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Original Article

Effect of different anaesthesia methods on perioperative cellular immune function and long-term outcome in patients undergoing radical resection of esophageal cancer: a prospective cohort study

Xuhui Cong[1], Zhoufeng Huang[2], Liyuan Zhang[1], Mingyang Sun[1], Enqiang Chang[1], Wei Zhang[1], Jiaqiang Zhang[1]

[1]Department of Anesthesiology, Zhengzhou University People's Hospital and Henan Provincial People's Hospital, Zhengzhou, Henan, P. R. China; [2]Laboratory Medicine, Zhengzhou University People's Hospital and Henan Provincial People's Hospital, Zhengzhou, Henan, P. R. China

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Abstract: To analyze the effects of different anaesthetic methods on perioperative cellular immunity and long-term outcome in patients who undergo esophageal cancer surgery. Participants: A total of 120 patients with esophageal cancer admitted to Zhengzhou University People's Hospital from January 2016 to January 2017 were recruited and randomly divided into a GA group (general anaesthesia, n = 40), a PG group (paravertebral nerve block with general anaesthesia, n = 40) and an EG group (epidural anaesthesia with general anaesthesia, n = 40). Methods: Self-rating anxiety scale and visual analogue scale scores were adopted to compare postoperative anxiety and the degree of pain of patients in the three groups. In addition, the adverse reactions of patients in the three groups were compared. The levels of interleukin-6 (IL-6), IL-4, tumor necrosis factor-α (TNF-α), interferon-γ (IFN-γ), and the survival of T-cell subsets (CD3+, CD4+, CD8+, CD4+/CD8+) before operation, at the end of operation, and on postoperative day (POD) 1 and POD 2 were measured by either ELISA or flow cytometry. Results: In the PG and EG group, the VAS scores were lower, and fewer opioids and vasoactive agents were used than in the GA group. In both the EG and PG groups, higher CD3+ and CD4+ cell survival and lower levels of Cor, IL-4, and IL-6 were identified at the end of or after the surgery than in the GA group. Moreover, the postoperative survival curves of the PG and EG groups were better than that of the GA group. Conclusions: The combination of paravertebral nerve block or epidural anaesthesia and general anaesthesia may improve perioperative immune function and long-term outcome in patients who undergo esophageal cancer surgery.

Keywords: Cellular immunity, cytokinesis, epidural block, esophageal cancer, long-term follow-up, paravertebral block

Introduction

Esophageal cancer (EC) is the sixth leading cause of cancer-related death worldwide due to its high malignant potential and poor prognosis [1]. Surgery is often performed to achieve locoregional control in EC patients; it offers the best chance to cure patients with localized terminal illness. Surgical stress, anesthetic agents, hypotension and other factors can reduce the cellular immune function of cancer patients during the perioperative period [2]. Perioperative immunosuppression may increase the likelihood of metastasis and the proliferation of tumor cells [3]. Accordingly, reducing perioperative immunosuppression is critical to the long-term prognosis of esophageal cancer. Previous studies have suggested that regional anesthesia may preserve immune functions and reduce the risk of cancer recurrence after surgery. Although the underlying mechanisms remain elusive, the attenuation of surgical stress responses and a decrease in dosage of general anesthetics have been suggested to avoid reduced immune function. Retrospective studies also found an association of the use of

perioperative regional anesthesia with an increase in the survival of overall cancer patients, instead of the rate of recurrence [4]. However, other studies also demonstrated that regional anesthesia may be associated with a lower recurrence rate in certain cancer types [5]. To the best of our knowledge, limited prospective data are available regarding how regional anesthesia affects cancer recurrence after surgery [5-7].

The conventional types of anesthesia used for radical resection of EC include general anesthesia (GA) or epidural anesthesia (EA) combined with GA. EA has the advantage of providing excellent analgesia both intraoperatively and postoperatively and ameliorating the perioperative immune functions of tumor patients [8]. However, this anesthetic technique may cause hemodynamic fluctuations, a slow heart rate, and extradural hematomas, among other effects [9]. Paravertebral blocks (PVBs) have been increasingly employed in clinical practice (e.g., during thoracic, breast and hepatobiliary surgery). As supported by ultrasound-guided techniques, the safety of PVBs can be ensured, and the success rate of PVBs has increased [10-12]. Moreover, research has also shown that thoracic PVBs (TPVBs) can improve immune function and reduce the postoperative tumor recurrence rate in patients with breast carcinoma [13]. PVB has been reported to reduce the use of opioids and other anesthetics during surgery, thereby achieving more stable hemodynamics and other favorable effects (e.g., improving the function of cell-mediated immunity); however, this is only an assumption.

Therefore, this study aimed to compare the effects of GA, epidural anesthesia (EA) combined with GA, and paravertebral blocks (PVBs) combined with GA on perioperative immune cell survival, cytokine changes, perioperative complications and the postoperative survival rate of EC patients.

Methods and materials

Participants

The study protocol was approved by the Ethics Committee of Zhengzhou University People's Hospital and Henan Provincial People's Hospital (Ethics, 201941, Trial registration: ChiCTR, 1900026213). Written informed consent was provided by each patient before the study. A total of 160 patients who underwent open radical resection of thoracic esophageal cancer by left thoracotomy were recruited from the People's Hospital of Zhengzhou University from January 2016 to January 2017. After excluding patients who developed hematopoietic dysfunction, autoimmune diseases, immunodeficiency diseases, severe coronary heart disease, and/or hypertension, 120 patients were ultimately recruited for the study. The patients were randomized by a computer-generated number sequence to receive total intravenous anesthesia alone (GA group, n = 40), epidural anesthesia combined with general anesthesia (EG group; n = 40) or paravertebral block based on general anesthesia (PG group; n = 40). The patients recruited for the study had no history of endocrine disease and had not undergone radiotherapy, chemotherapy, or hormone therapy before surgery.

