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ORIGINAL ARTICLE

The effects of desflurane and sevoflurane on hepatic and renal functions after right hepatectomy in living donors*

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desflurane, liver function tests, living-donor right hepatectomy, renal function tests, sevoflurane.

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Summary

We compared postoperative hepatic and renal functions between the two inhalational anesthetics, desflurane and sevoflurane in living donors undergoing right hepatectomy. Seventy-four adult donors were randomly allocated into Des group (n = 37) and sevo group (n = 37). Before the induction of anesthesia, morphine sulfate 400 μg was injected intrathecally. Anesthesia was maintained with one minimum alveolar concentration (MAC) of deflurane or sevoflurane plus continuous intravenous remifentanil. Liver and renal function tests were performed and analysed at preoperative period, immediately after operation, and on 1st, 2nd, 3rd, 5th, 7th, and 30th postoperative days (PODs). Aspartate aminotransferase (AST) showed significant elevations from the day of surgery to POD 3 and alanine aminotransferase (ALT) was significantly elevated on POD 1 and POD 3 in the sevo group. Albumin level was significantly lower on POD 2 in the sevo group. Creatinine was significantly higher on POD 3 and POD 30 and estimated glomerular filtration ratio was significantly lower on POD 3 and POD 30 in the sevo group. No patient developed hepatic or renal failures. The results of our study showed better postoperative hepatic and renal function test with desflurane than sevoflurane at equivalent dose of 1 MAC in living donors undergoing right hepatectomy, but further study is required to evaluate clinical importance.

Introduction

Living-donor liver transplantation has gained significant attention as a result of the exponential growth in the number of liver transplantation candidates along with the shortage of cadaver donors. The living-donor liver transplantation may be less frequently performed in some transplantation centers in Western countries, while it constitutes majority of liver transplantations in some Asian countries [1]. Currently, thanks to the improvements in surgical techniques and advances in anesthetic management, the living-donor hepatectomy is recognized as a relatively safe procedure. However, regarding the health condition of living donors and the obligation to insure living donor safety, the complications of various degrees still remain a great concern[2]. Considering the severity of living-donor right hepatectomy for adult liver transplantation, there are significant risks to the living donors, including substantial morbidity and even mortality [2–4]. Moreover, the large liver resection leads to transient alterations in hemostasis, metabolism and possibly, pharmacokinetics and pharmacodynamics of drugs administered [5]. Therefore, the safety of living donors is the cardinal issue mandating comprehensive anesthetic management regimen that encompasses all the aspects of vital organ functions such as hepatic and renal functions.

For living liver donors, no optimal anesthetic technique has been established for the maintenance of anesthesia. Typically, either the inhalational anesthesia or total intravenous anesthesia (TIVA) is used depending on the anesthesiologist's preference. Both anesthetic methods may be considered safe; however, our previous study demonstrated better outcomes in postoperative hepatic and renal functions in patients who received inhalational anesthetic, desflurane, than the ones with propofol-based TIVA [6]. Additionally, protective effect of inhalation anesthetic preconditioning in patients undergoing liver resection with inflow occlusion has been demonstrated by Beck-Schimmer *et al.* [7]. These results suggest that inhalational anesthesia may be a more appropriate anesthetic choice in patients undergoing liver surgeries. In general, various inhalational anesthetics (e.g. desflurane, sevoflurane, isoflurane, etc) are used in living liver donors [8,9]; however, the impact of these inhalational anesthetics on vital organ functions is still inconclusive. Therefore, the aim of this study was to compare the hepatic and renal functions between desflurane and sevoflurane, two most frequently used inhalational anesthetics with different degrees of hepatic metabolism, in living donors undergoing right hepatectomy.

Patients and methods

The institutional review board approved this study and all donors provided written informed consent. Seventy-four donors undergoing right hepatectomy during the period between May 2008 and May 2009 were enrolled and randomly allocated into two groups using a sealed envelop technique: desflurane group (Des group, $n = 37$) and sevoflurane group (sevo group, $n = 37$). Patients undergoing re-operation, those contraindicated to spinal injection of morphine sulfate (e.g. skin infection at the site of injection) or those with a known allergy to any of the drugs used in this study were excluded.

Anesthesia monitoring included electrocardiogram, continuous arterial and peripheral venous pressures (PVP), pulse oximetry, capnography, urine output, nerve stimulator, and esophageal core temperature.

