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Transcranial Doppler Ultrasound and Transesophageal Echocardiography for Intraoperative Diagnosis and Monitoring of Patent Foramen Ovale in Non-Cardiac Surgery

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Abstract: Background: perioperative stroke is one of the major complications after surgery. Patent foramen ovale (PFO) increases the risk of stroke in non-cardiac surgery by right-to-left shunt related to intraoperative hemodynamic alterations, leading to paradoxical embolism. Transesophageal echocardiography is the best tool for obtaining anatomical confirmation of PFO and essential details such as the PFO measure and the degree and direction of the shunt. Despite this, preoperative PFO screening is not routinely performed. Methods and results: we described the features of ten consecutive patients undergoing major abdominal surgery at the Abdominal Organ Transplant Intensive Care Unit, IRCCS Sant'Orsola, Bologna, Italy, who were screened for PFO using a PFO diagnostic and monitoring standardized intraoperative protocol by transesophageal echocardiography and transcranial color Doppler ultrasound. Finally, we highlighted the neurological and respiratory outcomes, the course and the management of three patients with intracardiac and extracardiac shunts. Conclusions: identifying an unknown PFO by a TCCD-TEE approach allowed the intraoperative monitoring of the shunt direction. It prevents the risk of complications secondary to paradoxical embolism in non-cardiac high-embolic-risk surgery.

Keywords: patent foramen ovale; transesophageal echocardiography; transcranial color Doppler ultrasound; micro embolic signal; liver transplantation

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1. Introduction

Perioperative stroke is one of the major complications after surgery, with an incidence reported from 0.2 to 9.7% and with consequences in terms of postoperative morbidity and 30-day mortality [1]. Congenital inter-atrial septum defects, such as patent foramen ovale (PFO), are an established risk factor for cryptogenic stroke in the general population [2]. Potential stroke mechanisms include paradoxical embolism, in situ PFO clot formation and atrial arrhythmias. PFO is also associated with a significant increased risk of stroke in non-cardiac surgery due to right-to-left shunt (RLS) related to intraoperative hemodynamic alterations, leading to paradoxical embolism. Major surgery exposes patients with PFO to various factors that can cause RLS, including positive pressure mechanical ventilation, a severe reduction in systemic vascular resistance, clamping of great vessels, fluid therapy, anesthetic drugs, and patient positioning [3,4]. In addition to neurological complications, PFO can also cause hypoxemia and platypnea–orthodeoxia syndrome due to right-to-left shunting of deoxygenated blood [5].

Standard PFO diagnostic techniques include contrast-enhanced transthoracic echocardiography (cTTE), contrast-enhanced transesophageal echocardiography (cTEE) and transcranial color Doppler ultrasound (TCCD). TEE is the best tool for obtaining an anatomical confirmation of PFO and essential details such as the PFO measure, degree and direction of the shunt, presence of atrial septal aneurysm and prominent Eustachian valve. TCCD, although more sensitive than cTTE in detecting PFO (96.1% vs. 45.1%), is unable to distinguish between intracardiac and extracardiac shunts [6]. A bubble test is recommended before and after the Valsalva maneuver with TCCD and echocardiography. cTTE confirmed the PFO diagnosis when the left ventricular bubble appeared within the first 3–5 cardiac cycles after right ventricular opacification. TCCD confirms the diagnosis when at least one bubble appears <25 s after injection with stirred saline [7,8].

Preoperative PFO screening is not routinely performed, although PFO was significantly associated with an increased risk of postoperative ischemic stroke [4]. Guidelines recommend antiplatelet therapy for secondary prevention of stroke in patients with PFO, but no definitive recommendations exist for the management of incidental PFO diagnosed perioperatively. Closure of an incidental PFO is reasonable in high-risk surgery, such as heart transplantation, ventricular assisted-device implantation or in surgical procedures involving atriotomy [9]. In non-cardiac high-embolic-risk surgery, such as liver transplantation (LT), the risk of PFO-related paradoxical embolism is expected to increase due to perioperative hemodynamic changes [10]. Despite such considerations, there are currently no indications of preoperative PFO closure in asymptomatic patients [11].

Since the intraoperative evaluation of a PFO shunt is essential to guide the anesthesiological conduct in real-time, and reduce the risk of stroke, we proposed a PFO diagnostic and monitoring protocol.

The objective of this study was to describe the feasibility and utility of the proposed protocol in patients undergoing non-cardiac major surgery with a high risk of embolic events.

We aimed to verify how many patients undergoing abdominal high-embolic-risk surgery with expected hemodynamic instability receive an intraoperative diagnosis of unknown PFO shunt using a standardized TCCD-TEE protocol (Figure 1). We also checked for shunt reversal during surgery and whether the presence of PFO was related to postoperative respiratory and neurological complications. Finally, we investigated whether the intraoperative diagnosis and monitoring of the PFO shunt led to different anesthetic management.

