

# Incidence of venous gas embolism during robotic-assisted laparoscopic radical prostatectomy is lower than that during radical retropubic prostatectomy†

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## Key points

- Transoesophageal echocardiography (TOE) can be used to detect venous gas embolism (VGE) during robotic-assisted laparoscopic radical prostatectomy (RALRP) and retropubic prostatectomy (RRP).
- In this study, the incidence of VGE during RALRP was lower compared with that during RRP using TOE.
- TOE was found to be useful in detecting VGE in both RALRP and RRP, thereby improving patient safety.

**Background.** Robotic-assisted laparoscopic radical prostatectomy (RALRP) is gaining popularity as a less traumatic and minimally invasive alternative to open radical retropubic prostatectomy (RRP). The aim of this study was to evaluate the incidence and grade of venous gas embolism (VGE) during RALRP compared with those during RRP using transoesophageal echocardiography (TOE).

**Methods.** Fifty-two patients undergoing RRP ( $n=26$ ) or RALRP ( $n=26$ ) were consecutively enrolled. TOE was continuously applied during surgery and VGE was graded by an independent researcher.

**Results.** The total incidence of VGE (proportion, 95% CI) in the RRP group was higher than that in the RALRP group [20/25 (0.80, 0.60–0.92) and 10/26 (0.38, 0.22–0.58), respectively]. Most VGE in the RALRP group occurred during the transection of the deep dorsal venous complex. There was no difference in the incidence of severe VGE between the two groups. No patients with cardiorespiratory instabilities even with severe VGE were observed in this study.

**Conclusions.** In contrast to general belief, VGE occurred less frequently during RALRP. Although the VGE in this study did not cause any cardiorespiratory instability, close monitoring for possibly fatal VGE must be considered during both types of radical prostatectomy because those who undergo radical prostatectomy frequently have cardiopulmonary co-morbidities.

**Keywords:** cardiorespiratory; embolism; prostate cancer; retropubic prostatectomy; robotic-assisted laparoscopic prostatectomy; transoesophageal echocardiography

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Radical prostatectomy is a standard management technique for localized prostate cancer due to its excellent survival rate. Robotic-assisted laparoscopic radical prostatectomy (RALRP) is gaining popularity because it is a less traumatic and minimally invasive alternative to open radical retropubic prostatectomy (RRP).<sup>1–2</sup> However, RALRP requires a prolonged pneumoperitoneum using carbon dioxide (CO<sub>2</sub>), which is known to be associated with venous gas embolism (VGE). On the other hand, a small number of fatal venous air embolisms during RRP in the Trendelenburg position have also been reported.<sup>3–5</sup> VGEs are often overlooked unless large amounts of gas bubbles are entrained, but since pre-existing cardiac or pulmonary diseases enhance the effect of VGE, relatively small amounts of gas may produce marked haemodynamic changes.

Despite the clinical relevance of the present topic, no studies have evaluated intraoperative embolisms in two different surgical approaches for radical prostatectomy. The aim of this study was to evaluate the incidence and grade of VGE during RALRP and compare them with those during RRP using transoesophageal echocardiography (TOE), which is the most sensitive and accurate method for detecting emboli.

## Methods

The study protocol was approved by the institutional review board, and written informed consent was obtained from all patients. Patients with ASA physical status I or II undergoing RALRP (RALRP group,  $n=26$ ) or RRP (RRP group,  $n=26$ ) were consecutively enrolled from March 2007 to November 2007 at a single university hospital.

