

# Risk Factors for an Intraoperative Arrhythmia during Esophagectomy

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**Purpose:** Arrhythmias after an esophagectomy (most commonly atrial fibrillation) are a significant contributing factor to patient morbidity. However, the significance of an intraoperative arrhythmia is not completely understood. The aim of this retrospective study was to determine the occurrence and risk factors for developing intraoperative arrhythmias in patients undergoing an esophagectomy. **Materials and Methods:** We reviewed the records of 427 patients who underwent a transthoracic esophagectomy between 2001 and 2005. Variables such as age, sex, hypertension, diabetes, cardiac disease, preoperative pulmonary function test (PFT) results, cancer level, combined radiochemotherapy, intrathoracic cavity adhesions and anastomosis site, hemoglobin, central venous pressure (CVP), fluid balance, serum potassium level, dose of vasopressors, temperature, and combined general and epidural anesthesia were analyzed as risk factors for the occurrence of an arrhythmia. We defined this arrhythmia as one not originating from the sinus node. **Results:** The incidence of intraoperative arrhythmia in this subset of patients was 17.1%, with a 37.2% reoccurrence rate during the first three postoperative days. Univariate and multivariate analysis revealed the presence of heart disease, poor PFTs, cervical anastomosis, elevated CVP, and higher ephedrine doses to be independent predictors of the development of an intraoperative arrhythmia. **Conclusion:** The incidence of intraoperative arrhythmia during esophagectomy was 17.1% with a 37.2% of reoccurrence rate.

**Key Words:** Arrhythmia, esophagectomy

## INTRODUCTION

A transthoracic esophagectomy with esophago-

gastrostomy for resection of an esophageal malignancy is associated with a high incidence of complications. Considerable progress has been made toward decreasing surgical complications (i.e., gastric fat necrosis, anatomic site leakage) because of standardization of surgical techniques.<sup>1</sup> However, pulmonary complications related to extensive lymphadenectomy and tachyarrhythmias still contribute to a poor outcome after an esophagectomy.<sup>2-6</sup> Anesthetic management for a transthoracic esophagectomy has focused on early extubation and fluid restriction to reduce postoperative lung complications.<sup>7</sup> However, little attention has focused on the development of arrhythmias during operation. Although it is unclear why an esophagectomy is associated with a high incidence of arrhythmia, right-sided heart strain and an imbalance of the autonomic nervous system associated with a radical dissection of the thoracic cavity have been suggested to be causative factors.<sup>3</sup> The incidence of postoperative arrhythmias related to an esophagectomy is as high as 13-64%,<sup>8,9</sup> and it has been shown to be associated with prolonged intensive care unit (ICU) and hospital stay, and an increase in mortality within the first 30 days after surgery.<sup>8</sup> Murthy et al. also reported increased pulmonary complication rates and surgical sepsis in cases involving arrhythmias.<sup>10</sup> Although age and an elevated body temperature have been recently reported as significant risk factors for supraventricular tachyarrhythmias after an esophagectomy, the pathogenesis is not completely understood.<sup>11</sup> To our knowledge, no information is available on the incidence and implications of an intraoperative arrhythmia during an esophagectomy; the

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aim of this study was to determine the incidence and risk factors for an arrhythmia in this setting. We intend to suggest anesthetic management by proposing intraoperative arrhythmia risk factors by retrospectively evaluating patients who did and did not develop an arrhythmia during surgery.

## MATERIALS AND METHODS

This study was performed after the approval of our Institutional Review Board. We reviewed the records of the patients who underwent a transthoracic esophagectomy for an esophageal cancer resection by a single surgeon from 2001 to 2005. All of the patients reviewed were operated upon through right posterolateral thoracotomy with a thoracic or cervical esophagogastronomy. Cases with incomplete information and with an unexpected surgical event, such as injury to adjacent vessel(s) and deviations in procedure protocol, were excluded. A total 427 patients were included in the study.

