The effect of preventive use of corticosteroids on postoperative complications after esophagectomy: A retrospective cohort study

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Research Article

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Abstract

Background: Although corticosteroids were known to reduce acute respiratory distress syndrome (ARDS) after esophagectomy, the efficacy of corticosteroid remains debatable. Moreover, the risk of anastomosis leakage or infection, which relates to the administration of corticosteroid is another concern. Therefore, we compared the incidence of composite complications between patients who received or not the preventive administration of corticosteroid in esophagectomy.

Methods: All patients who underwent esophagectomy from 2010 to 2015 at a tertiary care university hospital, were reviewed in this retrospective study (*n*=1,041). Patients were divided into Steroid (*n*=120) and Control (*n*=860) groups based on the preventive administration of corticosteroid during surgery. The primary endpoint was the incidence of composite complications (acute respiratory distress syndrome, wound dehiscence, and infection). Comparison between the two groups was performed after adjustment of co-variables.

Results: The incidence of composite complications was not different between Steroid and Control group (21.7% vs 17.4%, respectively; *P*=0.26). Incidence of complications in each category between Steroid and Control groups were not significantly different: acute respiratory distress syndrome (5.0% vs 3.8%; *P*=0.46), graft dehiscence (6.7% vs 4.8%; *P*=0.37), and infection (15.8% vs 12.8%; *P*=0.36). After propensity score matching, the difference between the groups was also not significant. In multivariable analysis, age, lower body mass index, diabetes mellitus and duration of operation were independent risk factors of composite complications. Additionally, intraoperative vasopressor was a risk factor of graft dehiscence (odds ratio, 2.06; 95% confidence interval, 1.03-4.12; *P*=0.0407).

Conclusions: The preventive use of corticosteroid was not related to the incidence of composite complications after esophagectomy. Application of corticosteroid for prevention of acute respiratory distress syndrome is not recommended due to its lack of apparent benefit.

Keywords: Acute respiratory distress syndrome, corticosteroid, esophagectomy.

Background

Despite improvements in surgical techniques and postoperative management, esophagectomy is an invasive and high-risk procedure in the thoracic surgeries as ever [1]. And respiratory complications, including acute respiratory distress syndrome (ARDS) are major causes of postoperative mortality and morbidity after esophagectomy [1]. Mortality exceeds 50% when ARDS occurs [2]. ARDS, which is not related to pneumonia or anastomotic leak, results from a massive release of inflammatory cytokines during esophagectomy due to the radical dissection of gastro-enteral organs [3-5] and one lung ventilation (OLV) which increases inflammatory cytokines in both dependent and non-dependent lungs [6]. Excessive neutrophils recruited in response to the pro-inflammatory cytokines increase pulmonary vascular permeability [7]. These reactions often precede systemic inflammatory response syndrome or ARDS [4, 8].

Preventive administration of corticosteroid was reported to reduce ARDS after esophagectomy by inhibiting inflammatory responses [9, 10]. However, there are also studies that showed no beneficial effect of corticosteroid on ARDS [3, 11]. Moreover, there are concerns that corticosteroid can impair the healing process of surgical wounds and produce leakage of the anastomosis site by anti-inflammatory effects and antagonistic effects on growth factors [12-14]. Abnormal immune defenses from the perioperative use of corticosteroid can cause surgical site infection and may increase the incidence of pneumonia [14-16]. Graft dehiscence and infection are another major morbidities in esophagectomy [1].

Due to the complex effects of corticosteroid, studies on its preventive use are required in terms of risk-benefit. However, a few studies have compared the composite complications (ARDS, graft dehiscence, infection) in esophagectomy. In this retrospective study, we reviewed our clinical data from a large group of patients who underwent esophagectomy to compare the incidence of composite complications until discharge in patients who received or not the preventive administration of corticosteroid. Preventive use of corticosteroid waspure ARDSc leak problem defined as an intravenous corticosteroid administered during surgery for the prevention of ARDS.

Methods

Patient records

This retrospective cohort study was approved by our institutional review board (approval No. 2017-11-004). The need for written informed consent from participant was waived because of non-interventional retrospective design. Electronic medical records for all patients who underwent esophagectomy from January 2010 to December 2015 in our institute, were reviewed in this study (*n*=1,041). Patients who received corticosteroid to prevent ARDS during operation were assigned to the Steroid group and patients who did not receive corticosteroid during the same period were assigned to the Control group. Preventive use of corticosteroid waspure ARDSc leak problem defined as an intravenous corticosteroid administered during operation for the preventive purpose of ARDS. A single bolus dose of 100 mg of hydrocortisone was usually administered during the surgery by anesthesiologist H. J. A. and thoracic surgeon Y. S. C. These two physicians routinely administered corticosteroid in esophagectomy for the prevention of ARDS during the study period. Other anesthesiologists and thoracic surgeons did not use corticosteroid for the preventive purpose.

