Original Article

Effects of propofol-based total intravenous anesthesia versus desflurane anesthesia on natural killer cell cytotoxicity after hepatocellular carcinoma resection

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Abstract

Background and Aims: Inhalation anesthesia suppresses the immune system and stimulates the growth of tumor cells, contrary to intravenous anesthesia. However, no consensus exists on which anesthetic technique is better for preventing cancer recurrence. Therefore, this study compared the effects of two different anesthetic techniques on natural killer cell cytotoxicity (NKCC) in hepatocellular carcinoma (HCC) patients undergoing open hepatic resection.

Material and Methods: Patients diagnosed with nonmetastatic HCC were scheduled for hepatic resection and randomly assigned to receive either propofol- or desflurane-based anesthesia. The primary outcome was pre- and postoperative NKCC assay. Cytokine levels were assessed by measuring interleukin (IL)-2, IL-4, IL-6, IL-10, tumor necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ) levels, and the secondary outcome was postoperative cancer recurrence evaluated using diagnostic imaging scans for 2 years.

Results: Twenty-eight patients were analyzed, including 15 and 13 in the total intravenous anesthesia (TIVA) and inhalation (INH) groups, respectively. Two patients in the INH group were excluded due to non-HCC postoperative pathologic results. At 24 h, the postoperative change in NKCC between both groups showed no significant differences at a ratio of effector cell: target cell = 1:1, 5:1, and 10:1 (P = 0.345, 0.345, and 0.565, respectively). Also, there were no significant differences in IL-2, IL-4, IL-6, IL-10, TNF-α, and IFN-γ levels (P = 0.588, 0.182, 0.730, 0.076, 0.518, 0.533, respectively). Postoperative tumor recurrence occurred in five and six patients in the TIVA and INH groups, respectively.

Conclusion: NKCC did not differ significantly among HCC patients undergoing open hepatic resection under either propofol or desflurane anesthesia 24 h postoperatively.

Keywords: Anesthesia, desflurane, hepatocellular carcinoma, natural killer cells, propofol

Introduction

Liver cancer is the leading cause of cancer-related deaths worldwide, and approximately 75%–85% of primary liver cancers are hepatocellular carcinomas (HCCs). Hepatic resection is an effective treatment for nonmetastatic HCC. However, the recurrence rate following the surgical treatment is significantly high, which is 50% within 2 years and 90% within 5 years postoperatively.[1,2]

Natural killer (NK) cells play an important role in nonspecific antitumor immunity, including in HCC, by producing

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cytokines against cancer. Therefore, impaired NK cell function is associated with disease progression.[3,4]

Although previous studies have inconsistently suggested that inhalation (INH) anesthetics suppress the immune system and stimulate the growth of tumor cells, while intravenous anesthetics are less likely to affect the immune system and might also inhibit the growth of cancer cells, there is still no consensus on which anesthetic technique is better for preventing cancer recurrence.[5-8]

This prospective, randomized study aimed to compare the effects of two different anesthetic techniques on NK cell cytotoxicity (NKCC) in patients with HCC undergoing hepatic resection. We hypothesized that propofol-based anesthesia would result in greater NKCC than that associated with desflurane-based anesthesia during the postoperative period in hepatic resection surgery. The primary outcome was NKCC, measured in an NKCC assay preoperatively and 24 h postoperatively. The secondary outcome was cytokine levels assessed by measuring interleukin (IL)-2, IL-4, IL-6, IL-10, tumor necrosis factor-alpha (TNF-α), and interferon gamma (IFN-γ) levels, as well as postoperative cancer recurrence evaluated using diagnostic imaging scans for 2 years.