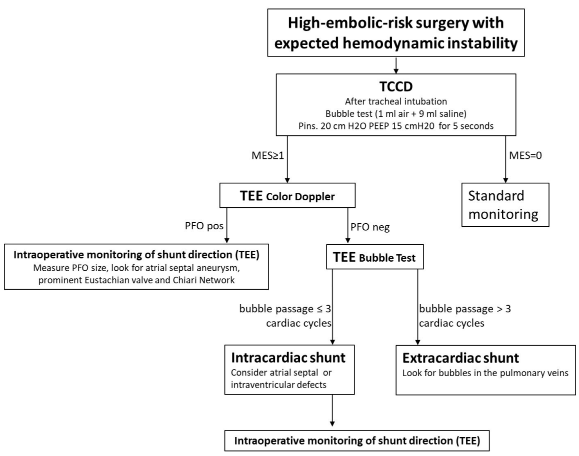

Figure 1. Flowchart of PFO diagnostic and monitoring standardized intraoperative TCCD-TEE protocol. TEE: transesophageal echocardiography; TCCD: transcranial—ecocolor Doppler; Pins: inspiratory pressure, PEEP: positive end expiratory pressure; PFO: patent foramen ovale; MES: microembolic signals.

2. Materials and Methods

2.1. Participants, Inclusion, and Exclusion Criteria

We described extensively the first ten consecutive patients enrolled prospectively in the MEIO21 study involving the execution of planned intraoperative TEE-TCD monitoring in subjects who underwent major abdominal surgery between 1 January 2023, and 31 August 2023, at the Abdominal Organ Transplant Intensive Care Unit, IRCCS Sant'Orsola, Bologna—Italy.

The inclusion criteria were as follows: patients age ≥18 years, undergoing major abdominal surgery with expected high-embolic risk and severe intraoperative hemodynamic instability, eligible for peri-operative TEE monitoring.

We selected patients with expected hemodynamic instability, as both the intraoperative variations in pre-load and after-load (biventricular) and the hemodynamic supports used can cause the inversion of the shunt (from right to left) and, therefore, paradoxical embolism.

Exclusion criteria were as follows: American Society of Anesthesiologists (ASA) physical status classification ≥ V, known intra- or extracardiac shunts in medical history, contraindications to TEE probe placement, severe encephalopathy (West Haven criteria > III) or severe chronic obstructive pulmonary disease (COPD—GOLD grade 4).

All patients signed their informed consent. Subjects undergoing LT were included in the MEIO21 study (ethics committee approval no. CE-AVEC: 983/2021) involving the execution of planned intraoperative TEE-TCD monitoring in the surgery setting. The study was conducted following the local guidelines of the Ethical Committee, the ethical guideline of the World Medical Association's Declaration of Helsinki and the guidelines for Good Clinical Practice [12,13].

2.2. Ultrasound Technique and Flowchart

We use a PFO diagnostic and monitoring standardized intraoperative TCCD-TEE protocol derived from the algorithm proposed by Pristipino et al. [14] (Figure 1). After orotracheal intubation and initiation of mechanical ventilation, TCCD with a bubble test was performed with the intravenous injection of 1 mL of air + 9 mL of saline solution. We conducted a bubble test in baseline conditions and after Induced Valsalva Maneuver (IVM) by applying a positive airway pressure of 20 cmH_2O for 5 s and a positive end-expiratory pressure (PEEP) of 15 cmH_2O, as described by Koroneos et al. [15]. TCCD was considered positive for the presence of an intracardiac or extracardiac shunt if at least one micro embolic signal (MES) was visualized in the Pulsed Doppler flow-line spectrum sampled in the Middle Cerebral Artery (<25 s). In the case of MES, we subsequently used color Doppler TEE to verify the presence of an unknown PFO. If PFO were not detected, we performed a TEE-bubble test to identify extracardiac shunts. No further investigations were conducted in case of the absence of MES. In the presence of PFO, we constantly monitored the direction of the shunt during the surgical phases using color Doppler TEE and noted the channel size. We also looked for the presence of atrial septal aneurysm, prominent Eustachian valve or Chiari Network.

To reduce inter-operator variability, a single experienced anesthesiologist performed the ultrasound examinations. The ultrasound machine used was GE-Venue with 6TC-RS (TEE) and 3Sc (TCCD) probes.

2.3. Postoperative Follow-Up

At the end of the surgery, we noted whether PFO modified the anesthetic management, through an anesthesiologist chart. We noted the postoperative neurological and respiratory complications within seven days after surgery and the ICU length of stay. The postoperative neurological complications considered were alteration of consciousness after discontinuation of sedative drugs (Glasgow Coma Scale), the onset of clinical signs of stroke and delirium (CAM-ICU scale), and worsening of the encephalopathy grade in cirrhotic patients (West Haven criteria). The postoperative respiratory complications considered were respiratory failure requiring nasal high-flow oxygen (HFNC), non-invasive ventilation (NIV) or reintubation. All the laboratory tests were obtained immediately after ICU admission, and just for glycemic control, we used our point-of-care testing device (POCT).

Finally, we collected the clinical data of the study population and described the futures of MES-positive patients in detail, attaching the more explanatory images (Table 1).

Table 1. Results and complications from standardized intraoperative TEE-TCCD protocol.