Information collected from patient’s medical record included administration of perioperative corticosteroids, age, gender, comorbidities, body mass index (BMI), American Society of Anesthesiologists (ASA) physical status, duration and type of surgery, preoperative hemoglobin and albumin, intraoperative administration of inotrope or vasopressor, perioperative transfusion, net volume of fluid administrated during and within 24 hours after the surgery, and method of postoperative analgesia (thoracic epidural analgesia or intravenous patient-controlled analgesia). Comorbid conditions included hypertension, diabetes mellitus, renal dysfunction (serum creatinine > 1.2 mg/dl), cerebrovascular disease, cardiac disease, and pulmonary dysfunction. Cerebrovascular disease included a history of cerebral infarction, cerebral hemorrhage, and Parkinson's disease/dementia/Alzheimer's disease. Cardiac disease included coronary artery disease, arrhythmia and heart failure. Pulmonary dysfunction included lung diseases (i.e., chronic obstructive pulmonary disease, bronchiectasis, asthma, and interstitial lung disease), preoperative forced expiratory volume in one-second (FEV_1) < 60% of predicted value, and current smoker. Current smoker was defined as patients who were smoking or had stopped smoking within 1 month before surgery.

Definition of postoperative complications

Composite complication was the primary outcome of this study. Three categories of complication until discharge were included: ARDS, graft dehiscence, and infection. ARDS was defined in according to the 2012 Berlin definition as acute (within one week of a known clinical insult) hypoxemic respiratory failure (a ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen [PaO_2/FiO_2] less than 300 mm Hg) requiring positive end-expiratory pressure (PEEP) of 5 cm H_2O or greater with bilateral opacities on chest imaging that are not fully explained by cardiac failure or fluid overload [17]. Graft dehiscence included the development of anastomotic leakage, significant esophageal fistula, perforation of bowel or stomach, bronchopulmonary fistula, and graft failure. Infection included pneumonia, empyema, surgical site infection, and catheter-related infection.

Anesthesia and postoperative management

Anesthesia and postoperative management were performed according to our institutional protocol. Most patients received a balanced anesthesia, which was a combination of volatile anesthetic agents, non-depolarizing neuromuscular blocking agents, and a continuous intravenous infusion of remifentanil. Maintenance fluid was lactated Ringer's solution, infused at a rate of 3 - 5 ml/kg/h. If volume deficiency was suspected, 5% human albumin (Green Cross Corp., Gyeonggi, Korea) or 6% hydroxyethyl starch (Fresenius Kabi, Seoul, Korea) was infused to the patients. In case of intraoperative bleeding, transfusion was performed for effective resuscitation (transfusion cut-off: hemoglobin < 8 g/dl). The protective ventilation protocol was applied to all patients. Mechanical ventilation during OLV was maintained with a tidal volume of 5-6 ml/kg predicted body weight at 5 cm H_2O PEEP. A recruitment maneuver to the dependent lung was performed immediately after OLV and at the restart of two lung ventilation.

For postoperative management, patients stayed in the intensive care unit (ICU) for two days. The postoperative analgesic methods were determined by surgeon's preference and existence of contraindications for regional analgesia. Maintenance fluid was administered at a rate of 2-3 ml/kg/h. ICU intensivists administered additional fluid based on the patient's vital sign. Patients were encouraged to ambulate from postoperative day (POD) 1 and received a daily physiotherapy program, which included deep-breathing exercises, incentive spirometry, and chest physiotherapy by physiotherapists and attending nurses during the ICU and the ward stays.

Statistics

Patient demographic and clinical data were summarized as frequency (percentage) for categorical variables and median (interquartile range) for continuous variables. Wilcoxon rank sum test was used to determine the significant differences in continuous variables between the Steroid and Control groups. Chi-square test or Fisher's exact test was used to compare categorical variables between the two groups. Multivariable logistic regression analysis was used for the risk factors of postoperative complications. Univariable analysis was done for all variables and variables with $P<0.2$ were further analyzed by multivariable analysis. Propensity score matching (PSM) was performed between the two groups. Matched variables were gender, age, body mass index, ASA classification, hypertension, diabetes mellitus, cardiac disease, pulmonary dysfunction, renal dysfunction, cerebrovascular disease, liver disease, preoperative hemoglobin, preoperative albumin, duration of surgery, intraoperative inotrope or vasopressor, transfusion, intraoperative fluid balance, minimally invasive surgery, and thoracic epidural analgesia. Based on the standard deviation of the logit of the estimated propensity score, one to one matching was performed using the nearest-neighbor method with a caliper width of 0.2 in pairwise manner. The matched data included n=115 for each group. For all analyses, a 2-sided $P<0.05$ was considered significant. Data were analyzed using SAS 9.4 software (SAS Institute, Inc, NC, USA).

Results

A total of 1,041 patients received esophagectomy in our institute between 2010 and 2015. Patients with incomplete data in their medical record were excluded (n=61). The final analysis included 980 patients. No patients received corticosteroid before operation. Overall, 120 patients received preventive use of corticosteroid and the remaining 860 patients were assigned to the Control group (Figure 1).

Hydrocortisone was administrated in most cases (100 mg per patient, n=95), but dexamethasone (10 mg per patient, n=15) or methylprednisolone (250 mg per patient, n=10) was used in a small number of cases.

Demographic and clinical characteristics between the groups are shown in Table 1. There were no differences in demography and underlying comorbidities between the Steroid and Control groups except in cardiac disease (1% vs 5%, Steroid vs Control; P=0.040). The Steroid group received more fluid (net fluid balance, median [interquartile range]: 533 [158-986] vs 381 [34-770]; P=0.006), transfusion (10% vs 5%; P=0.031), thoracic epidural analgesia (45% vs 35%; P=0.033) and underwent less minimally invasive surgery (7% vs 15%; P=0.018) than the Control group.