Material and Methods

This was a randomized controlled trial conducted at King Chulalongkorn Memorial Hospital, Bangkok, Thailand from October 2019 to September 2022, followed by a 2-year observational period for HCC recurrence (total: 3 years). The study was conducted in accordance with the Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines [Figure 1]. According to Cho *et al.*,[6] NKCC increased from 15.1% to 20.1% among patients undergoing breast cancer surgery who received propofol alone, whereas it decreased from 19.5% to 17.0% in the sevoflurane INH anesthetic group. Therefore, a sample size of 13 patients in each group would be required to compare the mean values between the two independent populations at a significance of $P < 0.05$, with 95% confidence intervals. We factored in a 10% dropout rate and enrolled 15 patients in each group.

Thus, 30 patients diagnosed with nonmetastatic HCC and aged 18 – 80 years, with American Society of Anesthesiologists (ASA) physical status I – III and scheduled for elective hepatic resection, were enrolled. The exclusion criteria were patient refusal to participate; diagnosis of recurrent HCC before participation in the research; known allergy to medications used in the research protocol; severe systemic diseases, such as cardiovascular, respiratory, or endocrine system conditions; chronic use of anxiolytics and/or opioids; addiction to alcohol or drug abuse; immunocompromised or receiving immunosuppressants < 6 months preoperatively; and postoperative lesion histopathology results excluding HCC as the diagnosis.

This study was approved by the Institutional Review Board (IRB) of the Faculty of Medicine, Chulalongkorn university (IRB No. 266/62). The trial was registered with the Thai Clinical Trials Registry (TCTR) (TCTR20210218001) issued on February 18, 2021. Patients were allocated randomly to the propofol or desflurane anesthesia group using a secure web-based randomization system (http://www.randomizer.org/, Research Randomizer, PA, USA) according to a table

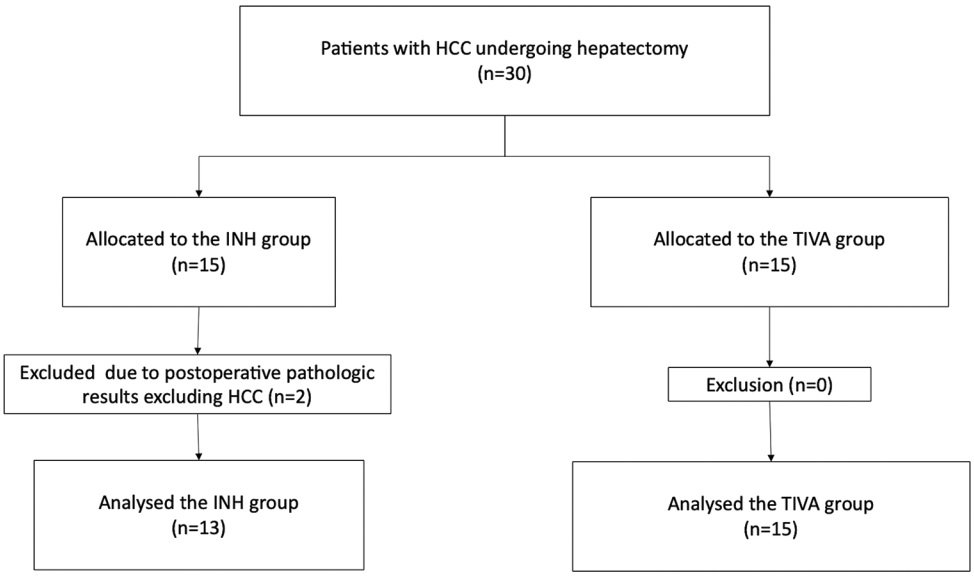

Figure 1: CONSORT diagram of the study. HCC = hepatocellular carcinoma, INH = inhalation, TIVA = total intravenous anesthesia

of random numbers. Written informed consent was obtained 1 day preoperatively.

On surgical day, standard ASA monitoring and end-tidal carbon dioxide ($ETCO_2$) monitoring were done, nasopharyngeal temperature was measured, and bispectral index (BIS) with four electrodes were applied before anesthetic induction. Also, preoperative blood samples were collected for analyzing NKCC and other cytokine levels. An epidural catheter was placed at thoracic T6 or T8 level, and 1.5% xylocaine with adrenaline (1:200,000) 3 mL was administered as a test dose; then, the catheter tip position was confirmed with epidural arterial pressure waveforms. In the propofol (total intravenous anesthesia [TIVA]) group, the plasma target regimen of the Schnider model propofol target-controlled infusion was administered during anesthetic induction and maintenance.[9] In the desflurane (INH) group, induction was performed with 4%−5% sevoflurane and maintained with desflurane. The concentrations of propofol and desflurane were titrated to maintain BIS in the range of 40–60.