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**Table 1** Staging of gas embolism by two-dimensional TOE. RA, right atrium; RV, right ventricle; RVOT, right ventricular outflow tract

Stage	Transoesophageal echocardiography
0	No emboli in RA, RV, and RVOT
I	Several gas bubbles in RA, RV, and RVOT
II	Gas emboli less than half the diameter of RA, RV, and RVOT
III	Gas emboli more than half the diameter of RA, RV, and RVOT
IV	Gas emboli completely filling the diameter of RA, RV, and RVOT

Standard intraoperative monitoring used in this study included ECG, invasive systemic arterial pressure and central venous pressure (CVP), pulse oximetry, nasopharyngeal temperature, infrared CO<sub>2</sub> analysis, inspired oxygen fraction, and minute ventilation. After induction of general anaesthesia, a nasogastric tube was inserted to remove intragastric air for the improvement of TOE (SONOS 4500, Philips, Boeblingen, Germany) visualization. A 5.0 MHz multiplane TOE probe was then inserted by an anaesthesiologist who was qualified in intraoperative TOE. Before surgery, the foramen ovale was observed with agitated saline for its patency, and complete TOE examination was performed. The gain setting was lowered to minimize artifact misinterpretation and the mid-oesophageal four-chamber view was continuously monitored and videotaped. Observations were continued till the end of surgery and the patient was returned to the horizontal supine position after gas exsufflation. When gas bubbles were seen in the right atrium (RA), the mid-oesophageal bicaval view was obtained to confirm its entrance from the inferior vena cava and the probe was adjusted to the right ventricle (RV) inflow–outflow view to document its pathway into the RV outflow tract (RVOT). If gas bubbles filled more than half the diameter of RA, RV, and RVOT, visual ventricular function was assessed with TOE. To avoid interobserver variability, an independent cardiac anaesthesiologist blind to the protocol reviewed the TOE videotapes. The cardiac anaesthesiologist evaluated the images three times and defined embolism as showing detectable emboli in the RA. The degree of embolism was classified as one of five stages (Table 1).<sup>6</sup> Severe VGE was defined as stages III and IV VGE.

If there was a sudden occurrence of cardiac arrhythmia including tachycardia, a sudden decrease in end-tidal CO<sub>2</sub> >10 mm Hg, a decrease in mean arterial pressure (MAP) >20 mm Hg, or abrupt peripheral pulse oximetric desaturation (Sp<sub>o2</sub>) <90% during embolic events, it was defined as cardiovascular instability due to VGE. When cardiovascular instability occurred, the surgeon was notified for intervention.

During surgery, anaesthesia was maintained with 50% O<sub>2</sub>/50% air, sevoflurane, and target-controlled remifentanyl. Ventilation was controlled to maintain the end-tidal CO<sub>2</sub> partial pressure (P<sub>E'CO<sub>2</sub></sub>) in a range of 30–40 mm Hg. Fluids

were administered before anaesthesia to replace those lost during preoperative fasting (2 ml kg<sup>-1</sup> h<sup>-1</sup>) and intraoperative fluid administration was adjusted to maintain a urine output ≥1 ml kg<sup>-1</sup> h<sup>-1</sup>. To avoid artifacts on TOE images resulting from fluids rapidly infused through a central venous catheter to the RA, the infusion rate was limited to a minimum. All injections of i.v. medications were administered via a peripheral intravascular catheter. Hypotension (systolic arterial pressure <90 mm Hg or more than a 20% decrease from the baseline value) was treated with fluid infusion and ephedrine. When the patient's vital signs became unstable with a decrease in haematocrit (<28%), packed red cells were administered.

RRP was performed by a single surgical team (Y.D.C.) and RALRP by another team (K.H.R.) who had performed more than 180 RALRP cases. The same standard surgical technique was performed for RRP. For RALRP, the Vattikuti technique<sup>7</sup> was performed using the da Vinci surgical system (PS2000, Intuitive Surgical, Sunnyvale, CA, USA) under a pneumoperitoneum created with a variable-flow insufflator (High-Flow Insufflator, Stryker, San Jose, CA, USA). The insufflating needle was carefully inserted with a trocar to avoid injuring blood vessels. Gas insufflation was started at a low flow rate of 1 litre min<sup>-1</sup> to minimize the risk of embolism at the beginning of pneumoperitoneum and increased slowly as needed. We also kept the insufflation pressure and flow rate low until we were certain that uneventful insufflation was occurring. The intraperitoneal pressure was maintained at 15 mm Hg after moving patients into a 30° head-down tilt Trendelenburg position during surgery.