The incidence of composite complications was not different (21.7% in the Steroid group and 17.4% in the Control group, P=0.26) (Table 2). The incidence of complications in each category was also not different between the Steroid and Control groups: ARDS (5.0% vs. 3.8%; P=0.46), graft dehiscence (6.7% vs. 4.8%; P=0.37), and infection (15.8% vs. 12.8%; P=0.36) (Table 2).

PSM was performed to adjust confounders between the two groups (PSM balance in Figure 2, n=115 for each group). Composite complication (21.7% vs. 20.9%, Steroid vs Control; P=0.86) and individual categories of complication were not different between the two groups after PSM (ARDS [5.2% vs. 4.3%; P=0.76], graft dehiscence [7.0% vs. 2.6%; P=0.14], and infection [15.7% vs. 16.5%; P=0.85]) (Table 3).

Multivariable logistic regression analysis showed that preventive administration of corticosteroid did not affect the development of composite complications (OR [odds ratio], 1.33; 95% CI [confidence interval] 0.82 to 2.18; P=0.25). Instead, age, lower BMI, diabetes mellitus and longer duration of operation were independent risk factors of composite complications (Table 4). We also conducted multivariable logistic regression analysis in each category of complication in the same manner to confirm independent risk factors of subcategory. In these analyses, we could not find the variables that are related to ARDS. Duration of surgery (OR, 1.01; 95% CI, 1.00 to 1.01, per minute; P<0.0001) and use of vasopressor (OR, 2.06; 95% CI, 1.03 to 4.12; P=0.0407) were related to graft dehiscence. Age (OR, 1.04; 95% CI, 1.02 to 1.07; P=0.0009), BMI (OR, 0.92; 95% CI, 0.86 to 0.99; P=0.0180), and duration of surgery (OR, 1.00; 95% CI, 1.00 to 0.01, per minute; P=0.0003) were related to infection (Table 5-7).

Discussion

In the current study, the preventive administration of corticosteroid did not affect the occurrence of composite complications after esophagectomy, nor to any individual category of the complications (i.e., ARDS, graft dehiscence, and infection).

Corticosteroids inhibit the transcription of mRNA that encodes inflammatory cytokines, thus reducing the production of cytokines and acute-phase reactants [18]. And by this mechanism, corticosteroids have been used to suppress inflammatory reactions in many clinical conditions [14, 19]. Previous studies have shown reduction of pro-inflammatory cytokines with the use of corticosteroids in esophagectomy [10, 11, 20, 21]. Interleukin (IL)-6 and IL-8 were shown to be decreased with the preventive use of corticosteroids in a meta-analysis [22]. However, few publications have shown reduction of pulmonary complications [9, 10].

A randomized controlled trial (RCT), which included a total of 66 patients undergoing esophagectomy, showed that corticosteroids administered 30 minutes before the surgery reduced IL-6 and IL-8 levels and organ failure of heart, lung, kidney, and liver (33% vs 61%, steroid vs control) [10]. However, the definition of organ failure was quite broad in that study [10]. In addition, another RCT (n=40) [11] did not show statistical differences in the incidence of postoperative complications according to the preoperative use of corticosteroids.

A retrospective study (*n*=234) showed that corticosteroids administered after graft anastomosis reduced C-reactive protein level and acute respiratory failure (acute lung injury, ARDS and pneumonia; 2 vs 16 patients, steroid vs control) [9]. However, the sample size was relatively small as a retrospective study and the incidence of complications was low for analysis.

A meta-analysis in 2014 reported that the preoperative use of corticosteroid during esophagectomy reduced organ failure, cardiovascular complications, and pulmonary morbidity [22]. However, another meta-analysis [3] that was based on the same RCTs did not show significant differences in the incidence of postoperative complications between steroid and control group [3]. These meta-analyses were comprised of small studies (minimum 17 patients to maximum 66 patients) published more than a decade ago (between 1994 and 2005).

The strength of our study is that, although not an RCT, we included a large group of patients who were treated using a uniform protocol (anesthesia, operation, and perioperative care) and investigated composite complications including three major complication categories after esophagectomy. Each category was defined more comprehensive than the previous studies.

In multivariable analysis, old age, lower BMI, diabetes mellitus and longer duration of operation were risk factors of composite complications. These results are in line with previous reports except lower BMI that is newly reported in our study. Patients with esophageal cancer have the highest incidence of malnutrition (79.8%) among various cancers [23]. Perioperative malnutrition can cause biochemical or immunological abnormalities which are critical to the postoperative healing process and defense system against infection [24]. In addition, preoperative malnourishment was likely to be correlated with esophageal cancer progression [25].

Interestingly, the use of vasopressor during esophagectomy was a risk factor of postoperative graft dehiscence. Since avoiding overload of fluid is important to prevent postoperative acute lung injury after esophagectomy, vasopressors are frequently used to restore systemic blood pressure [26, 27]. However, vasopressors can impair blood flow in the graft while providing adequate perfusion to vital organs [28, 29]. In swine model, the esophageal graft was shown to experience severe hypoperfusion after the administration of vasopressor especially in hypovolemic state [28]. Poor perfusion of the graft, in turn, correlates to increased incidence of anastomotic leaks after esophagectomy [30]. Our data also showed that the decision to use vasopressors need to be made with a caution due to the risk of graft dehiscence. A goal directed fluid therapy may be recommended for adequate graft perfusion [31].