Anesthesia regimen and postoperative analgesia method

All patients fasted from solid food and clear liquids for 6 h and 2 h, respectively. All patients were administered intramuscular injections of 0.5 mg of atropine and 0.1 g of phenobarbital sodium and intravenously injected with lactated Ringer's solution 30 min before operation. In the GA group, an intravenous drip containing 0.2 mg/kg of midazolam (batch number: 20151224, Jiangsu Enhua Pharmaceuticals, Xuzhou, China), 0.5 μg/kg of sufentanyl (batch number: 1150708, Hubei Yichang Human-well Pharmaceuticals, Hubei, China), 0.5 mg/kg of rocuronium bromide (batch number: 160701, Zhejiang Xianju Pharmaceuticals, Zhejiang, China), and 1.5 mg/kg of propofol (batch number: 16IK2424, Fresenius Kabi Co Ltd, Beijing, China) was given to each patient. Double-lumen endotracheal tubes were placed with the help of anesthesia induction. To maintain the bispectral index (BIS) at 45±5, propofol was continuously administered by target-controlled infusion (TCI) when necessary. Remifentanil (batch number: 6161101, Hubei Yichang Human-well Pharmaceuticals, Hubei, China) and rocuronium bromide were injected intermittently throughout the operation.

Patients in the EG group were treated with 3 ml of 2% lidocaine and anesthesia was performed

after determining the block level. Patients then had double-lumen endotracheal tubes implanted. A solution consisting of propofol was continuously injected according to the BIS, and 10 ml 0.375% ropivacaine (batch number: 6161101, AstraZeneca, Wilmington, DE, USA) was injected into the epidural space. The remifentanil and rocuronium bromide were injected intermittently, and the injection lasted from the beginning to the end of the operation.

For the PG group, the patients were injected with 15 ml of 0.375% ropivacaine (100 mg/10 ml) in the thoracic paravertebral space at T4-5 and T6-7 and anesthesia was performed once the level of the regional block reached the expected level for the surgical procedure. Patients then had double-lumen endotracheal tubes inserted and propofol, remifentanil, and rocuronium bromide were continuously injected. During the operation, blood oxygen saturation, electrocardiogram readings, and intra-airway pressure of patients were all closely monitored.

Postoperatively, patients in the three groups were connected to a PCIA analgesia pump for 2 days. The PCIA protocol was as follows: butorphanol 2 ug/kg + Ketolorac Ambutriol 210 mg + tropisetron 10 mg, and they were diluted to 100 ml with normal saline. The PCIA parameters were as follows: loading dose 2 ml, background dose 2 ml/h, PCA 2 ml each time with a locking time of 15 min.

Postoperative treatment

Administration of propofol, remifentanil, and rocuronium bromide was stopped at the end of the suture and neostigmine was used to help patients regain their spontaneous breathing. After the patient resumed spontaneous breathing, deoxygenation was observed for 10 min. If patients maintained a SpO_2 higher than 95%, their endotracheal tube was pulled out and they were sent to the anesthesia recovery room (PACU) for anesthesia recovery.

Flow cytometry

A total of 6 ml of venous blood was collected from every patient in the GA, EG, and PG groups at four different time points: before anesthesia induction, at the end of the surgical procedure, and on postoperative day POD 1 and on POD 2. The respective samples were collected in heparinized anticoagulation tubes. A total of 1 ml of anticoagulated whole blood was obtained at the previously discussed time point and centrifuged for 5 mins at 500-1000 r/min. Red blood cells in the lower layer (50 μl) were washed three times with PBS followed by centrifugation and removal of the supernatant. A red blood cell suspension was then made by mixing red blood cells with PBS, and the suspension was divided into five separate test tubes (100 μl/per tube). Subsequently, 0.01 ml of monoclonal antibody marked by cluster of differentiation 3: peridinin chlorophyll protein complex-labeled mouse anti-human CD3, fluorescein isothiocyanate-labeled mouse anti-human CD4, and PE-labeled mouse anti-human CD8 monoclonal antibodies (Becton Dickinson, Franklin Lakes, NJ, USA) and labeled with CD16 FITC and CD56 PE were added, thoroughly mixed and incubated for 30 min at room temperature under dark conditions. The mixture was then washed with 1 ml of PBS and centrifuged, and then the supernatant was discarded. Another 500 μl of PBS was added and thoroughly mixed, and then a flow cytometer (FC500; Beckman Coulter, Hialeah, America) was used for detection purposes.

Enzyme-linked immunosorbent assay (ELISA)

A total of 2 ml of whole blood was also collected at each time point and centrifuged. Plasma was obtained, and the levels of inflammatory cytokines, including cortisol (Cor, cat. no. KGE008), interleukin-6 (IL-6, cat. no. D6050), interleukin-4 (IL-4, cat. no. D4050), tumor necrosis factor-α (TNF-α, cat. no. MTA00B) and interferon-γ (IFN-γ, cat. no. DIF50) were detected using ELISA kits (R and D Systems, Minneapolis, MN, USA) according to the manufacturer's protocol. When both the reaction and coloration had been terminated, the optical density (OD) value was obtained at a wavelength of 150 nm using an enzyme-labeled meter. The standard concentration represented the horizontal ordinate, while the OD value of 450 nm was the vertical coordinate.

