



Clinical Research

Portal Hypertension Is Associated With Congestive Encephalopathy and Delirium After Cardiac Surgery

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ABSTRACT

Background: Venous congestion might lead to congestive encephalopathy after cardiac surgery. However, objective signs of congestion have yet to be associated with delirium. Portal vein flow pulsatility is a congestion marker that may identify a subgroup of patients at risk.

Methods: We performed a retrospective study and a prospective study in patients undergoing cardiac surgery. Adult patients who underwent portal vein Doppler imaging by the attending physician during usual care in the intensive care unit were included in the retrospective cohort. For the prospective cohort, patients had a cognitive and echocardiographic evaluation the day before surgery and daily for 3 days after surgery. Delirium was independently assessed by the nursing staff in the prospective cohort.

Results: A total of 237 patients in the retrospective cohort and 145 patients in the prospective cohort were included, for whom 1074

RÉSUMÉ

Contexte : La congestion veineuse peut entraîner une encéphalopathie congestive après une chirurgie cardiaque. Toutefois, aucune association n'a été établie jusqu'à présent entre les signes objectifs de la congestion et le délire. La pulsativité du flux de la veine porte est un marqueur de la congestion qui pourrait permettre de distinguer un sous-groupe de patients à risque.

Méthodologie : Nous avons effectué une étude rétrospective et une étude prospective portant sur des patients subissant une chirurgie cardiaque. Des patients adultes qui se sont prêtés à un examen de la veine porte par imagerie Doppler, réalisé par le médecin dans le cadre des soins standard dispensés à l'unité des soins intensifs, ont été inclus dans la cohorte rétrospective. Pour la cohorte prospective, les patients avaient fait l'objet d'une évaluation cognitive et échocardiographique la veille de l'intervention chirurgicale et

Postoperative delirium is a frequent complication after cardiac surgery, with incidences reported from 10% to 70% in cardiac intensive care units (ICUs).¹ Delirium is a clinical syndrome corresponding to clinically significant neuropsychiatric abnormalities or encephalopathy. To prevent delirium, identification of modifiable risk factors would offer the opportunity to develop targeted strategies based on the mechanism of

development rather than limiting the management to empirical approaches or the indiscriminate use of psychoactive medication. The latter approach has, so far, failed to reduce the rate of delirium in clinical trials.²

During the perioperative period, intravenous fluid administration remains one of the most frequent interventions. Although the appropriate use of fluid therapy can reestablish organ perfusion via the optimization of cardiac output, there are potential drawbacks with overzealous fluid administration. Fluid overload can result in venous hypertension, particularly in the setting of right ventricular dysfunction. Venous hypertension results in a decreased arteriovenous pressure gradient and can lead to interstitial edema in the setting of critical illness.³ Venous congestion may be responsible for organ dysfunction as it was

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portal Doppler evaluations were performed. An association was found between delirium and portal vein pulsatility in the retrospective cohort (odds ratio [OR], 2.69; confidence interval [CI], 1.47-4.90; $P = 0.001$). In the prospective cohort, significant associations were found between the presence of portal vein pulsatility and the development of cognitive dysfunction and asterixis assessed by the investigators (OR, 2.10; CI, 1.25-3.53; $P = 0.005$ and OR, 2.23; CI, 1.13; 4.41; $P = 0.02$, and delirium detected by the nursing staff (hazard ratio, 2.63; CI, 1.13-6.11; $P = 0.025$). Higher N-terminal pro-beta natriuretic peptide measurements (OR, 4.03; CI, 1.78-9.15; $P = 0.001$) and cerebral desaturations (OR, 2.54; CI, 1.12-5.76; $P = 0.03$) were associated with cognitive dysfunction.

Conclusion: These data present an association among hepatic congestion, delirium, and encephalopathy in patients undergoing cardiac surgery. Further studies should explore whether those neurological complications may have a congestive origin in some patients.

demonstrated for the kidney, liver, bowel, and lung.³ It is likely that venous congestion also may affect cerebral function in some settings where significant cardiac dysfunction can occur, such as in cardiac surgery. In critically ill patients, a positive fluid balance has been shown to be an independent risk factor for delirium.⁴

Hemodynamic repercussions of venous hypertension on the brain are not easily assessed at the bedside. Central venous pressure (CVP) is susceptible to measurement errors and may not be representative of the impact of venous congestion on end organs.⁵ Portal vein flow pulsatility is an echocardiographic sign of portal hypertension originally described in patients with congestive heart failure,^{6,7} in whom it is associated with an increased risk of adverse outcomes.⁸ More recently, portal pulsatility has been investigated in the perioperative period and has been linked to acute kidney injury and other major complications.^{9,10} The kidney and the brain both have a limited capacity to expand without resulting in an exponential increase in interstitial pressure.¹¹ Therefore, portal pulsatility could be the hallmark of significant venous hypertension resulting in a detrimental impact on multiple organs.