This study has some limitations. First, this is a retrospective study. Uncontrolled data inherent in the retrospective designed study might have influenced the results. In this study, we performed multivariable logistic regression and PSM analysis to adjust and minimize confounding variables between the groups. Second, we only focused on major complications related to corticosteroids, but other complications such as hyperglycemia may also be related to the use of corticosteroids. Third, the type and dose of corticosteroids were not controlled. In our study, hydrocortisone was the most commonly administered corticosteroid, while most previous studies used methylprednisolone. There are no studies comparing different types of corticosteroids on postoperative complications, but the difference between corticosteroids is considered negligible [32]. In previous studies, various doses of corticosteroids were used [3, 9, 10]. But no differences existed with doses [3, 9, 11, 22]. The lack of standard on the steroid types and doses can be a significant hurdle to draw any solid conclusions in this and future studies.

Conclusions

The preventive use of corticosteroid was not related to the incidence of composite complications after esophagectomy. Application of corticosteroid for prevention of ARDS is not recommended due to its lack of apparent benefit.

Abbreviations

ARDS: acute respiratory distress syndrome; OLV: one lung ventilation; BMI: body mass index; ASA: American Society of Anesthesiologist; FEV_1: forced expiratory volume in one-second; PEEP: positive end-expiratory pressure; ICU: intensive care unit; POD: postoperative day; PSM: propensity score matching; OR: odds ratio; CI: confidence interval; IL: interleukin; RCT: randomized controlled trial.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Samsung Medical Center (approval number, SMC 2017-11-004-001). The IRB waived the need for written informed consent from participant because of non-interventional retrospective design.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author’s contributions

HJ and JWC contributed equally as first author. They contributed to the study design, data analysis, and wrote the manuscript. HJA, DKK, and BSS analyzed and interpreted the patient data, and were major contributors on writing the manuscript. JAK, MY, and JKK supervised the study and co-wrote the manuscript. MP, SHL, YK, and YJC performed the data collection and helped with the data analysis. All authors read and approved the final manuscript.

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References

1. Wright CD, Kucharczuk JC, O'Brien SM, Grab JD, Allen MS. Predictors of major morbidity and mortality after esophagectomy for esophageal cancer: a Society of Thoracic Surgeons General Thoracic Surgery Database risk adjustment model. J Thorac Cardiovasc Surg 2009;137:587-95.
2. Tandon S, Batchelor A, Bullock R, Gascoigne A, Griffin M, Hayes N, Hing J, Shaw I, Warnell I, Baudouin SV. Peri-operative risk factors for acute lung injury after elective oesophagectomy. Br J Anaesth 2001;86:633-8.
3. Weijs TJ, Dieleman JM, Ruurda JP, Kroese AC, Knape HJ, van Hillegersberg R. The effect of perioperative administration of glucocorticoids on pulmonary complications after transthoracic oesophagectomy: a systematic review and meta-analysis. Eur J Anaesthesiol 2014;31:685-94.
4. D'Journo XB, Michelet P, Marin V, Diesnis I, Blayac D, Doddoli C, Bongrand P, Thomas PA. An early inflammatory response to oesophagectomy predicts the occurrence of pulmonary complications. Eur J Cardiothorac Surg 2010;37:1144-51.
5. Haga Y, Beppu T, Doi K Nozawa F, Mugita N, Ikei S, Ogawa M. Systemic inflammatory response syndrome and organ dysfunction following gastrointestinal surgery. Crit Care Med 1997;25:1994-2000.
6. Zingg U, Forberger J, Frey DM, Esterman AJ, Oertli D, Beck-Schimmer B, Zollinger A. Inflammatory response in ventilated left and collapsed right lungs, serum and pleural fluid, in transthoracic esophagectomy for cancer. Eur Cytokine Netw 2010;21:50-7.

7. Baudouin SV. Lung injury after thoracotomy. Br J Anaesth 2003;91:132-42.
8. Morita M, Yoshida R, Ikeda K, Egashira A, Oki E, Sadanaga N, Kakeji Y, Ichiki Y, Sugio K, Yasumoto K, Maehara Y. Acute lung injury following an esophagectomy for esophageal cancer, with special reference to the clinical factors and cytokine levels of peripheral blood and pleural drainage fluid. Dis Esophagus 2008;21:30-6.
9. Park SY, Lee HS, Jang HJ, Joo J, Zo JI. Efficacy of intraoperative, single-bolus corticosteroid administration to prevent postoperative acute respiratory failure after oesophageal cancer surgery. Interact Cardiovasc Thorac Surg 2012;15:639-43.
10. Sato N, Koeda K, Ikeda K, Kimura Y, Aoki K, Iwaya T, Akiyama Y, Ishida K, Saito K, Endo S. Randomized study of the benefits of preoperative corticosteroid administration on the postoperative morbidity and cytokine response in patients undergoing surgery for esophageal cancer. Ann Surg 2002;236:184-90.
11. Yano M, Taniguchi M, Tsujinaka T, Fujiwara Y, Yasuda T, Shiozaki H, Monden M. Is preoperative methylprednisolone beneficial for patients undergoing esophagectomy? Hepatogastroenterology 2005;52:481-5.
12. Brauchle M, Fassler R, Werner S. Suppression of keratinocyte growth factor expression by glucocorticoids in vitro and during wound healing. J Invest Dermatol 1995;105:579-84.
13. Park JE, Barbul A. Understanding the role of immune regulation in wound healing. Am J Surg 2004;187:11s-6s.
14. Ismael H, Horst M, Farooq M, Jordan J, Patton JH, Rubinfeld IS. Adverse effects of preoperative steroid use on surgical outcomes. Am J Surg 2011;201:305-8.
15. Byrne D. Adverse impact of surgical site infections in English hospitals. J Hosp Infect 2006;62:392.
16. Turan A, Sessler DI. Steroids to ameliorate postoperative pain. Anesthesiology 2011;115:457-9.
17. Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, Camprorta L, Slutsky AS. Acute respiratory distress syndrome: the Berlin Definition. Jama 2012;307:2526-33.
18. Rhen T, Cidlowski JA. Antiinflammatory action of glucocorticoids--new mechanisms for old drugs. N Engl J Med 2005;353:1711-23.
19. Fauci AS. Mechanisms of corticosteroid action on lymphocyte subpopulations. II. Differential effects of in vivo hydrocortisone, prednisone and dexamethasone on in vitro expression of lymphocyte function. Clin Exp Immunol 1976;24:54-62.
20. Matsutani T, Onda M, Sasajima K, Miyashita M. Glucocorticoid attenuates a decrease of antithrombin III following major surgery. J Surg Res 1998;79:158-63.
21. Takeda S, Takeda S, Kim C, Ikezaki H, Nakanishi K, Sakamoto A, Okawa K, Miyashita M, Sasajima K, Tajiri T, Tanaka K, Ogawa R. Preoperative administration of methylprednisolone attenuates cytokine-induced respiratory failure after esophageal resection. J Nippon Med Sch 2003;70:16-20.
22. Gao Q, Mok HP, Wang WP, Xiao F, Chen LQ. Effect of perioperative glucocorticoid administration on postoperative complications following esophagectomy: A meta-analysis. Oncol Lett 2014;7:349-56.