Observation of postoperative complications, visual analog scale scores, and Riker Sedation-Agitation Scale scores

The incidences of postoperative nausea and vomiting (PONV), bucking, dizziness, and chest

Table 1. Comparison of clinicopathologic features and intraoperative baseline features of esophageal cancer patients among the three groups

Feature	GA group	EG group	PG group	*P* value
Age, y	60±4.2	58±6.35	57.4±7	0.174
Gender				0.512
Male	25	27	22	
Female	15	13	18	
BNM kg/m^2	23.35±2.6	23.16±1.6	22.02±1.8	0.271
ASA classification				0.25
ASAI	26	21	28	
ASAII	14	19	12	
TNM staging				0.34
I-II	12	10	16	
III-IV	28	30	24	
Anesthetic induction, min,	4.20±1.10	4.40±1.30	4.0±1.10	0.245
Anesthesia maintenance, min	210±42	200±36	190±45	0.38
Operative duration, min	205±37	184±31	172±38	0.31
Intraoperative urinary output, mL	736.07±126.7	756.30±235.7	687.32±154.4	0.34

BMI = body mass index; ASA = American Society of Anesthesiologists; TNM = Tumor Node Metastasis. Data are mean ± SD.

tightness were recorded for 48 h after the surgery. Tropisetron was employed for symptomatic treatment if vomiting occurred, and the relevant dose was recorded. The visual analog scale (VAS) and the Riker Sedation-Agitation Scale (SAS) scores were used to assess patients at 20 min after extubation, at 6 h postoperatively, on POD 1 and on POD 2. At the end of the operation, the amounts of remifentanil, propofol, and vasoactive drugs were recorded.

Follow-up

All patients received a 3-year follow-up consisting of a re-examination and a telephone call every 3 months. Local recurrence and distant metastasis of the cancer were recorded, as were the 1-, 2- and 3-year survival rates. The follow-up periods ranged from the time of diagnosis to January 1, 2019. No patients were lost to follow-up.

Statistical analysis

The sample size was calculated using the online software "Power and Sample Size.com". Based on our preliminary study, the CD4+/CD8+ at POD-1 was 0.58. Assuming a 20% difference with an alpha error of 0.05 (the alpha error was corrected by three pairwise comparisons) and a power of 0.8, the minimum necessary number of patients in each group was 34. Allowing for dropouts, we aimed to recruit 40 patients in each group with a total of 120 patients. Statistical data and the standard curves were analyzed with SPSS version 21.0 software (IBM Corp., Armonk, NY, USA). The measured data were presented as the mean ± standard deviation (SD). Normal distributions were compared using unpaired and paired *t*-tests. Comparisons among multiple groups were conducted by one-way analysis of variance (ANOVA), while comparisons between two groups were performed using Fisher's least significant difference (LSD) test. Measured data without a normal distribution were compared using a rank-sum test. Furthermore, comparisons of cytokine concentrations and the ratio of lymphocyte subsets were detected using the variance of repeated measured data. Enumerated data were presented as a percentage or ratio, and the chi-square test was used for comparisons. $P<0.05$ was considered significant.

Results

Demographic and intraoperative baselines

Among all esophageal cancer patients in the three groups, no significant differences were identified in age, weight, gender, American Society of Anesthesiologists (ASA) classification, tumor-node-metastasis stage, anesthesia induction time, anesthesia maintenance time, surgery duration, or intraoperative urinary output (all $P>0.05$) (**Table 1**).

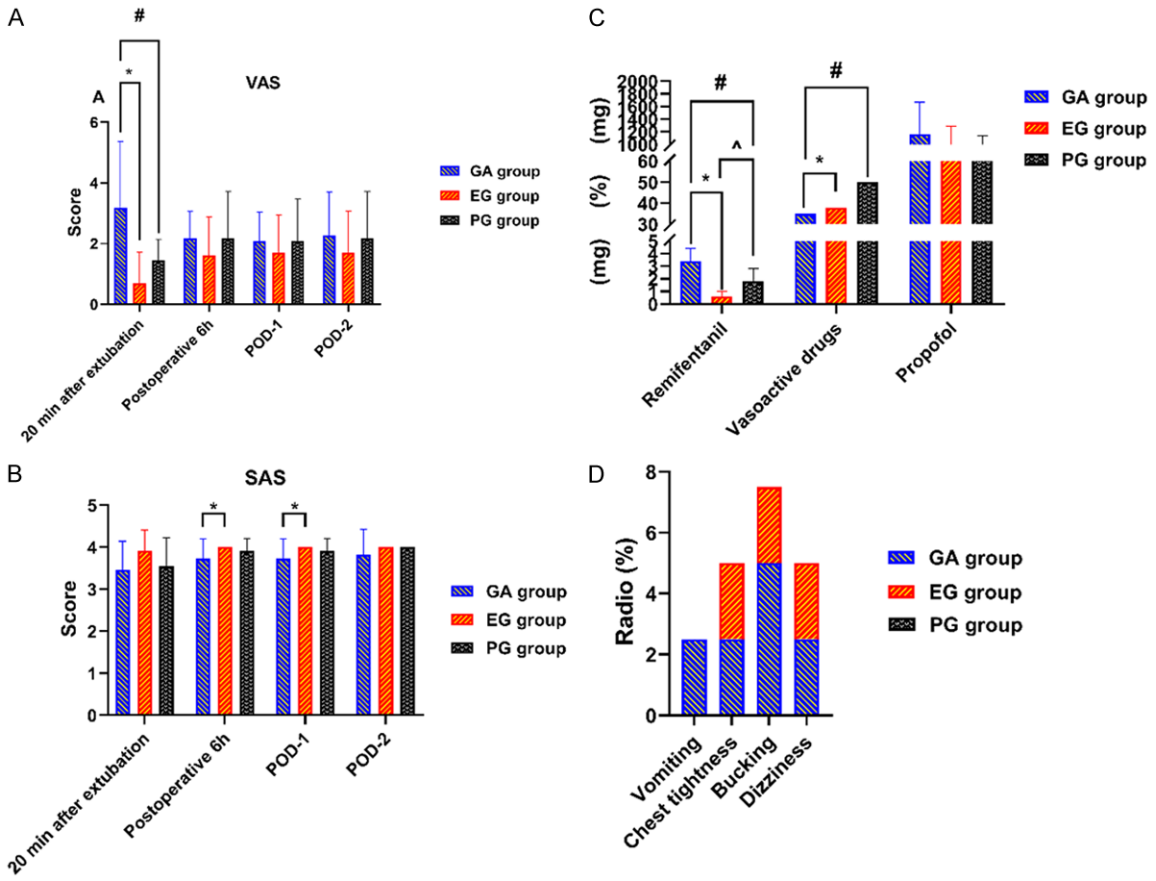


Figure 1. Comparison of VAS scores (A), SAS scores (B), Anesthetic and vasoactive drug consumption (C) and postoperative adverse reactions (D) among three groups. *P<0.05: the EG group vs the GA group at the corresponding time point; #P<0.05: the PG group vs the GA group at the corresponding time point; ^P<0.05: the PG group vs the EG group at the corresponding time point. POD-1 = postoperative day 1; POD-2 = postoperative day 2.