All patients were intubated with cisatracurium 0.2 mg/kg, and ventilation was controlled with a tidal volume of 8 mL/kg, respiratory rate of 10 − 12 beats/min, and $ETCO_2$ of 35 − 40 mmHg. Invasive blood pressure monitoring via radial arterial cannulation using a 20 G catheter was performed after anesthetic induction to closely monitor mean blood pressure maintained within 20% of the baseline values. During skin preparation, epidural injection with 3 − 5 mL of 1% xylocaine was administered, and 0.2% bupivacaine with fentanyl 2 μg/mL was titrated between 4 and 10 mL/h for continuous epidural anesthesia. A balanced salt solution of 2 − 4 mL/kg/h and fentanyl at a maximum of 4 μg/kg were administered throughout the surgery. Blood transfusion was performed when the hematocrit level was <25%.

Postoperative analgesia was provided as patient-controlled epidural analgesia (PCEA) with 0.1% bupivacaine and fentanyl 2 μg/mL. Initial PCEA settings were background infusion of 5 mL/h with a bolus of 5 mL, lockout interval of 15 min, and 4-h limit at 80 mL. In addition, blood samples were collected for analyzing NKCC and other cytokine levels 24 h postoperatively.

To measure NKCC by flow cytometry, blood samples were obtained before anesthetic induction and 24 h postoperatively. Whole blood was mixed with the same volume of 1X phosphate-buffered saline, and peripheral blood mononuclear cells (PBMCs) were isolated from peripheral blood by standard Ficoll separation using Ficoll-Paque Plus density gradient medium (GE Healthcare, Chicago, IL, USA). Finally, NK cells were isolated from PBMCs using an NK Cell Isolation Kit (Miltenyi, Bergisch Gladbach, Germany).

Cytotoxicity assay was performed by labeling K562 cells (targeted cell [T]; 2×10^4 cells/well) with 0.25 μM carboxyfluorescein succinimidyl ester (CFSE; BioLegend, San Diego, CA, USA) and culturing them together with NK cells (effector cell, E: targeted cell, T). They are then seeded in the well at a ratio of E: T = 0:1, 1:1, 5:1, and 10:1 and incubated for 4 h at 37°C in 5% CO_2. Dead cells were counterstained by propidium iodide. Finally, NKCC of effector cells was measured using flow cytometry, and the cytotoxicity percentage was calculated as follows:

% cytotoxicity = [(experimental cells – target spontaneous lysis cells)/(target maximum lysis cells – target spontaneous lysis cells)] ×100

The maximum target cell lysis was 100%, which should yield complete lysis of target cells. Cytokine levels were measured preoperatively and 24 h postoperatively. Blood serum was obtained, centrifuged at 3000 rpm for 5 min, and then stored at −20°C. Cytokine levels of IL-2, IL-4, IL-6, IL-10, TNF-α, and IFN-γ in the serum were measured using a commercial BD® Cytometric Bead Array (BD biosciences, Haryana, India) and analyzed by flow cytometry.

Patient data was collected. Baseline characteristics, including age, sex, weight, height, ASA classification status, underlying comorbidity, diagnosis, details of operation, size and location of the tumors, and use of antiviral medication, were recorded.

At the end of the surgery, the total volume of epidural infusion, amount of propofol or desflurane, amount of intravenous fentanyl, operative time, number and duration of the Pringle maneuver, volume of blood loss, volume of fluid replacement, use of blood product replacement, and use of vasopressors were recorded.

