Effects of Different Anaesthesia Methods on Perioperative Cellular Immune Function and Long-term Outcomes in Patients Undergoing Radical Resection of Esophageal Cancer: A Prospective Cohort Study

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Abstract

Background The present study aimed to analyse the effects of different an anaesthetic method on perioperative cellular immunity and long-term outcomes in patients having undergone oesophageal cancer surgery.

Design A Prospective Cohort Study

Participants 120 cases of patients with oesophageal cancer in the Zhengzhou University People's Hospital from January 2016 to January 2017 were recruited and randomly split into GA group (general anaesthesia, n=40), PG group (Paravertebral nerve blocks with general anaesthesia, n = 40) and 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 of the three groups. Besides, adverse reactions of patients in the three groups were compared. Pre-operation, the end of operation, postoperative day (POD) 1 and POD 2 levels of interleukin-6 (IL-6), IL-4, tumour necrosis factor-α (TNF-α), interferon-γ (IFN-γ) and the survival of T-cell subsets (CD3+, CD4+, CD8+, CD4+/CD8+) were measured with by either ELISA or flow cytometry.

Results In the PG or EG group, VAS scores were lower, and fewer opioids and vasoactive agents were used, as compared with those of 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 those in the GA group. Moreover, the postoperative survival cure of the PG and EG groups was better than that of the GA group.

Conclusions The combination of paravertebral nerve blocks or epidural anaesthesia and general anaesthesia may improve the perioperative immune function and the long-term outcome for patients having undergone oesophageal cancer surgery.

Background

Esophageal Cancer (EC) is the sixth primary cause of cancer-related death worldwide for 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 localityterminal illness. Surgical stress, anaesthetic agents, hypotension and some 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 proliferation of tumour cells [3]. Accordingly, reducing perioperative immunosuppression is critical to the long-term prognosis of patients with oesophageal cancer. Previous studies suggested that regional anaesthesia may preserve immune functions and reduce the risk of

cancer recurrence after surgery. Though the underlying mechanisms remain elusive, the attenuation of surgical stress responses and the decrease in dosages of general anaesthetics have been suggested to avoid the reduction of immune functions. Retrospective studies also found an association of the use of perioperative regional anaesthesia with an increase in the survival of overall cancer patients, instead of the rate of recurrence [4]. However, other studies also demonstrated that regional anaesthesia 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 anaesthesia affects cancer recurrence after surgery [5–7].

The conventional type of anaesthesia for radical resection of EC is General Anaesthesia (GA) or Epidural Anaesthesia (EA) combined with GA. EA has an advantage that it can provide excellent analgesia both intraoperatively and postoperatively and ameliorate perioperative immune functions of tumour patients [8]. However, this Anaesthetic technique may cause hemodynamic fluctuations, a slow heart rate, extradural hematoma, etc. [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 also showed that thoracic PVBs (TPVBs) can improve immune functions and reduce the postoperative tumour recurrence rate in patients with Breast Carcinoma [13]. PVB has been reported to reduce the use of opioid and other anaesthetics during surgery, thereby achieving more stable hemodynamic and other favourable effects (e.g., improving the function of cell-mediated immunity); however, this is only an assumption.

As a result, this study aimed to compare the effects of Epidural Anaesthesia (EA) combined with GA, Paravertebral Blocks (PVBs) combined with GA and GA on perioperative immune cell survival, cytokines changes, perioperative complications and the postoperative survival rate of EC patients.

Methods

Participants

The study protocol was approved by the Ethics Committee of People's Hospital of Zhengzhou University (Henan, China). The written information consent was provided by each patient before the study. A total of 160 patients having undergone open radical resection of thoracic oesophageal cancer by left thoracotomy were recruited from the People's Hospital of Zhengzhou University from January 2016 to January 2017. After patients developing hematopoietic dysfunctions, autoimmune diseases, immunodeficiency diseases, severe coronary heart disease, and/or hypertension were excluded, 120 patients were finally recruited for the study. They were randomized via a computer-generated number sequence to receive total intravenous anaesthesia alone (GA group, n = 40), epidural anaesthesia combined with general anaesthesia (EG group; n = 40) or paravertebral blocks based on general anaesthesia (PG group; n = 40). Those patients recruited for the study had no history of endocrine disease and had not undergone radiotherapy, chemotherapy and hormonotherapy before surgery.