No premedication was given in any of the donors. In our transplantation center, it is routine procedure to perform spinal analgesia using intrathecal opioid for the postoperative pain control [10]. Before the induction of anesthesia, dural puncture was performed at the L3–L4 or L4–L5 level with a 27-gauge pencil-pointed spinal needle after local anesthesia. Four milliliters of cerebrospinal fluid was withdrawn through the spinal needle and mixed with morphine sulfate 400 μg and then slowly injected back into the intrathecal space. In both groups, anesthesia was induced with thiopental sodium 5 mg/kg and continuous infusion of remifentanil 0.15 μg/kg per min. Vecuronium (0.15 mg/kg) was administered to achieve muscle relaxation before endotracheal intubation. End-tidal desflurane or sevoflurane concentrations during the induction were limited to 2 MAC. Concentrations of inhalational anesthetics were measured using an anesthetic gas analyser (Datex-Ohmeda, Helsinki, Finland). For the maintenance of anesthesia, the inspired desflurane or sevoflurane concentration was carefully titrated to maintain the end-tidal concentration of 1 MAC. A constant fresh gas flow of 3 l/min (medical-grade air in oxygen to make inspiratory oxygen fraction 0.5) was used during the maintenance of anesthesia. Ventilation was controlled with a tidal volume of 7–10 ml/kg and ventilatory rate was adjusted to maintain an end tidal CO_2 of 35–40 mmHg. Continuous infusion of remifentanil (0.02–0.15 μg/kg) was titrated to maintain intraoperative blood pressure (BP) and heart rate (HR) within 20% of preoperative values. When mean value of BP exceeded 20% of preoperative values using above methods, then nitroglycerine was started at 0.5 μg/kg per min and increased at incremental doses of 0.5 μg/kg per min, as necessary. Additional vecuronium was administered as appropriate. Bispectral index (BIS) monitoring (Aspect Medical System Inc., Norwood, MA, USA) was used to ensure unawareness during the operation [11]. Nerve stimulator was used to monitor neuromuscular blockade on the right adductor pollicis. Hypotension (a drop in systolic BP to the extent of 30% or more or the systolic BP being less than the preoperative values) was treated with volume replacement and, when necessary, with intravenous ephedrine in incremental doses of 5 mg. Bradycardia (HR < 50 beats per min) was treated with 0.5 mg atropine if needed. The PVP was used instead of central venous pressure [12]. The PVP was maintained ≤8 mmHg during the hepatic parenchymal dissection phase by the surgeons' request on the basis of their clinical experience in an effort to reduce blood loss and facilitate liver dissection. Five-hundred milliliter colloid solution (6% hydroxyethyl starch) was administered for intravascular volume expansion following liver resection in all donors. The same surgical team performed all operations, and neither vascular clamping nor the Pringle maneuver was used. After operation, all donors were transferred to postanesthesia care unit (PACU) for close monitoring and further management. They remained in PACU until they met the criteria of postanesthesia recovery score (modified Aldrete's score) [13] in addition to assessment of pain, nausea/vomiting, and surgical bleeding, and all of the donors were discharged to the ward within 3 h of arrival at the PACU.

Another anesthesiologist who was blinded to the group assignment collected the postoperative data. Total liver volume (TLV), graft volume (GV), remnant liver volume

(RLV) ratio, surgical and anesthetic times, administered fluids, estimated blood loss, urine output, duration of postoperative hospital stay, blood products transfusion and complications were investigated. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (TB), prothrombin time (PT) expressed in international normalized ratio (INR), albumin, blood urea nitrogen (BUN), creatinine (Cr), BUN/Cr ratio, estimated glomerular filtration rate (GFR, calculated using Modification of Diet in Renal Disease Study Equation) [14], platelet count (PLT), and hemoglobin (Hb) were analysed at preoperative period, immediately after operation, and on the 1st , 2nd, 3rd, 5th, 7th, and 30th postoperative days (PODs). All donors were interviewed about the possibility of intraoperative recall at the PACU and on the 2nd or 3rd POD, using the modified Brice interview [15].

Statistical methods

The sample size of the donors was determined by power analysis ($\alpha = 0.05$, $\beta = 0.80$), which showed that 37 patients would be required in each group to reveal a significant difference in ALT values on POD 1 between the two groups. This was based on our pilot study of 27 patients in each group with mean difference of 42 and standard deviation (SD) of 54 and 75 in ALT values on POD 1 in each group. Data are presented as mean ± SD. For continuous variables, Student's *t*-test or Mann–Whitney rank sum test was employed to compare the inter-group difference, and chi-squared test was adopted for categorical variables. The difference was regarded as statistically significant when the $P < 0.05$.

Results

All donors were graded as American Society of Anesthesiologists physical status I. Two donors (one in each group) were excluded from the study because of postoperative bleeding secondary to surgical factors requiring bleeding control operation on POD 2. Intraoperative findings of the donor in the Des group revealed arterial bleeding in the gallbladder bed site and the donor in the sevo group revealed small artery branch bleeding near the bile duct. Therefore, two more donors (one in each group) were recruited. There were no significant differences in demographic data (Table 1). The TLV, GV, RLV ratio, and fatty changes (macrovesicular and microvesicular) were similar between the two groups. The surgical and anesthetic data are shown in Table 2. Intraoperative hemodynamic parameters including HR, mean BP, and PVP values were divided into three stages: prehepatectomy, intrahepatectomy, and posthepatectomy and were similar between the two groups in all three stages (Table 3).

Table 1. Demographic data.