Data regarding age, sex, hypertension, diabetes, cardiac disease, preoperative poor pulmonary function test (PFT) results, cancer level, and concurrent combined radiochemotherapy were analyzed. Poor PFTs were defined as  $< 70\%$  of forced expiratory volume in 1 second ( $FEV_1$ ), and  $< 70\%$  of  $FEV_1$ /forced vital capacity (FVC) of predicted values. Patients were classified as having previous cardiac disease if they showed signs of arrhythmias or abnormalities of the ST segment, or there was evidence of old myocardial infarction (OMI) on a review of the preoperative EKG, or they had received medications related to previous cardiac disease. Patients with chronic arrhythmias were also included as having arrhythmias based on a preoperative EKG. The patient was placed into two categories at the same time if they had at least two cardiac risk factors. The existence of adhesion in the thoracic cavity, anastomosis site (thoracic or cervical), hemoglobin level, central venous pressure (CVP), intraoperative total fluid balance, intraoperative potassium level, dose of vasopressor before the development of arrhythmias, temperature measured at transthoracic period, and the use of combined intraoperative general and epidural anesthesia were

also analyzed. We examined the occurrence of intraoperative arrhythmias and their relation to postoperative occurrence of arrhythmias. Arrhythmia was defined as not having originated from the sinus node.

No premedication was administered. Anesthesia was induced with thiopental sodium and  $O_2$ /sevoflurane (isoflurane), followed by vecuronium to facilitate tracheal intubation. Anesthesia was maintained with sevoflurane/isoflurane,  $O_2$ /air, opioids when necessary, and one-lung ventilation was applied during transthoracic esophagectomy. In the case of combined general and epidural anesthesia, an epidural catheter was inserted at T4-5 or T5-6 interspace. A 5- to 10-mL solution of 0.25% or 0.125% bupivacaine was injected through the epidural catheter at an infusion rate of 2 mL/hr; 0.125% bupivacaine was continued throughout the operation. Patient monitoring included the use of EKGs, oxygen saturation by pulse oximetry, temperature, urine output, CVP, and direct arterial pressure. Anesthesia was performed by the same protocol. Ringer's lactate solution/normal saline was infused at a rate of 5 mL/kg/hr, and 500 mL of colloid or packed red blood cells were infused according to the anesthesiologist's decision, based on the intravascular volume status and the vital signs. CVP was maintained between 0 and 10 mmHg during the operation. Ephedrine was used when systolic blood pressure was  $< 20\%$  of the preoperative value, and continuous dopamine infusion was begun when repeated uses of ephedrine were necessary.

All patients underwent an initial abdominal exploration through an upper abdominal laparotomy. The stomach was mobilized and all lymph nodes involved were resected. A pyloroplasty was performed. After the abdominal stage, a right posterolateral thoracotomy was performed. The esophagus was mobilized with all the paraesophageal and subcarinal lymph nodes. Upper mediastinal, right and left paratracheal lymphatic tissues, including lymph nodes of recurrent laryngeal nerve, were removed. The esophagogastronomy was located in the thoracic inlet or cervical level (T/C). An EKG of the patients was monitored continuously in the ICU or subICU for at least three days after the operation.

Statistical analysis was performed with the SAS

program (version 8.2). Normal distribution of values was assessed by the Kolmogorov-Smirnov test. Univariate analysis was done using unpaired t-test or Mann-Whitney U-test, as indicated by the distribution of the parameters. Categorical parameters were analyzed by chi-square test. In order to prevent the loss of suspected variables, parameters for those *p*-value less than 0.25 after univariate analysis or thought to be important for medical reasons were entered in an explorative stepwise logistic model to identify the factors relevant to the incidence of intraoperative arrhythmias. A *p*-value less than 0.05 was considered significant.

## RESULTS

Thirty-six patients were excluded because of incomplete medical records. The incidence of an intraoperative arrhythmia was 17.1% (*n* = 73), which was managed as follows: supplementation of electrolyte solution (68.1%), short acting beta-blocker (66.7%), calcium-channel blocker (63.2%), digitalis (31.2%), adenosine (26.3%), and cardioversion (7.2%). In only eight cases was arrhythmia sustained to the end of operation. The types of arrhythmia included all ectopic atrial and ventri-

cular rhythms; 37.2% (27/73) of intraoperative arrhythmias reoccurred within three days following the operation. In cases of intraoperative arrhythmias, the following postoperative complications were found: pulmonary complications (chylothorax, pneumothorax, pneumonia), wound infections, gastric fat necrosis, and anastomosis leakage (58.2%, 4.2%, 3.8%, and 3.5%, respectively).