Patients	Age	Type of Surgery	MES	PFO Shunt	Extra-Cardiac Shunt	Neurologic Complication	Post-Operative ARF	Needs for Re-Intubation	ICU-LOS
1	55	LT	N	N	N	N	N	Y	7
2	62	LT	Y	Y	N	Y	N	N	5
3	62	LT	N	N	N	N	N	N	4
4	67	LT	N	N	N	N	N	N	4
5	64	LT	N	N	N	N	N	N	5
6	65	LT	Y	N	Y	N	N	N	12
7	70	LT	N	N	N	N	N	N	5
8	59	LT	N	N	N	N	N	N	2
9	46	LT	N	N	N	N	N	N	2
10	64	Other	Y	Y	N	N	Y	Y	12

MES: microembolic signals detected by transcranial Doppler. PFO: patent foramen ovale. ARF: acute respiratory failure. ICU-LOS: length of stay in intensive care unit. LT: liver transplantation. Y: present; N: absent.

3. Results

We described first ten patients enrolled prospectively in the MEIO21 study undergoing surgery with high embolic risk and expected severe intraoperative hemodynamic instability: nine LT and one nephrectomy with thrombectomy/caval resection with intraoperative veno-venous bypass. The features of the study population are reported (Table 1). The average age was 61.4 ± 6.8 years while the mean ICU length of stay was 5.8 ± 3.6 days. Seven patients were TCCD MES-negative while three had >1 MES. The three MES-positive patients subsequently underwent intraoperative TEE. Two patients had PFO shunt while one patient had an extracardiac shunt (case n° 3, Figure 2). Both patients with PFO had intraoperative phases with shunt reversal secondary to hemodynamic changes. In nine patients, the postoperative neurological status was unchanged or better than the preoperative one. One patient with an intraoperative diagnosis of PFO shunt (case n° 2) experienced postoperative reversible delirium (CAM-ICU positive) and worsening of the West Haven score from I to III without lateral neurological deficits. No patients had ischemic stroke within 30 days after surgery. In nine patients, there were no postoperative respiratory complications, while one patient (with PFO Shunt—case n° 1) had a postoperative respiratory failure with the need for reintubation, NIV and HFNC oxygen therapy. The mean ICU length of stay was 5.8 ± 3.6 days. Intraoperative PFO-diagnosis and shunt-direction monitoring guided the anesthetist in choosing ventilatory and hemodynamic supports to avoid the right–left shunting. We described TCCD MES-positive cases below.

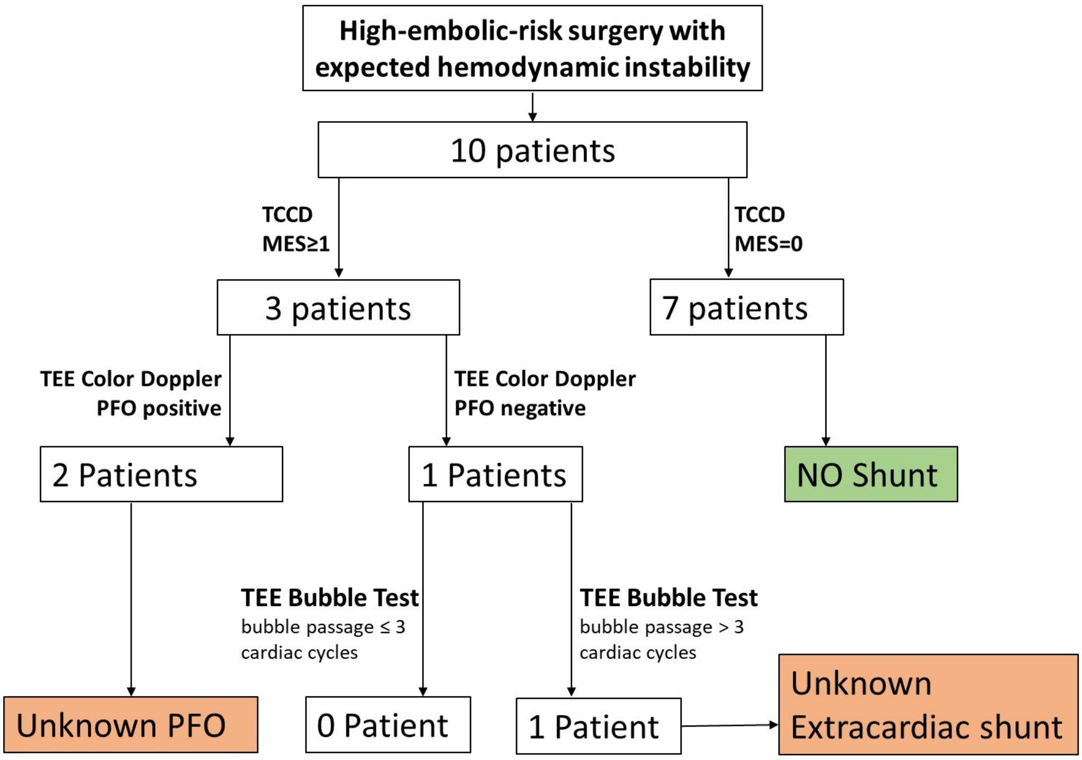

Figure 2. Patients enrolled in the study.