	Des group (n = 37)	Sevo group (n = 37)
Age (years)	32.0 ± 10.7	33.2 ± 11.0
Gender (M/F)	19/18	24/13
Height (cm)	165.5 ± 8.3	168.2 ± 8.6
Body weight (kg)	62.1 ± 9.2	66.4 ± 10.1

Values are expressed as mean ± SD or as numbers of donors. Des group, desflurane group; sevo group, sevoflurane group; SD, standard deviation; M, male; F, female.

Table 2. Surgical and anesthetic data.

	Des group (n = 37)	Sevo group (n = 37)
TLV (ml)	1008.4 ± 215.9	1089.3 ± 174.0
GV (ml)	657.1 ± 148.5	703.8 ± 119.1
RLV ratio (%)	34.8 ± 6.7	35.3 ± 4.2
Sevo group (n = 37)		
Macrovesicular (%)	6.5 ± 3.7	7.0 ± 4.1
Microvesicular (%)	7.9 ± 4.8	10.2 ± 6.6
Surgical time (min)	366.0 ± 46.3	376.8 ± 50.7
Anesthetic time (min)	408.3 ± 50.4	417.1 ± 52.3
Anesthetic exposure (MAC-hour)	6.8 ± 0.8	6.9 ± 0.9
BIS values	35 ± 6	39 ± 8*
Administered crystalloid (ml)	2300.0 ± 555.0	2282.4 ± 586.4
Estimated blood loss (ml)	479.7 ± 268.6	423.5 ± 138.1
Urine output (ml)	306.8 ± 198.3	398.2 ± 280.4
Administered remifentanil (mg)	1.52 ± 0.68	1.77 ± 0.95
Postoperative hospital stay (days)	18 ± 7	17 ± 4

Values are expressed as mean ± standard deviation. Des group, desflurane group; sevo group, sevoflurane group; TLV, total liver volume; GV, graft volume; RLV ratio, remnant liver volume ratio; MAC, mean alveolar concentration; BIS values, bispectral index values. *$P < 0.05$ compared with Des group.

Table 3. Intraoperative hemodynamic variables.

	Des group (n = 37)			Sevo group (n = 37)		
	HR	MBP	PVP	HR	MBP	PVP
Prehepatectomy	77 ± 10	85 ± 13	8 ± 2	74 ± 7	84 ± 9	9 ± 3
Intrahepatectomy	78 ± 12	77 ± 9	6 ± 2	76 ± 9	77 ± 9	6 ± 2
Posthepatectomy	81 ± 11	79 ± 10	10 ± 3	77 ± 9	79 ± 9	9 ± 2

Values are expressed as mean ± SD. Des group, desflurane group; sevo group, sevoflurane group; HR, heart rate; MBP, mean blood pressure; PVP, peripheral venous pressure.

Three donors in each group required continuous infusion of nitroglycerine 0.5 μg/kg per min to maintain hemodynamic stability during the incision. BIS values showed sufficient depth of anesthesia in both groups but mean BIS value was significantly lower ($P = 0.023$) in the Des group. No intraoperative awareness was observed in any

