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Short title: CO2 insufflation in EVH

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Human Ethics and Consent to Participate declarations:

After obtaining approval from the local ethics committee, patients who agreed to participate gave their signed informed consent after explanation of the trial benefits and hazards. All procedures were carried out in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. The study received the approval of ethical committee of faculty Medicine, Menoufia University (No.10/2025CARS6).

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It was taken from every patient before being included in this work.

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Available to be handled.

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Nil.

Abstract

Objectives: The objectives of this study were to determine the efficacy of endoscopic saphenous vein harvesting in coronary artery bypass grafting (CABG) and to determine the time course of the carbon dioxide (CO₂) embolism with transesophageal echocardiography (TEE) monitoring.

Methods: A total of 260 consecutive cardiac patients scheduled for off-pump coronary artery bypass graft using saphenous vein harvesting were included. These cases were randomly divided into 2 groups, Group A using low-flow CO₂, and Group B for high-flow CO₂ insufflation during saphenous vein harvesting. Echocardiography was done throughout the procedure by monitoring CO₂ bubbles in the inferior vena cava and circulatory system.

Results: In this study, a total of 260 patients were studied to determine the outcomes of patients who underwent CO₂ insufflation during saphenous vein harvesting at CABG in terms of demographic, operative, and postoperative variables. The ROC curve shows 87% sensitivity of TEE in the prediction of CO₂ embolism according to the quantity of bubbles during harvesting of the vein. There are non-significant differences between values of arterial blood gases (ABG, O₂/CO₂) nor end-tidal CO₂ before, during, and after vein harvesting with fewer logistic regression curves for low-flow over high-flow groups according to levels of End-tidal CO₂ across the procedure.

Conclusions: We conclude that the incidence of CO₂ embolisms during endoscopic vein harvesting could be reduced using lower CO₂ insufflation pressure, which, in combination with increased surgical experience and continuous TEE monitoring of the inferior vena cava, helps to reduce the risks of massive CO₂ embolism.

Keywords: CO₂ embolism, Echocardiography, Trans-esophageal, Saphenous vein.

Abbreviations

CABG: coronary artery bypass graft

TEE: transesophageal echocardiography

ABG: arterial blood gases

EVH: endoscopic saphenous vein harvesting

CO2: Carbon Dioxide

Introduction

The traditional method of harvesting the great saphenous vein to be used in coronary artery bypass grafting (CABG) surgery is through an open wound in the thigh. There are new trends to harvest the saphenous vein endoscopically, thus minimizing the operative timing and postoperative complications. This new technique is used also to decrease the hospital stay and maximize the patient's satisfaction. Insufflation of carbon dioxide (CO₂) could be used to create a subcutaneous tunnel to do endoscopic saphenous vein harvesting (EVH) [1].

The mid- and long-term outcomes are instead still controversial issues. This controversy may be partly due to the fact that the event-free survival rate over periods from 2 to 5 years is commonly taken as a surrogate marker for graft failure, since postoperative angiographic studies, the gold standard to evaluate the long-term influence of vein harvest technique on graft patency, are not widely used owing to their low practicality and high costs [2].

In coronary artery bypass grafting surgery, arterial conduits are preferred because of more favorable long-term patency and outcome. Anyway, the greater saphenous vein continues to be the most commonly used bypass conduit. Minimally invasive endoscopic saphenous vein harvesting is increasingly being investigated in order to reduce the morbidity associated with conventional open vein harvesting, including postoperative leg wound complications, pain, and patient satisfaction. However, to date the short- and the long-term benefits of the endoscopic technique remain controversial [3].

There are very low reported cases of venous CO₂ embolism after its usage in laparoscopic surgery, but there are insufficient reports about this complication when this technique is applied during EVH with CO₂ insufflation in coronary artery bypass. The published literature showed lower incidence of carbon dioxide embolisms related to CABG using endoscopic saphenous grafting with lower CO₂ insufflation pressure. Most of these literatures suggested more experience about this technique with continuous trans-esophageal echocardiography monitoring of the inferior vena cava to minimize the morbidity and mortality [4].