Description Of Anaesthesia

Patients were fasted for 6 h from solid food and 2 h from clear liquids. The EG group underwent epidural puncture between T6 and T7 in the left lateral position; subsequently, an epidural catheter was inserted using the paramedian approach and the loss-of-resistance method. A test injection of 3 mL of 2% lidocaine was administered through the epidural catheter when no blood or cerebrospinal fluid was aspirated. Next, 10 ml of 0.375% ropivacaine (Astrazeneca, Wilmington, DE, USA) was injected after the general anaesthesia induction was conducted. For the PG group, the paravertebral block was performed in a left lateral position under ultrasound guidance with a high-frequency linear probe (7–13 MHz) (P07576 type, Sonosite company, Seattle, America). After the back skin was produced using the 2% chlorhexidine solution, the ultrasound probe was covered with a sterile transparent dressing (3M Health Care, St. Paul, Minnesota), and the sterile gel acted as a coupling medium.

The ultrasound probe was placed parasagittal to the long axis of the thoracic vertebrae that was approximately 3 to 4 cm lateral to the spine. When the ultrasound probe was moved, the tip of the transverse process was obviously observed. Subsequently, the paravertebral space was visualized between the parietal pleura and the costotransversarium ligamentum. The in-plane technique was adopted to insert a 16-G needle (Pajunk; Medizintechnologie GmbH, Geisingen, Germany) until the tip of the needle could be observed on the screen. The hydrolocation technique with 0.5 mL normal saline was applied to identify the needle tip until the pleural drift was observed, demonstrating that the needle tip was located in the paravertebral space, and 15 ml of 0.375% ropivacaine (100 mg/10 ml) was injected into the thoracic paravertebral space at T4–5 and T6–7.

Once the level of the regional block reached the expected level for the surgical procedure, general anaesthesia would be induced. All patients in the three groups underwent routine intravenous inductions with 0.2 mg/kg of midazolam (Jiangsu Enhua Pharmaceuticals, Xuzhou, China), 0.05 μg/kg of sufentanil (Hubei Yichang Human-well Pharmaceuticals, Hubei, China) and 0.1 mg/kg of vecuronium bromide (Zhejiang Xianju Pharmaceuticals, Zhejiang, China). Afterwards, the patients were intubated with double-lumen endotracheal tubes, and their lungs were mechanically ventilated.

Anaesthesia was maintained with intravenous infusions of propofol by Target-Controlled Infusion (TCI) and remifentanil, together with vecuronium bromide at 0.1 μg/kg/min (intravenous (i.v.)) when necessary to keep the bispectral index (BIS) at 45 ± 5. The induction and maintenance of anaesthesia for patients in the GA group were identical to those adopted for patients in the EG and PG groups, except for the absence of epidural blocks or paravertebral block.

Monitored Indicators And Experimental Procedures

Venous blood samples (6 mL from each patient) were taken via an intravenous catheter at 30 min before the anaesthesia induction, at the end of the surgical procedure, on the postoperative day POD 1 and on POD 2. A three-channel flow cytometer (FC500; Beckman Coulter, Hialeah, America) was adopted to

