independent. Preoperative vascular imaging demonstrated largely separate cerebral arterial inflow to each brain through the carotid and vertebrobasilar systems. No shared circle of Willis configuration or major arterial fusion was observed, while minimal fronto-parietal cortico-pial arterial communications were seen. In fact, no major arterio-arterial cross-circulation capable of sustaining systemic hemodynamic coupling was identified. During the arterial phases of digital subtraction angiography, these microscopic flows were directed from Twin A toward Twin B. They were abolished during Valsalva maneuvers performed on Twin B, supporting the interpretation that these communications were not hemodynamically relevant. The absence of macroscopic arterial cross-circulation made a

primary arterial mechanism unlikely to account for the magnitude and persistence of the systemic pressure gradient.

Venous drainage was shared, asymmetric, and preferentially directed toward Twin A. Contrast-enhanced CT angiography and MR venography confirmed complex venous fusion, with a dominant "circular sinus" draining predominantly from Twin A toward a shared torcular confluence (Fig. 2A).

The venous phase showed marked asymmetry in drainage capacity. Twin A displayed a more developed venous outflow scaffold, including a dominant dural drainage pathway resembling an enlarged vein of Labbé and a large deep venous collector compatible with a markedly developed internal cerebral venous channel (Fig. 2B). Deep venous drainage was also asymmetric favoring Twin A.

Preferential venous drainage toward Twin A was further supported during provocative angiographic testing. During Valsalva maneuvers performed by Twin A, drainage from the circulation of Twin B persisted toward the transverse sinus of Twin A. This finding supported the presence of a dominant venous pathway toward Twin A and supported the interpretation that the shared sinus system behaved as an asymmetric downstream venous compartment. Balloon occlusion testing of the dominant deep venous channel draining Twin A in the circular sinus showed preserved venous clearance with a rerouting in the skull base sinuses, without delayed venous phase. This supported tolerance to partial venous sacrifice and provided functional evidence that staged venous rerouting could be attempted. The staged strategy was therefore based on progressive modification of the shared venous system, including venous sinus disconnection, partial parenchymal division, scalp expansion and final separation. These procedures progressively altered the topology of the shared venous compartment and provided serial physiological perturbations of the coupled circulation (Fig. 3).

Systemic arterial pressure showed persistent but dynamic inter-twin divergence. Longitudinal monitoring showed a persistent systemic arterial pressure difference between the twins. Twin A had higher SBP and MAP than Twin B during most observation periods.

At baseline, Twin A had an SBP of 116 mm Hg and MAP of 84.5 mm Hg, whereas Twin B had an SBP of 94 mm Hg and MAP of 68.8 mm Hg. This baseline difference persisted after Stage I, with Twin A showing an SBP of 118 mm Hg and MAP of 90.6 mm Hg, compared with an SBP of 88 mm Hg and MAP of 64.4 mm Hg in Twin B. Before Stage II, the pressure gradient remained present, with Twin A MAP of 93.0 mm Hg and Twin B MAP of 71.8 mm Hg.

The divergence became most marked after major venous modification. After Stage II, Twin A MAP increased to 117.1 mm Hg, whereas Twin B MAP remained 70.9 mm Hg. During the Stage III period, the pressure difference persisted, although with partial attenuation, with Twin A MAP of 94.6 mm Hg and Twin B MAP of 75.9 mm Hg.

The inter-twin pressure difference was not fixed. A transient convergence occurred before the Stage III intervention, when Twin A and Twin B showed MAP values of 84.6 and 89.4 mmHg, respectively. After Stage III, the dominant Twin A pressure phenotype reappeared, with Twin A MAP of 116.9 mm Hg and Twin B MAP of 67.9 mm Hg. Before final separation, Twin A remained hypertensive relative to Twin B, with MAP values of 112.5 and 66.8 mmHg, respectively.