Transesophageal echocardiography (TEE) is one of the most sensitive maneuvers usually used to detect venous CO₂ embolism when compared with end-tidal CO₂ and pulmonary artery pressure monitoring [5].

The primary outcome of this study was to investigate the incidence and severity of CO₂ embolism during EVH with CO₂ insufflation in patients undergoing CABG with TEE

monitoring. The secondary outcome of this work is to investigate the role of trans-esophageal echocardiography in monitoring the incidence of CO₂ embolism and the accuracy of its results in the management of such cases.

Methods and materials:

This prospective case series study included 260 consecutive patients scheduled for CABG surgery using EVH (either low-pressure or high-pressure CO₂ insufflation) in the period from July 2021 to February 2025. The collected data were recorded from patients admitted to our Cardio-thoracic Surgery Department of our University Hospital. Then, the included patients were divided into two equal groups: Group A for low-pressure CO₂ insufflation (10-12 mmHg, 130 cases) and Group B for high-pressure CO₂ insufflation (15-20 mmHg, 130 cases).

To avoid any bias in the methodology in the selection of included patients, there was blinded collection of these patients with computer randomization for determining the procedure for any patient. For observer bias, the procedure was done by the same team of surgeons with the same echocardiography consultant.

The study protocol was approved by the Ethics Committee of our University Hospital with the reference number (No.10/2025CARS6). A written informed consent was obtained from all patients. Patients were excluded if they had prior saphenous vein harvesting for peripheral arterial occlusive disease or CABG surgery. Trial registration was already done with the number (PACTR202607767851615).

All patients had a preoperative assessment that included demographic data and past history of chronic diseases such as hypertension, diabetes, and cardiac or chest problems. Vital data, central venous pressure (CVP), arterial blood gases (ABG), and End-tidal CO₂ were done for all cases before, during, and after the procedure. Antibiotic prophylaxis was taken for all patients with a preoperative dose of first-generation cephalosporin or vancomycin. Harvesting time was measured, and length of the segment was also taken. Numbers of grafts taken for harvesting in the CABG were also recorded.

All patients were operated under general anesthesia using 5 mg/kg thiopental and three to five g/kg fentanyl, plus 0.1 mg/kg rocuronium was used to facilitate intubations. Monitoring of vital signs and data through a thermometer, pulse oximetry, arterial line, end-tidal CO₂, and central venous catheter. Trans-esophageal echocardiography was done by a multiplane probe (6T, GE Vingmed Medical) that was inserted after anesthetic induction and intubation. Routine TEE was

done before, during, and after the procedure for evaluation of the regional wall motion and cardiac functions. The inferior vena cava was monitored continuously with TEE by an anesthesiologist, and during EVH, images taken from TEE were recorded by a certain recorder.

The procedure of EVH was done to all patients by the same main surgeon with another assistant physician. Firstly, the skin incision was done just above the knee joint (longitudinal incision, 2 cm). Using the Vasoview Uniport System (Guidant), the vein dissector was used to separate the saphenous vein with the flexible bipolar scissors that were introduced through a trocar. The initial skin incision was made just above the joint line and was 2 cm long in a longitudinal fashion.

At 15 mmHg pressure, CO₂ was insufflated through an incision achieved by port insertion. This was done to create a subcutaneous tunnel. Dissection of the great saphenous vein was made till it reached the area of the groin using the endoscopy. Bipolar scissors were applied to divide the branches of the saphenous vein to prevent the occurrence of the possible CO₂ embolism and to minimize the bleeding. The proximal end of the vein was also ligated and divided through another skin incision in situ.