analyse the survival of T-cell subsets (a cluster of differentiation CD3+, CD4+, CD8+, CD4+/CD8+). The numbers of T-cell subsets were determined with peridinin chlorophyll protein complex-labelled mouse anti-human CD3, fluorescein isothiocyanate-labelled mouse anti-human CD4, as well as PE-labelled mouse anti-human CD8 monoclonal antibodies (Becton Dickinson, Franklin Lakes, NJ, USA). A double antibody sandwich enzyme-linked immunosorbent assay (ELISA) (R and D Systems, Minneapolis, MN, USA) was performed to determine the levels of Cortiso (Cor), (interleukin-6) IL-6, IL-4, tumour necrosis factor-α (TNF-α) and interferon-γ (IFN-γ). The incidences of postoperative nausea and vomiting (PONV), bucking, dizziness, and chest tightness were recorded for 48 h after the surgery. Tropisetron was employed for the symptomatic treatment if vomiting occurred, and the relevant dose was recorded. The visual analog scale (VAS) and the Riker Sedation-Agitation Scale (SAS) were used to assess patients at 20 min after the extubation, at 6 h postoperatively, and on POD 1 and on POD 2. At the end of the operation, the amounts of remifentanil, propofol, and the vasoactive drugs were recorded.

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

Statistical Analysis

The patients were recruited based on CD4 + cells and CD3 + cells in a comparison between PVB and GA published previously [14] at β = 0.2 (i.e., 80% power). The sample size in each group at α = 0.05 was 35 patients per group (StatMate version 2.00; GraphPad, San Diego, California, USA). Statistical data were analysed with SPSS version 21.0 software (IBM Corp., Armonk, NY, USA), and the data are denoted as the mean ± Standard Deviation (SD). Pairwise comparisons were verified by an independent ttest. If normally distributed, the data were statistically analysed by the analysis of variance, followed by Norman Keul's test for in-depth comparison; otherwise, the data were analysed by Mann–Whitney test. The survival rate was calculated using KaplanMeier survival curve and a significance analysis of survival rate by a log-rank test. A P value less than 0.05 was considered showing statistical significance.

Results

Demographic And Intraoperative Baselines

Among all oesophageal cancer patients in the three groups, no significant difference was identified in age, weight, gender, American Society of Anaesthesiologists (ASA) classification, tumour–node–metastasis stage, anaesthesia induction time, anaesthesia maintenance time, surgery duration, or intraoperative urinary output (all P > 0.05) (Table 1).

Table 1
Comparisons of clinicopathologic features and intraoperative baseline features of oesophageal-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
ASA I	26	21	28	
ASA II	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	1162 ± 510	912 ± 381	883 ± 255	0.203
Operative duration, min	1102 ± 450	847 ± 306	758 ± 245	0.109
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.

Intraoperative doses of anaesthetics and use radio of vasoactive drugs

The remifentanil consumption in both the PG and EG groups decreased significantly at the end of the surgical procedure, compared with it in the GA group, though it was even lower in the EG group than that in the PG group ($P < 0.05$) (Table 2). Furthermore, the use radios of vasoactive drugs in the PG and the EG groups were lower than those in the GA group ($P < 0.05$) (Table 2).

Table 2
Comparisons of intraoperative dose of anaesthetics and the use of vasoactive drugs among the three groups

Group	n	Remifentanil (mg)	Propofol (mg)	Vasoactive drugs (%)
PG	40	1.8 ± 1[#]	883 ± 255	35[#]
EG	40	0.6 ± 0.4[*^]	913 ± 381	38[*]
GA	40	3.4 ± 1	1162 ± 510	50

Data are mean ± SD. [*]P < 0.05, The EG group was compared with 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.

Postoperative Adverse Reactions, Vas And Sas Scores

The VAS and SAS scores in patients among the three groups are presented in (Fig. 1). One patient had vomiting (Table 3), and one and two patients had bucking in the EG group and GA group, 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 difference was 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 group and PG group decreased significantly at 20 min after the extubation (P < 0.05). 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).

Table 3
Comparisons of postoperative adverse reactions among the three groups.