Overall, the arterial pressure pattern was characterized by persistent directionality favoring Twin A, dynamic modulation across staged venous interventions, transient convergence before Stage III, and re-emergence of the higher-pressure Twin A phenotype after subsequent venous modification (Fig. 4). Because cardiac output and systemic vascular resistance were not directly measured, these pressure patterns were interpreted as systemic hemodynamic phenotypes rather than as

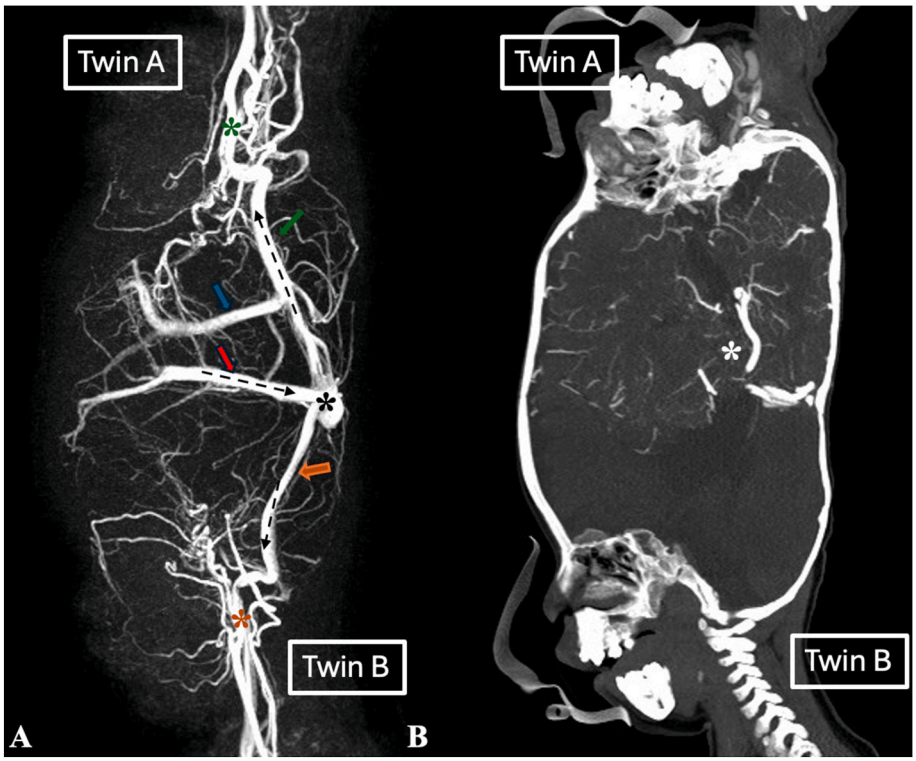

Fig. 2. The first MR angiography (A) showed a circular sinus shared by both twins (red arrow), converging into a large common torcular in the occipito-parietal region (black asterisk). Two transverse–sigmoid sinus systems (orange and green arrows) arose from this torcular and represented the dominant venous drainage pathways for both twins, draining into the right internal jugular vein of Twin A (green asterisk) and the left internal jugular vein of Twin B (orange asterisk). The contralateral sinuses and jugular veins were hypoplastic. A lateral intradural venous channel, continuation of the circular sinus toward Twin A, was also identified, resembling a sort of vein of Labbé (blue arrow). Black dotted arrows show the blood flow direction. Panel B highlights the large deep venous trunk of Twin A (white asterisk), which was occluded during the second stage of the separation procedure, with subsequent rerouting of venous drainage through skull-base venous pathways.