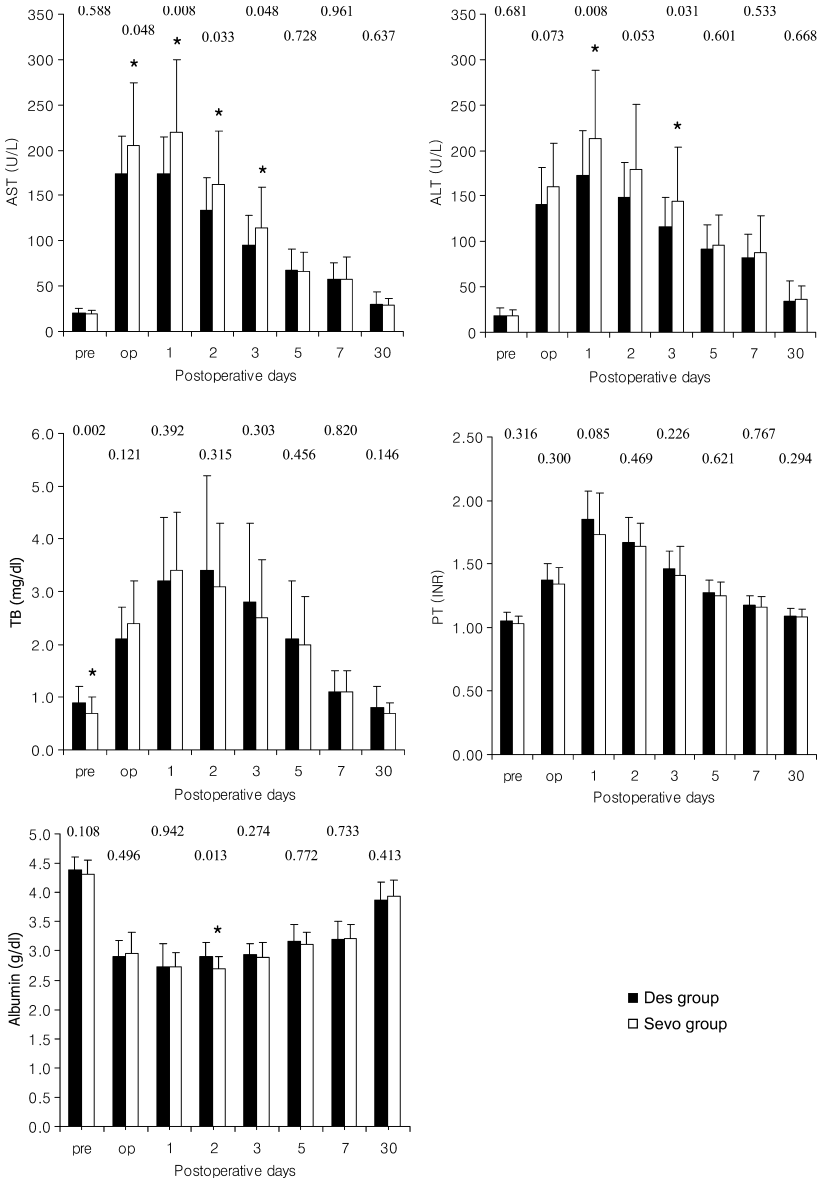

Figure 1 Serial changes in perioperative aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (TB), prothrombin time [PT(INR)], and albumin. Des group, desflurane group; sevo group, sevoflurane group. Values are expressed as mean ± SD. *$P < 0.05$ compared with Des group. (numbers in the figures indicate *P*-values.)

of the patients. Serial changes in the perioperative AST, ALT, TB, PT (INR), and albumin are shown in Fig. 1. Mean values of AST, ALT, TB, and PT (INR) reached a maximum within POD 2 and showed gradual reduction, thereafter, close to preoperative levels on POD 30. AST values were significantly elevated on the day of operation and POD 1, 2, and 3 in the sevo group when compared with the Des group. ALT values were significantly elevated on POD 1 and 3 in the sevo group. Albumin level was significantly lower on POD 2 in the sevo group. Serial changes in the perioperative BUN, Cr, BUN/Cr ratio, and estimated GFR are shown in Fig. 2. BUN, Cr, and BUN/Cr ratio remained decreased until POD 7 and showed increasing trend toward preoperative values from POD 7 to POD 30. The estimated GFR remained increased until POD 7 and decreased toward preoperative values on POD 30, and these values showed similar trends between the two groups. BUN level was significantly higher on POD 30, Cr level was significantly higher on POD 3 and 30 and estimated GFR was significantly lower on POD 3 and 30 in the sevo group. Perioperative Hb and PLT values were similar between the two groups.

Postoperative complications are listed in Table 4. There was no significant difference in number of donors who experienced complications between the two groups. One donor in the sevo group received of five units each of RBC and FFP until POD 2 because of the blood discharge from the JP drain (approximately 2300 cc until POD 2), but no surgery was required for bleeding control. There was no sustained hepatic dysfunction or hepatic failure,

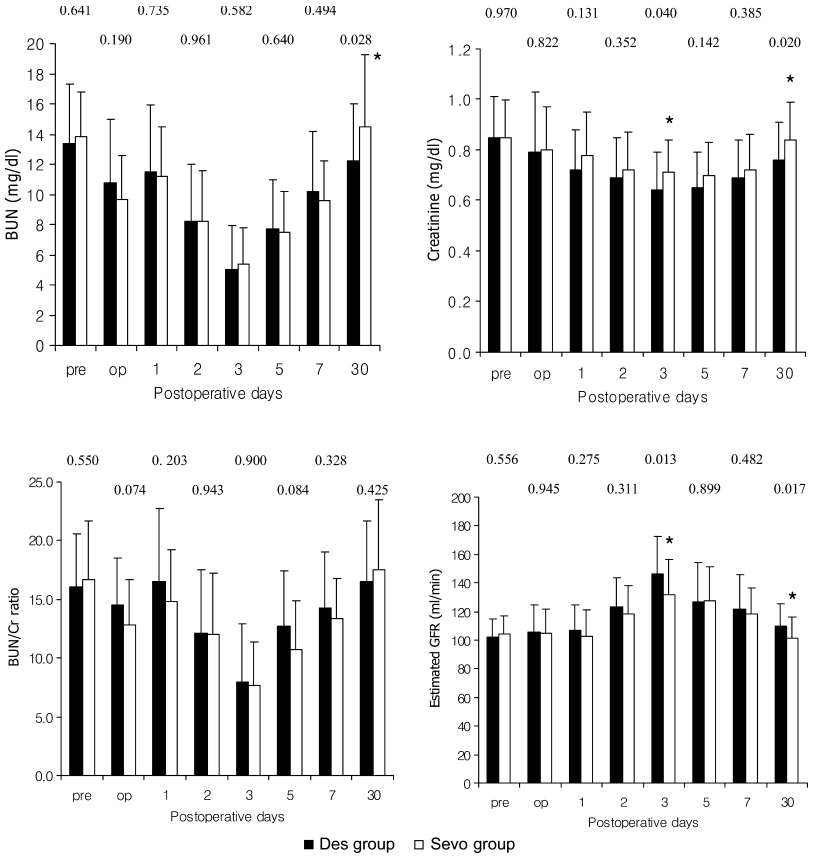

Figure 2 Serial changes in perioperative blood urea nitrogen (BUN), creatinine (Cr), BUN/Cr ratio and estimated glomerular filtration ratio (GFR). Des group, desflurane group; sevo group, sevoflurane group. Values are expressed as mean ± SD. *$P < 0.05$ compared with Des group. (numbers in the figures indicate *P*-values.)