Adverse reaction	GA group (n = 40)	EG group (n = 40)	PG group (n = 40)	P value
Vomiting, %	2.5	0	0	0.365
Chest tightness, %	2.5	2.5	0	0.601
Bucking, %	5	2.5	0	0.359
Dizziness, %	2.5	2.5	0	0.601

Ratio Of Lymphocyte Subsets

There were fewer CD3 + and CD4 + cells at the end of the surgery, on the POD1, and on POD2 than those before surgery in the EG group ($P < 0.05$) (Fig. 2). In the PG and GA groups, there were fewer CD3 + and CD4 + cells at the end of the surgery and on POD 1 than those before the surgery ($P < 0.05$). The ratio of CD4+/CD8 + cells in the EG group at the end of the surgery on POD 1 and on POD 2 was lower than that before the surgery ($P < 0.05$). In the EG group, there were fewer CD8 + cells on POD 2 than those before the surgery ($P < 0.05$). On the POD 1, the ratio of CD3 + cells in the EG group and PG group were evidently higher than that in the GA group ($P < 0.05$). Except for on the POD 1, there were significantly fewer CD4 + cells in the EG and PG groups than those in the GA group ($P < 0.05$).

Cytokine Concentrations

Before anaesthesia, no noticeable differences in cytokine levels (Cor, IL-6, TNF-α, IFN-γ, IL-4) were noted among the three groups ($P > 0.05$) (Table 4). In the GA group, compared with the time points before the surgery, the Cor levels were significantly different at the end of the surgery, on the POD 1 and on the POD 2 ($P < 0.05$). Moreover, the IL-6, IFN-γ, IL-4 levels were also significantly different on the POD 1 and on the POD 2 ($P < 0.05$). In the EG and PG groups, the Cor, IL-6, IFN-γ, IL-4 levels on the POD 2 were evidently different compared with those at the time points before the surgery ($P < 0.05$). Moreover, in the PG group, the IL-6 levels on the POD 1 were higher than those at the time points before the surgery ($P < 0.05$).

Table 4
Comparison of cytokine levels of oesophageal-cancer patients among three groups at all-time points.

Time point	Group	Cor	IL-6	TNF-β	IFN-γ	IL-4
		(ng/ml)	(pg/ml)	(ng/ml)	(pg/ml)	(pg/ml)
Before surgery	GA	135.850.2	108.116.5	34.15.6	12.43.8	6.02.2
	EG	145.849.8	105.420.5	32.16.6	11.94.2	5.91.8
	PG	142.845.6	107.425.5	36.56.8	12.63.5	5.42.1
The end of surgery surgery	GA	210.843.6$^{a*\#}$	118.532.5$^{*\#}$	35.88.5	11.84.2	6.32.4
	EG	175.656.5	94.121.1	33.54.8	12.33.6	5.82.3
	PG	173.442.5	97.528.5	35.17.2	12.14.1	5.61.7
POD-1	GA	235.541.5$^{a*\#}$	152.630.5$^{a*\#}$	33.16.1	9.13.6$^{a*\#}$	7.83.4$^{a*\#}$
	EG	160.750.9	109.525.6	34.58.2	11.83.8	5.62.4
	PG	168.544.3	114.223.1^{a}	37.14.9	11.64.3	5.51.9
POD-2	GA	223.464.5^{a}	134.234.2^{a}	35.64.2	7.53.2$^{a*\#}$	6.82.3^{a}
	EG	235.471.2^{a}	121.527.5^{a}	35.66.5	9.53.5^{a}	6.62.1^{a}
	PG	215.658.5^{a}	120.520.5^{a}	36.55.4	8.94.1^{a}	6.11.9^{a}

Data are mean ± SD. $^{a}P < 0.05$, the cytokine levels of this time point was compared with the cytokine levels at the time point of before ansthesia in all groups; $^{*}P < 0.05$, the EG group was compared with the GA group at the corresponding time point; $^{\#}P < 0.05$, the PG group vs the GA group at the corresponding time point; $^{\wedge}P < 0.05$, the PG group vs the EG group at the corresponding time point.