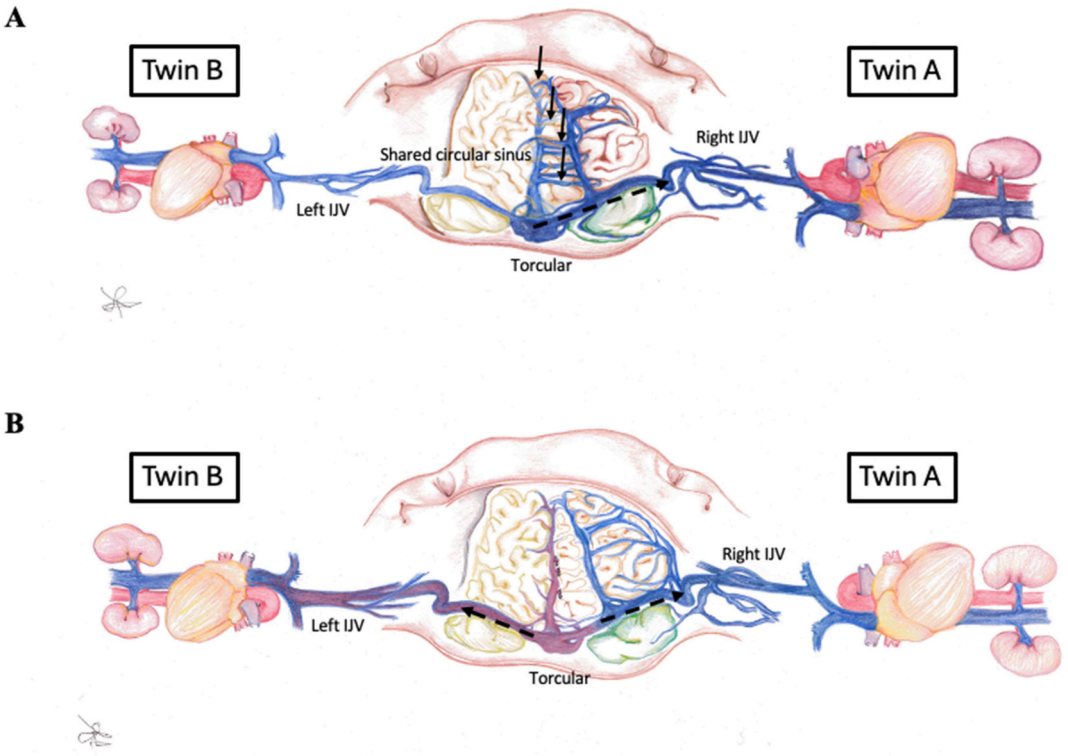

Fig. 3. Staged venous uncoupling in total vertical craniopagus twins. Schematic representation of the shared intracranial venous drainage architecture before and after staged venous modification. Panel A illustrates the native shared venous anatomy: the twins have independent systemic circulations and largely independent cerebral arterial inflow but remain coupled through a partially shared dural venous compartment. Venous drainage preferentially follows the dominant venous outflow pathway of Twin A (black dotted arrow), resulting in asymmetric venous outflow conditions and a potential mechanism for systemic hemodynamic divergence. Small black arrows indicate the cortical bridging and deep veins connecting Twin A to the shared circular sinus. These veins represent the principal targets of the staged venous separation. In panel B, staged venous disconnection and redistribution of shared venous channels have been illustrated and the independent drainage have been highlighted by two black dotted arrows, heading toward each twin's venous outflow pathways. The figure illustrates the proposed transition from a shared venous drainage system to two progressively independent venous outflow pathways.

direct measurements of flow.

Central venous pressure followed the systemic pressure asymmetry. Available CVP measurements showed a parallel inter-twin difference. During the earlier coupled stages, Twin A maintained relatively stable CVP values of approximately eight to 10 mm Hg, whereas Twin B showed lower values, typically 0 to five mm Hg. This venous pressure asymmetry was directionally consistent with the systemic arterial pressure pattern, in which Twin A displayed the higher-pressure phenotype and Twin B the lower-pressure phenotype.

As staged separation progressively reduced shared venous drainage, available measurements suggested partial convergence of the CVP difference. Although complete stage-specific median CVP values were not available, the available measurements supported a relationship between venous drainage conditions and systemic hemodynamic divergence.

Renal output paralleled arterial pressure divergence. Renal output provided an independent physiological signal consistent with the systemic pressure pattern. Twin A, who maintained higher systemic arterial pressure, also had greater urine output. During early ICU monitoring, Twin A showed MAP values of approximately 85 to 95 mm Hg associated with polyuria of approximately four to seven mL/kg/h. Twin B had lower MAP values–approximately 55 to 65 mm Hg, lower urinary output, and intermittent oliguria.

This pattern was directionally correlated with differences in effective renal perfusion pressure. Twin B also had intermittent metabolic acidosis during intercurrent illness, in association with lower arterial pressure and lower urine output. No evidence suggested primary intrinsic renal failure as the main driver of the urine output divergence. The parallel divergence of arterial pressure and urine output supported a systemic hemodynamic mechanism.