Intraoperative doses of anesthetics and use ratios of vasoactive drugs

The remifentanil consumption in both the PG and EG groups decreased significantly at the end of the surgical procedure compared with that in the GA group and was lower in the EG group than in the PG group (P<0.05) (**Figure 1**). Furthermore, the rates of using vasoactive drugs in the PG and EG groups were lower than those in the GA group (P<0.05) (**Figure 1C**).

Postoperative adverse reactions, VAS and SAS scores

One patient experienced vomiting in the GA group (**Figure 1D**), and one and two patients experienced bucking in the EG and GA groups, respectively. No vomiting or bucking was identified in the PG group. In the GA group, one patient suffered from chest tightness and one had dizziness; an identical scenario was noted in the EG group. These adverse reactions were not identified in patients in the PG group. Among the three groups, no significant differences were identified in the prevalence of vomiting, chest tightness, bucking, or dizziness (all P>0.05). Compared with those in the GA group, the VAS scores of patients in the EG and PG groups decreased significantly at 20 min after extubation (P<0.05) (**Figure 1A**). At 6 h postoperatively and on POD 1, the SAS scores of patients in the EG group increased significantly compared with those of patients in the GA group (P<0.05) (**Figure 1B**).

Cytokine concentrations

At the end of the surgery, the concentrations of Cor and IL-6 in the EG and PG groups were significantly lower than those in the GA group (P<0.05). On POD 1, the Cor, IL-6, and IL-4 lev-

els in the EG and PG groups significantly decreased compared with those in the GA group ($P<0.05$). Moreover, the IFN-γ levels in the EG and PG groups on POD 1 and POD 2 significantly increased compared with those in the GA group ($P<0.05$). The ratio of IFN-γ/IL-4 at POD 1 was increased in the PG and EG groups compared with the GA group ($P<0.05$). See **Figure 2**.

Ratio of lymphocyte subsets

There were fewer CD3+ and CD4+ cells at the end of the surgery, on POD 1, and on POD 2 than before surgery in the EG group ($P<0.05$) (**Figures 3**, **4**). In the PG and GA groups, there were fewer CD3+ and CD4+ cells at the end of the surgery and on POD 1 than before the surgery ($P<0.05$). The ratios of CD4+/CD8+ cells in the EG group at the end of the surgery and on POD 1 and on POD 2 were lower than that before the surgery ($P<0.05$). In the EG group, there were fewer CD8+ cells on POD 2 than before the surgery ($P<0.05$). On POD 1, the ratios of CD3+ cells in the EG and PG groups were higher than that in the GA group ($P<0.05$). Except on POD 1, there were significantly fewer CD4+ cells in the EG and PG groups than in the GA group ($P<0.05$).

Postoperative long-term prognosis

In terms of the overall survival rate, the 1-, 2-, and 3-year survival rates following surgery in the GA group were 82.40, 38.20 and 28.60%, respectively, those in the EG group were 85.22, 47.27 and 44.34%, respectively, and those in the PG group were 87.62, 57.24 and 54.10%, respectively. As revealed by the log-rank test results, the postoperative survival curves of the PG and EG groups were better than that of the GA group ($P<0.05$) (**Figure 5**).

Discussion

Our study detected the concentrations of immunologic factors such as Cor, IL-6, IL-4, and IFN-γ in serum, providing evidence that esophageal cancer patients in the PG and EG groups exhibited lower serum concentrations of Cor, IL-6, and IL-4 and higher serum concentrations of IFN-γ than those in the GA group. Zao et al. [14] found the TNF-α, IL-6 and IL-8 levels to be significantly lower in the GEA group and suggested that this anesthesia method protected immune functions by inducing a reduced stress response. In many different studies, when compared to general anesthesia, serum IFN-γ levels have been found to be high in patients undergoing cancer surgery and for whom combined GEA was applied [15, 16]. Regional anesthesia achieved with paravertebral nerve blocks may preserve the antimetastatic and anti-inflammatory functions of patients during the operative period, which is critical to improve outcomes after cancer surgery [17]. This study found that under the conditions of epidural anesthesia combined with general anesthesia or paravertebral nerve blocks based on general anesthesia, patients achieved more stable hormone levels, which may be related to the effects of paravertebral and epidural nerve blocks on the reduction of perioperative stress and the inflammatory response in patients with esophageal cancer.

A further finding of our study was in relation to the detection of the increased expression of T-cell subsets (CD3+, CD4+) in the EG and PG groups in comparison with the GA group. T lymphocytes participate in the immune system and are extensively involved in immune regulation, inflammation, and protective immune mechanisms [18]. Existing studies have suggested that regional anesthesia can maintain the Th1/Th2 balance and may increase the number and improve the function of T lymphocytes [19, 20]. Kun et al. [8] also reported that epidural anesthesia may help maintain perioperative immunity in patients who have undergone gastric cancer surgery. An elegant study compared cytokines and NK cells and reported that the serum from patients who had undergone paravertebral nerve block combined with general anesthesia did not exhibit alterations in NK cell expression or cytokine levels, whereas the serum from general anesthesia patients showed a decreased amount of activating receptors on NK cells [21]. Our results demonstrated that the use of epidural anesthesia combined with general anesthesia or paravertebral nerve blocks based on general anesthesia had a relatively minor effect on the expression of T-cell subsets compared to general anesthesia. In general, it is reasonable to hypothesize that GEA or PVB combined with GA affects cellular immune functioning less so than GA alone.