Arterial blood gas analysis was conducted and serum haematocrit was examined before and after induction of anaesthesia and repeated at 1 h intervals. If VGE was detected on TOE, arterial blood gas was immediately analysed. Intraoperative characteristics including operating time, amount of infused fluid, urine output, estimated blood loss and transfusion, and incidences of hypotension and treatment during surgery were recorded. Any symptoms or signs related to common clinical signs of thromboembolic complications were evaluated during the postoperative period.

The sample size was calculated based on a pilot study. The incidence of VGE during RALRP and RRP was 50% and 90%, respectively, with an  $\alpha$  error of 0.05 and a power of 0.8. As a result, in each group, 25 patients were required, but 26 patients were recruited to compensate for the dropout rate of 5%.

Statistical analysis was performed using SAS 9.1 for Windows (SAS Institute Inc., Cary, NC, USA). Data were expressed as mean (SD) or number of patients (%). The Mann–Whitney *U*-test, Student's *t*-test, and Fisher's exact test were used to determine statistical differences between the two groups where appropriate. A *P*-value of <0.05 was considered significant.

## Results

Of the 52 subjects, one patient in the RRP group was excluded from the study due to TOE insertion failure.

The patient characteristics and intraoperative characteristics are presented in Table 2. There was no difference in patient characteristic data between the two groups. Two patients in each group had patent foramen ovale. There were significant differences in the intraoperative characteristics between the groups. The RALRP group had a significantly longer surgical time but less fluid administration, less urine output, and less estimated blood loss than the RRP group. One patient (3.8%) in the RALRP group required an intraoperative transfusion of 250 ml of packed red blood cells, whereas 14 patients (56%) in the RRP group received transfusions of 200–1600 ml [621 (sd 366), mean (sd)] ( $P < 0.05$ ).

The incidence of VGE in each stage is listed in Table 3. The total incidence of VGE (proportion, 95% CI) in the RRP group was higher than that in the RALRP group [20/25 (0.80, 0.60–0.92) and 10/26 (0.38, 0.22–0.58), respectively]. Most embolic episodes occurred during the transection of the deep dorsal venous complex. In the RALRP group, there was no detection of emboli after gas exsufflation and the position of the patient was made horizontal supine again. There was no difference in the incidence of severe VGE between the two groups. There were no patients with cardio-respiratory instabilities even with severe VGE in this study. All bubbles were cleared from the right heart cavities within a minute, and no interatrial septal shift or paradoxical embolism was detected in any patient during embolic events (Fig. 1). There was no correlation between episodes of embolism and blood gas variables or  $Pe'_{CO_2}$  in both groups. No complications related to TOE were noted after surgery. No clinical signs or symptoms of thromboembolic complications were observed in any patient on postoperative day 7.

## Discussion

This study demonstrated that the incidence of VGE during RRP (80%) was significantly higher than that during RALRP (38%). All VGEs were in the subclinical range without significant haemodynamic or respiratory changes.

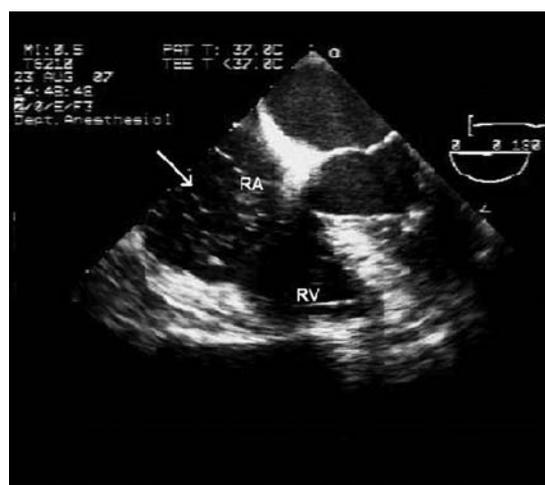
Previous studies on VGE during laparoscopic surgeries reported varying degrees of VGE, including fatal massive gas embolism.<sup>8–11</sup> Recently, we reported that subclinical gas embolisms occurred in 17.1% of laparoscopic radical prostatectomies and this procedure has the potential for a serious gas embolism.<sup>12</sup> Another study in our institution reported that while the incidence of VGE was only 15% during total abdominal hysterectomy, the incidence of VGE was 100% during total laparoscopic hysterectomy.<sup>11</sup> It also reported that the grade was higher during total laparoscopic hysterectomy. This was explained by the increased pressure difference between the injured vascular lumen and the RA due to the positive pressure insufflation of the peritoneal cavity. However, in this study, the incidence of VGE was lower during RALRP, which is in contrast to general belief. In addition, there was no difference in the severity of VGE. This may be explained in part by the extreme Trendelenburg position during RALRP. Usually, the steep Trendelenburg