During the vein harvesting, TEE was used to monitor the occurrence of any bubbles in the monitor. If this event is recorded at any time, the procedure (CO₂ insufflation) should be stopped immediately. Resuming the insufflation of CO₂ can be done only after intimate examination of the vein system. End-tidal CO₂ was done to all cases before, during, and after the procedure away from going on or off pump bypass timing without heart manipulation. Also, the temperature and arterial blood pressure were monitored to be in the normal range during assessment of End-tidal CO₂ with constant ventilator settings. These precautions were followed during measuring ABG (CO₂/O₂) , thus are aimed to avoid any bias in values measured the procedure.

All collected data were studied in tables and figures, and then they were statistically analyzed using the Statistical Package for Social Sciences version 20.0 for Windows (SPSS Inc., Chicago, IL, USA). Data was expressed as mean, standard deviation (SD), and range for continuous variables and as frequencies (percentages) for categorical variables. Chi-square test and t-test were used as statistical methods for comparison of qualitative or quantitative variables between both groups. A P-value of 0.05 was used to determine significance, where a P-value >0.05 was considered statistically insignificant and a P-value ≤0.05 was considered statistically significant.

Results:

In this study, a total of 260 patients were included. Outcomes of patients who underwent CABG using saphenous vein harvesting were presented in terms of demographic, operative, and postoperative variables. The mean average age was noted to be 57.55 ± 15.87 . There was male predominance (208 cases were male, 52 cases were female). The mean BMI was 27.6 ± 4.92 . There were 186 cases presented with hypertension, and 172 cases presented with diabetes, while only 18 cases were diagnosed with chronic obstructive pulmonary disease, as noted in Table 1.

Table 1: Demographic data

Demographic data		No of patients = (260 cases)
Age (mean $\pm$ SD)		57.55 ± 15.87
Gender	-Male	208 (80%)
	-Female	52 (20%)
Smoker	Yes	177 (68%)
	No	83 (32%)
BMI		27.6 ± 4.92
Chronic diseases - Hypertension		186 (71.5%)
-Diabetes mellitus		172 (66.1%)
-Chronic obstructive pulmonary disease		18 (7%)

SD = standard deviation, BMI: body mass index.

Table 2 shows mean harvesting time was 44.03 ± 15.72 , while mean length of harvested segment was 38.25 ± 14.36 . The mean operative time was 187.41 ± 65.38 , mean clamp time was 97.22 ± 31.15 , and mean bypass time was 125.49 ± 47.43 . While majority of cases (52.7%) had at least 3 segments, and 25.3% of cases had at least 4 grafts. Only 17.7% of cases had only 2 segments. The mean critical care stay, in days, was 4.00 ± 3.50 .

Table 2: Operative data

Variables	Mean $\pm$ SD
Harvesting time	44.03 ± 15.72
Length of segment	38.25 ± 14.36

No. of grafts	1	6 (2.3%)
	2	46 (17.7%)
	3	137 (52.7%)
	4	66 (25.3%)
	5	5 (2%)
Operation time		187.41 ± 65.38
Clamp time		97.22 ± 31.15
Bypass time		125.49 ± 47.43
Critical care admission (days)		4.00 ± 3.50

SD = standard deviation

Table 3 shows non-significant differences between before, during, and after the procedure according to values of either ABG (CO₂/O₂) or end-tidal CO₂ comparing both groups or for each group separately.

Table 3: Monitoring of ABG (CO₂/O₂) and End-tidal CO₂ before, during and after the maneuver in both groups

Parameters		Results (Mean ± SD)			p-value
		Before	During	After	
ABG (CO₂/O₂)	Group A	1.15 ± 16.15	1.22 ± 16.13	1.84 ± 16.14	0.329
	Group B	1.32 ± 14.29	1.58 ± 13.26	1.91 ± 11.77	0.419
End-tidal CO₂	Group A	34.4 ± 14.6	35.0 ± 14.6	35.3 ± 14.6	0.528
	Group B	34.8 ± 13.2	36.9 ± 14.4	33.1 ± 12.5	0.457
p-value		0.091 for ABG 0.918 for CO ₂ %	0.115 for ABG 0.412 for CO ₂ %	0.719 for ABG 0.369 for CO ₂ %	

SD = standard deviation, ABG: arterial blood gases, CO₂: carbon dioxide.

