Hemodynamic effects of sevoflurane versus propofol anesthesia for laparoscopic radiofrequency ablation of liver tumors

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THE EDITOR

Curative liver resection is suitable for only 10-20% of patients with metastatic liver cancer.[1] Several interstitial ablation techniques have been employed for the treatment of inoperable hepatic neoplasm.[2] Laparoscopic cryo-ablation of the liver caries the risk of hemodynamic instability, due to bleeding, hypothermia and reperfusion injury.[3-4] This may be worsened by the cardiovascular effects of laparoscopy and anaesthetic agents.[5-7]

As opposed to cryoablation, laparoscopic radiofrequency ablation (LRFA) has not been associated with hemodynamic instability.[8] Sevoflurane may attenuate arterial baroreflex function during anesthesia, which may adversely affect the hemodynamic stability of the patients receiving sevoflurane anesthesia.[7] Thus, our hypothesis was that sevoflurane as opposed to propofol anesthesia might lead to hemodynamic instability during LRFA surgery due to its possible effect on baroreceptors. We, therefore, investigated the hemodynamic profiles of patients undergoing LRFA of liver tumors under either sevoflurane or propofol anesthesia.

Purpose

Laparoscopic radiofrequency ablation of liver tumors, as opposed to cryoablation, is characterized by hemodynamic stability. Our hypothesis was that sevoflurane as opposed to propofol anesthesia, might lead to hemodynamic instability during LRFA surgery, due to its possible effect on baroreceptors.

Methods

To calculate the necessary sample size for the study, a power analysis was performed. We defined a difference of at least 15% of mean arterial pressure, heart rate, and cardiac index between groups, with pooled SD of 15 mmHg, 10 beats per minute, and 0.5 L/min/m^2 for mean arterial pressure, heart rate, and cardiac index, respectively, to be of clinical importance. To achieve an 80% power to detect such a difference with an α of 0.05, 17 patients were calculated to be required in each group. Therefore, 20 patients were enrolled in each study group.

After obtaining the relevant approval and patient written informed consent, 40 patients (20 per group) aged 18-80 yr, scheduled to undergo elective LRFA of liver tumors were assigned to this prospective, randomized, double blind study. Patients with irresectable hepatic lesions of less than 3 cm in diameter with no documented extrahepatic involvement at laparoscopic ultrasound examination were included in the study. Excluded from the study were patients with ASA classification of IV, NYHA (New York Heart Association) class >2 and/or left ventricular ejection fraction (LVEF) <40%, if recorded.

Protocol

Thirty min before surgery, patients received sublingual brotizolam, 0.25 mg. The assignment to a specific anaesthetic technique was randomly performed before the induction of anesthesia. The randomization was undertaken with the closed envelope technique.

After 3 minutes of preoxygenation, anesthesia was induced with propofol 2-2.5 mg/kg, fentanyl 2 μg/kg, and succinylcholine 1 mg/kg. Rocuronium 0.4 mg/kg was administered after intubation. Standard ASA monitoring was employed. In addition, central and arterial indwelling catheters were placed prior to induction of anesthesia. Following endotracheal intubation, anesthesia was maintained according to the group assignment: 1) sevoflurane (1-2% end tidal concentration) with 70% N$_2$O in 30% oxygen or 2) a continuous propofol infusion of 100-150 μg.kg^{-1}.min^{-1} plus 70% N$_2$O in 30% oxygen. The end-tidal sevoflurane concentrations and the propofol infusion rates were changed to maintain a BIS

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value between 40-50. In both groups, 50 µg fentanyl was given every 30 min. At the end of the procedure, muscle relaxants were reversed and the patient was extubated and taken to the PACU. Normal saline solution 0.9% was administered throughout the procedure at a rate of 5 mL.kg^{-1}.hr^{-1}.

The primary endpoints of the study which characterized hemodynamic instability were the number of episodes of changes greater than 30% from the baseline (preanesthetic value) in mean arterial pressure (MAP), heart rate (HR), cardiac index (CI - measured with thoracic bioimpedance), systemic vascular resistance index (SVRI) and central venous pressure (CVP). These were recorded at predetermined times, with the need for hemodynamic pharmacological interventions (for hypo/hypertension or brady/tachycardia), as previously defined. Hypotension with a MAP < 60 mmHg was treated with 5 mg ephedrine intravenously (ivi). Bradycardia, defined as a heart rate of < 45 beats per min (bpm) with stable MAP or < 60 bpm associated with MAP < 60 mmHg, was treated with 0.5 mg ivi atropine. Hypertension (MAP>120 mmHg) and tachycardia (HR>100 bpm) were treated with aliquots of 5 mg ivi esmolol. Postoperatively, patients were followed up until they met the standard discharge criteria from PACU (Aldrete).