Regarding the prognosis of esophageal cancer patients, our study found that patients who

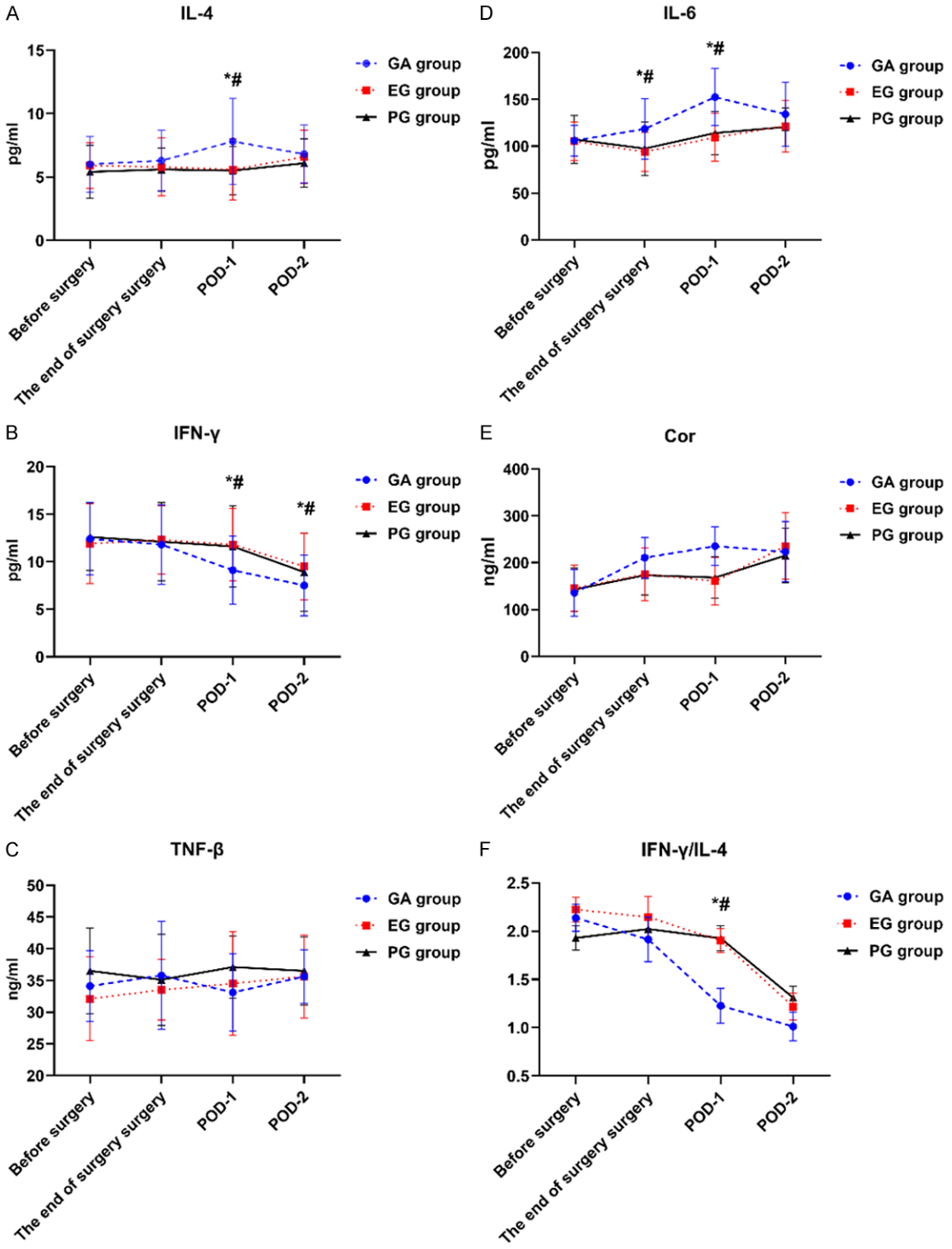


Figure 2. The cytokine levels as measured by ELISA in all groups; *P<0.05: the EG group vs the GA group at the corresponding time point; #P<0.05: the PG group vs the GA group at the corresponding time point; POD-1 = postoperative day 1; POD-2 = postoperative day 2.

underwent GEA or PVB combined with GA exhibited less pain and higher survival rates than those who underwent GA alone. Almost all postoperative cancer-associated deaths result