**Table 2** Patient characteristics and intraoperative characteristics. Data are mean (sd) or number of patients (%). PFO, patent foramen ovale; EBL, estimated blood loss during surgery. Hypotension, systolic arterial pressure  $< 90$  mm Hg or more than a 20% decrease from baseline value. \* $P < 0.05$

Variables	RRP group (n=25)	RALRP group (n=26)
Age (yr)	68.6 (4.9)	66.0 (6.9)
Weight (kg)	66.2 (9.0)	66.7 (6.9)
Height (cm)	168.7 (7.0)	167.2 (5.1)
Incidence of PFO	2 (8%)	2 (8%)
Duration of surgery* (min)	236.5 (67.3)	279.6 (34.2)
Fluid administered* (ml)	3564 (1609)	2021 (500)
Urine output* (ml)	432.6 (245.5)	246.4 (121.3)
EBL* (ml)	1410 (901)	457 (281)
Hct (%)		
Preoperative	35.9 (3.3)	36.6 (2.6)
Postoperative*	28.8 (4.1)	32.5 (2.8)
Transfusion*	14 (56%)	1 (3.8%)
Hypotension*	13 (52%)	3 (11.5%)

**Table 3** Incidence of intraoperative VGE. Data are number of patients (%)

Stage	RRP group (n=25)	RALRP group (n=26)
I	9 (36%)	4 (15%)
II	6 (24%)	2 (8%)
III	5 (20%)	2 (8%)
IV	0 (0%)	2 (8%)
Total	20 (80%)	10 (38%)



**Fig 1** Gas embolism detected by TOE during the transection of deep dorsal complex. Gas emboli are filling more than half the diameter of RA in the RALRP group. Arrows indicate bubbles entering the RA. RA, right atrium; RV, right ventricle.

position is assumed as a 15° head-down position during gynaecological surgery, but during RALRP a 30° head-down position was made to facilitate the acquisition of working space. The extreme Trendelenburg position increases RA pressure, which in turn increases the venous pressure, and this may have prevented the entrainment of gas through the broken vein.<sup>13</sup> Despite this beneficial effect on embolic events, of course, the extreme head-down position has some possibilities of complications. It may cause deep venous thrombosis of the lower extremities due to poor blood circulation. Furthermore, in any positions in which the head is at a different level than the heart, the effect of the hydrostatic gradient on cerebral arterial and venous pressures should be carefully considered in terms of cerebral perfusion pressure.<sup>14</sup>

Most serious gas emboli during laparoscopic surgery in previous studies developed principally at the beginning of pneumoperitoneum.<sup>15 16</sup> However, every embolic event in the RALRP group occurred during transection of the deep dorsal venous complex and not during gas insufflation. This may have been due to careful gas insufflation administered at a slow rate from the start, because slowly diffused CO<sub>2</sub> dissolves better in the blood and clears faster in the lungs than that entering through the broken vein.<sup>12</sup> Kim and colleagues<sup>11</sup> also reported that the VGE during total laparoscopic hysterectomy occurred during round ligament transection and broad ligament dissection, and not at the time of insufflation.