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 the POD 1, the Cor, IL-6, and IL-4 levels in the EG and PG groups significantly decreased, compared with those in the GA group ($P < 0.05$). Moreover, the IFN-γ level in the EG and PG groups on the POD 1 and the POD 2 significantly increased, as compared with those in the GA group ($P < 0.05$).

Postoperative long-term prognosis

In terms of the overall survival rate, the 1-, 2-, 3- year survival rates following the 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 reached 87.62, 57.24 and 54.10%, respectively. As revealed from Log-rank test results, the postoperative survival curve of the PG group and the EG group was better than that of the GA group ($P < 0.05$) (Fig. 3).

Discussion

The present study investigated the possibility of using paravertebral nerve blocks or epidural anaesthesia to improve the survival of T cells and lower cytokine levels in patients carrying oesophageal cancer. The results here demonstrated that the paravertebral nerve blocks combined with general anaesthesia can improve the total postoperative survival of patients carrying oesophageal cancer compared with those using epidural anaesthesia combined with general anaesthesia or general anaesthesia alone. This finding is significant since it offers the possibility of using the paravertebral nerve block or epidural anaesthesia to facilitate the long-term prognosis of patients with oesophageal cancer. T lymphocytes participate in the immune system and are extensively covered in immune regulation, inflammation and protective immune mechanisms [15]. Cytokines are split into Th1 or Th2 in accordance with the cell of release [16]. Th1 cells and T cytotoxic lymphocytes release Th1 cytokines, which imposes stimulatory actions on cell-mediated immunity [17]. Th1 cytokines are released by Th1 cells and T cytotoxic lymphocytes, thereby stimulating cell-mediated immunity. Th2 lymphocytes release IL-4, which is the important Th2 cytokine [18]. The balance between Th1 / Th2 cytokines appears to be relevant to the formation and development of cancer [19]. Existing studies suggested that regional anaesthesia can maintain the Th1 / Th2 balance and may increase the number and improve the function of T lymphocytes [20, 21].

The anaesthetic regimen of epidural anaesthesia combined with general anaesthesia has been reported to exhibit the advantages of maintaining normal hormone levels and requiring less general anaesthetics and/or opioids [9, 22], which complies with the case in this study. A recent study [23] revealed that thoracotomy with a thoracic epidural block exerts a decreased impact on postoperative lymphocyte responses compared with surgery performed under general anaesthesia. Kun et al. [8] also reported that epidural anaesthesia may help maintain perioperative immunity in patients having undergone gastric cancer surgery. In this study, we found that the ratio of CD3 + and CD4 + cells in the three groups was lower after surgery than before anaesthesia, demonstrating that cellular immunity may have been affected by surgical stimulation and anaesthetics. However, the percentage of CD3 + and CD4 + cells on POD 2 increased to the preoperative level in the EA + GA group. Though epidural anaesthesia has several advantages, nerve or spinal injury remains a risk associated with this procedure. Moreover, intraoperative blood pressure fluctuation (primarily decreased blood pressure and heart rate) during surgery is concerning particularly in elderly patients whose vital organs can get injured even with a relatively short decrease in perfusion perioperatively [24–27].

As fuelled by the development of ultrasound technology, the application of paravertebral nerve blocks has become popular clinically. One existing study showed that paravertebral nerve blocks decrease surgical stress and are associated with a lower risk of metastasis in patients having undergone breast cancer surgery [13]. Paravertebral nerve blocks have been suggested to reduce opioid consumption, and opioids are generally known to have immunosuppressive effects not conducive to cancer patients. Regional anaesthesia achieved with paravertebral nerve blocks may preserve the anti-metastatic and anti-inflammatory functions of patients during the operative period, which is critical to improve outcomes

after cancer surgery [28]. An elegant study compared cytokines and NK cells and reported that the serum from patients having undergone paravertebral nerve blocks combined with general anaesthesia did not achieve altered NK cell expression or cytokine levels, whereas the serum from general anaesthesia patients showed a decreased amount of the activating receptors of NK cells [29]. The release of catecholamines, plasma cortisol and other stress-induced hormones caused by surgical stress can inhibit the immune functions of the body. However, if the activity of the autonomic nerve system can be reduced, the effects on the hypothalamus-pituitary-adrenal cortical axis can decrease, and the immune functions of the body can be better maintained [30].