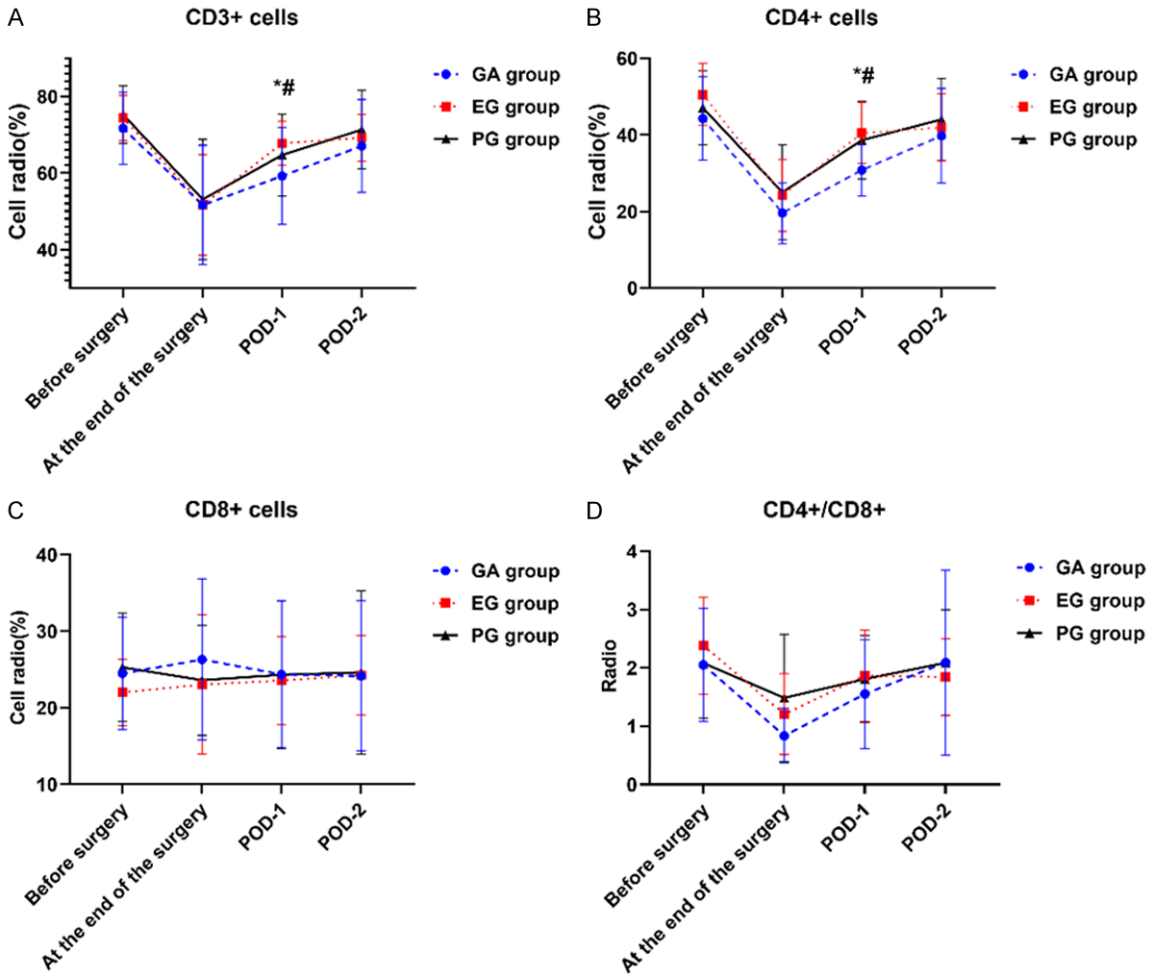
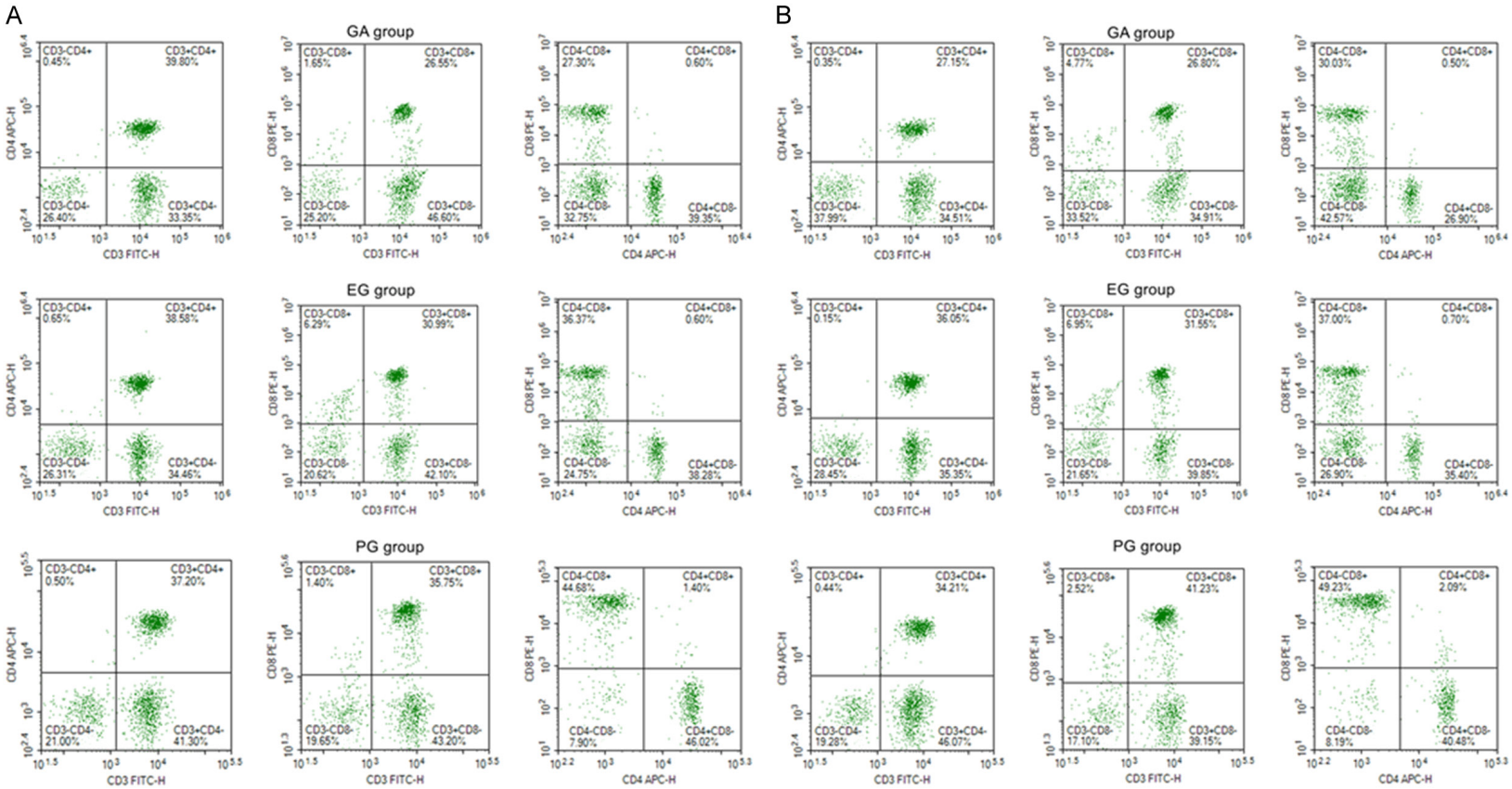