Measurements

Hemodynamic measurements were undertaken at specific time-points during anesthesia and surgery.

Mean arterial pressure (MAP) and heart rate (HR) measured oscillometrically, cardiac index determined with thoracic bioimpedance readings , systemic vascular resistance index, central venous pressure, nasopharyngeal temperature, EtCO^2, and SpO$_2$ were recorded every 10 minutes and additionally at seven specific time points: 1) before anesthesia, 2) before tracheal intubation, 3) three min after intubation, 4) three min after patient was placed in head-down table position, 5) three min after patient was placed in head up table position, 6) at maximal abdominal inflation (15 mmHg) with gas, and 7) three min after extubation. This seven additional measurement time points were considered as events with potential for occurrence of hemodynamic changes. At the same times, we recorded the amount of bleeding, fluids and blood infused, and the need for administration of atropine, ephedrine or esmolol (hemodynamic pharmacological interventions). Episodes of hypo/hypertension and brady/tachycardia documented at any given time throughout the procedure were also recorded. The systemic vascular resistance index was calculated for each time point from the standard cardiac output formula (9).

Complications such as arrhythmias (defined as runs of ventricular tachycardia, ventricular fibrillation, paroxysmal supraventricular tachycardia, atrial fibrillation, or cardiac arrest) were recorded, as were cardiovascular complications (intraoperative myocardial ischemia defined as a new 2-mm ST depression or new 1-mm ST elevation on an automatic ST analyzer, and myocardial infarction), significant bleeding (>10 mL/kg) and a switch to open surgery.

The amount of bleeding, urinary output, fluid infused, duration of surgery and total MAC hours for sevoflurane, and the total volume of propofol used was also recorded. The anaesthesiologist performing the measurements was ''blinded'' throughout surgery to the type of anaesthetic

administered by concealing the vaporizers and the infusion pump (a ''dummy'' infusion pump was connected to the sevoflurane patients). Length of PACU stay and patient's satisfaction presented on a two-point scale (satisfied or unsatisfied) obtained 24 hours after surgery were also recorded.

Data analysis

Data were evaluated for normal distribution using the Kolmogorov-Smirnov test. Continuous variables with distribution significantly differing from normal were compared using the Mann-Whitney U or median tests. Parametric data are expressed as means ± SD. Categorical data are described using frequency counts and percentages and compared using Chi square (with Yates correction) or Fisher's exact tests, as appropriate. All results were considered significant at P < 0.05. Main outcomes were analysed and compared with the multivariable logistic regression, while dynamic chronological changes between and within the groups were analysed with the general linear model for repeated measurements.

Results

Demographic data, number of resected tumors per patient, duration of surgery, urinary output, blood loss, the amount of fluid infused, total MAC hours for sevoflurane, total volume of propofol, length of PACU stay and patient satisfaction were similar between the groups and are presented in Table 1. Heart rate, cardiac index, systemic vascular resistance index,

Table 1: Demographic and Intraoperative Data			
	Sevoflurane	**Propofol**	
			P
	N = 20	**N = 20**	
Age (yr)	64 ± 13	63 ± 8	0.800
Male/Female (%)	64 / 36	64 /36	1.000
ASA I / II/ III (N)	6/ 12 /2	8 /11 /1	0.800
Number of resected tumors per patient	1.45 ± 0.69	1.3 ± 0.47	0.500
Duration of surgery (min)	143 ± 13	136 ± 24	0.280
Blood loss (mL)	100 ± 50	120 ± 50	0.300
Total IV fluids (mL)	2391 ± 491	2255 ± 242	0.400
Urinary output (mL.kg^{-1}.h^{-1})	0.9 ± 0.2	1 ± 0.3	0.800
Temperature at the end of surgery (ºC)	36.0 ± 0.4	35.9 ± 0.3	0.300
Total MAC hours of sevoflurane	2.18 ± 0.3	-	
Total dose of propofol (mg.h^{-1})	-	440 ± 50	
Length of PACU stay (min)	60 ± 10	65 ± 13	0.500
Patient satisfaction (N)			
-Satisfied	17	18	0.900
-Unsatisfied	3	2	

Data are expressed as mean ± SDs, absolute numbers (N) or percentage of total.

central venous pressure, temperature (Table 2), EtCO$_2$ and SpO$_2$, were similar in the two groups. There were no cases with significant bleeding or intraoperative complications in either group.