Table 4 shows complications recorded after vein harvesting as (10 cases presented with bleeding, 7 cases presented with infection at the wound site, and only 2 cases presented with conversion) in group A, while in group B there were complications recorded as (12 cases presented with bleeding, 11 cases presented with infection at the wound site, and only 5 cases presented with conversion).

Table 4: Complications

Complications	Group A	Group B	p-value
CO2 embolism	5	7	0.934
Bleeding	10	12	
Wound infection	7	11	
Conversion	2	5	

In group A, there were five cases only with minimal CO2 bubbles detected by TEE during the procedure that was stopped immediately, and the operator got enough one to two grafts that were enough. While in group B, there were seven cases that developed massive CO2 embolisms that were monitored in critical care for at least one week. Only one case died in the critical unit after 2 days. Complications in both groups were discussed in table 4.

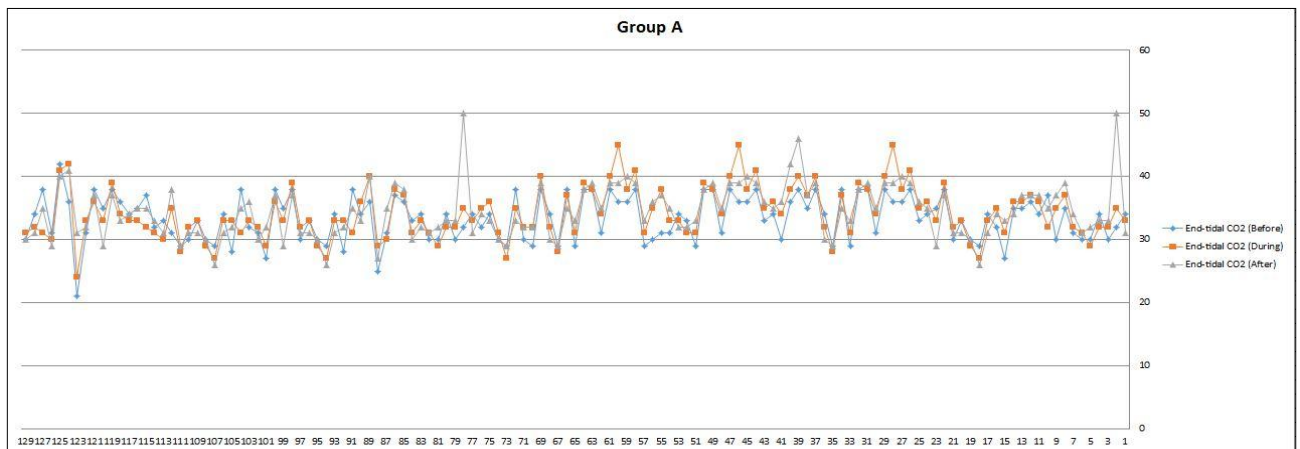


Figure (1): End-tidal CO2 before, during and after the procedure in Group A