We hypothesize the presence of portal pulsatility during the perioperative period is associated with delirium in patients undergoing cardiac surgery. In addition, we explored the associations among changes in cerebral oximetry measured by near-infrared spectroscopy, detection of asterixis, and N-terminal pro-beta natriuretic peptide (NT-pro-BNP) levels.

Material and Methods

Two distinct cohort studies were performed in a single specialized cardiac surgery center. Data were collected retrospectively in a first cohort and subsequently validated in a substudy within a prospective cohort study (clinicaltrials.org identifier: NCT02831907).¹² Both studies were approved by the Montreal Heart Institute Ethics Committee. Written

quodienement pendant les 3 jours suivant la chirurgie. Dans la cohorte prospective, le délire était évalué de façon indépendante par le personnel infirmier.

Résultats : Au total, 237 patients ont été inclus dans la cohorte rétrospective et 145 patients dans la cohorte prospective, chez lesquels 1074 examens Doppler de la veine porte avaient été effectués. Une association a été observée entre le délire et la pulsativité de la veine porte dans la cohorte rétrospective (rapport de cotes [RC] : 2,69; intervalle de confiance [IC] : de 1,47 à 4,90; $p = 0,001$). Dans la cohorte prospective, les chercheurs ont observé des associations significatives entre la présence d'une pulsativité de la veine porte et l'apparition d'une dysfonction cognitive et d'un astérisis (RC : 2,10; IC : de 1,25 à 3,53; $p = 0,005$ et RC : 2,23; IC : de 1,13 à 4,41; $p = 0,02$) ainsi que le délire détecté par le personnel infirmier (RC : 2,63; IC : de 1,13 à 6,11; $p = 0,025$). Des valeurs élevées du fragment propeptide natriurétique de type B N-terminal (RC : 4,03; IC : de 1,78 à 9,15; $p = 0,001$) et la désaturation cérébrale (RC : 2,54; IC : de 1,12 à 5,76; $p = 0,03$) étaient associées à une dysfonction cognitive.

Conclusions : Ces données montrent l'association existant entre la congestion hépatique, le délire et l'encéphalopathie chez des patients subissant une chirurgie cardiaque. Des études additionnelles devraient être menées dans le but de voir si ces complications neurologiques pourraient avoir une origine congestive chez certains patients.

informed consent was obtained for all participants in the prospective cohort.

Methods specific to the retrospective cohort

Participants. All patients, 18 years or older, from May 2015 to November 2016 who had portal vein Doppler imaging by the attending intensive care physician within 7 days after cardiac surgery were eligible. The files of all consecutive patients who were under the care of an experienced intensive care physician with National Board Certification in Critical Care Ultrasound from the American College of Chest Physicians. Patients were excluded if they had known liver cirrhosis or if the cognitive status was not assessed for the entire observation period, such as when deep sedation was used.

Cognitive status assessment. Data were collected from the medical chart once daily for 7 days after surgery. Delirium in the retrospective cohort was defined as the mention of encephalopathy, confusion, or delirium in the medical notes at the time of portal flow assessment in the ICU. Asterixis was documented as present when reported in the medical notes and absent if documented as absent or not mentioned.

Ultrasound assessment. The results of the portal vein Doppler imaging were recorded as noted by the attending physician in the medical record. Portal flow Doppler was integrated into the routine postoperative care of this physician since 2014 when it was first described in patients who developed complications after surgery.¹³

Other information. The following information was also collected: age, gender, duration of cardiopulmonary bypass (CPB), type of surgery, the context of surgery, the preoperative risk evaluated using the European System for Cardiac

Operative Risk Evaluation (euroSCORE) II,¹⁴ and duration of ICU stay and hospital stay in days.