Biochemical and hormonal measurements did not support a primary neuroendocrine mechanism. Available biochemical and hormonal measurements did not support a primary osmotic, renal, or neuroendocrine explanation for the persistent arterial pressure gradient. Plasma osmolality was 279 mOsm/kg, urinary osmolality was 312 mOsm/kg, serum sodium was 136 mmol/L, potassium was 4.5 mmol/L, and creatinine was 0.2 mg/dL. Plasma ADH was 11.0 pmol/L, within the reported reference range of 1.9 to 13 pmol/L.

These findings did not support sustained ADH-mediated water balance dysregulation, major electrolyte disturbance, or renal dysfunction as the primary explanation for the hemodynamic divergence. Although subtle neuroendocrine influences cannot be excluded, the available data were more consistent with a hemodynamic mechanism related to asymmetric venous drainage.

4. Discussion

This case provides a model of two otherwise independent circulatory systems mechanically coupled through a partially shared intracranial venous drainage network.

The most relevant observation is that systemic arterial pressure divergence was temporally and anatomically associated with asymmetric venous architecture, in the absence of major arterial cross-circulation, myocardial dysfunction or overt neuroendocrine differences. Twin A, characterized by a larger and more developed venous drainage scaffold, consistently exhibited higher arterial pressure and greater urine output, whereas Twin B displayed relative hypotension, compensatory tachycardia, and intermittent oliguria.

The physiological value of this case lies in the presence of two

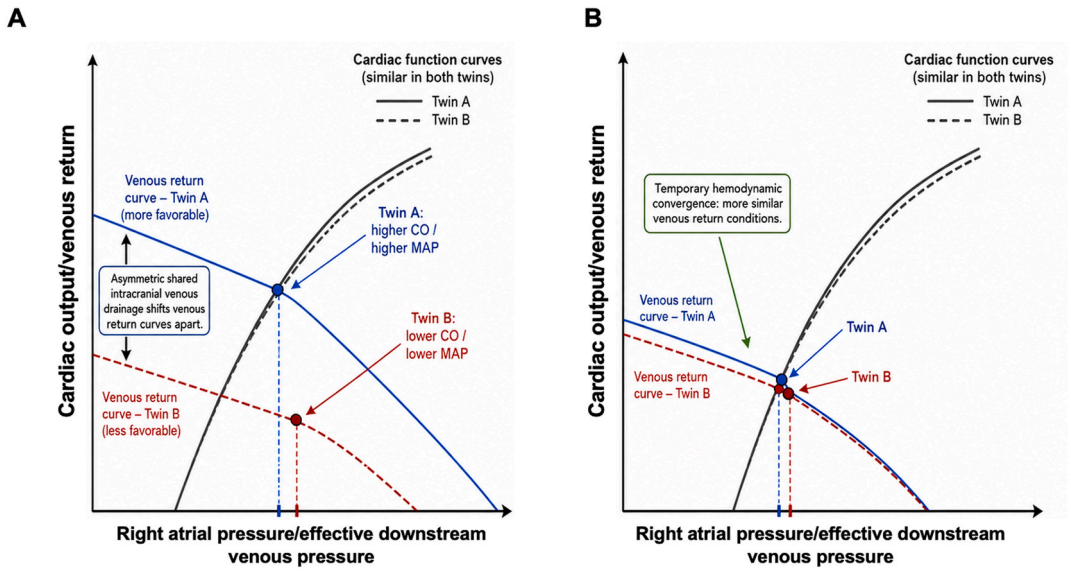

Fig. 4. Conceptual Guyton-based venous return model of systemic hemodynamic divergence during staged separation. The figure illustrates a proposed potential physiological mechanism by which asymmetric drainage through a shared intracranial venous compartment may alter the venous return conditions of two otherwise independent circulations. In panel A, Twin A operates on a more favorable venous return curve and is schematically represented at a higher operating point, consistent with higher arterial pressure and greater renal output. Twin B operates on a less favorable venous return curve and a lower operating point, consistent with relative hypotension and lower urine output. In panel B, staged modification of the shared venous pathways transiently reduces the asymmetry of venous return conditions, bringing the operating points of the two circulations closer together before subsequent re-establishment of asymmetric drainage. Cardiac function curves are intentionally depicted as broadly similar to illustrate that the proposed perturbation primarily involves venous return rather than intrinsic myocardial dysfunction, although baseline physiological differences between the twins may also have contributed to their overall cardiovascular status. The curves, operating points, and effective downstream venous pressure are schematic and intended solely to illustrate the proposed physiological interpretation. They are not derived from direct quantitative measurements or mathematical fitting. Intracranial venous pressure, cardiac output, systemic vascular resistance, mean systemic filling pressure, and venous return resistance were not directly measured. Accordingly, this figure should be interpreted as a hypothesis-generating conceptual model rather than a validated quantitative representation of cardiovascular physiology.