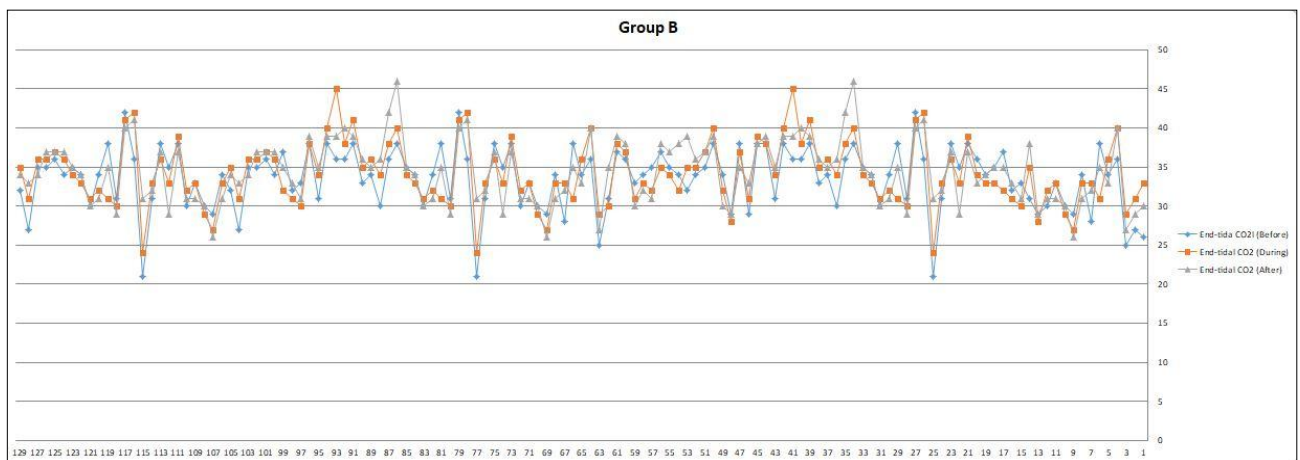


Figure (2): End-tidal CO2 before, during and after the procedure in Group B

Figures (1, 2) showed the values of end-tidal CO₂ recorded before, during, and after the procedure. Logistic regression of the occurrence of minimal to massive carbon dioxide embolization is not affected by harvesting time, the length of segmented grafts, or the number of grafts taken (11.25%, 10.95%, and 9.24%, respectively).

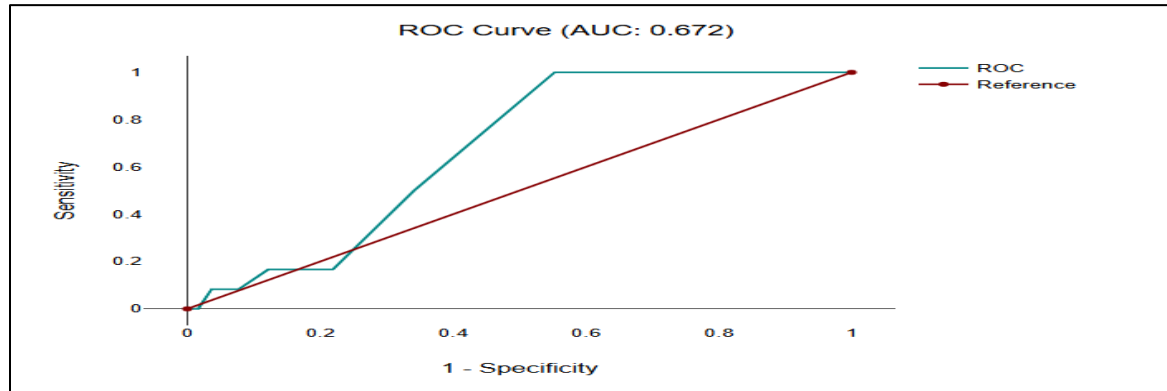


Figure (3): ROC curve for detection of CO₂ bubbles after induction of saphenous vein harvesting

The ROC curve was studied to discuss the efficacy of trans-esophageal echocardiography for the prediction of pulmonary embolism as shown in Figure 3. TEE showed (sensitivity, 87% and specificity, 82%) for pulmonary embolism occurrence with detection of five CO₂ bubbles or more. The area under the curve was (0.672) with high sensitivity that means that the operating team could depend on TEE in detection and prediction of many cardiac events with CO₂ embolism.