Figure 3. Comparison of the ratios of (A) CD3+, (B) CD4+, (C) CD8+ lymphocyte subsets and (D) CD4+/CD8+ lymphocytes among the three groups. $^{*}P<0.05$: the EG group vs. the GA group at the corresponding time point; $^{\#}P<0.05$: the PG group vs. the GA group at the corresponding time point; POD-1 = postoperative day 1; POD-2 = postoperative day 2.

from metastases or recurrence [22]. It has been hypothesized that anesthetic management impacts the long-term outcome following surgery, and that an anesthetic treatment exhibiting low potential for immunosuppression reduces relapse [23]. Pei et al. [24] reported that EA may improve the outcome for patients with prostate cancer, and they hypothesized that EA is involved in immunoreaction and oncocytology. The statistical analysis in this study confirmed this hypothesis and found that thoracic paravertebral nerve block combined with general anesthesia improved the postoperative survival of patients with esophageal cancer more than epidural anesthesia combined with general anesthesia. The underlying mechanism might be that a higher success rate and more stable hemodynamics in PVB may have resulted in fewer complications and better postoperative management and overall survival in PVB than in TEA. However, it was reported that anesthesia had a minor impact on immune systems [25]. Multiple clinical trials should be conducted to verify this conclusion.

This study innovatively observed the effects of different anesthesia methods on perioperative T lymphocyte subsets and cytokines and the postoperative long-term survival rate of patients with esophageal cancer. However, this study was an observational cohort study with a relatively small sample size. Subsequent studies with larger sample sizes and randomized trials are required to verify the findings here in depth.

In brief, the results described here demonstrated that the combination of PVBs or EA with GA


A
GA group
EG group
PG group
B
GA group
EG group
PG group
CD3-CD4+ 0.45%
CD3+CD4+ 39.80%
CD3-CD4- 26.40%
CD3+CD4- 33.35%
CD3-CD8+ 1.65%
CD3+CD8+ 26.55%
CD3-CD8- 25.20%
CD3+CD8- 46.60%
CD4-CD8+ 27.30%
CD4+CD8+ 0.60%
CD4-CD8- 32.75%
CD4+CD8- 39.35%
CD3-CD4+ 0.65%
CD3+CD4+ 38.58%
CD3-CD4- 26.31%
CD3+CD4- 34.46%
CD3-CD8+ 6.29%
CD3+CD8+ 30.99%
CD3-CD8- 20.62%
CD3+CD8- 42.10%
CD4-CD8+ 36.37%
CD4+CD8+ 0.60%
CD4-CD8- 24.75%
CD4+CD8- 38.28%
CD3-CD4+ 0.50%
CD3+CD4+ 37.20%
CD3-CD4- 21.00%
CD3+CD4- 41.30%
CD3-CD8+ 1.40%
CD3+CD8+ 35.75%
CD3-CD8- 19.65%
CD3+CD8- 43.20%
CD4-CD8+ 44.68%
CD4+CD8+ 1.40%
CD4-CD8- 7.90%
CD4+CD8- 46.02%
CD3-CD4+ 0.35%
CD3+CD4+ 27.15%
CD3-CD4- 37.99%
CD3+CD4- 34.51%
CD3-CD8+ 4.77%
CD3+CD8+ 26.80%
CD3-CD8- 33.52%
CD3+CD8- 34.91%
CD4-CD8+ 30.03%
CD4+CD8+ 0.50%
CD4-CD8- 42.57%
CD4+CD8- 26.90%
CD3-CD4+ 0.15%
CD3+CD4+ 36.05%
CD3-CD4- 28.45%
CD3+CD4- 35.35%
CD3-CD8+ 6.95%
CD3+CD8+ 31.55%
CD3-CD8- 21.65%
CD3+CD8- 39.85%
CD4-CD8+ 37.00%
CD4+CD8+ 0.70%
CD4-CD8- 26.90%
CD4+CD8- 35.40%
CD3-CD4+ 0.44%
CD3+CD4+ 34.21%
CD3-CD4- 19.28%
CD3+CD4- 46.07%
CD3-CD8+ 2.52%
CD3+CD8+ 41.23%
CD3-CD8- 17.10%
CD3+CD8- 39.15%
CD4-CD8+ 49.23%
CD4+CD8+ 2.09%
CD4-CD8- 8.19%
CD4+CD8- 40.48%
CD4 APC-H
CD3 FITC-H
CD8 PE-H