independent cardiac pumps and systemic circulations coupled downstream through a shared venous compartment. This configuration created a kind of natural experiment in which progressive modifications of the shared venous anatomy provided an opportunity to explore whether venous topology influenced the overall hemodynamic profile of each circulation. This ultimately may have additional relevance to the assessment of perioperative risk, as during the staged separation Twin B experienced complications of systemic hypoperfusion that prevented viable anatomic independence.

Twin B presented with global developmental delay, hypotonia, nutritional fragility, iron deficiency, and hypoalbuminemia, all of which may have contributed to baseline physiological differences and may have influenced systemic hemodynamics and renal function. However, these factors alone are unlikely to account for the dynamic hemodynamic changes observed during sequential venous modifications, including the transient convergence following major venous occlusions and the subsequent re-establishment of hemodynamic divergence. These observations support the hypothesis that alterations and asymmetry in venous return represented an important additional determinant of the observed physiological behavior and should therefore be interpreted as complementary to, rather than replacing, the contribution of these baseline factors.

In this context, the observed venous anatomy offers a possible physiological explanation for the divergent systemic hemodynamic phenotypes observed in the two twins. Twin A had a more developed venous outflow scaffold, including a dominant lateral dural drainage pathway resembling a hypertrophic vein of Labbé and a large deep venous collector compatible with a markedly developed internal cerebral venous channel. This architecture may have provided Twin A with a larger effective venous drainage system and a more favorable outflow pathway.

From a hemodynamic perspective, a larger and preferential venous outflow pathway could reduce the effective resistance to cerebral venous outflow and facilitate drainage toward the dominant venous system. Conversely, partial dependence of Twin B drainage on shared venous pathways could increase effective venous resistance for Twin B, reduce the effective venous return gradient, and contribute to lower arterial pressure with compensatory tachycardia.

In this scenario, venous dominance should be interpreted not only as a surgical risk factor, but also as a potential physiological determinant of circulatory behavior in this coupled system. In the present case, the twin with the more developed venous drainage scaffold consistently displayed the higher-pressure phenotype, whereas the twin with less favorable venous drainage showed relative hypotension, tachycardia, and intermittent oliguria. Conceptually, the shared sinus may have acted as an intermediate downstream compartment modifying the effective pressure opposing cerebral venous drainage. If this downstream constraint differed between twins because of asymmetric venous drainage capacity, it could have contributed to the distinct systemic hemodynamic phenotypes observed despite broadly similar cardiac function.

Staged venous modification provided sequential perturbations of the shared venous topology. The temporal modulation of systemic pressure divergence, including the transient convergence and subsequent re-emergence of the higher-pressure phenotype in Twin A, is consistent with the hypothesis that changes in the shared venous system contributed to the observed hemodynamic behavior, in addition to baseline physiological differences.

The physiological plausibility of this interpretation is supported by established principles of circulatory physiology. In simplified cardiovascular physiology, mean arterial pressure is determined by the interaction between cardiac output and systemic vascular resistance ($MAP \approx CO \times SVR$), whereas, at steady state, cardiac output equals venous return ($CO = VR$).

According to the Guytonian model, venous return is governed by the pressure gradient between mean systemic filling pressure and right atrial pressure, divided by the resistance to venous return (VR = [Pms − Pra]/Rvr).

Although cardiac output, mean systemic filling pressure, resistance to venous return, and intracranial venous pressure were not directly measured in the present case, these relationships provide a conceptual physiological framework through which alterations in venous drainage conditions could influence systemic hemodynamic behavior. Within this framework, progressive modifications of the shared venous anatomy may have altered the effective conditions governing venous return, thereby contributing to the dynamic changes in systemic arterial pressure observed during staged separation.