23. Larrea J, Vega S, Martinez T, Torrent JM, Vega V, Nunez V. The nutritional status and immunological situation of cancer patients. Nutr Hosp 1992;7:178-84.
24. Wu GH, Liu ZH, Wu ZH, Wu ZG. Perioperative artificial nutrition in malnourished gastrointestinal cancer patients. World J Gastroenterol 2006;12:2441-4.
25. Ouattara M, D'Journo XB, Loundou A, Trousse D, Dahan L, Doddoli C, Seitz JF, Thomas PA. Body mass index kinetics and risk factors of malnutrition one year after radical oesophagectomy for cancer. Eur J Cardiothorac Surg 2012;41:1088-93.
26. Chau EH, Slinger P. Perioperative fluid management for pulmonary resection surgery and esophagectomy. Semin Cardiothorac Vasc Anesth 2014;18:36-44.
27. Kita T, Mammoto T, Kishi Y. Fluid management and postoperative respiratory disturbances in patients with transthoracic esophagectomy for carcinoma. J Clin Anesth 2002;14:252-6.
28. Theodorou D, Drimousis PG, Larentzakis A, Papalois A, Toutouzas KG, Katsaragakis S. The effects of vasopressors on perfusion of gastric graft after esophagectomy. An experimental study. J Gastrointest Surg 2008;12:1497-501.
29. Jaeger JM, Collins SR, Blank RS. Anesthetic management for esophageal resection. Anesthesiol Clin 2012;30:731-47.
30. Zehetner J, DeMeester SR, Alicuben ET, Oh DS, Lipham JC, Hagen JA, DeMeester TR. Intraoperative Assessment of Perfusion of the Gastric Graft and Correlation With Anastomotic Leaks After Esophagectomy. Ann Surg 2015;262:74-8.
31. Ng JM. Update on anesthetic management for esophagectomy. Curr Opin Anaesthesiol 2011;24:37-43.
32. Sue MA, Kwong FK, Klaustermeyer WB. A comparison of intravenous hydrocortisone, methylprednisolone, and dexamethasone in acute bronchial asthma. Ann Allergy 1986;56:406-9.

Tables

Table 1. Baseline characteristics of patients and operations

Variables	Control (n=860)	Steroid (n=120)	P value
Preoperative data			
Age	63 [57-70]	65 [60-70]	0.06
Male	786 (91)	109 (91)	0.84
Body mass index (kg/m^2)	23 [20-25]	23 [21-25]	0.25
Hemoglobin (mg/dl)	14 [12-15]	14 [13-15]	0.64
Albumin (g/dl)	4 [4-5]	4 [4-5]	0.52
ASA physical status ≥3	47 (6)	5 (4)	0.52
Stage 3, 4	135 (19.0)	21 (18.8)	0.95
Neoadjuvant CCRT[a]	91 (13.6)	21 (13.5)	0.95
Comorbid condition			
Hypertension	332 (39)	40 (33)	0.27
Diabetes mellitus	130 (15)	17 (14)	0.79
Pulmonary dysfunction[b]	253 (29)	39 (32)	0.49
Cardiac disease	43 (5)	1 (1)	0.0389
Cerebrovascular disease	42 (5)	7 (6)	0.66
Renal dysfunction	7 (1)	1 (1)	1.00
Intraoperative data			
Duration of surgery (min)	276 [237-348]	268 [237-355]	0.80
Type of surgery			
Ivor Lewis operation	480 (56)	74 (62)	0.16
Three fields operation	161 (19)	27 (23)	
Three holes operation	107 (12)	8 (7)	
Etc.[c]	51 (6)	5 (4)	
Minimally invasive surgery[d]	125 (15)	8 (7)	0.0184
Net balance of fluid (ml)	381 [34-770]	533 [158-986]	0.0064
Use of inotrope	203 (24)	29 (24)	0.89
Use of vasopressor	485 (56)	79 (66)	0.05

Transfusion	44 (5)	12 (10)	0.0308
Thoracic epidural analgesia	301 (35)	54 (45)	0.0328
Hospital days (day)	13 [11-16]	12.5 [11-16]	0.75
ICU stay (day)	2 [2-3]	2 [2-3]	0.92

Values are presented as median [interquartile] or *n* (%).