Methods specific to the prospective cohort

Participants. Patients 18 years and older undergoing cardiac surgery with the use of CPB from August 2016 to August 2017 were eligible to participate. Patients were screened by 2 investigators. Patients were excluded if they had severe chronic kidney disease (estimated glomerular filtration rate < 15 mL/min/1.73 m² or dialysis), they underwent renal transplantation, they had a critical preoperative state before surgery (defined as aborted sudden death, preoperative cardiac massage, preoperative mechanical ventilation, preoperative vasopressor or inotropes support, or intra-aortic counter pulsation balloon pump), they already had documented acute kidney injury or delirium before surgery, or they had known or suspected cirrhosis or portal vein thrombosis. Patients admitted for urgent surgery were otherwise eligible if none of the previously mentioned features were absent. These exclusion criteria were predefined for the main study.¹²

Patient assessment

Cognitive status assessment. Assessments were performed by the investigators from the day before surgery to postoperative day 3. Patients unable to communicate because of sedation or mechanical ventilation were not assessed. Cognitive dysfunction was defined as a score of more than 0 on any component of the delirium index scale according to the evaluation by the investigators at the bedside before the ultrasound exam. This scale include signs of inattention, disorganized thinking, altered level of consciousness, disorientation, memory impairment, perceptual disturbances, and psychomotor agitation/retardation (Supplemental Appendix S1 of shows details).¹⁵ The presence of asterix was evaluated by asking the participant to raise his/her arms at a 90° angle with the body and to perform wrist dorsiflexion during 30 seconds. The presence of bilateral jerking movements of the hand or flapping tremors was defined as asterix.¹⁶ The presence of asterix was assessed systematically by the investigators before the ultrasound assessment.

Delirium was defined as a nurse-reported Intensive Care Delirium Screening Checklist (ICDSC) of ≥ 4 at any point during a 24-hour period (Supplemental Appendix S1).¹⁷ This method is part of standard care at the Montreal Heart Institute and was performed independently from the investigators. The nurses were not informed of the results of the ultrasound assessment and routinely perform the ICDSC assessment at least once per 8 hours according to the institutional policy.

Cerebral oximetry. Bilateral frontal cerebral oximetry was assessed by near-infrared spectroscopy using the O3 Regional Oximeter System (Masimo Corporation, Irvine, CA) once daily from the day before surgery to postoperative day 3. Values were recorded at the time of cognitive evaluation by installing the sensor on the forehead of the patient until an unchanged value appeared for at least 30 seconds, and the mean of both values was considered. A decrease of $\geq 15\%$ compared with the preoperative baseline was considered significant on the basis of previous literature.^{18,19}

Ultrasound assessment. From the day before surgery to postoperative day 3, the investigators (A.B. and W.B.S.) performed ultrasound assessment daily at the bedside. Ultrasound evaluation in the prospective cohort was performed with the Sparq system (Philips Healthcare, Amsterdam, The Netherlands) with a phased array transducer (S4-2) or a convex array transducer (C6-2). Interobserver reliability assessment was performed and has been published.¹²

Portal vein Doppler measurements were performed using a coronal view of the liver, as previously described.¹² The peak and nadir velocities during the cardiac cycle were recorded. The portal flow pulsatility fraction (PF) was defined as the difference between the maximal and the minimal velocities, divided by the maximal velocity, and expressed as a percentage. Portal flow pulsatility was defined as a PF of $\geq 30\%$ on the basis of the available data as described in Supplemental Appendix S2.

Other information. The following information was also collected: age, gender, comorbidities, duration of CPB, type of surgery, context of surgery, and preoperative risk evaluated using the euroSCORE II.¹⁴ Measurements of NT-pro-BNP were performed before surgery and daily on postoperative days 1, 2, and 3. In addition, a baseline cognitive assessment was performed before surgery using the Mini-Mental State Examination.²⁰ The use of antipsychotic medications, including typical antipsychotics (haloperidol) and atypical antipsychotics (quetiapine, olanzapine, risperidone), was recorded in the first postoperative week after surgery by reviewing pharmacy profiles.

Statistical analysis

The association between portal pulsatility and delirium in the retrospective cohort or cognitive dysfunction at the time of assessment in the prospective cohort was tested using a generalized estimating equation analysis with a logistic regression function. This type of analysis accounts for the study design in which multiple assessments were performed for each patient. The associations are presented in odds ratio (OR) with a 95% confidence interval (CI) representing the association between portal flow pulsatility and the detection of cognitive dysfunction at the same time point. In addition, the time of assessment was included as a factor in the analysis, and the interaction between the studied variable and the time of ultrasound assessment was tested. In the presence of a significant interaction with time ($P < 0.05$), the association would have been presented for each time point. A robust estimator for the covariance matrix and an independent structure for the working correlation matrix were used. The same method was used to assess the association between portal pulsatility and other neurologic parameters (asterixis, cerebral desaturation). Additional analyses were performed to determine whether the PF as a continuous variable is associated with cognitive dysfunction and the delirium index score as a continuous variable.