3.1. TCCD MES-Positive Case 1

A 64-year-old man underwent left nephrectomy and inferior vena cava (IVC) thrombectomy for renal cell carcinoma. The surgical procedure required total IVC clamping and venotomy. Due to surgical needs, we placed a femoro-jugular veno-venous bypass.

Remote pathological history revealed mild COPD (GOLD 1) in a previous smoker, without functional limitations. No evidence of neurological disease was reported.

TCCD with a bubble test was performed after induction of general anesthesia and orotracheal intubation. The test was negative in basal conditions while numerous MES (MES > 10) appeared during IVM. (Figure 3, Video 1) TEE confirmed the presence of PFO (5 mm) with left-to-right shunt and shunt reversal after increasing intrathoracic pressures (Figures 4 and 5, Video 1). Additional findings were atrial septal aneurysm and a prominent Eustachian valve.

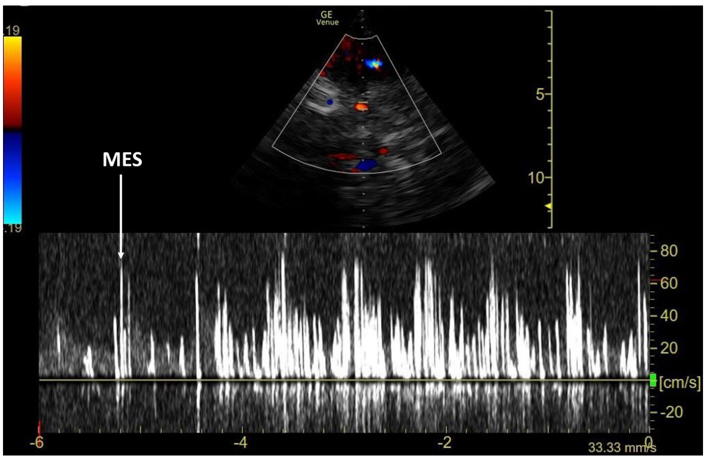

Figure 3. TCCD, middle cerebral artery. Numerous MES appeared on TCCD spectrum during the Induced Valsalva Maneuver. MES = Micro-Embolic signals.

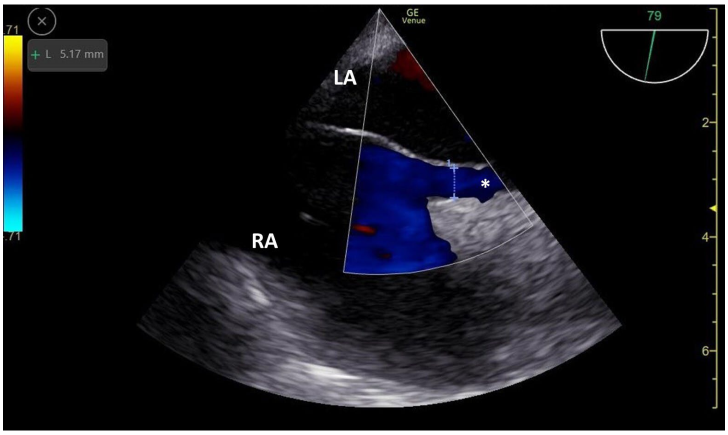

Figure 4. TEE Mid-esophageal view. PFO (5 mm) with left-to-right shunt (Blue). LA = Left Atrium, RA = Right Atrium, * PFO = Patent Foramen Ovale.

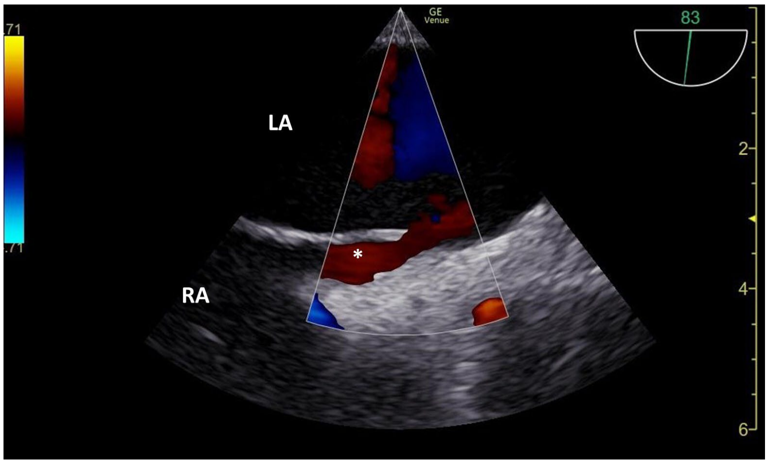

Figure 5. TEE Mid-esophageal view. Reversal of the PFO-shunt direction (right-to-left shunt, Red) during the Induced Valsalva Maneuver. LA = Left Atrium, RA = Right Atrium, * PFO = Patent Foramen Ovale.

The PFO-shunt direction was monitored during surgery using color Doppler TEE. Spontaneous shunt reversal was observed in some surgical phases following the reduction in systemic arterial pressure.