Table 1 shows the patient data, including preoperative demographics. The patients with cardiac disease were classified as patients with arrhythmias (*n* = 26), an ST abnormality/OMI on EKG (*n* = 65), and medications related to a history of cardiac disease (*n* = 49). In each case, the incidence of arrhythmia during an operation was 45.6%, 17.5%, and 21.3% respectively (*p* < 0.05). Table 2 lists the intraoperative factors investigated for their potential effects on the occurrence of arrhythmia. In 355 patients, an esophagogastrotomy was performed at the thoracic inlet, while in 72 patients, this was performed at the cervical level. The incidence of arrhythmia was higher in patients undergoing cervical anastomosis (26.4% vs. 15.2%). In cases of thoracic esophagejejunostomy, all arrhythmias developed during the thoracotomy. However in six (6/19, 31.6%) of the cervical cases, the arrhythmias were detected

**Table 1.** Patient Characteristics associated with Intraoperative Occurrence of Arrhythmias

Variables	Without arrhythmia ( <i>n</i> = 354)	With arrhythmia ( <i>n</i> = 73)	P1 (Univariate analysis)	P2, RR (CI) (Multivariate analysis)
Age (yrs)	61.7 ± 7.8	63.9 ± 8.5	0.22	0.10, 1.18 (0.92 - 2.91)
Sex (M/F)	323/31	67/6	0.94	
Hypertension (%)	86 (24.2)	18 (24.6)	0.93	
Diabetes (%)	56 (15.9)	13 (17.5)	0.81	
Heart disease (%)	85 (24.0)	29 (39.7)	0.04	0.03, 1.80 (1.11 - 2.87)
Poor PFTs (%)	17 (4.8)	18 (24.7)	< 0.01	0.01, 1.05 (1.01 - 1.07)
Cancer level (U/M/L)	46/163/145	11/35/27	0.79	
Radiochemotherapy (%)	57 (15.4)	17 (23)	0.19	0.059, 1.42 (0.98 - 2.01)

Data are presented as No (%), or mean ± SD.

P1 represents the probability value from t-test or Fisher's exact test.

RR (CI) represents relative risk (95% confidence interval).

P2 represents the probability value from multiple regression analysis.

Poor PFTs: < 70% FEV<sub>1</sub> and < 70% FEV<sub>1</sub>/FVC of predicted values.

Cancer level (U/M/L); cancer level (upper/middle/lower).

**Table 2.** Intraoperative Factors associated with the Occurrence of Arrhythmias

Variables	Without arrhythmia (n = 354)	With arrhythmia (n = 73)	P1 (univariate analysis)	P2, RR (CI) (multivariate analysis)
Adhesion (%)	131 (37.0)	27 (36.9)	0.90	
Anastomosis site (T/C)	301/53	54/19	0.03	0.03, 2.75 (1.55 - 5.32)
Hemoglobin (mg/dL)	12.5 ± 1.2	11.9 ± 3.5	0.72	
Central venous pressure (mmHg)	4.4 ± 2.6	7.8 ± 4.0	0.07	0.04, 1.08 (1.00 - 1.15)
Crystalloid solution (mL/kg/hr)	4.2 ± 0.2	4.4 ± 0.3	0.81	
Urine output (mL/kg/hr)	0.75 ± 0.21	0.69 ± 0.30	0.69	
Serum potassium (mmol/L)	3.7 ± 0.4	3.7 ± 0.6	0.87	
Dose of ephedrine (mg/kg)	0.13 ± 0.04	0.38 ± 0.06	0.05	0.03, 2.97 (1.15 - 7.37)
Temperature (°C)	35.4 ± 0.5	35.1 ± 0.5	0.81	
Combined anesthesia (%)	156 (44.1)	24 (33.3)	0.10	0.09, 1.24 (0.91 - 2.90)

Data are presented as No (%). or mean ± SD.