The NKCC and cytokine levels between the two groups before anesthetic induction and 24 h postoperatively were compared. Also, 24 h postoperative volume of PCEA consumption, pain numeric score at rest and in motion, and postoperative volume of fluid replacement were assessed.

The postoperative pathological results and early cancer recurrence within 2 years of the surgery were also recorded.

The primary aim was to compare the effects of the two anesthetic techniques on the immune function assessed by NKCC, measured preoperatively and at 24 h postoperatively. Also, the secondary outcome was cytokine levels, that is, the

levels of IL-2, IL-4, IL-6, IL-10, TNF-α, and IFN-γ, as well as postoperative cancer recurrence evaluated using diagnostic imaging scans for 2 years.

Categorical data (demographics and pre- and intraoperative characteristics of patients) are presented as frequency and percentage and compared between groups using Fisher's exact test. Continuous data with normal distribution are presented as mean and standard deviation and compared between groups using the *t*-test, while continuous data with non-normal distribution are presented as the median and interquartile range (IQR) and compared between groups using the Mann − Whitney U test. Immunologic data are presented as median, IQR, and range and compared *between* groups using the Mann − Whitney U test and *within* groups using the Wilcoxon signed-rank test. Postoperative data were described and compared using the same approaches as preoperative data. Statistical significance was set at $P < 0.05$. All statistical analyses were performed using Stata 14.0 (Stata Corp, College Station, TX, USA).

Results

This study enrolled 30 patients, of whom two were excluded due to postoperative pathologic results excluding HCC. Therefore, 13 and 15 patients in the INH and TIVA groups, respectively, were analyzed [Figure 1]. There were no significant differences in preoperative patient characteristics [Table 1], intraoperative values [Table 2], and 24-h postoperative values [Table 3].

At 24 h postoperatively, the changes in NKCC between the INH and TIVA groups showed no significant differences *between* groups at a ratio of 24-h postoperative E:T concentrations = 1:1, 5:1, 10:1 ($P = 0.345$, 0.345, and 0.565, respectively) [Table 4, Figure 2]. However, the results exhibited a downward trend in both groups postoperatively compared to the baseline [Figure 3].

There were statistically significant differences in NKCC *within* groups between preoperative (at 0 h) and 24-h postoperative values in the TIVA group at all ratios ($P = 0.006$, 0.008, and 0.017, respectively) and in the INH group at a ratio of 5:1 ($P = 0.028$) [Table 4].

Table 1: Preoperative characteristics

Characteristics	INH (*n*=13)	TIVA (*n*=15)	*P**
Age (years), median (range)	56 (51–67)	64 (58–68)	0.596
Sex, *n* (%)			0.686
Female	3 (23)	5 (33)	
Male	10 (77)	10 (67)	
Weight (kg), median (range)	60 (59–68)	62 (56–68)	0.678
Height (cm), median (range)	165 (161–168)	166 (157–170)	0.963
ASA physical status, *n* (%)			0.433
I	1 (7)	0 (0)	
II	7 (54)	11 (73)	
III	5 (38)	4 (27)	
Comorbidity			
HCV, *n* (%)	2 (15)	2 (13)	1.000
HBV, *n* (%)	6 (46)	8 (53)	1.000
Cirrhosis, *n* (%)	3 (23)	5 (33)	0.686
DM type, *n* (%)	2 (15)	5 (33)	0.396
Diagnosis of HCC, *n* (%)			0.852
Right	9 (69)	11 (73)	
Left	3 (23)	2 (13)	
Both sides	1 (8)	2 (13)	
Segmentectomy, *n* (%)			1.000
>3 segments	9 (69)	10 (67)	
≤3 segments	4 (31)	5 (33)	
Antiviral medication, *n* (%)			0.705
Nonantiviral	9 (69)	9 (60)	
Antiviral	4 (31)	6 (40)	

*ASA=American Society of Anesthesiologists, DM=Diabetes mellitus, HBV=Hepatitis B virus, HCC=Hepatocellular carcinoma, HCV=Hepatitis C virus, INH=Inhalation, TIVA=Total intravenous anesthesia. *Analyzed by the Fisher's exact test for comparison of proportions. Otherwise, the Mann−Whitney U test was used*