Considering the high risk of paradoxical embolism, we decided to insert two embolus traps into the bypass circuit and administer heparin to maintain an activated clotting time (ACT) >180 s despite the high hemorrhagic risk (some embolic fragments were blocked by the bypass filter—Figure 6). We carefully avoided hemodynamic and ventilatory conditions that could favor the reversal of the shunt, e.g., increase in ventilatory pressures or in vascular resistance. Vascular accesses were constantly monitored to avoid accidental air intravasations. We did not observe intraoperative embolic or hemorrhagic complications.

The postoperative period was characterized by hypoxemic respiratory failure with platypnea–orthodeoxia (minimum P/F < 90). The patient was extubated 16 h after surgery and required NIV and HFNC oxygen therapy for hypoxemia. The patient was then reintubated due to hypoxemia refractory. We excluded pulmonary embolism, pleuro-parenchymal pathology, and bronchial obstruction by CT–angiography (computer tomography angiography) and fibro bronchoscopy. TCCD and TTE documented the presence of a persistent postoperative right-to-left intracardiac shunt.

Respiratory symptoms gradually improved, and the patient was subsequently extubated and discharged from the intensive care unit 12 days after surgery. The right to left shunt was absent during spontaneous breathing, as shown by a negative TCCD-MES at discharge.

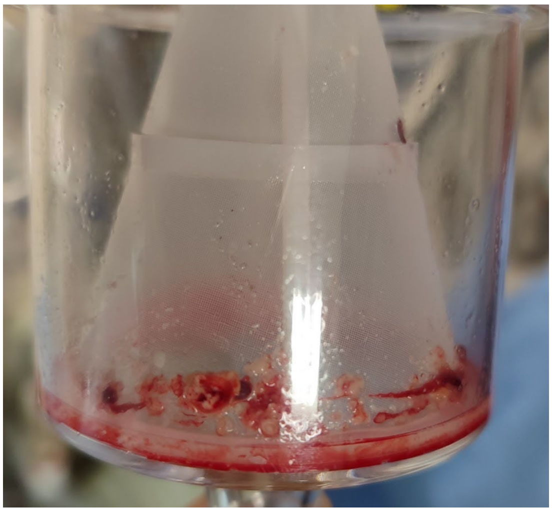

Figure 6. Some embolic fragments blocked by the bypass filter.

3.2. TCCD MES-Positive Case 2

A 61-year-old man underwent LT for dysmetabolic cirrhosis complicated by hepatocellular carcinoma with MELD 15.

Medical history noted mild COPD (GOLD 1) in a former smoker, obesity and diabetes mellitus type 2. No neurological (West Haven criteria = 0) or cardiovascular pathology was described. A preoperative cTTE showed biatrial dilatation with thickening of the mitral and aortic valves.

TCCD with a bubble test was performed in the operating room after endotracheal intubation. No MES was identified in baseline conditions (PEEP 5), while rare MES appeared during the IVM maneuver. (Figure 7) TEE was subsequently performed and a small PFO with left to right shunt was found in baseline conditions (Figure 8).

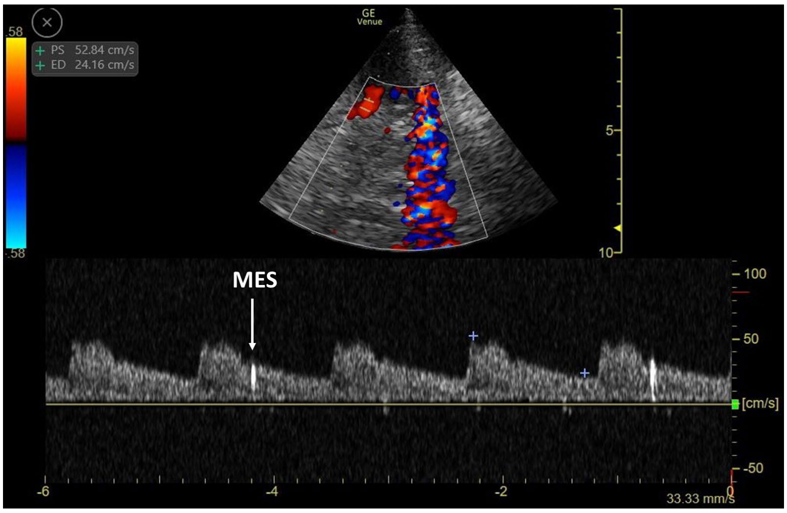

Figure 7. TCCD, middle cerebral artery. Rare MES appeared on TCCD spectrum during the Induced Valsalva Maneuver. MES = Micro-Embolic signals.

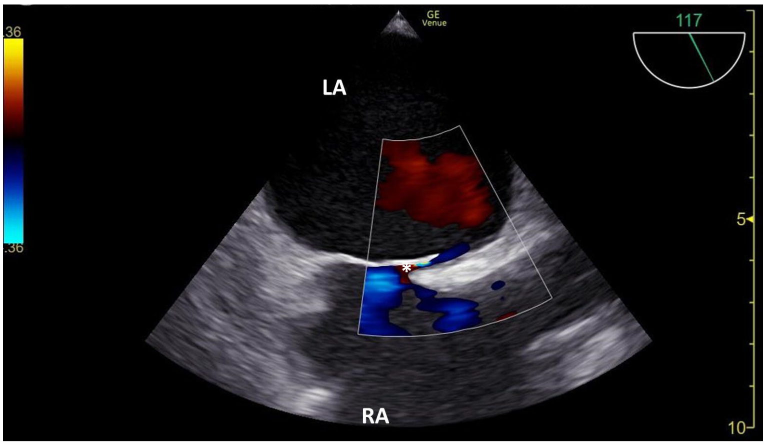

Figure 8. TEE mid-esophageal view. Small PFO with left-to-right shunt (Blue). LA = Left Atrium, RA = Right Atrium, * PFO = Patent Foramen Ovale.