There were no episodes of hemodynamic instability as defined previously, nor were hemodynamic pharmacological interventions required.

Mean arterial blood pressure was significantly lower in the sevoflurane group (90 ± 12 mmHg) at 3 minutes after changing to head-up position of the patient than in the propofol group (103 ± 10 mmHg - P = 0.009). This difference remained significant for the next 5 minutes.

Multivariable logistic regression analysis revealed that the type of anesthesia was not associated with the hemodynamic variables measured.

Lack of patient satisfaction in all 5 cases 3 with sevoflurane and 2 with propofol) was caused be postoperative nausea managed by ondansetron, 0.1 mg.kg-^{1}, intravenously.

Discussion

The results of the study do not support our hypothesis that hemodynamic changes during LRAF may differ with the type of anesthesia and this is a limitation of the study. However, the decrease in the MAP during head-up position encountered with sevoflurane but not with propofol, may suggest a positional change related hemodynamic lability during sevoflurane anesthesia.

Hemodynamics during anesthesia can be affected by at least three independent factors: type of anesthesia, type of surgery and patients' cardiovascular status. The last two factors were presumably similar among the patients as they all had reasonably normal left ventricular function and were scheduled for elective laparoscopic radioablation surgery. All patients had the same type of surgery, were on a normal diet the day before surgery and apparently had similar hydration states; thus the impact of the other factor, anesthesia, on patients' hemodynamics could be evaluated. Laparoscopic surgery by itself is associated with hemodynamic disturbances.[10-12] Reports of the influence of pneumoperitoneum on the patient's hemodynamics had demonstrated a decrease in cardiac output and venous return, an increase in intraabdominal pressure and systemic vascular resistance and a decrease in portal vein blood flow (10-12). We chose LRFA surgery for our study, as it has not been reported to cause any hemodynamic impairment.[8]

In our series, cardiac index, SVRI and CVP were not different at differing time-points within the same group. This may reinforce the conclusion of the study by Nguyen et al, that the hemodynamic changes related to laparoscopy itself may not have serious clinical significance.[13]

As mentioned previously, it appears that in contrast to cryotherapy, radiofrequency does not induce hemodynamic instability. In an animal study, hepatic artery blood flow and peripheral blood pressure did not change significantly during peritoneal insufflation for radiofrequency ablation surgery.[8]

We did not intend to investigate the effects of LRFA itself on the hemodynamics. To accomplish this, we will need to compare two types of surgery (i.e. LRFA vs. cryo-ablation). Rather, we estimated the hemodynamic effects of sevoflurane vs. propofol, during this specific surgical procedure which has not previously been associated with significant hemodynamic