[a]Neoadjuvant CCRT was analyzed in 823 patients (Control vs. Steroid; 667 vs. 156, respectively) due to missed data.

[b]Pulmonary dysfunction included lung diseases (chronic obstructive pulmonary disease, bronchiectasis, asthma, interstitial lung disease), preoperative forced expiratory volume in one-second (FEV_1) < 60% of predicted value and current smoker; current smoker was defined as patients who kept smoking or stop smoking within 1 month before surgery.

[c]Etc. included esophagocolonogastrostomy, esophagocolonojejunostomy, transhiatal esophagectgomy, and total gastrectomy.

[d]Minimally invasive surgery indicated a video assisted and robotic esophagectomy. Abbreviations: ASA American society of anesthesiologist, CCRT concurrent chemoradiotherapy, ICU intensive care unit.

Table 2. Postoperative complications between Control and Steroid groups

Complication [n (%)]	Control (n=860)	Steroid (n=120)	P value
Composite complication	150 (17.4)	26 (21.7)	0.26
ARDS	33 (3.8)	6 (5)	0.46
Graft dehiscence	41 (4.8)	8 (6.7)	0.37
Infection	110 (12.8)	19 (15.8)	0.36
Other complications			
Chylothorax	27 (3.1)	4 (3.3)	0.78
Atelectasis	19 (2.2)	2 (1.7)	1.00
Secretion retention	6 (0.7)	0	1.00
Arrhythmia (A.fib)	58 (6.7)	10 (8.3)	0.52
Arrhythmia (non A.fib)	52 (6)	7 (5.8)	0.93
Myocardial infarction	1 (0.1)	0	1.00
Cerebral infarction	3 (0.4)	1 (0.8)	0.41
Delirium	39 (4.5)	9 (7.5)	0.16
Seizure	2 (0.2)	0	1.00
Acute kidney injury	8 (0.9)	1 (0.8)	1.00
Pulmonary thromboembolism	2 (0.2)	1 (0.8)	0.32
Postoperative bleeding	6 (0.7)	1 (0.8)	0.60
Vocal cord paresis	131 (15.2)	20 (16.7)	0.68
Death[a]	1 (0.1)	0	1.00

Values are presented as n (%). [a]Death within 30 days after surgery.

Abbreviations: ARDS acute respiratory distress syndrome, PSM propensity score matching, A.fib atrial fibrillation, PTE pulmonary thromboembolism.

Table 3. Postoperative complications between Control and Steroid groups after propensity score matching

Complication [*n* (%)]	Control (*n*=115)	Steroid (*n*=115)	*P* value
Composite complication	24 (20.9)	25 (21.7)	0.86
ARDS	5 (4.3)	6 (5.2)	0.76
Graft dehiscence	3 (2.6)	8 (7.0)	0.14
Infection	19 (16.5)	18 (15.7)	0.85

Values are presented as *n* (%). Abbreviations: ARDS acute respiratory distress syndrome, PSM propensity score matching.

Table 4. Multivariable logistic regression

Composite complications						
Variables	Univariable			Multivariable		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Group	1.31	0.82 - 2.09	0.26	1.33	0.82 – 2.18	0.25
Age, per year	1.02	1.01 - 1.04	0.0143	1.03	1.00 - 1.05	0.0178
Male	1.94	0.95 - 3.94	0.07			
BMI (kg/m^2)	0.91	0.86 - 0.96	0.0005	0.90	0.85 - 0.96	0.0010
Hemoglobin (mg/dl)	0.89	0.82 - 0.98	0.02			
Albumin (g/dl)	0.58	0.39 - 0.88	0.01			
Duration of surgery, per min	1.00	1.00 - 1.01	<0.0001	1.00	1.00 - 1.01	<0.0001
Use of inotrope	1.61	1.12 - 2.31	0.01			
Use of vasopressor	1.49	1.06 - 2.10	0.02			
Transfusion	1.91	1.04 - 3.50	0.04			

All variables underwent univariable analysis and variables with *P* <0.2 were entered into multivariable analysis.

Variables with *P* <0.2 in univariable analysis were presented in this table. Abbreviations: OR odds ratio, CI confidence interval, BMI Body mass index.

Table 5. Multivariable logistic regression for acute respiratory distress syndrome

Acute respiratory distress syndrome						
Variables	Univariable			Multivariable		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Group	1.32	0.54 - 3.22	0.54	1.24	0.50 - 3.06	0.64
Age, per year	1.03	0.10 - 1.08	0.08			
Male	3.72	0.51 - 27.47	0.20			
Body mass index (kg/m^2)	0.92	0.82 - 1.02	0.12			
Pulmonary dysfunction[a]	1.68	0.87 - 3.22	0.12			
Use of vasopressor	1.69	0.85 - 3.38	0.14			

All variables underwent univariable analysis and variables with P <0.2 were entered into multivariable analysis.

Variables with P <0.2 in univariable analysis were presented in this table.