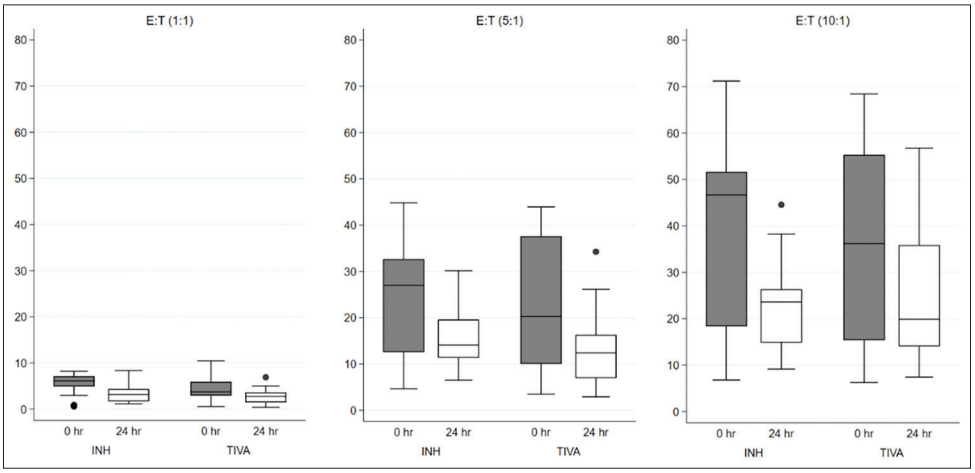

Figure 2: Natural killer cell cytotoxicity preoperatively and 24 h postoperatively. E = effector cell, INH = inhalation, T = targeted cell, TIVA = total intravenous anesthesia

Table 2: Intraoperative values

Intraoperative characteristics	INH (*n*=13)	TIVA (*n*=15)	*P**
0.2% Bupivacaine with fentanyl 2 μg/mL, median (IQR)	20 (17–36)	25 (20–36)	0.239
Propofol (mg/kg/min), median (IQR)	-	0.097 (0.077–0.148)	
Desflurane (mL/kg/min), median (IQR)	0.0047 (0.0038–0.0050)	-	
Intravenous fentanyl (μg)	100 (50–100)	75 (50–100)	0.866
Operation time (min)	330 (272–375)	301 (200–380)	0.549
Duration of Pringle maneuver (min), median (IQR)	55 (45–90)	60 (34–87)	0.590
The number of Pringle maneuver, median (IQR)	4 (3–6)	4 (2–6)	0.696
Total blood loss (mL), median (IQR)	600 (450–1100)	450 (200–1000)	0.204
Crystalloid (mL), median (IQR)	1800 (1500–2200)	1 500 (1300–2100)	0.332
Colloid (mL), median (IQR)	500 (500–1000)	500 (500–750)	0.660
Use of PRC, *n* (%)	2 (15)	3 (20)	1.000
Use of FFP, *n* (%)	2 (15)	2 (13)	1.000
Use of vasopressor, *n* (%)	10 (77)	13 (87)	0.639

*FFP=Fresh frozen plasma, INH=Inhalation, IQR=Interquartile range, PRC=Packed red cells, TIVA=Total intravenous anesthesia. *Analyzed by the Fisher's exact test for comparison of proportions. Otherwise, the Mann–Whitney U test*

Table 3: Postoperative values

Postoperative characteristics	INH (*n*=13)	TIVA (*n*=15)	*P**
0.1% bupivacaine + fentanyl 2 μg/kg (mL), median (IQR)	169 (107–237)	140 (116–195)	0.608
Pain, median (IQR)			
At rest	1 (1–5)	0 (0–3)	0.104
On motion	4 (2–7)	4 (2–5)	0.626
Crystalloid (mL), median (IQR)	2130 (1750–2480)	2000 (1710–2650)	0.982
Colloid (mL), median (IQR)	745 (345–1463)	250 (250–705)	0.325
Tumor size (mm), median (IQR; range)	14.3 (5.6–16.5; 2.6–18)	8.0 (6.5–15.5; 1.1–24)	0.433
Vascular invasion, *n* (%)	8 (61.5)	7 (47)	0.841
AFP high risk (score ≥3), *n* (%)	10 (77)	13 (87)	0.639
Recurrent rate in 2 years, *n* (%)	6 (46)	5 (33)	0.488