This study found that under the conditions of epidural anaesthesia combined with general anaesthesia or paravertebral nerve blocks based on general anaesthesia, patients achieved more stable hormone levels, more CD4+, CD3+, and CD8 + cells, and higher CD4+/CD8 + compared with those using general anaesthesia alone. Pintaric, et al. [31] reported that paravertebral nerve blocks combined with general anaesthesia can achieve similar analgesic effects to those obtained with epidural blocks and are more conducive to hemodynamic stability for the attenuation of sympathetic nerve suppression from the spinal canal. In this study, PVBs exerted almost the same analgesic effect and a fewer complication than epidural anaesthesia based on general anaesthesia. Almost all cancer-associated deaths in the post operation result from metastases or recurrence [32]. It has been hypothesized that the anaesthetic management impacts the long-term outcome following surgery, and that an anaesthetic treatment exhibiting low potential for immunosuppression reduces relapse [33]. Pei et al. [22] reported that EA may improve the outcome for patients with prostate cancer; they hypothesized that EA is concerned with immunoreaction and oncocytology. The statistical analysis in this study confirmed this hypothesis. However, it was reported that anaesthesia had a minor impact on immune systems [34]. Thus, a mass of clinical trials should be conducted to verify this conclusion.

In brief, the results here demonstrated that the combination of PVBs or EA with GA may lead to less endocrine disturbances and better perioperative cellular immunity than GA. Besides, the PVBs with GA were reported to elevate the total postoperative survival rate of patients with oesophageal cancer to some extent. Nevertheless, this study was an observational cohort study with a relatively small sample size, and subsequently studies with a large sample size and randomized trials are required to verify the findings here in depth.