[a]Pulmonary dysfunction included lung diseases (chronic obstructive pulmonary disease, bronchiectasis, asthma, interstitial lung disease), preoperative forced expiratory volume in one second (FEV_1) < 60% of predicted value and current smoker; current smoker was defined as patients who kept smoking or stop smoking within 1 month before surgery. Abbreviations: OR odds ratio CI confidence interval.

Table 6. Multivariable logistic regression for graft dehiscence

Graft dehiscence						
Variables	Univariable			Multivariable		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Group	1.43	0.65 - 3.12	0.37	1.43	0.61 - 3.36	0.41
Body mass index (kg/m^2)	0.88	0.80 - 0.97	0.0134			
Hemoglobin (mg/dl)	0.85	0.73 - 0.99	0.0375			
Albumin (g/dl)	0.45	0.23 - 0.90	0.0240			
Hypertension	0.46	0.23 - 0.91	0.0248			
Duration of surgery, per min	1.01	1.01 - 1.01	<0.0001	1.01	1.00 - 1.01	<0.0001
Net balance of fluid	1.00	1.00 - 1.00	0.0006			
Use of inotrope	1.77	0.96 - 3.25	0.07			
Use of vasopressor	2.11	1.11 - 4.04	0.0234	2.06	1.03 - 4.12	0.0407
Transfusion	3.00	1.28 - 7.02	0.0113			

All variables underwent univariable analysis and variables with $P < 0.2$ were entered into multivariable analysis.

Variables with $P < 0.2$ in univariable analysis were presented in this table. Abbreviations: OR odds ratio CI confidence interval.

Table 7. Multivariable logistic regression for infection

Infection						
Variables	Univariable			Multivariable		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Group	1.28	0.76 - 2.18	0.36	1.27	0.74 - 2.19	0.39
Age, per year	1.04	1.02 - 1.06	0.0005	1.04	1.02 - 1.07	0.0009
Male	1.76	0.79 - 3.90	0.16			
Body mass index (kg/m^2)	0.92	0.87 - 0.98	0.0108	0.92	0.86 - 0.99	0.0180
Hemoglobin (mg/dl)	0.90	0.81 - 0.99	0.0330			
Albumin (g/dl)	0.58	0.37 - 0.92	0.0205			
ASA physical status ≥3	1.84	0.92 - 3.68	0.08			
Diabetes mellitus	1.52	0.95 - 2.44	0.08			
Duration of surgery, per min	1.00	1.00 - 1.01	0.0001	1.00	1.00 - 1.01	0.0003
Use of inotrope	1.61	1.07 - 2.41	0.0209			
Use of vasopressor	1.50	1.02 - 2.21	0.0406			

All variables underwent univariable analysis and variables with P <0.2 were entered into multivariable analysis.

Variables with P <0.2 in univariable analysis were presented in this table. Abbreviations: OR odds ratio CI confidence interval.