Exclusively for the prospective cohort, a Cox proportional hazards model analysis was used to assess the association between the detection of portal pulsatility and subsequent delirium identified by the nursing staff. Portal pulsatility was treated as a segmented time-dependent variable, thus ensuring

that the temporal relationship between its detection and assessment of delirium was consistent, and accounting for the fact that portal flow might change between individual measurements in the same patient. Other risk factors for postoperative delirium were assessed. A multivariable model was constructed including all variables with $P < 0.15$ in univariate analysis with backward stepwise selection using the likelihood ratio method. The results are presented as hazard ratio (HR) with a 95% CI. An additional analysis was performed to determine if the PF as a continuous variable is associated with delirium using the same method.

Results are presented in number and percentage (%) for dichotomous variables and in mean \pm standard deviation or median and interquartile range (IQR) for continuous variables, where appropriate. Comparisons between 2 groups for continuous variables were performed using the t test or Mann–Whitney U test for independent sample, and comparison between 2 groups for categorical variables was performed using the chi-square test. Comparison between more than 2 groups was performed using 1-way analysis of variance or Kruskal–Wallis test followed by multiple comparison with Bonferroni correction. All statistical tests were performed in SPSS version 24 (IBM, Armonk, NY). Additional details about the determination of sample size are available in [Supplemental Appendix S2](#).

Results

Retrospective cohort

After review of 342 consecutive patient files, 237 cases (69.3%) were included in the retrospective cohort ([Fig. 1](#)). Characteristics of patients are presented in [Table 1](#). Patients had a mean age of 67 ± 12.3 years and a median euroSCORE II of 2.1% (IQR, 1.2–3.7), and 29.1% were women. Isolated coronary artery bypass graft was performed in 106 patients (44.7%), and 27 procedures (11.4%) were performed in an emergency setting. Median duration of CPB was 80 minutes (IQR, 62–114). The mean cumulative fluid balance during surgery was 1.4 ± 1.2 L. The median length of mechanical ventilation was 1 day (IQR, 1–1). Patient median stay in the ICU was 3 days (IQR, 2–6). Median hospital length of stay was 7 days (IQR, 5–10). During hospitalization, 9 patients (4%) died.

A total of 515 ultrasound evaluations were compiled through the 7 postoperative days for a mean of 2.2 examinations per patient. Portal pulsatility was detected in 259 examinations (50.3%), and 155 patients (65%) had at least 1 assessment showing portal pulsatility during their ICU stay. The relative prevalence of abnormal portal flow is presented in [Figure 2](#). A total of 969 cognitive examinations were performed by the attending physician, and delirium was noted in 161 examinations (17%). Seventy-two patients (30%) had at least 1 abnormal cognitive status assessment during their ICU stay. In total, 366 individual assessments in 237 patients combining portal and cognitive assessment were available for analysis. The distribution of portal flow assessment and PF distribution are presented in [Supplemental Table S1](#) in [Supplemental Appendix S3](#).

A significant association was found between the presence of portal pulsatility and both delirium (OR, 2.69; CI, 1.47–4.90;

$P = 0.001$) and asterixis (OR, 5.19; CI, 2.27–11.88; $P < 0.001$) ([Table 2](#)). Age (for each year above 60 years) and the euroSCORE II were associated with delirium (OR, 1.06; CI, 1.02–1.09; $P < 0.001$ and OR, 1.05; CI, 1.003–1.11; $P = 0.038$). The association between portal pulsatility with both delirium and asterixis remained after adjustment for age and euroSCORE II (OR, 2.70; CI, 1.47–2.99; $P = 0.001$) ([Supplemental Table S2](#) in [Supplemental Appendix S3](#)).

Prospective cohort

For the prospective study, 145 participants were included ([Fig. 1](#)). Patient characteristics are described in [Table 1](#). Patients had a mean age of 66 ± 12.9 years and a median euroSCORE II of 2.96% (IQR, 1.7–4.8), and 26.2% were women. Before surgery, only 2 patients (1.4%) had a Mini-Mental State Examination score of 24 or less, compatible with cognitive impairment, and no patient had cognitive dysfunction based on the delirium index scale.