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Figures

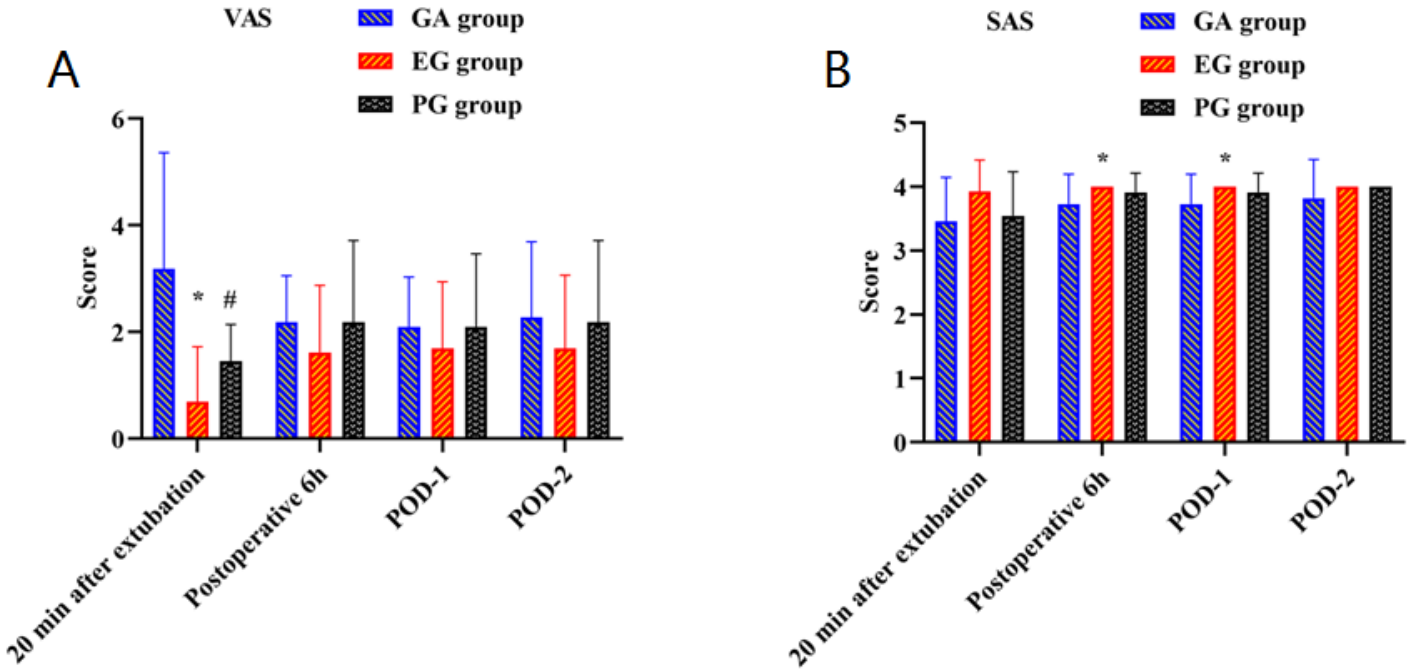

Figure 1

Comparisons of postoperative VAS values and SAS scores among the three groups. Data are mean ± SD (n = 40). *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 = the postoperative day 1; POD - 2 = the postoperative day 2.