Discussion

The main target of the application of Carbon dioxide in endoscopic saphenous vein harvesting is to minimize the incidence of postoperative pain, and wound infections plus shortening hospital stay. This also needs to lower the pressure of insufflation during EVH during CABG using CO₂. The gas inflate during the endoscopic surgery aimed to create the most applicable space to facilitate introduction of tools to perform the procedures. This technique is targeted to minimize the incidence of trauma and hematoma postoperatively [6]. There are conflict about the safety of the usage of CO₂ due to the reports that detect the incidence of massive CO₂ embolism [7]. In one recent study, in which 15 mmHg of CO₂ insufflation pressure was used during endoscopic

vein harvesting, carbon dioxide embolism already was recorded in 17.1% of patients. The main outcome of that study as reduction of pressure of carbon dioxide insufflation during the procedure as reduction of embolism occurrence postoperatively. Although reducing the pressure of insufflation more than 12 mmHg would hinder the technique with less space to proceed, so that it is better to keep the pressure ranging from 12 to 15 mmHg [8].

Carbon dioxide embolism could be probably happened through direct rapid invasion of CO₂ to the injured vessels. There are no massive carbon dioxide embolism recorded in this study [9, 10]. However in another study, the operator noticed that there were 2 recorded incidents with carbon dioxide embolization which lead to immediate stoppage of insufflation by lowering the pressure of carbon dioxide.

The appearance of CO₂ bubbles in the IVC in another study was found in 49 patients (9.9% of all patients). As well as in our study, the incidence of CO₂ bubbles in the high-flow group of patients was significantly higher than that in the low-flow group (13.3% vs 6.5%, $p < 0.05$). During the study period, two episodes of a shower of CO₂ bubbles in the IVC resulted in the immediate cessation of CO₂ insufflation in the high group of patients. There was only a slight drop of blood pressure and mixed venous oxygen saturation at that time, with no significant hemodynamic alterations. In contrast to our study, no massive CO₂ embolisms with significant hemodynamic alterations happened in either group. The pulmonary artery pressure, the end-tidal CO₂, oxygen saturation, blood pressure, and other hemodynamic variables did not differ significantly between the two groups of patients [11].

In a study also conducted by Lin TY et al. in which 15 mm Hg of insufflation pressure was used during EVH with CO₂, we found CO₂ embolism occurred in 17.1% of patients, while devastating CO₂ embolism presenting as sudden cardiovascular collapse happened in 0.5% of patients. Because of the technical difficulties in creating the subcutaneous tunnel if the insufflation pressure was set at 10 mm Hg or lower in our experience, we used 12 mm Hg in the current study to determine whether lower insufflation pressure was helpful in reducing the risks of CO₂ embolism. Our results demonstrated that lower CO₂ insufflation pressure did reduce the incidence of CO₂ embolism. In addition, the similar incidence of CO₂ embolism (13.3% vs 17.1%) between the patients using the same 15 mm Hg as the insufflation pressure in the current and previous studies suggested that the most important factor for the reduction of CO₂ embolism is the lower CO₂ insufflation pressure [12].

It is mandatory on the operator to notice any vascular bubbles could be detected using transesophageal echocardiography throughout the procedure till it finished. TEE is one of the most diagnostic tool in prediction of CO₂ embolism. Trans-gastric images of the echocardiography could be easily obtained during the procedure to monitor any bubbles. This view is easily obtained, not interfered by microbubbles from the central venous pressure lines, and very sensitive to monitor the appearance of CO₂ bubbles in the inferior vena cava. [10]

In a study presented by Lin et al., the concentrations measured for end-tidal carbon dioxide intraoperatively didn't show noticeable differences among group of patients without carbon dioxide embolism (31.4 ± 2.4 mmHg) and patients with minimal and moderate-to-massive bubbles of carbon dioxide (31.6 ± 2.4 and 32.4 ± 2.2 mm Hg, respectively) in the venous system [1]. While in our study, there are no to minimal appearance of CO₂ bubbles, showed end-tidal CO₂ before, during and after the procedure as following (34.4 ± 14.6 , 35.0 ± 14.5 , & 35.3 ± 14.6 respectively) and the carbon dioxide/oxygen ratio (by ABG) showed non-significant vales comparing before, during and after EVH as (1.15 ± 16.15 , 1.22 ± 16.13 , & 1.84 ± 16.14).