Isolated coronary artery bypass grafting was performed in 42 patients (29%), and 48 procedures (33.1%) were urgent. Median duration of CPB was 68 minutes (IQR, 48–94). Mean fluid balance after surgery was 1.3 ± 1.0 L. The median length of mechanical ventilation in patients was 4 hours (IQR, 3–7). The median stay in the ICU for patients was 45 hours (IQR, 23–73). The median hospital length of stay was 8 days (IQR, 6–9). No patients died during hospitalization.

A total of 559 ultrasound evaluations and 379 cognitive assessments were completed during the study period. The distribution of portal pulsatility in the postoperative period is shown in [Figure 2](#). After surgery, cognitive dysfunction was present in 36.9% (139/379) of all assessments, with a median severity of 3 points (IQR, 2–4 points) on the delirium index scale. The distribution of delirium and cognitive dysfunction is presented in [Figure 3](#). During the week after surgery, 25 patients (17.2%) developed delirium. Antipsychotic medications were prescribed in 25 patients (17.8%), including 11 patients with delirium and 10 patients with sub-syndromal delirium (ICDSC > 0 and < 4). Portal pulsatility was present in 42.3% (237/559) of all ultrasound assessments.

A significant association was found between the presence of portal pulsatility and cognitive dysfunction (OR, 2.10; CI, 1.25–3.53; $P = 0.005$) ([Table 2](#)). A significant association was also present between PF as a continuous variable and cognitive dysfunction (OR, 1.20; CI, 1.08–1.32; $P = 0.001$ for each increase of 10% in PF), and an association was found between the severity of cognitive dysfunction based on the delirium index score as a continuous variable and the PF (R -estimate: 0.13 CI, 0.03–0.23; $P = 0.01$ for each increase of 10% in PF). We also observed a significant association between portal pulsatility and asterixis (OR, 2.23; CI, 1.13–4.41; $P = 0.02$), as well as cerebral desaturations (OR, 2.23; CI, 1.12–4.71; $P = 0.02$). Apart from the detection of portal pulsatility, higher NT-pro-BNP measurements were associated with cognitive dysfunction (OR, 4.03; CI, 1.78–9.15; $P = 0.001$), asterixis (OR, 4.26; CI, 1.73–10.59; $P = 0.002$), and cerebral desaturations (OR, 2.54; CI, 1.12–5.76; $P = 0.03$). These associations were also significant if the PF was analyzed as a continuous variable, as shown in [Supplemental Table S3](#) in [Supplemental Appendix S3](#). On the contrary, CVP measurements and cumulative fluid balance were not ([Table 3](#)).

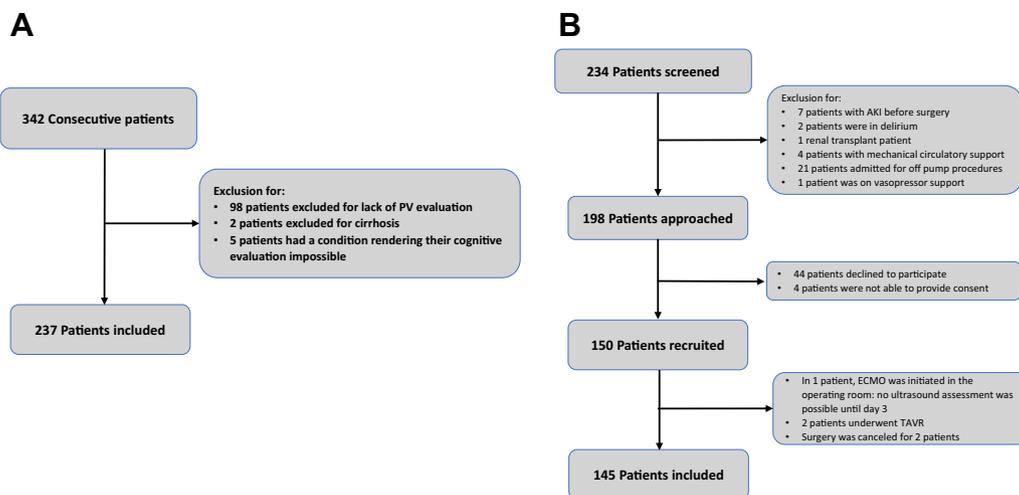


Figure 1. Flowchart of patient inclusion for the (A) retrospective and (B) prospective cohorts.

Clinical variables associated with portal pulsatility are presented in [Supplemental Table S3](#) in [Supplemental Appendix S3](#). Vasopressor use (number of vasopressors, dose of norepinephrine) was not associated with portal flow pulsatility, but inotrope use was associated with a higher portal PF (β estimate = 15.7; CI, 4.2-27.2; $P = 0.008$, no interaction with time of assessment) ([Supplemental Fig. S2](#) in [Supplemental Appendix S3](#)).