TEE documented reversal of the PFO-Shunt (right to left) after graft reperfusion during reperfusion syndrome due to decreased systemic blood pressure, need for fluid challenge and increased pulmonary pressure (Video 2). During reperfusion, some spontaneous hyperechoic gas emboli were visualized in the left atrium and left ventricle caused by shunt reversal (Figure 9, Video 3).

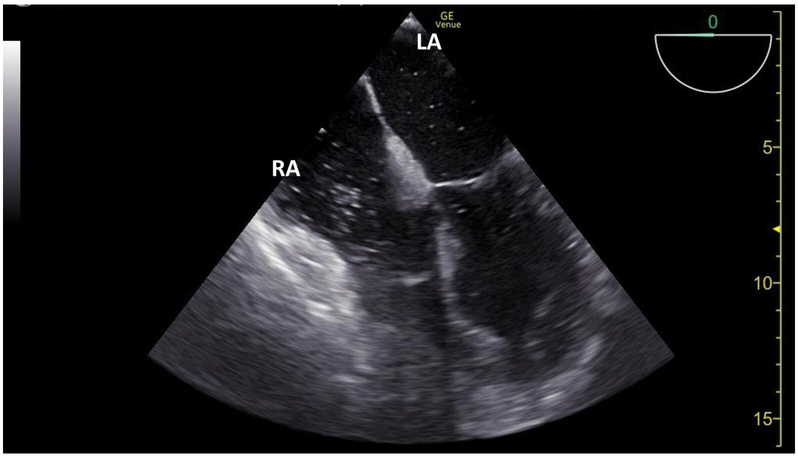

Figure 9. TEE mid-esophageal four-chamber view. Appearance of spontaneous hyperechoic air emboli in the left atrium and left ventricle due to shunt reversal following graft reperfusion. LA = Left Atrium, RA = Right Atrium.

Intraoperative TEE monitoring of the PFO-shunt direction guided the anesthesiologist in choosing of ventilatory and hemodynamic supports to avoid right-to-left shunt.

TEE excluded paradoxical thromboembolism, while gas emboli were visualized in some surgical phases (Figure 9, Video 3). No respiratory or neurological complications occurred during the surgery.

The patient was extubated 12 h after surgery. There were no postoperative respiratory complications, while significant hyperkinetic delirium with confusion and gross disorientation appeared in the first days after surgery (CAM-ICU scale positive for delirium, West Haven criteria III). No significant metabolic alterations were present, and the blood levels of ammonium, urea, and tacrolimus were within the normal range. No objectifiable focal neurological deficits appeared. Discharge from intensive care occurred five days after surgery.

3.3. TCCD MES-Positive Case 3

A 65-year-old man with alcoholic cirrhosis underwent LT (MELD 30). He had liver disease complicated by ascitic decompensation and hepatorenal syndrome. His medical history noted arterial hypertension with secondary hypertrophic heart disease and moderate mitral insufficiency. No pneumopathy or other significant elements were reported.

After intubation, the TCCD bubble test showed sporadic spontaneous MES (without ventilatory maneuvers). Color Doppler TEE did not identify intracardiac shunts. The TEE bubble test showed gas emboli in the left atrium after six cardiac cycles, suggesting the presence of extracardiac shunts. The presence of an extracardiac shunt was confirmed by visualization of gas emboli in the pulmonary veins (Figure 10, Video 4).