Table 4. Postoperative complications.

Complications	Des group (n = 37) (%)	Sevo group (n = 37) (%)
Number of donors experienced complications	17 (46)	16 (43)
Overall complications	18 (49)	19 (51)
Major complications	1 (3)	1 (3)
Bile duct leakage	1 (3)	0
Postoperative bleeding requiring transfusion	0	1 (3)
Minor complications	17 (46)	18 (49)
Atelectasis	2 (5)	2 (5)
Pleural effusion	5 (14)	6 (17)
Wound infection or dehiscence	3 (8)	4 (11)
Wound hematoma or seroma	7 (19)	6 (17)

Values are expressed as number (percentage) of donors. Des group, desflurane group; sevo group, sevoflurane group.

renal failure, thromboembolism, sepsis, or death in our donors.

Discussion

In conclusion, sevoflurane induced greater alterations in functions based on hepatic and renal function tests after surgery than desflurane in living donors undergoing right hepatectomy.

The surgical technique for living donor operation has been standardized in recent years, therefore, the effect of surgical incursion on postoperative donor outcome may be considered similar in each group. However, the effect of anesthesia on living donors still requires further investigation owing to its various types and combinations of anesthetic regimens. In general, various inhalational anesthetics have been used during hepatobiliary surgeries including living-donor operation [8,9]. Most of the halogenated inhalational anesthetics have been suggested to induce hepatocellular injury in animals and humans to a variable degree and produce mild alterations in functions based on hepatic and renal function tests after surgery, although clear connection of the anesthetic itself is still ambiguous [16–21]. In this regard, there is a concern about the impact and probable clinical significance of inhalational anesthetics on hepatic functions in living donors. Therefore, in this study, we investigated two inhalational anesthetics with different degrees of metabolism, desflurane and sevoflurane, and their effects on postoperative hepatic and renal functions in living donors undergoing right hepatectomy.

The mechanisms of hepatic injury pertaining to inhalational anesthetics include decreased hepatic blood flow [22–24] and biotransformation of toxic metabolites [25]. It is generally accepted that all the inhalational anesthetics alter hepatic blood flow and oxygenation that may lead to changes in hepatocellular functions [22–24]. The decrease in total hepatic blood flow (THBF) is primarily because of decreased cardiac output and imposes various compromising effects on hepatic oxygen supply [22]. Sevoflurane, like isoflurane, preserved THBF at up to 1 MAC, but THBF was reduced in tandem with increased MAC [23]. However, desflurane is shown to better preserve THBF than halothane or isoflurane in animal studies [24]. To our knowledge, no study has been performed on the comparison of THBF between desflurane and sevoflurane, and further studies (either animal or clinical) are warranted to determine the effects of these inhalational anesthetics on THBF, and subsequently, on postoperative hepatic functions. All inhalational anesthetics undergo biotransformation and the possibility for organ toxicity associated with the metabolites is a concern with each and every inhalational anesthetic agent. The degree of biotransformation of inhalational anesthetics is measured by the serum and urinary concentrations of fluoride, and fluoride has been implicated in organ toxicity after some inhalational anesthesia [25]. Among the currently available inhalational anesthetics, desflurane is reported to be highly stable and undergo significantly less biotransformation than other halogenated inhalational anesthetics [26]. In contrast, the peak plasma concentration of fluoride after sevoflurane anesthesia is approximately 50 times higher than those after desflurane [27,28]. Numerous studies have demonstrated that sevoflurane does not adversely affect hepatic function in adult surgical patients [17,18]. However, mild postoperative increases in liver function tests (e.g. bilirubin and transaminases) after sevoflurane anesthesia [16], especially in morbidly obese patients [29], and several case reports of associated hepatotoxicity [30,31] raised the safety issue in patients with underlying disease. In this regard, the safety of sevoflurane in healthy liver donors must be carefully evaluated because of the lengthy duration (approximately 7 h in our study) and extensive hepatic resections in donor right hepatectomy may increase the likelihood for organ toxicity, and the alterations in biochemical markers to a degree of injury that may be considered unacceptable to some clinicians.