As well as in a study presented by Felisky CD, et al. [13] that there are no significant differences between conventional vein harvesting and EVH with CO₂ insufflation according to harvesting time. There were CO₂ bubbles appeared in the venous system with tributaries divided from the great saphenous system and with the surgical manipulation of the venous system. There are also no significant results with multiple logistic regression analysis as risk factors related to obesity, history of chronic diseases, harvesting time, length of segment or number of grafts. These factors showed no relation with development of minimal CO₂ bubbles without embolization, as well as a study presented by Lin et al. [1] although they showed 2 cases with massive CO₂ embolism.

The incidence of significant CO₂ embolism during endoscopic saphenous vein harvesting with CO₂ insufflation procedures showed wide range of values as it was in a study conducted by Lin et al. 2003 (more than 4%). While it was in our study ranging between 3.8% in low-flow CO₂ group and 5.3% in high-flow CO₂ group. Lin et al. showed that minimal, moderate, and massive CO₂ embolisms occurred in 13.1%, 3.5%, and 0.5%, respectively. This could be explained by that the occurrence of moderate and massive CO₂ embolisms was frequently associated with the surgical manipulation of branches of saphenous veins. Continuous transesophageal echocardiographic monitoring of the CO₂ bubbles in the inferior vena cava is essential in early detection and can help to prevent the development of significant CO₂ embolisms in these

patients [14]. In contrast, many previous studies have highlighted that the systemic absorption of CO₂ and rarely gas embolism can lead to life-threatening events, which has led to questions about the safety of EVH [15].

Another study showed that only rare cases of complications concerning CO₂ insufflation have been reported, while severe CO₂ embolism necessitating emergency cardiopulmonary bypass occurred in a large study in 0.5% of patients [16]. In contrast, Lopes and colleagues found that endoscopic vein harvesting was associated with higher rates of death, myocardial infarction, and repeat revascularization at 3 years (hazard ratio, 1.22; 95% Confidence Interval, 1.01 to 1.47; $p = 0.04$) [17]. The clinical equipoise stemming from these conflicting results highlights the need for a randomized clinical trial with long-term follow-up of clinical outcomes to directly compare endoscopic vs open saphenous

This study has several limitations. First, the greater sample of patients is needed for detection of more studied of echocardiographic findings during insufflation of CO₂. Second, transesophageal echocardiography was not performed continuously, so the possibility that some bubbles were missed cannot be excluded. Lack of continuous monitoring might be the reason for wide variation in the detection rate of bubbles across studies. Finally, although TEE monitoring may contribute to early detection of cardiac events, it is not realistic to use this method routinely in the clinical setting because of the cost, equipment, and personnel required, and the need for prolonged placement in the esophagus. However, our experience is that if any cardiac event is suspected, it can be diagnosed immediately by TEE, and if vital signs are stable after insufflation is stopped, surgery can be continued more safely with monitoring using TEE.

Conclusion

We conclude that the incidence of CO₂ embolisms during EVH could be reduced with lower CO₂ insufflation pressure, which, in combination with increased surgical experience and continuous TEE monitoring of the inferior vena cava, helps to reduce the risks of massive CO₂ embolism. Continuous transesophageal echocardiographic monitoring of the CO₂ bubbles in the inferior vena cava is essential in early detection and can help to prevent the development of significant CO₂ embolisms in these patients.

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Figure legend:

Figure (1): End-tidal CO₂ before, during and after the procedure in Group A

Figure (2): End-tidal CO₂ before, during and after the procedure in Group B

Figure (3): ROC curve for detection of CO₂ bubbles after induction of saphenous vein harvesting

Table legends:

Table 1: Demographic data

Table 2: Operative data

Table 3: Monitoring of ABG (CO₂/O₂) and End-tidal CO₂ before, during and after the maneuver in both groups

Table 4: Complications