Figures

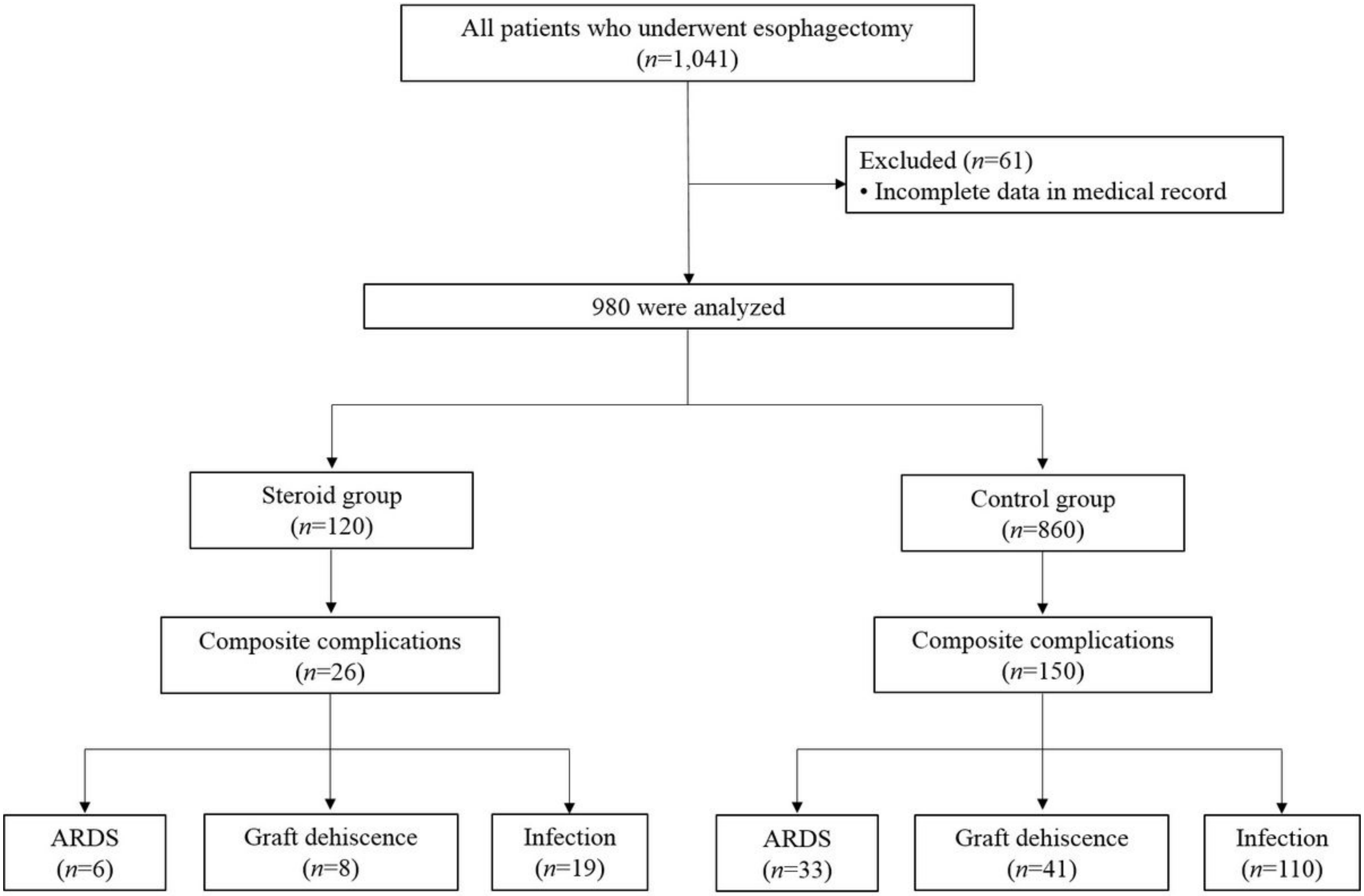

Figure 1

Flow diagram and the incidence of complications in each group. Abbreviation: ARDS Acute respiratory distress syndrome.

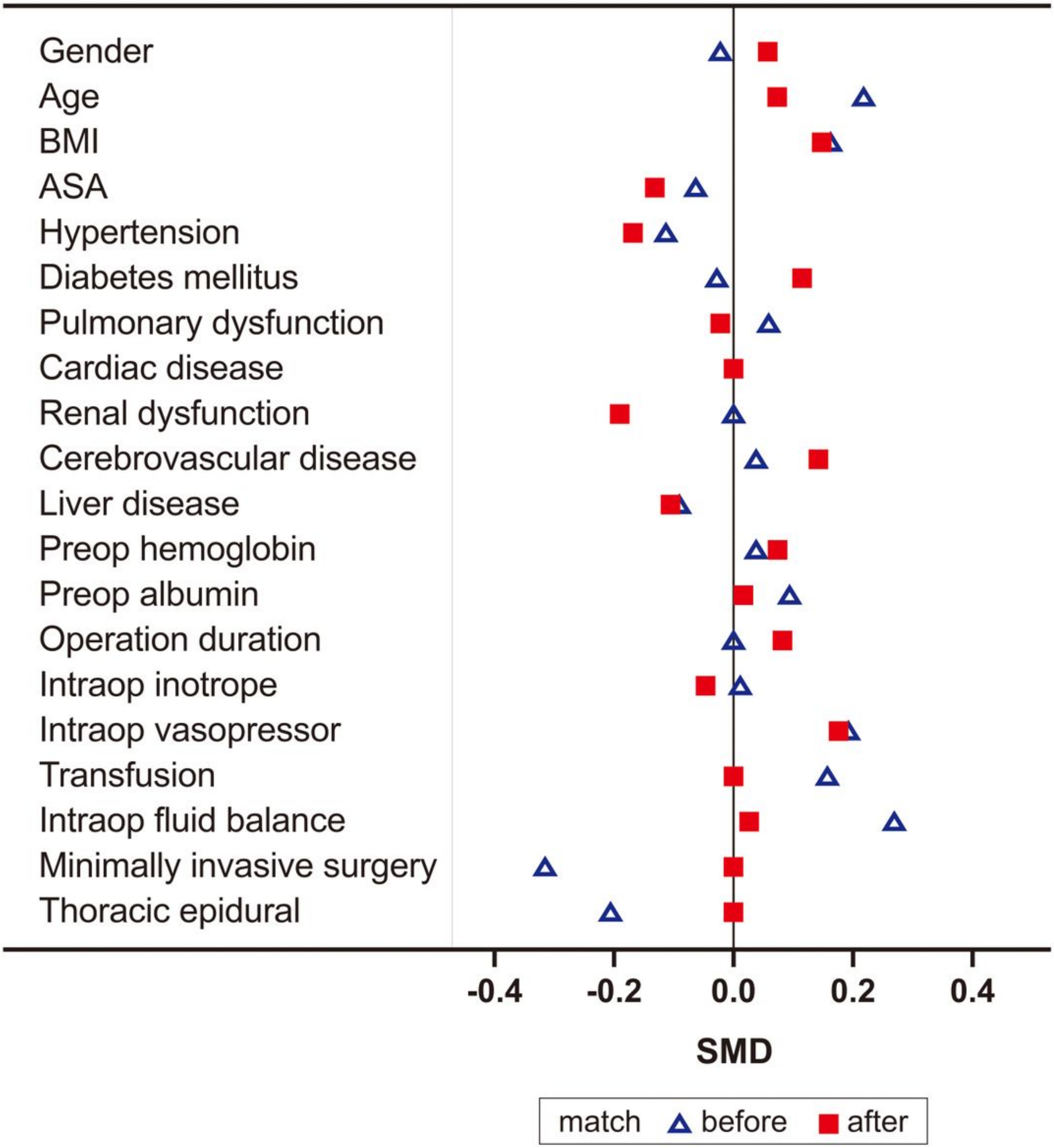

Figure 2

Covariance balance plots of standardized mean differences before (blue triangle) and after (red square) propensity score matching. Abbreviations: BMI Body mass index, ASA American Society of Anesthesiologist.