In clinical practice, the elevations in AST and ALT values are considered as the 'gold standard' for anesthetic-related hepatic toxicity. In this study, although the comparable TLV, GV and RLV ratio in each group may be viewed as an indirect reflection of comparable degree of surgical incursion, the significant elevations in postoperative AST on the day of operation and POD 1, 2, and 3 and ALT on POD 1 and 3 in the sevo group when compared with the ones in the Des group imply greater extent of hepatocyte injury in the sevo group. Although liver enzyme elevations indicated structural damages to hepatocytes, hepatic synthetic functions, best measured by TB, PT (INR), and albumin showed similar trends between the two groups, except for significant decrease in albumin on POD 2 in the sevo group. The careful evaluation of these results implies that there might have been a greater degree of liver damage after anesthesia with sevoflurane than with desflurane when anesthetic exposure was almost equal (6.9 vs. 6.8 MAC-h respectively) between the two groups. This hypothesis may be supported, in part, by the different degrees of THBF and the metabolism between the two anesthetics where sevoflurane is reported to undergo intermediate metabolism (1–5%) which is significantly higher (approximately 100 times greater) than the ones of desflurane (0.02%) in humans [32]. In addition, sevoflurane is reported to produce extra metabolite, Compound A [fluoromethyl-2,2-difluoro-1-(difluoromethyl) ether], produced via chemical reactions with CO_2 absorbents [33,34]. Most of the studies on Compound A have highlighted its effect on kidney, but several studies have suggested that Compound A might also be hepatotoxic as shown by transient increase in postoperative liver function tests [17,21]. Therefore, although desflurane and sevoflurane show similar pharmacokinetic properties [35,36], the desflurane may be viewed more stable than sevoflurane in that it resists degradation by standard carbon dioxide absorbents [37] and undergo minimal metabolism by the liver [28]. These unique properties of desflurane might have contributed to better postoperative hepatic function test results in the Des group.

In our study, the renal function test results including BUN, Cr, BUN/Cr ratio, and estimated GFR were preserved and showed similar postoperative trends in both groups. Although, postoperative Cr was consistently higher in the sevo group with significantly higher values on POD 3 and 30, these values were within normal ranges. Moreover, estimated GFR level was generally lower in the sevo group with significantly lower values on POD 3 and 30. In animal studies, a link between Compound A and renal injury has been demonstrated [34], but it is still unresolved in clinical settings [18,20,21]. In addition, inorganic fluoride from anesthetic metabolism raised concern for nephrotoxicity because some correlation was observed between its peak concentration and the degree of renal injury [38]. The presumed threshold for inorganic fluoride-related nephrotoxicity is 50 μmol/l and a number of patients undergoing sevoflurane anesthesia showed fluoride concentrations exceeding 50 μmol/l [39].

However, anesthetic factor alone can not be ascribed as the main contributing factor for the statistically significant alterations in some of liver and renal functions, because there are other important factors such as patient- and surgery-related factors pertaining to the living-donor right hepatectomy. Furthermore, in our study, the duration of hospital stay and the incidence and severity of complications were similar between the two groups, and thus, the clinical implication of the altered biochemical findings requires further investigation.

Clinically, major abdominal surgeries usually require more than 1 MAC to ensure hemodynamic stability when inhalational anesthetic is used alone. In this study, as 1 MAC of each inhalational anesthetic may not provide adequate control of intraoperative hemodynamics, remifentanil was co-administered as an adjuvant to inhalational anesthetics, and the total amount of remifentanil administration was similar between the two groups. In addition, intrathecal morphine given before the induction of anesthesia might have provided some analgesic effect intraoperatively [10]. Therefore, the MAC-sparing effect of remifentanil and intrathecal morphine made it possible to proceed with the donor right hepatectomy with only 1 MAC of inhalational anesthetics. In addition, intraoperative hemodynamic parameters including HR, mean BP, and PVP values during prehepatectomy, intrahepatectomy, and posthepatectomy stages were similar between the two groups, and especially, the comparable PVP values after right lobectomy suggests that outflow and congestion of the residual liver were similar, and thus, similar degree of its influence on LFTs between the two groups. Noticeably, in this study, the ALT and AST values until POD 2 in the Des group were lower than the ones of our previous study, desflurane vs. propofol-based TIVA [10]. The AST and ALT values at POD 0, 1, and 2 of previous study versus this study are: 199 ± 55 vs. 174 ± 42 ($P = 0.031$), 198 ± 53 vs. 174 ± 41 ($P = 0.038$), 140 ± 41 vs. 133 ± 37 ($P = 0.49$) and 168 ± 51 vs. 141 ± 40 ($P = 0.021$), 203 ± 56 vs. 173 ± 49 ($P = 0.018$), and 168 ± 53 vs. 148 ± 39 ($P = 0.068$) respectively. This may be explained by the different anesthetic methods used in the two studies where in our previous study, anesthesia was maintained with only desflurane and thus, various degrees of MAC (often higher than 1 MAC) were employed to maintain intraoperative BP and HR within 20% of preoperative values. In contrast, in this study, desflurane was fixed at 1 MAC and anesthesia was supplemented with remifentanil and intrathecal morphine. As potential organ toxicity of inhalational anesthetics is dependent on the dose and duration of exposure, the higher desflurane concentration in our previous study might have contributed to greater derangements in hepatic function tests. In addition, the results of this study might have been influenced by an interaction of the regional and the general anesthetics. Based on these findings, it may be deduced that a multimodal anesthetic approach using minimal inhalational anesthetic dose with intravenous opioid and regional analgesia may have more favorable effect on hepatic function in the living donors.