The staged separation procedures further strengthened this interpretation because they acted as sequential perturbations of the shared venous system. Systemic hemodynamic divergence changed in temporal association with progressive modification of the venous pathways. This dynamic pattern is consistent with the hypothesis that changes in the shared venous system contributed to the observed hemodynamic behavior, in addition to baseline physiological differences.

Moreover, in addition to reducing venous communication between the twins, staged venous modification may have transiently altered intracranial venous drainage resistance within portions of the dural sinus system. Cranial tissue expansion, although primarily reconstructive, may also have influenced extracranial venous drainage through modifications of diploic or emissary venous pathways. Collectively, these changes may have altered venous drainage conditions and thereby contributed to the dynamic systemic hemodynamic changes observed during staged separation. The value of this observation is not that it provides quantitative proof of altered venous return, but that it identifies a rare configuration in which intercirculatory coupling occurred anatomically downstream, within the venous compartment.

Renal output provided an additional physiological observation consistent with the systemic hemodynamic differences between the two twins. Twin A consistently showed greater urine output in parallel with higher arterial pressure, whereas Twin B experienced intermittent oliguria during periods of lower arterial pressure. This pattern is compatible with established pressure-dependent regulation of renal perfusion and diuresis and suggests more favorable effective renal perfusion conditions in the higher-pressure circulation.

It is already well-known that renal perfusion depends on the balance between arterial inflow and downstream venous pressure. Although renal venous pressure was not measured and central venous pressure represents only an imperfect surrogate of downstream venous pressure, the parallel behavior of arterial pressure and urine output is physiologically consistent with the proposed hemodynamic interpretation.

Notably, Twin A exhibited both higher arterial pressure and higher central venous pressure yet maintained greater urine output, indicating that the observed renal differences cannot be explained simply by lower venous pressure. Rather, they are compatible with more favorable overall renal perfusion conditions despite the higher downstream venous pressure. Conversely, Twin B's lower arterial pressure, despite lower central venous pressure, was associated with reduced urine output and intermittent oliguria, further supporting the interpretation that effective renal perfusion differed between the two circulations. Finally, the absence of major differences in available biochemical, osmotic, and hormonal parameters argues against a primary endocrine or osmoregulatory mechanism as the principal explanation for the observed divergence in urine output.

Several alternative confounders may have contributed to short-term hemodynamic variability, including baseline developmental and nutritional differences, prolonged ICU exposure, infection, anticoagulation, fluid balance, vasoactive therapy, anesthetic conditions, mechanical ventilation, and intercurrent illness. To facilitate interpretation of these potential confounders, a chronological overview integrating these events with staged venous interventions and longitudinal hemodynamic changes has been shown in Fig. 1.

Although these factors likely contributed to transient fluctuations, they do not completely explain the reproducible temporal relationship between staged venous modifications and the observed pattern of divergence, transient convergence, and subsequent re-divergence of systemic hemodynamics.

5. Limitations

Several limitations must be acknowledged. Direct intracranial venous pressure measurements were not available, and the proposed mechanism therefore remains inferential.

The absence of direct measurements of intracranial venous pressure, cardiac output, systemic vascular resistance, mean systemic filling pressure, and resistance to venous return precludes validation of the proposed physiological mechanism. Accordingly, the present model should not be interpreted as demonstrating causality or quantitatively describing cardiovascular behavior. Rather, it represents a conceptual framework designed to integrate the observed anatomical, angiographic, and longitudinal hemodynamic findings into a physiologically plausible hypothesis.

Urine output and CVP data were not available as complete median values for all time windows in the current dataset. The observations derive from a single extremely rare anatomical configuration and cannot be generalized to normal physiology. Incomplete availability of central venous pressure and urine output measurements across all observation windows limited the completeness of the quantitative analysis. Consequently, the reported trends should be interpreted descriptively and integrated with the overall chronological evolution of the physiological variables.

Moreover, no dedicated pharmacokinetic studies or continuous physiological analyses specifically designed to quantify systemic cross-circulation were performed. Although atropine and remifentanil administered to one twin produced no clinically evident effects in the other, we are aware that these observations cannot definitively exclude possible minimal systemic cross-circulation. Rather, they suggest that any potential cross-circulation was unlikely to be clinically significant under the observed conditions.