During the first postoperative week, an association was observed between detection of portal pulsatility and delirium reported by the nursing staff (HR, 2.63; CI, 1.13-6.11; $P = 0.025$). This association was also present when portal PF was considered as a continuous variable (HR, 1.20; CI, 1.05-1.36; $P = 0.007$ for each increase of 10% in PF). Other known risk factors associated with delirium are presented in [Supplemental Table S4](#) of [Supplemental Appendix S3](#). In a multivariable model, the association between portal pulsatility and delirium was still observed (HR, 2.57; CI, 1.01-6.57; $P = 0.049$) ([Table 4](#)).

Table 1. Baseline characteristics of included participants

	Retrospective cohort (n = 237)	Prospective cohort (n = 145)
Age (y)	67.2 ± 12.3	66 ± 12.9
Female gender (n)	69 (29.1%)	38 (26.2%)
euroSCORE II (%)	2.13 (1.16-3.71)	2.96 (1.70-4.79)
CPB duration (min)	80 (62-114)	90 (69-120)
Type of surgery (n)		
Isolated CABG	106 (44.7%)	42 (29.0%)
1 procedure other than CABG	71 (29.9%)	38 (26.2%)
2 procedures	50 (21.1%)	50 (34.5%)
3 procedures	1 (0.4%)	11 (7.6%)
Surgery on thoracic aorta	13 (5.5%)	10 (6.9%)
Cardiac transplantation	5 (2.1%)	2 (1.4%)
Context of surgery (n)		
Elective	211 (89.0%)	96 (66.2%)
Urgent	NA	48 (33.1%)
Emergency	27 (11.4%)	0 (0.0%)

CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; euroSCORE, European System for Cardiac Operative Risk Evaluation; NA, not available.

Discussion

This study explored a possible link between venous congestion manifesting as delirium after cardiac surgery. Our observations in the retrospective cohort led to the initial identification of the association between portal pulsatility and cognitive dysfunction in the postoperative period. This observation was confirmed in the prospective cohort. The detection of portal pulsatility was associated with the presence of asterix in both studies and higher NT-pro-BNP and cerebral desaturations in the prospective study. Finally, the detection of portal pulsatility was associated with an increased risk of subsequent delirium, which was independently assessed by the nursing staff.

Portal flow pulsatility is an echocardiographic marker originally described in patients with congestive heart failure that is created by the transmission of pressure variations in the right atria during the cardiac cycle to the portal circulation through a noncompliant venous system. Portal flow assessment using Doppler ultrasound is a reproducible measurement that can be performed bedside with basic training in almost all patients undergoing cardiac surgery and might be of use to evaluate the impact of venous hypertension. In support of this, we previously reported the hemodynamic factors and echocardiographic factors associated with pulsatile portal flow in the prospective cohort, including larger inferior vena cava diameter, higher NT-pro-BNP, alteration in intrarenal venous flow, and lower perfusion pressure.¹² Furthermore, we previously demonstrated that pulsatile portal flow is also a marker of right ventricular dysfunction during cardiac surgery.¹⁰ In these studies, the detection of portal flow pulsatility during or after cardiac surgery was associated with acute kidney injury¹² and major postoperative complications.¹⁰ Beyond being a marker for the abdominal organs, the detection of portal flow pulsatility might indicate venous congestion of clinical significance for the brain. This is further supported by the association between portal pulsatility and relative cerebral desaturations at the time of assessment seen in the prospective cohort. The association between postoperative delirium and cerebral desaturation occurring in the ICU²¹ and the operating room²² has been reported. Venous congestion may reduce brain oximetry by increasing the relative contribution