*AFP=Alpha fetoprotein, INH=Inhalation, IQR=Interquartile range, TIVA=Total intravenous anesthesia. *Analyzed by the Fisher's exact test for comparison of proportions. Otherwise, the Mann–Whitney U test was used*

Table 4: NK cell cytotoxicity

NK cell cytotoxicity	INH (*n*=13)	TIVA (*n*=15)	*P*
E:T (1:1)			
At 0 h	6.1 (4.9–7.1; 0.6–8.2)	3.7 (3.0–6.0; 0.6–10.5)	0.240
At 24 h	3.2 (1.7–4.4; 1.2–8.4)	2.8 (1.5–3.6; 0.4–6.9)	0.345
Difference (0–24 h)	2.43 (−1.08–4.46; −1.97–5.86)	2.11 (0.27–2.53; −2.03–6.96)	0.872
*P***	0.055	0.006	
E:T (5:1)			
At 0 h	26.9 (12.6–32.6; 4.6–44.8)	20.2 (10.0–37.6; 3.4–43.9)	0.695
At 24 h	14.1 (11.3–19.6; 6.5–30.2)	12.4 (6.9–16.3; 2.9–34.2)	0.345
Difference (0–24 h)	6.1 (0.8–14.8; −9.1–32.6)	9.7 (0.44–14.7; −8.0–25.2)	0.800
*P***	0.028	0.008	
E:T (10:1)			
At 0 h	46.7 (18.4–51.6; 6.8–71.2)	36.2 (15.3–55.3; 6.2–68.4)	0.872
At 24 h	23.6 (14.8–26.3; 9.1–44.5)	19.9 (14.0–35.9; 7.4–56.7)	0.565
Difference (0–24 h)	10.4 (−6.6–28.2; −13.8–44.9)	8.8 (0.74–19.7; −14.5–39.7)	0.662
*P***	0.064	0.017	

*E=Effector cell, INH=Inhalation, IQR=Interquartile range, NK=Natural killer, T=Targeted cell, TIVA=Total intravenous anesthesia. Values in cells are median (IQR; range). *Analyzed using the Mann–Whitney U test. **Comparisons change from 0 to 24 h within groups using the Wilcoxon signed-rank test*

Innate immune cells release proinflammatory cytokines (IL-6), anti-inflammatory cytokines (IL-10), and TNF-α (macrophage activation), whereas adaptive immune cells release cytokines that play roles in cytotoxic function (IL-2), humoral function (IL-4), and IFN-α (T-helper cell stimulation; the byproduct of NK cells). There were no differences in the