In this study, the incidence of VGE was higher in the RRP group than in the RALRP group. There have been a small number of reports concerning fatal RRP-related air embolism till now.<sup>3-5</sup> Those cases were detected only because there were catastrophic haemodynamic and respiratory changes during the surgery. As the result of this study shows, the incidence of subclinical air embolism is quite high. The conditions for creating VGE during laparotomic surgeries differ from those during laparoscopic surgery. During RRP, the entrained gas is air, which is not readily absorbed in the blood like CO<sub>2</sub>, and air can be passively drawn into an open, non-collapsed vein by negative intrathoracic venous pressure. Furthermore, a pressure gradient of as little as 5 cm H<sub>2</sub>O is sufficient to allow air entry via open veins.<sup>17</sup> The gradient increases if hypovolaemia from surgical blood loss is inadequately compensated, causing a decrease in CVP and a greater risk of venous air embolism. The higher incidence of VGE during RRP compared with that during RALRP may be explained by the lack of the tamponade effect of the pneumoperitoneum, which can be of significant benefit because increased intraabdominal pressure more than 20 mm Hg can collapse the injured vessel.<sup>18</sup>

The diagnosis of embolism depends on the detection of emboli in the right heart or on recognition of the physiological changes from embolization such as tachycardia, cardiac arrhythmias, hypotension, desaturation, or electrocardiographic changes. However, since all these clinical changes are rarely consistently positive, the detection of emboli in the heart with TOE is the most sensitive method and is

considered the 'gold standard'.<sup>19</sup> TOE can detect emboli as small as 0.05 ml with no haemodynamic or respiratory changes, which usually signifies an embolus volume of 1 ml kg<sup>-1</sup>.<sup>20</sup> In previous reports, incidences of embolism with or without cardiorespiratory consequences have been reported as often as in 69% of cases during laparoscopic cholecystectomy, 76% during neurosurgery in the sitting position, and up to 68–100% during laparoscopic hepatic resection when TOE was used for monitoring.<sup>6 8 21 22</sup>

No patient in this study demonstrated any cardiorespiratory instability or abrupt  $P_{E'_{CO_2}}$  changes. This may be because only healthy patients or those with only mild systemic disease without any functional limitation (ASA physical status I and II) were included in this study. We may expect that since pre-existing cardiac or pulmonary disease enhances the effects of venous air embolism, a relatively small amount of air may have produced marked haemodynamic changes in those with severe systemic disease (ASA physical status III and IV). In the RALRP group, even the two patients with a high grade of VGE (grade IV) were haemodynamically stable. This is consistent with other studies of VGE during laparoscopic surgeries.<sup>8 11</sup> This is likely because the entrained gas was CO<sub>2</sub>, which is extremely soluble in the presence of red blood cells and therefore much less life threatening than an identically sized intravascular bolus of air.<sup>23</sup> Rapid elimination also increases the margin of safety in cases of i.v. injection of CO<sub>2</sub>. Patent foramen ovale exists in 10–35% of the population and is the most common route for paradoxical air embolism.<sup>24</sup> In this study, two patients in each group had a patent foramen ovale, but there was no major neurological complication that may result from paradoxical air embolism.

There are several limitations in this study. This was a prospective, same-surgeon series, but patients were not randomized because the primary parameter influencing the selection of surgical approach was patient preference. Patient characteristics such as history of surgery may have influenced the result of this study because it has been reported to increase the risk of embolism.<sup>25</sup> However, it is unlikely because no patient had a history of abdominal surgery. Another limitation is the inclusion criteria, which was ASA physical status I and II, which means patients with severe cardiopulmonary disease were excluded. This may have affected the cardiorespiratory and  $P_{E'_{CO_2}}$  consequences of VGE.

In conclusion, the incidence of VGE during RALRP (38%) was lower than that during RRP (80%) and most emboli occurred during transection of the deep dorsal vein. Although the VGE in this study did not cause any cardiorespiratory instability, close monitoring for possibly fatal VGE must be considered during both types of radical prostatectomy because those who undergo radical prostatectomy frequently have cardiopulmonary co-morbidities.

## Conflict of interest

None declared.

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