Table 2: Hemodynamic measurements			
	Sevoflurane	**Propofol**	*P*
Mean Arterial Pressure (mmHg)			
Baseline (before anesthesia)	96 ± 20	103 ± 15	0.400
Intraoperative mean value	96 ± 15	100 ± 25	0.600
Before tracheal intubation	94 ± 28	106 ± 18	0.200
3 min after intubation	99 ± 24	98 ± 16	0.900
3 min after head-down position	94 ± 20	106 ± 12	0.200
3 min after head-up position	90 ± 12	103 ± 10	*0.009*
At maximal abdominal inflation	99 ± 23	97 ± 12	0.900
End of surgery	94 ± 20	104 ±17	0.300
Heart Rate (beats per minute)			
Baseline (before anesthesia)	75 ± 15	69 ± 12	0.400
Intraoperative mean value	72 ± 10	70 ± 13	0.800
Before tracheal intubation	69 ± 12	70 ± 13	0.900
3 min after intubation	68 ± 14	69 ± 13	0.900
3 min after head-down position	70 ± 15	68 ± 13	0.800
3 min after head-up position	70 ± 16	70 ± 15	1.00
At maximal abdominal inflation	74 ± 16	71 ± 12	0.600
End of surgery	71 ± 15	67 ± 26	0.700
Cardiac Index (L·min^{-1}·m^{-2})			
Baseline (before anesthesia)	2.9 ± 0.4	2.7 ± 0.9	0.500
Intraoperative mean value	2.6 ± 0.8	2.5 ± 0.5	0.800
Before tracheal intubation	2.7 ± 0.9	2.8± 0.7	0.900
3min after intubation	2.7 ± 0.9	2.7 ± 0.7	1.00
3 min after head-down position	2.5 ± 0.4	2.3 ± 0.4	0.400
3 min after head-up position	2.5 ± 0.8	2.3 ± 0.5	0.600
At maximal abdominal inflation	2.7 ± 0.9	2.5 ± 0.6	0.400
End of surgery	2.7 ± 0.7	2.7 ± 0.7	0.800
Systemic Vascular Resistance Index (dynes·sec·cm^{-5}·m^{-2})			
Baseline (before anesthesia)	2670 ± 490	3000 ± 1240	0.300
Intraoperative mean value	2880 ± 1100	3050 ± 1000	0.500
Before tracheal intubation	2600 ± 1030	2800 ± 920	0.600
3 min after intubation	33070 ± 3000	2670 ± 960	0.500
3 min after head-down position	3280 ± 2730	3363 ± 970	0.900
3 min after head-up position	2890 ± 1600	3150 ± 650	0.600
At maximal abdominal inflation	2670 ± 830	2840 ± 620	0.600
End of surgery	2547 ± 885	2878 ± 732	0.400
Central Venous Pressure (mmHg)			
Baseline (before anesthesia)	12 ± 4	13 ± 4	0.700
Intraoperative mean value	13 ± 3	13 ± 5	0.900
Before tracheal intubation	15 ± 6	14 ± 4	0.900
3 min after intubation	13 ± 5	14 ± 4	0.900
3 min after head-down position	13 ± 4	14 ± 4	0.700
3 min after head-up position	14 ± 4	13 ± 5	0.900
At maximal abdominal inflation	13 ± 4	13 ± 4	1.00
End of surgery	12 ± 3	12 ± 3	0.600

Data are expressed as mean ± SDs.

changes. Thus, by standardizing the effect of surgery and laparoscopy, we could estimate the hemodynamic effect of the specific anaesthetic agent employed.

In a study by Watson and Shah in spinal surgery, the cardiovascular stability was good and comparable with both sevoflurane and propofol.[14] In a study of patients undergoing carotid surgery, there were a similar number of episodes of hypotension, hypertension, and tachycardia amongst groups, but the incidence of bradycardia was less with propofol compared with sevoflurane. Also, the duration of episodes of hypotension was shorter with propofol compared with sevoflurane.[15]

Keyl et al demonstrated that both sevoflurane and desflurane increased the delay of systolic blood pressure response to baroreceptor stimulation.[16]

Sevoflurane may attenuate arterial baroreflex function during anesthesia and this may adversely affect the hemodynamic stability of the patients receiving sevoflurane anesthesia.[7] This might explain the greater decrease in MAP during head-up position in the patients who received sevoflurane as compared with the propofol group. In contrast to sevoflurane anesthesia, the baroreceptor reflex sensitivity is maintained during propofol anesthesia.[17]

We evaluated the influence of the anaesthetic technique on hemodynamic stability through changes in MAP, HR, CI, SVR as well as the need for pharmacological therapeutic interventions. With univariate analysis we found that the MAP was lower in the sevoflurane group, 3 minutes after changing to head-up position of the table (P=0.009). This may suggest a tendency for less hemodynamic stability with sevoflurane as compared with propofol with positional changes during laparoscopic procedures.

The thoracic bioimpedance monitoring provided us with important hemodynamic information in addition to standard monitoring. The bioimpedance technique has been shown to provide reliable hemodynamic information in patients undergoing laparoscopic abdominal surgery.[5] These measurements showed that the trends of cardiac output and systemic vascular resistance remained unchanged throughout surgery.

In conclusion, our hypothesis that sevoflurane might lead to more hemodynamic instability as compared with propofol, due to a presumable effect on the baroreceptors is supported by a significantly lower mean arterial pressure with isoflurane in the head-up position.

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