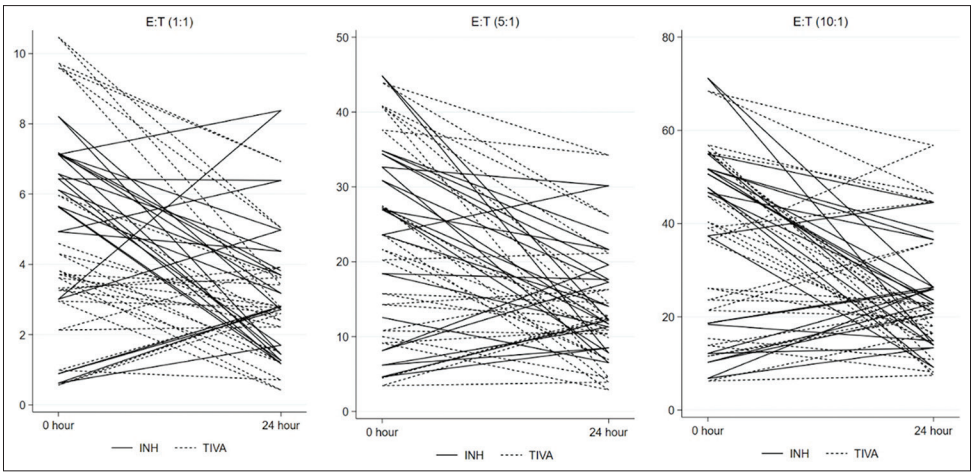

Figure 3: Individual visualization of E:T trend from 0 to 24 h. E = effector cell, INH = inhalation, T = targeted cell, TIVA = total intravenous anesthesia

levels of IL-2, IL-4, IL-6, IL-10, TNF-α, and IFN-γ *between* groups at 24 h postoperatively ($P = 0.588$, 0.182, 0.730, 0.076, 0.518, and 0.533, respectively).

However, compared *within* groups between preoperative and 24-h postoperative values, this study demonstrated that IL-6 and IL-10 levels in both groups were significantly elevated 24 h postoperatively ($P < 0.05$). In contrast, IL-2, IL-4, TNF-α, and IFN-γ levels were not significantly different compared to their baseline values [Table 5].

Six (46%) and five (35%) patients in the INH and TIVA groups, respectively, were diagnosed with recurrent HCC within 2 years postoperatively. However, there was no significant difference in the recurrence rate of HCC between the two groups ($P = 0.689$).

Table 5: Cytokine levels

Cytokine	INH (*n*=13)	TIVA (*n*=15)	*P**
IL-2, median (IQR)			
At 0 h	0.22 (0–6.95)	0.87 (0–2.29)	0.621
At 24 h	0.06 (0–7.22)	0.56 (0–2.32)	0.588
*P**	0.882	0.206	
IL-4, median (IQR)			
At 0 h	1.85 (0–7.16)	1.25 (0.12–2.18)	0.944
At 24 h	0.69 (0–6.91)	1.51 (0–57.9)	0.182
*P**	0.613	0.292	
IL-6, median (IQR)			
At 0 h	5.61 (0.24–9.93)	5.09 (1.57–15.3)	0.447
At 24 h	272 (144–432)	177 (121–426)	0.730
*P**	0.0015	0.0007	
IL-10, median (IQR)			
At 0 h	1.49 (0.68–7.03)	1.55 (0.96–3.71)	0.872
At 24 h	12.1 (7.24–20.1)	6.38 (2.51–15.3)	0.076
*P**	0.0015	0.0010	
TNF-α, median (IQR)			
At 0 h	0.37 (0–5.91)	0.96 (0.64–1.61)	0.460
At 24 h	1.16 (0.51–5.74)	0.91 (0.48–2.03)	0.518
*P**	0.124	0.650	
IFN-γ, median (IQR)			
At 0 h	1.63 (0.24–9.34)	0.76 (0.27–9.34)	0.321
At 24 h	0.99 (0.07–8.09)	0.92 (0–2.89)	0.533
*P***	0.056	0.977	

*IFN-γ=Interferon gamma, IL=Interleukin, INH=Inhalation, IQR=Interquartile range, TIVA=Total intravenous anesthesia, TNF-α=Tumor necrotic factor-alpha. *Analyzed using the Mann–Whitney U test. **Comparisons change from 0 to 24 h within groups using the Wilcoxon signed-rank test*

Discussion

This study revealed no significant difference in NKCC between patients with HCC undergoing hepatic resection in the INH and TIVA groups at 24 h postoperatively. Interestingly, both groups had a significant decrease in NKCC postoperatively within 24 h compared to their baseline values.