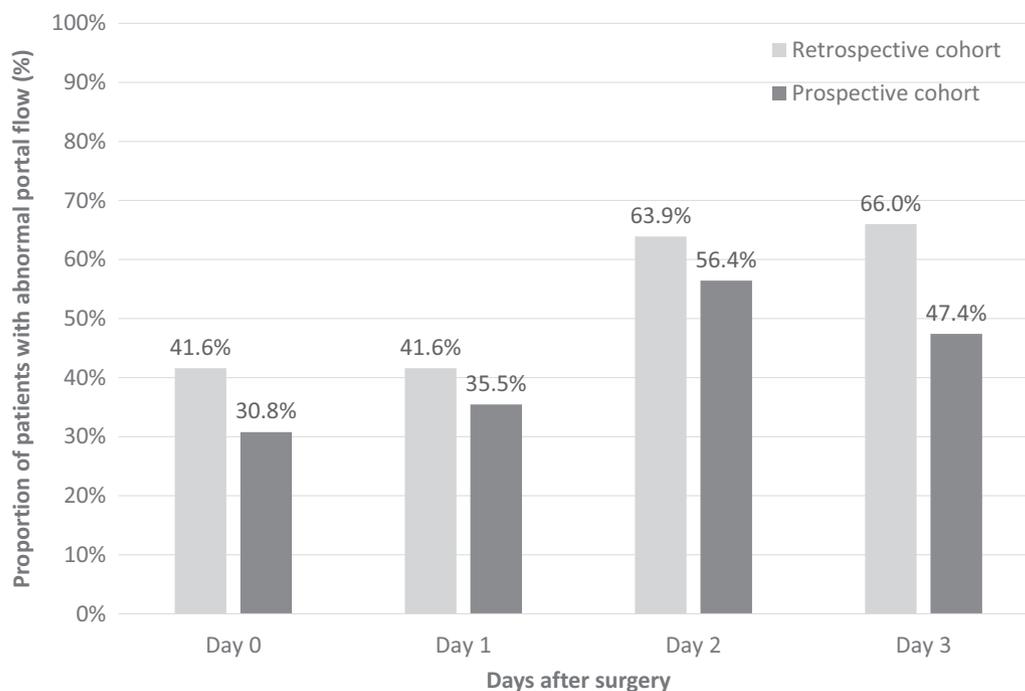


Figure 2. Relative prevalence of abnormal portal flow after cardiac surgery in the retrospective and prospective cohorts.

of venous blood to the oximetry reading and by directly impairing brain perfusion via an elevation of intracranial pressure.

Delirium is an important complication after cardiac surgery associated with adverse outcomes and increased health-care costs.²³ The pathophysiology is complex and depends both on baseline patient characteristics and on events during the perioperative period. The identification of a mechanism for cognitive dysfunction leading to delirium would be critical because a precise targeted intervention may result in a rapid improvement in a selected subgroup of patients. Although the possible contribution of venous congestion as a mechanism leading to cerebral dysfunction has been scarcely studied, the adverse effects of venous hypertension on other organs have been described in congestive heart failure and in critically ill patients.³ Furthermore, venous congestion as a pathophysiological mechanism for cognitive dysfunction has been suggested in animal models²⁴ and in humans.^{4,25,26}

Study limitations

Some of the limitations in the retrospective study were addressed in the prospective study. Asterixis assessment was

done sporadically in the retrospective cohort and was considered negative if missing, whereas it was systematically performed in the prospective cohort. The clinician performing the cognitive evaluation in the retrospective cohort was not blinded to the ultrasound assessment, whereas the cognitive assessment in the prospective cohort was systematically performed before ultrasound assessment. Delirium in the prospective cohort was reported by the nurse evaluation, which was independent of the investigator assessment. Although nurse screening using the ICDSC or other methods is known to have suboptimal sensitivity for delirium especially of the hypoactive subtype,²⁷ the use of sensitive criteria during the evaluation by the investigators to detect subtle alteration in cognitive status was chosen to circumvent this issue.

Despite these strengths, some limitations are still present. Both studies were performed in a single center, which limits the generalizability of these findings. The cognitive assessments performed by the investigators were not validated by a delirium expert, and the same team of investigators performed both the neurological and the ultrasound assessments. The limited sample size limits the identification of potential confounding factors and the number of variables to be included in

Table 2. Association between portal flow pulsatility and neurologic parameters at the time of assessment

Neurologic parameters at the time of assessment	Retrospective cohort (236 patients, 366 assessments)			Prospective cohort (145 patients, 379 assessments)		
	OR	CI	P value	OR	CI	P value
Abnormal cognitive evaluation	2.69	1.47-4.90	0.001	2.10	1.25-3.53	0.005
Asterixis	5.19	2.27-11.88	< 0.001	2.23	1.13-4.41	0.02
Cerebral desaturation (≥ 15% decrease from baseline values)				2.23	1.12-4.71	0.02

CI, confidence interval; OR, odds ratio.

Generalized estimating equation analysis was performed using a logistic link function. For each model, the studied neurologic variable and the time of assessment were included as factors. Interaction with time was tested for each model.