Nevertheless, this case offers an exceptional human model in which progressive modification of venous drainage architecture was associated with measurable systemic hemodynamic changes. The observations should therefore be interpreted as providing physiological plausibility, rather than quantitative proof, of altered venous return conditions.

6. Conclusions

This case supports the physiological plausibility of the concept that shared venous architecture may influence systemic circulatory equilibrium. In total vertical craniopagus twins with largely independent arterial inflow and preserved cardiac structure, asymmetric intracranial venous drainage may act as a downstream coupling node that modifies effective venous return conditions and contributes to systemic arterial pressure divergence. Venous dominance, therefore, should be considered not only a determinant of surgical risk, but also a potential physiological determinant of systemic hemodynamic behavior in coupled human circulations.

This unique clinical configuration provided an exceptional opportunity to explore the physiological consequences of progressive modification of a shared cerebral venous system. The temporal association between staged venous interventions and reproducible changes in systemic hemodynamic behavior, together with asymmetric venous anatomy, preserved cardiac structure and function, and concordant renal physiological observations, supports the physiological plausibility that shared venous architecture contributed to the observed circulatory differences. Although this hypothesis cannot be established from a single observational case, the findings suggest that, in total vertical

craniopagus twins with largely independent arterial inflow, asymmetric intracranial venous drainage may function as a downstream coupling site capable of influencing venous return conditions and systemic arterial pressure. Accordingly, venous dominance should be considered not only a determinant of surgical planning and operative risk, but also a potential contributor to systemic hemodynamic behavior in rare human circulatory systems involving shared venous drainage.

Ethics statement

This study is based on a retrospective physiological analysis of clinical data generated during the perioperative management of total vertical craniopagus twins. The clinical course was reviewed and supported throughout by an institutional Clinical Ethics Committee. According to the policies of our Institution, formal Institutional Review Board (IRB)/Ethics Committee approval is not required for single case reports. Written informed consent was obtained from the patients' parents for the surgical procedure. An additional informed consent was obtained and signed by the parents for publication and for the use of protected health information. An explicit consent was obtained from the parents for the use of the patients' photos, videos, radiological images and clinical data, including identifiable information, in this manuscript.

Data availability

Source data for this study are not publicly available due to privacy and ethical restrictions related to identifiable pediatric patient data and imaging. Deidentified source data may be made available to verified researchers upon reasonable request to the corresponding author, subject to institutional approval and applicable consent restrictions.

Grants

None.

Disclosures

No conflicts of interest, financial or otherwise, are declared by the authors.

Disclaimers

No disclaimers are declared.

Authors contribution

C.G., G.C., and I.R. conceived and designed the study. C.G., I.R., G.C., A.T., R.L., F.M., C.G., A.M., A.P., A.M., and G.C. contributed to clinical management, data acquisition, and interpretation of clinical findings. P. R. contributed to vascular imaging acquisition and interpretation. I.R. contributed to physiological interpretation and hemodynamic analysis. C.G., G.C., I.R. and A.T. drafted the manuscript. All authors critically revised the manuscript for important intellectual content, approved the final version, and agree to be accountable for all aspects of the work.

Acknowledgments

The authors gratefully acknowledge the Mouhamad Rassoul Dieng Foundation for its generous philanthropic support of the project. This support was made possible through the collaboration and facilitation of Smile House Fondazione ETS, which played a key role in connecting the Foundation with the clinical team and supporting the broader care pathway.

The authors also wish to thank the ad hoc Ethics Committee, established in collaboration with Regione Lombardia and Fondazione IRCCS San Gerardo dei Tintori, for its continuous oversight and guidance throughout all stages of the separation process. Its contribution was essential in supporting the ethical governance of this exceptionally complex clinical and surgical pathway. We acknowledge Dr. Assunta Filippini for the graphic contribution of Fig. 3.

References

Browd, S.R., Goodrich, J.T., Walker, M.L., 2008. Craniopagus twins. J. Neurosurg. Pediatr. 1, 1–20. https://doi.org/10.3171/ped-08/01/001.