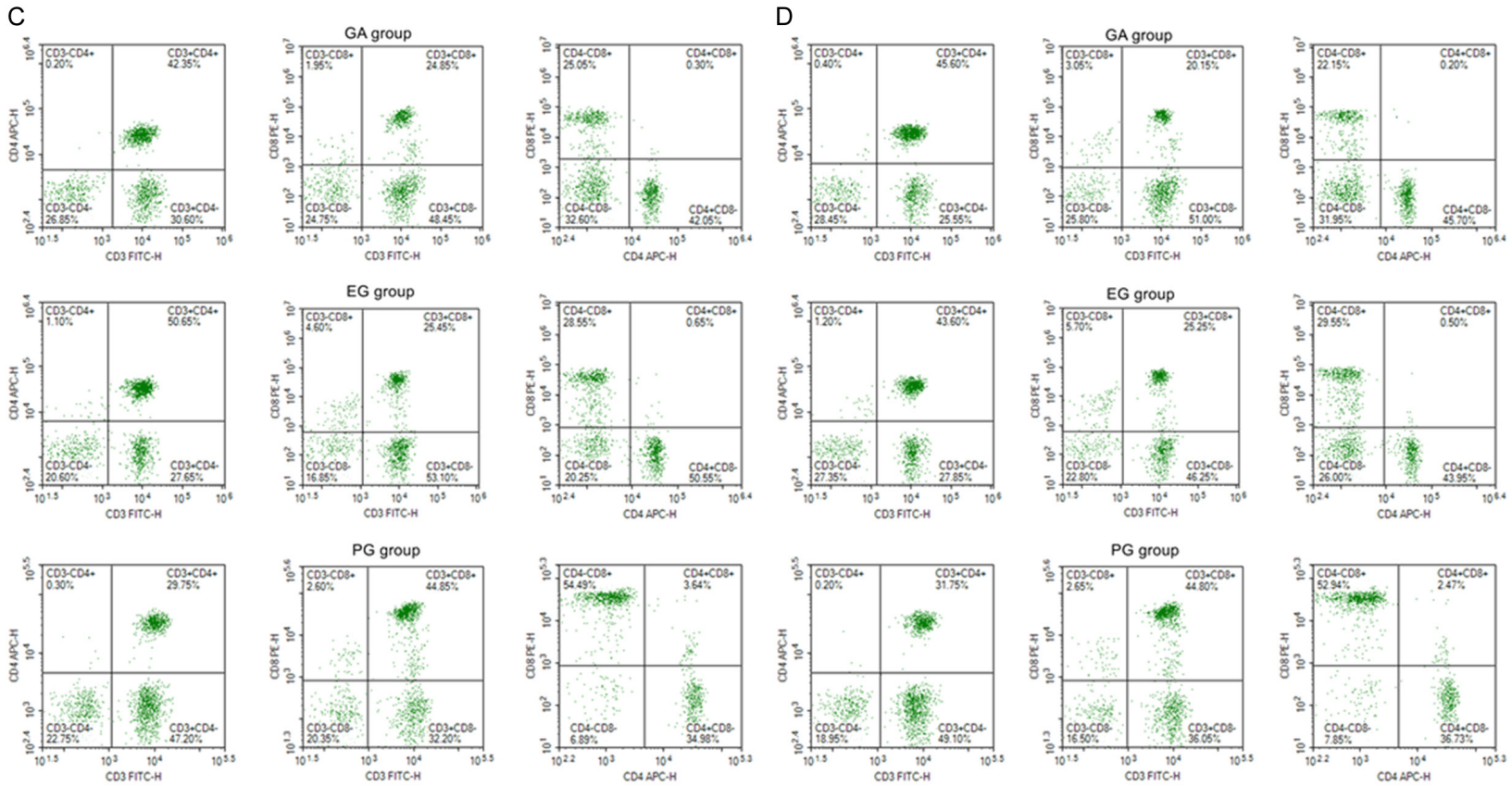


Figure 4. Flow cytometry analyses of T-lymphocyte subsets at different time points among the three groups. A. CD3+ cell levels, CD4+ cell levels, CD8+ cell levels, and CD4+ cell levels/CD8+ cell levels at the time point of before surgery among the three groups; B. CD3+ cell levels, CD4+ cell levels, CD8+ cell levels, and CD4+ cell levels/CD8+ cell levels at the time point of the end of surgery among the three groups; C. CD3+ cell levels, CD4+ cell levels, CD8+ cell levels and CD4+ cell levels/CD8+ cell levels at the time point of POD-1 among the three groups; D. CD3+ cell levels, CD4+ cell levels, CD8+ cell levels and CD4+ cell levels/CD8+ cell levels at the time point of POD-2 among the three groups; POD-1 = postoperative day 1; POD-2 = postoperative day 2.

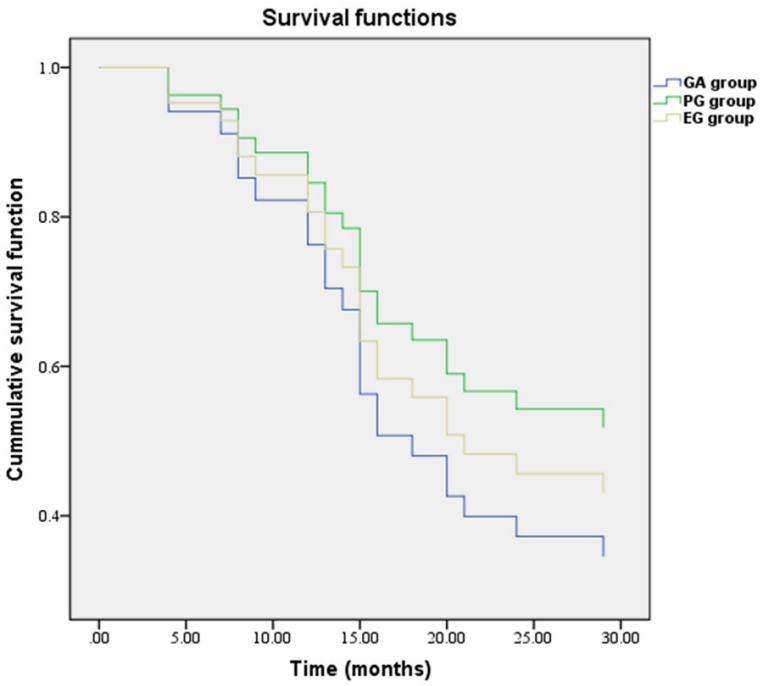


Figure 5. K-M curves of esophageal cancer patients among the three groups.

may lead to fewer endocrine disturbances and better perioperative cellular immunity than GA. In addition, PVBs with GA were found to elevate the total postoperative survival rate of patients with esophageal cancer to some extent.

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Disclosure of conflict of interest

None.

Address correspondence to: Jiaqiang Zhang, Department of Anesthesiology, Zhengzhou University People's Hospital and Henan Provincial People's Hospital, Zhengzhou, Henan, P. R. China. Tel: +86-18538298056; Fax: +86-5928-8887-777; E-mail: 844452331@qq.com

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