The limitations of our study were that we measured common parameters of hepatic and renal functions. More specific markers for hepatic injury like glutamate dehydrogenase or functional tests like the indocyanine green clearance and the more accurate biomarkers for the nephrotoxicity such as urinary glucose, albumin, α- and π-glutathione S-transferase (GST) might have elucidated further the contributing effect of each anesthetic on postoperative hepatic and renal functions. In addition, further in-depth studies to determine the effects of inhalational anesthetics on liver at histological levels by performing liver biopsies or at molecular levels by measuring oxidative stress or nitric oxide synthase expression might be needed. Second, the sample size of this study was based on our preliminary study which the primary endpoint was a change in ALT on POD 1. Thus the study was powered only for this hepatic parameter and not for renal parameters. Therefore, our results may be considered more of a type of a pilot study not powered for renal outcomes and it may be warranted to validate the results of our study by conducting a study with larger sample size. Also, at 1 MAC, mean BIS values were below 40 in each group which may be considered as a quite deep anesthesia, but our study design was to assess postoperative hepatic and renal functions at equivalent dose of each inhalational anesthetic and not adjust the anesthetic dose based on the BIS values.

In conclusion, the results of our study showed better postoperative hepatic and renal function test with desflurane than sevoflurane at equivalent dose of 1 MAC in living donors undergoing right hepatectomy, but further study is required to evaluate clinical importance.

Authorship

JSK: designed research, wrote the paper. MSG: performed research. SJC: performed research. MY: collected data. MJK: analysed data. JYL: analysed data. GSK: designed research, wrote the paper. CHDK: performed statistical analysis. JWJ: collected data.