Edun, T.R., Al Aujan, A.A., Al Khalaf, H.A., Azzubi, M.A., Al Namshan, M.K., Al Mohrij, S. A., Al Rabeeah, A.A., 2025. Extrauterine twin-twin transfusion syndrome in conjoined twins: prevalence and clinical implications. Pediatr. Surg. Int. 41 (1), 126. https://doi.org/10.1007/s00383-025-06026-6. Erratum in: Pediatr Surg Int. 2025 Oct 25;41(1):320. doi: 10.1007/s00383-025-06210-8. PMID: 40295339; PMCID: PMC12037641.

Frawley, G., 2020. Conjoined twins in 2020 – state of the art and future directions. Curr. Opin. Anaesthesiol. 33, 381–387. https://doi.org/10.1097/aco.0000000000000864.

Goldman-Yassen, A.E., Goodrich, J.T., Miller, T.S., Farinhas, J.M., 2020. Preoperative evaluation of craniopagus twins: anatomy, imaging techniques, and surgical management. Am. J. Neuroradiol. 41, 951–959. https://doi.org/10.3174/ajnr.a6571.

Goodrich, J.T., Staffenberg, D.A., 2004. Craniopagus twins: clinical and surgical management. Childs Nerv. Syst. 20, 618–624. https://doi.org/10.1007/s00381-004-1001-8.

Gupta, D., Kedia, S., Rath, G.P., Pandia, M.P., Chauhan, S., Sharma, R., Raheja, A., Darbari, S., Kamra, D., Malik, V., Saxena, A., Hote, M., Lodha, R., Gulati, S., Jauhari, P., Sankar, J., Sinha, A., Bagga, A., Kapil, A., Singhal, M., Chauhan, S., Tiwari, R., Prabhakar, A., Gaikwad, S.B., Takizawa, K., Sabapathy, S.R., Mazzeo, A. T., Jaryal, A., Kale, S.S., Mahapatra, A.K., 2022. A century with craniopagus twin separation surgeries: nihilism to optimism. Neurosurgery 91, 27–42. https://doi.org/10.1227/neu.0000000000001962.

Gupta, D.K., Mahapatra, A.K., AIIMS Team Craniopagus, 2020. Addressing the shared circumferential sinus in craniopagus conjoined twins: is venous bypass an option? World Neurosurg. 133, 421–422. https://doi.org/10.1016/j.wneu.2019.10.121. PMID: 31881558.

Kulhari, S., Rastogi, A., Kanaujia, A., Biswas, P., Singh, P.K., 2016. Anesthetic management of premature conjoined twins posted for nonseparation emergency surgery. Pediatr Anesthesia 26, 1204–1205. https://doi.org/10.1111/pan.12975.

Lasjaunias, P., Kwok, R., Goh, P., Yeong, K.Y., Lim, W., Chng, S.M., 2004. A developmental theory of the superior sagittal sinus(es) in craniopagus twins. Childs Nerv. Syst. 20, 526–537. https://doi.org/10.1007/s00381-004-1007-2.

O'Connell, J.E., 1976. Craniopagus twins: surgical anatomy and embryology and their implications. J. Neurol. Neurosurg. Psychiatry 39 (1). https://doi.org/10.1136/jnnp.39.1.1.

Parameswari, A., Vakamudi, M., Raghupathy, V., Siddhartha, R., 2010. Anaesthetic management of total craniopagus twins for magnetic resonance imaging and cerebral angiography. Br. J. Anaesth. 105, 368–370. https://doi.org/10.1093/bja/aeq165.

Shafarenko, M.S., Zuker, R.M., 2022. Conjoined twin separation: review of 30-Year case experience and lessons learned. Plast. Reconstr. Surg. 150, 133–144. https://doi.org/10.1097/prs.0000000000009267.

Stone, J.L., Goodrich, J.T., 2006. The craniopagus malformation: classification and implications for surgical separation. Brain 129, 1084–1095. https://doi.org/10.1093/brain/awl065.

Walker, M., Browd, S.R., 2004. Craniopagus twins: embryology, classification, surgical anatomy, and separation. Childs Nerv. Syst. 20, 554–566. https://doi.org/10.1007/s00381-004-0991-6.