There was a strong correlation between the number of infiltrating and $CD56^+$ NK cells and HCC cell apoptosis, as well as patient survival. A study regarding NK cell-based immunotherapy has demonstrated impaired cytotoxic ability, IFN-γ production, and NK cell number, especially $CD56^+$ $CD16^+$ NK cells in HCC patients.[10] This implied that NK cells play a major role in eliminating HCC cells.[11,12] Regarding anesthetics, their effect on human immune function, especially NKCC, has been controversial over the decades. Anesthetic agents have exhibited different effects on NKCC in animal and human studies. Propofol preserved NKCC and cytotoxic T-lymphocyte activity and suppressed tumor growth.[13,14] Also, propofol has cyclooxygenase-2 inhibiting activity, reducing the production of prostaglandin E_2, a mediator of pain and inflammation that inhibits NKCC.[15] A recent study reported increased NKCC in the propofol–ketorolac group, whereas NKCC was inhibited in the sevoflurane–fentanyl group.[6] In addition, an *in vitro* study demonstrated that propofol can promote NKCC.[16] However,

the present study demonstrated no difference in NKCC between the different types of anesthetics in patients with HCC undergoing hepatic resection. Consequently, we support the idea that anesthetics neither suppress nor affect NKCC more than others.

Previous studies related to NKCC were normally conducted on less invasive surgeries, such as breast cancer surgery.[6,7,17] The present study was conducted on open hepatic resection for two main reasons. First, open hepatic resection is an extensive major surgery that stimulates massive immunity and inflammatory responses, including NKCC. Consequently, the effects of anesthetics on NKCC were reasonably expected to be detected in such an operation. Second, hepatic resection itself may lead to hematologic tumor spreading due to intraoperative tumor manipulation, and the recurrence rate of HCC after surgical resection is approximately 10% per year and reaches 50% after 2 years, which is relatively high compared to other cancers.[18,19] Therefore, the present study aimed to determine the anesthetic technique that preserves NKCC during the surgery and thus compare the recurrence rate of HCC between groups as the secondary outcome.

Cytokines are a critical part of the antitumor response of NKCC. For instance, IL-2 and IL-10 enhance NK cell function, while IL-4 and IL-6 have the opposite effect[20,21] and INF-γ and TNF-α are secreted by NK cells responding to tumor cells.[22] A previous *in vivo* study demonstrated that intravenous anesthetics, especially propofol, suppress immune cells less than inhalation anesthetics do, including sevoflurane and desflurane.[23] Herein, we assessed various cytokine levels to assess the association of changes in NKCC with cytokine levels postoperatively. Our study demonstrated no significant differences in all cytokine levels between groups. However, there was a significant increase in IL-6 and IL-10 levels compared to the baseline values within the INH and TIVA groups, but there was no difference in other cytokine levels.

In a previous study, propofol anesthesia for colon cancer surgery was associated with a lower incidence of local recurrence and distant metastasis than that associated with desflurane anesthesia.[24] The rate of cancer recurrence in our study is comparable to that in the previous study; however, there was no difference between the two groups.[1,2]

This study had limitations. First, previous studies collected blood samples and analyzed NKCC three times at 6–24 h intervals to show the trend of NKCC changes.[25,26] We analyzed NKCC at 24 h postoperatively because previous studies indicated that NKCC was most suppressed at 24 h postoperatively.[17] Second, attending anesthesiologists could not be blinded to allocation due to the study design. However, the laboratory staff who analyzed the laboratory results were completely unaware of the assignment of the interventions. Finally, postoperative pain and several anesthetic drugs used in this study, including opioids and local anesthetics, may affect NKCC and are considered potential confounders.[8,27,28] Therefore, we demonstrated that both groups received similar amounts of these drugs and were adequately controlled for postoperative pain.

Conclusion

There was no significant difference in NKCC and the rate of cancer recurrence in patients with HCC undergoing open hepatic resection under either propofol or desflurane anesthesia at 24 h postoperatively. However, there was a significant decrease in NKCC in both groups postoperatively.

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Data availability

The data that support the findings of this study are available from the corresponding author (P. S.) upon reasonable request.

Patient consent

Informed consent was obtained from all participants in this study.

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Conflicts of interest

There are no conflicts of interest.

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