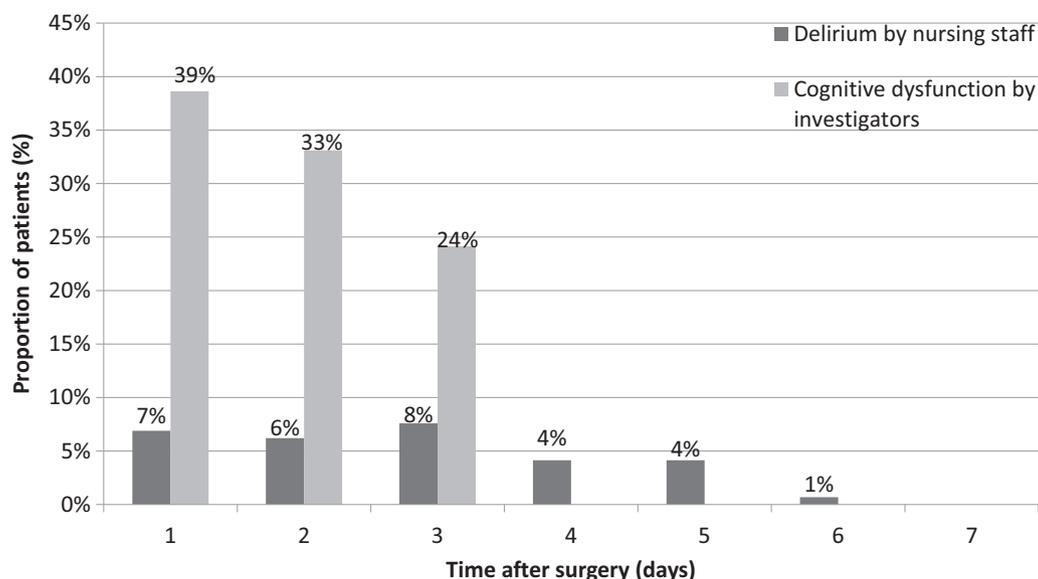


Figure 3. Prevalence of cognitive dysfunction assessed by the investigators and delirium assessed by the nursing staff in the prospective cohort. Cognitive dysfunction was not assessed on day 4 to 7.

multivariable models. Consequently, residual confounding could be present. The portal PF used was not compared with other Doppler measurements, such as the portal congestion index.⁸ Furthermore, we did not perform transcranial Doppler²⁸ or measurement of optic nerve diameter in these patients.²⁹ The method used to choose the cutoff to define clinically significant portal pulsatility resulted in adopting a cutoff that is slightly lower than reported by others.^{10,12} However, the association was also present when portal PF was analyzed as a continuous variable, supporting the validity of the association. Finally, because invasive monitoring is usually discontinued during the day after cardiac surgery at our institution, portal Doppler was not systematically compared with other invasive hemodynamic markers, such as CVP. However, this relationship has been demonstrated.¹⁰

Table 3. Other clinical predictors of cognitive dysfunction in the prospective cohort

Clinical parameter at the time of assessment	OR	CI	P value
NT-pro-BNP measurement (per 1 log of increase)	4.03	1.78-9.15	0.001
Cumulative fluid balance (per 1 L of increase)	1.11	0.96-1.29	0.17
CVP (per 1 mmHg of increase above 10 mmHg)	1.11	0.96-1.28	0.15
Cerebral desaturation ($\geq 15\%$ decrease from baseline values)	2.54	1.12-5.76	0.03

Generalized estimating equation analysis was performed using a logistic link function. For each model, the studied neurologic variable and the time of assessment were included as factors. Interaction with time was tested for each model.

CI, confidence interval; CVP, central venous pressure; NT-pro-BNP, N-terminal pro-beta natriuretic peptide; OR, odds ratio.

Conclusion

Portal pulsatility is a noninvasive ultrasound sign of venous congestion associated with encephalopathy and delirium after cardiac surgery. Further studies will be required to determine if portal flow assessment could lead to the identification of a subgroup of patients with delirium who may respond to a more specific and targeted intervention.

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Table 4. Multivariable proportional hazard regression models for the risk of delirium after cardiac surgery

	HR (CI)	P value
Portal flow pulsatility*	2.57 (1.01-6.57)	0.049
Previous stroke or transient ischemic attack	2.18 (0.44-6.47)	0.16
Chronic kidney disease (eGFR < 60)	1.40 (0.62-3.16)	0.43

CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio.

* Programmed as a time-segmented variable.

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Disclosures

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Supplementary Material

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