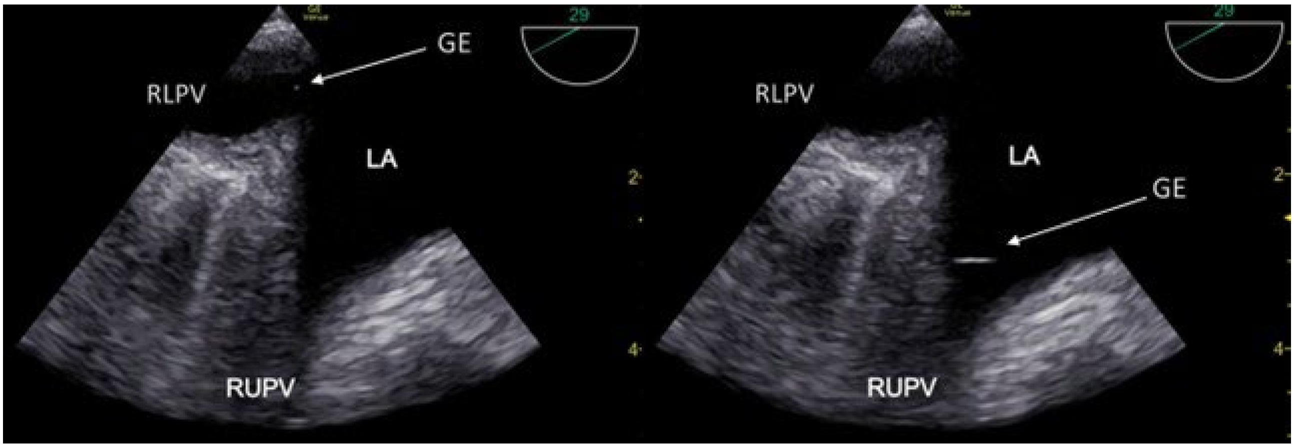

Figure 10. TEE mid-esophageal right pulmonary vein view. Gas emboli in the pulmonary veins. GE = gas emboli, RLPV = right lower pulmonary vein, RUPV = right upper pulmonary vein, LA = left atrium.

Blood oxygenation in spontaneous breathing (PaO_2 70 mmHg) and ultrasound findings suggest unknown subclinical hepato-pulmonary syndrome.

Extubation occurred 14 h after surgery. There were no neurological or respiratory complications. In the postoperative period, there were surgical complications that required an extension of hospitalization in intensive care unit (12 days).

4. Discussion

PFO is a fetal cardiovascular structure that remains open in approximately 20–25% of adults due to the non-fusion of the atrial septum primum and septum secundum [2,16]. It is usually asymptomatic; however, under certain circumstances, it can result in RLS and cause serious complications, including ischemic stroke and hypoxemia [12]. The main risk factors for stroke are PFO diameter, shunt degree, the presence of atrial septal aneurysm, a prominent Eustachian valve and deep vein thrombosis [17].

PFO is also associated with a significant increase in stroke risk during major non-cardiac surgery [3,18–21]. In a recent large retrospective cohort study that included 182,393 adults who underwent non-cardiac surgery, preoperatively diagnosed PFO was significantly associated with an increased risk of ischemic stroke within 30 days after surgery (3.2% vs. 0.5%) [4]. The overall incidence of thrombo-embolism after major abdominal surgery, such as hepatobiliary surgery, has been accounted for in the literature as between 10% and 40% [22]. Liver transplantation could be considered a procedure with a higher embolic risk in this context. The placement of central lines, veno-venous bypass, caval clamping, and liver graft reperfusion are some of the procedures that lead to thrombotic or gas emboli formation [18,23]. In addition, coagulation disorders related to end-stage liver disease predispose one to the development of thromboembolism.

In the LT setting, intraoperative hemodynamic changes, involving preload, afterload, and performance of both ventricles, can increase right atrial pressures and cause RLS, exposing the patient to embolic events, especially during graft reperfusion (Video 3) [10,19]. In our study, both patients with PFO had intraoperative phases with shunt reversal secondary to hemodynamic changes.

There are several strategies in the hands of the anesthesiologist to achieve intraoperative stroke risk reduction by limiting the RLS. Optimization of airway pressure (especially PEEP) during mechanical ventilation, patient position, fluids, and vasoconstrictor drugs may play a role in maintaining a pressure gradient between the right and left atrium, thus limiting RLS [24–26]. Positive inotropic drugs (e.g., epinephrine, milrinone), nitric oxide, or both may also limit RLS in the setting of pulmonary hypertension or right ventricular failure [27,28].

Antiplatelet and anticoagulant therapy or PFO closure can also reduce the risk of stroke in selected cases. In clinical practice, prophylactic antiplatelet and anticoagulant therapy are often suspended in the perioperative period due to the risk of bleeding. As pointed out by Ng et al. [4], further studies are needed to examine whether these patients would benefit from intensified stroke prevention measures in the perioperative and intraoperative periods as they have an increased risk of developing neurological complications [7].

Other PFO-related neurological diseases have been reported such as migraine, sleep-disordered breathing, and cognitive dysfunction [7]. Some authors investigated whether a PFO was associated with an increased risk of postoperative delirium; however, given the very low incidence of PFO and postoperative delirium, they were could not draw any conclusions [10,27]. In our case studies, no severe ischemic adverse events occurred despite the evidence of PFO but one patient developed postoperative delirium, assessed by the CAM-ICU scale. The patient presented at the same time with a rise in levels of ammonium (177 mcg/dL) and glycemia (284 mg/dL), which could only partially explain the development of such complications. Sodium, urea, tacrolimus, tox screen and PaO_2 levels were within normal range.

PFO is also associated with some respiratory complications. Shunt reversal, under certain circumstances, can cause hypoxemia and acute respiratory failure [4]. Platypnea orthodeoxia syndrome is one the possible clinical manifestation of RLS [28]. In the perioperative setting of cardiac surgery, for example, reopening of PFO has been associated with worsening respiratory outcomes, need for reintubation, and a longer ICU length of stay [29]. In our series, one PFO patient developed acute respiratory failure with platypnea orthodeoxia syndrome and the presence of persistent postoperative RLS.

Also, in laparoscopic procedures, the presence of PFO could predispose a person to hypoxemia and paradoxical carbon dioxide gas embolism. RLS occurs during all phases of laparoscopy, especially in the Trendelenburg position.