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References

1. de Villa VH, Lo CM, Chen CL. Ethics and rationale of living-donor liver transplantation in Asia. *Transplantation* 2003; **75**: S2.
2. Pomfret EA. Early and late complications in the right-lobe adult living donor. *Liver Transpl* 2003; **9**: S45.
3. Trotter JF, Adam R, Lo CM, Kenison J. Documented deaths of hepatic lobe donors for living donor liver transplantation. *Liver Transpl* 2006; **12**: 1485.
4. Akabayashi A, Slingsby BT, Fujita M. The first donor death after living-related liver transplantation in Japan. *Transplantation* 2004; **77**: 634.
5. Schumann R, Zabala L, Angelis M, Bonney I, Tighiouart H, Carr DB. Altered hematologic profiles following donor right hepatectomy and implications for perioperative analgesic management. *Liver Transpl* 2004; **10**: 363.
6. Ko JS, Gwak MS, Choi SJ, *et al.* The effects of desflurane and propofol-remifentanil on postoperative hepatic and renal functions after right hepatectomy in liver donors. *Liver Transpl* 2008; **14**: 1150.
7. Beck-Schimmer B, Breitenstein S, Urech S, *et al.* A randomized controlled trial on pharmacological preconditioning in liver surgery using a volatile anesthetic. *Ann Surg* 2008; **248**: 909.
8. Chhibber A, Dziak J, Kolano J, Norton JR, Lustik S. Anesthesia care for adult live donor hepatectomy: our experiences with 100 cases. *Liver Transpl* 2007; **13**: 537.
9. Siniscalchi A, Begliomini B, De Pietri L, *et al.* Increased prothrombin time and platelet counts in living donor right hepatectomy: implications for epidural anesthesia. *Liver Transpl* 2004; **10**: 1144.
10. Ko JS, Choi SJ, Gwak MS, *et al.* Intrathecal morphine combined with intravenous patient-controlled analgesia is an effective and safe method for immediate postoperative pain control in live liver donors. *Liver Transpl* 2009; **15**: 381.
11. Punjasawadwong Y, Boonjeungmonkol N, Phongchiewboon A. Bispectral index for improving anaesthetic delivery and postoperative recovery. *Cochrane Database Syst Rev* 2007; **17**: CD003843.
12. Choi SJ, Gwak MS, Ko JS, *et al.* Can peripheral venous pressure be an alternative to central venous pressure during right hepatectomy in living donors? *Liver Transpl* 2007; **13**: 1414.
13. Chung F. Discharge criteria – a new trend. *Can J Anaesth* 1995; **42**: 1056.
14. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of diet in Renal Disease Study Group. *Ann Intern Med* 1999; **130**: 461.
15. Pollard RJ, Coyle JP, Gilbert RL, Beck JE. Intraoperative awareness in a regional medical system: a review of 3 years' data. *Anesthesiology* 2007; **106**: 269.
16. Bito H, Ikeda K. Renal and hepatic function in surgical patients after low-flow sevoflurane or isoflurane anesthesia. *Anesth Analg* 1996; **82**: 173.
17. Obata R, Bito H, Ohmura M, *et al.* The effects of prolonged low-flow sevoflurane anesthesia on renal and hepatic function. *Anesth Analg* 2000; **91**: 1262.
18. Ebert TJ, Frink EJ Jr, Kharasch ED. Absence of biochemical evidence for renal and hepatic dysfunction after 8 hours of 1.25 minimum alveolar concentration sevoflurane anesthesia in volunteers. *Anesthesiology* 1998; **88**: 601.
19. Ebert TJ, Messana LD, Uhrich TD, Staacke TS. Absence of renal and hepatic toxicity after four hours of 1.25 minimum alveolar anesthetic concentration sevoflurane anesthesia in volunteers. *Anesth Analg* 1998; **86**: 662.
20. Eger EI II, Gong D, Koblin DD, *et al.* Dose-related biochemical markers of renal injury after sevoflurane versus desflurane anesthesia in volunteers. *Anesth Analg* 1997; **85**: 1154.
21. Eger EI II, Koblin DD, Bowland T, *et al.* Nephrotoxicity of sevoflurane versus desflurane anesthesia in volunteers. *Anesth Analg* 1997; **84**: 160.
22. Gelman S. General anesthesia and hepatic circulation. *Can J Physiol Pharmacol* 1987; **65**: 1762.
23. Frink EJ Jr, Morgan SE, Coetzee A, Conzen PF, Brown BR Jr. The effects of sevoflurane, halothane, enflurane, and isoflurane on hepatic blood flow and oxygenation in chronically instrumented greyhound dogs. *Anesthesiology* 1992; **76**: 85.
24. Hartman JC, Pagel PS, Proctor LT, Kampine JP, Schmeling WT, Warltier DC. Influence of desflurane, isoflurane and halothane on regional tissue perfusion in dogs. *Can J Anaesth* 1992; **39**: 877.
25. Mazze RI, Calverley RK, Smith NT. Inorganic fluoride nephrotoxicity: prolonged enflurane and halothane anesthesia in volunteers. *Anesthesiology* 1977; **46**: 265.
26. Jones RM, Koblin DD, Cashman JN, Eger EI II, Johnson BH, Damask MC. Biotransformation and hepato-renal function in volunteers after exposure to desflurane (I-653). *Br J Anaesth* 1990; **64**: 482.
27. Kharasch ED, Armstrong AS, Gunn K, Artru A, Cox K, Karol MD. Clinical sevoflurane metabolism and disposition. II. The role of cytochrome P450 2E1 in fluoride and hexafluoroisopropanol formation. *Anesthesiology* 1995; **82**: 1379.
28. Sutton TS, Koblin DD, Gruenke LD, *et al.* Fluoride metabolites after prolonged exposure of volunteers and patients to desflurane. *Anesth Analg* 1991; **73**: 180.
29. Al-Ghanem SM, Massad IM, Al-Barazangi B, Al-Mustafa M, Daoud FS, Abu-Ali H. Effects of sevoflurane on postoperative liver functions in morbidly obese as compared to the non-obese patients. *Middle East J Anesthesiol* 2009; **20**: 207.
30. Lehmann A, Neher M, Kiessling AH, Isgro F, Koloska A, Boldt J. Case report: fatal hepatic failure after aortic valve

replacement and sevoflurane exposure. *Can J Anaesth* 2007; **54**: 917.
31. Turillazzi E, D'Errico S, Neri M, Riezzo I, Fineschi V. A fatal case of fulminant hepatic necrosis following sevoflurane anesthesia. *Toxicol Pathol* 2007; **35**: 840.
32. Reichle FM, Conzen PF. Halogenated inhalational anaesthetics. *Best Pract Res Clin Anaesthesiol* 2003; **17**: 29.
33. Holaday DA, Smith FR. Clinical characteristics and biotransformation of sevoflurane in healthy human volunteers. *Anesthesiology* 1981; **54**: 100.
34. Keller KA, Callan C, Prokocimer P, *et al.* Inhalation toxicity study of a haloalkene degradant of sevoflurane, Compound A (PIFE), in Sprague-Dawley rats. *Anesthesiology* 1995; **83**: 1220.
35. Yasuda N, Lockhart SH, Eger EI 2nd, *et al.* Kinetics of desflurane, isoflurane, and halothane in humans. *Anesthesiology* 1991; **74**: 489.
36. Yasuda N, Lockhart SH, Eger EI 2nd, *et al.* Comparison of kinetics of sevoflurane and isoflurane in humans. *Anesth Analg* 1991; **72**: 316.
37. Eger EI 3rd. Stability of I-653 in soda lime. *Anesth Analg* 1987; **66**: 983.
38. Cousins MJ, Mazze RI. Methoxyflurane nephrotoxicity. A study of dose response in man. *JAMA* 1973; **225**: 1611.
39. Bito H, Ikeda K. Plasma inorganic fluoride and intracircuit degradation product concentrations in long-duration, low-flow sevoflurane anesthesia. *Anesth Analg* 1994; **79**: 946.