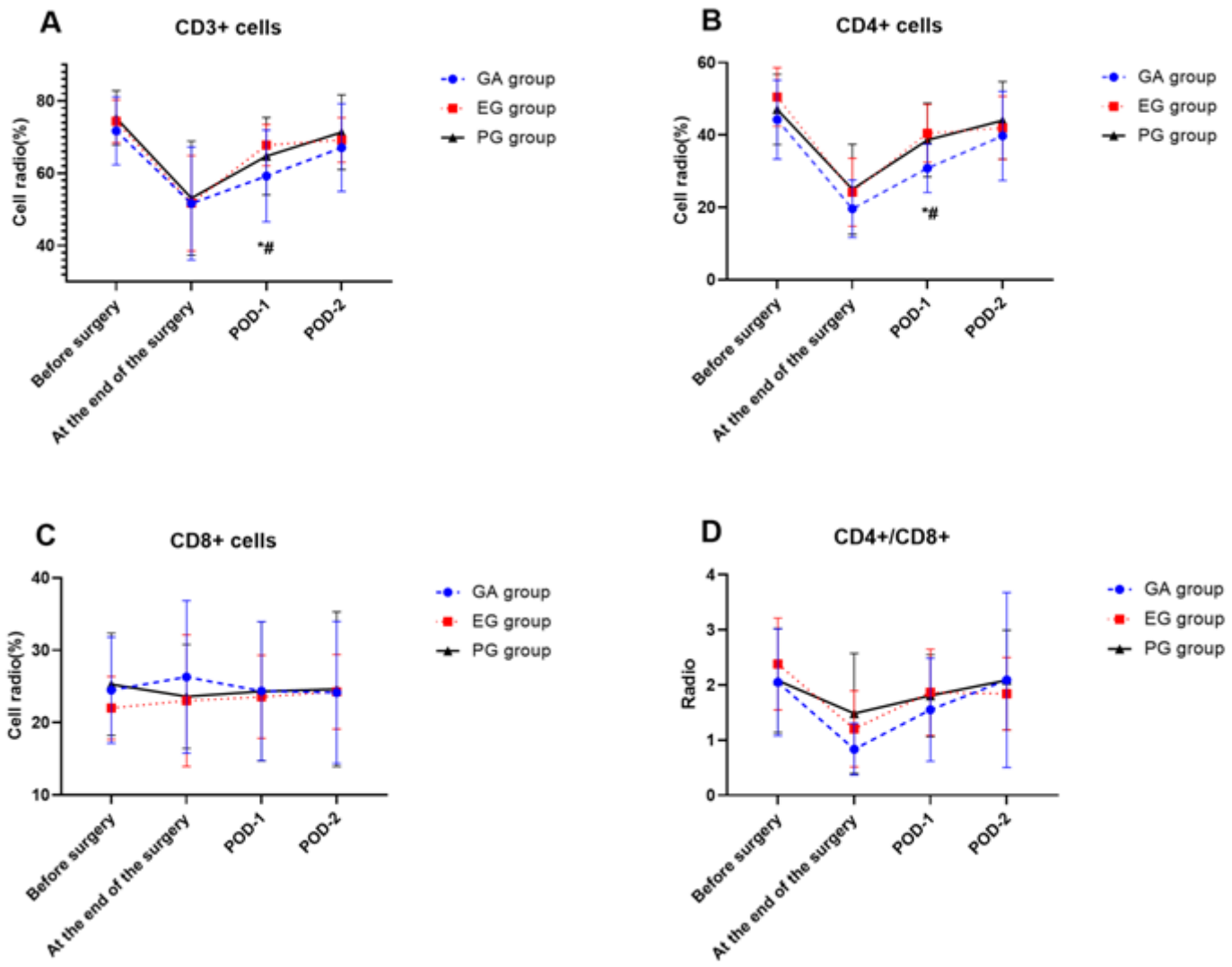

Figure 2

Comparison of the ratio of (A) CD3+, (B) CD4+, (C) CD8+ lymphocyte subsets and (D) CD4+/CD8+ among the three groups. Data are mean ± SD (n = 40). *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 = the postoperative day 1; POD - 2 = the postoperative day 2.

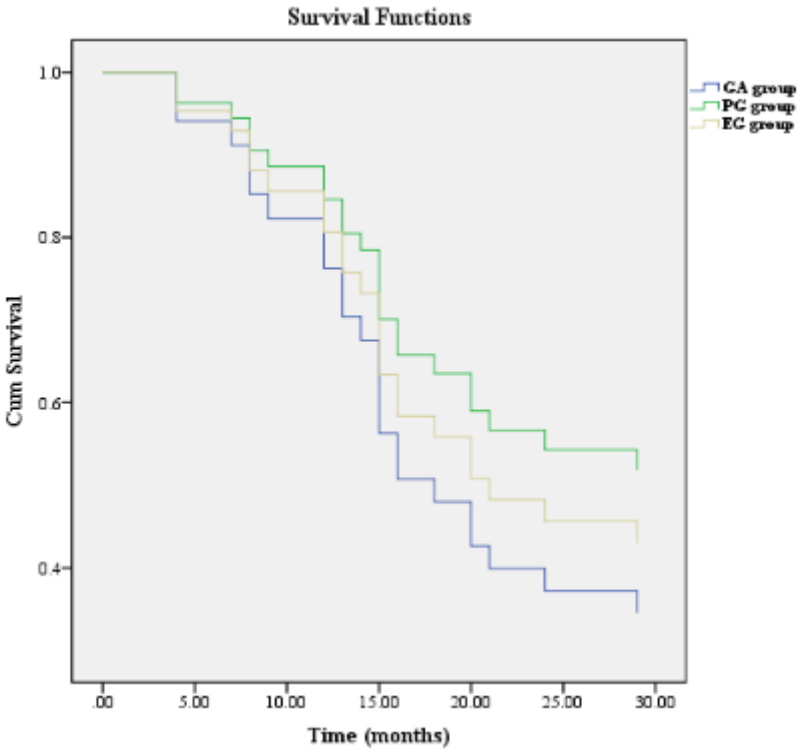

Figure 3

Survival curves of esophageal cancer patients among the three groups.