Despite such clinical implications, preoperative PFO screening is not routinely performed in high-embolic-risk surgeries. In these patients, an intraoperative diagnosis of PFO is usually not made, exposing them to the risk of complications [30].

For these reasons, we proposed a PFO diagnostic and monitoring intraoperative protocol applied to non-cardiac high-embolic-risk surgery with expected significant hemodynamic changes and a risk of shunt reversal. The proposed TCCD-TEE protocol identified two patients with an unknown PFO shunt (incidence 20%, similar to the general population) and one patient with an extracardiac shunt. We verified the reversal of the shunt direction during surgery in both patients with PFO by TEE (Table 1).

Both patients with PFO developed postoperative complications: the patient with the most significant PFO shunt developed respiratory complications while the patient with the smaller one developed neurological complication.

This protocol allowed us to guide the choice of ventilatory and hemodynamic supports, in order to avoid RLS (cases 1 and 2). These objectives were also achieved by optimizing anticoagulant therapy and placing antithrombotic filters during veno-venous bypass.

This preliminary case series of the prospective MEIO21 study highlighted, although monocentric, the feasibility of the TCCD-TEE protocol for the diagnosis and intraoperative monitoring of PFO in non-cardiac high embolic risk surgery. The search for a correlation between the presence of PFO and the occurrence of neurological and respiratory postoperative complications will require larger samples in prospective cohorts.

However, many confounding factors should be considered in the next studies to establish a correlation between PFO and neurological and respiratory outcomes: the different surgical interventions, the hemodynamic instability, the perioperative metabolic derangement such as pre-operative encephalopathy, chronic obstructive pulmonary disease, end-stage liver disease MELD-Na score, acute kidney injury (AKI), perioperative infections and hemodynamic instability, ischaemia–reperfusion injury (PRS), and levels of ammonium, glucose and sodium [26,31–42]. In this case series, the main variables that could interfere with the development of neurological complications were evaluated (see Table 2). Perioperative infections and hemodynamically significant carotid artery disease were excluded in every patient.

Table 2. Main confounding factors of postoperative neurologic and respiratory complications in the studied cohort.

Pts	MELD Na^+ [32,33,37]	Acute Diseases [32–34,36,37,41–43]	MAP (mmHg) [37–41]	Chronic Diseases [32,44]	Ammonia (mcg/dL) [37,40]	Na^+ Shift (mmol/L) [37,40]	Glucose Shift (mg/dL) [37,40]
1	30	Preop-AKI Preo-infections PRS	<65		43	5	39
2	19	Preop-AKI	<65	COPD	118	4	168
3	9	PRS	<65 >105		50	2	98
4	15				102	2	61
5	9	PRS	<65	COPD	42	3	32
6	22	Preop-infections			49	6	153
7	17				88	6	−26
8	14	Preop-infections	>105	COPD	64	16	61
9	11	PO-AKI	<65	CKD	39	8	43
10	//	PO-AKI Preop-infections Peri-operative arrhythmias		COPD	//	5	91

Pts: patients; Preop: pre-operative; AKI: acute kidney injury; COPD: chronic obstructive pulmonary disease; MELD Na^+: Mayo end-stage Liver Disease containing sodium; Na^+: sodium; CKD: chronic kidney disease; MAP: mean arterial pressure (peri-operative); PRS: post-reperfusion syndrome; PO-AKI: post-operative acute kidney injury.

Despite these limitations, it showed the potential role of the proposed PFO TCCD-TEE intraoperative protocol in guiding anesthetic management and in preventing postoperative complications.

5. Conclusions

The increase in average age and comorbidity of patients undergoing major abdominal surgery and LT predisposes them to the development of neurological and respiratory complications. PFO, a relatively frequent finding in general population, is a known risk factor for such complications. The occurrence of a right-to-left shunt related to hemodynamic alterations can lead to paradoxical embolism and respiratory complications during surgery. The proposed TCCD-TEE protocol, by identifying an unknown PFO, allowed us to monitor the shunt direction intraoperatively and guided the use of strategies to prevent the risk of paradoxical embolism in non-cardiac high embolic risk surgery. Further studies are needed to evaluate the correlation between the presence of PFO and the occurrence of neurological and respiratory postoperative complications.

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Data Availability Statement: Data supporting reported results can be found at IRCCS Azienda Ospedaliero–Universitaria di Bologna, department of digestive, hepatic and endocrine–metabolic diseases. Post-Surgical and Transplant Intensive Care Unit.

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Abbreviations

ACT	activated clotting time
ASA	American society of anesthesiologists
CAM-ICU	confusion assessment method in intensive care unit
COPD	chronic obstructive pulmonary disease
CT	computer tomography
HFNC	high-flow nasal cannula
ICU	intensive care unit
LT	liver transplantation
MELD	Mayo-end stage liver disease
MES	microembolic signals
NIV	non-invasive ventilation
PEEP	positive-end-expiratory pressure
PFO	patent foramen ovale
POCT	point-of-care testing device
RLS	right-to-left shunt
TCCD	Transcranial–ecocolor Doppler
TEE	transesophageal echocardiography

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