P1 represents the probability value from t-test or Fisher's exact test.

RR (CI) represents relative risk (95% confidence interval).

P2 represents the probability value from multiple logistic regression analysis.

Anastomosis site (T/C); Anastomosis site (Thoracic inlet/cervical).

during the cervical anastomosis. There was no difference in the intraoperative fluid balance between the two groups ( $p = 0.67$ ). Intraoperative combined general and epidural anesthesia was performed in 180 patients (42.1%) and was not a significant factor in the development of arrhythmia ( $p = 0.09$ ).

Univariate analysis revealed age, cardiac disease, poor PFTs, concurrent radiochemotherapy, anastomosis site, CVP, dose of ephedrine, and combined general and epidural anesthesia to be predisposing factors ( $p < 0.25$ ). After multivariate analysis, cardiac disease, poor PFTs, anastomosis site, elevated CVP, and the ephedrine dose were the significant independent parameters ( $p < 0.05$ ). Concurrent combined radiochemotherapy was borderline significant ( $p = 0.059$ ).

## DISCUSSION

In our analysis, heart disease, poor PFTs, cervical anastomosis, elevated CVP, and higher doses of ephedrine appeared to increase the risk of intraoperative arrhythmias during transthoracic esophagectomy.

It is well established that patients with limited pulmonary function are more prone to perioperative complications after noncardiac thoracic surgery, including an esophagectomy, because of diminished cardiopulmonary reserve.<sup>5</sup> This study also revealed that poor PFTs is a important risk factor.

CVP is determined by an interaction between the cardiac function and the return of blood from the vascular reservoir to the heart.<sup>12</sup> An increase in cardiac function without an increase in the return function results in a rise in cardiac output with a fall in the CVP.<sup>13</sup> The converse is true for a decrease in the cardiac or return functions.<sup>13</sup> It is possible that elevated CVP, with the same fluid balance between the two groups, is a consequence of a more compromised heart function suffered by this group of patients. It is remarkable to be a statistically different CVP between the two groups, even though this difference might not be clinically meaningful.

This study has one important limitation. An exact explanation of the blood pressure during operation is not available because this is a retrospective analysis; however, it is presumed that acceptable vital signs were maintained throughout

the operation in both groups. Stippel et al. explained that the administration of a vasopressor during the postoperative period was not secondary to a lack of body fluid but instead might reflect the imminent inflammatory reaction.<sup>6</sup> However, they did not measure inflammatory mediators such as cytokines. Our result is in agreement with that reported by Stippel et al., who showed that the vasopressor dose was higher in those patients who developed arrhythmias. However, because the ephedrine dose used before the new onset of arrhythmias was almost parallel with the occurrence of arrhythmia, the time intervals were insufficient to reflect inflammatory reactions in this study. It is believed that the ephedrine dose used to maintain the acceptable range of vital signs was higher in the patients who developed arrhythmias, which might reflect the difference in the heart function between the groups.

An elevated temperature measured at 24 and 48 hours postoperatively was the most important predisposing factor for arrhythmias.<sup>6</sup> An inflammatory reaction and subsequent adrenergic stimulation was suggested as a possible predictor of postoperative supraventricular tachyarrhythmias.<sup>6</sup> We evaluated the temperature measured at the transthoracic portion of the operation. The temperature did not differ  $< 36.5^{\circ}\text{C}$  in both groups. This was attributed to the effects of impairment in the temperature regulatory function, an open thoracic cavity, and infused fluid during anesthesia.

In this study, the transthoracic esophagectomy through a right thoracotomy was completed, followed by an intrathoracic or cervical anastomosis. Cervical anastomosis was generally performed when the tumor was located in the upper third of the esophagus.<sup>14</sup> In the case of a cervical anastomosis, a more traumatic surgical dissection was applied in accordance with the displacement of the original cardioesophageal junction up to a more proximal anatomical site, which could induce arrhythmia.

Increases in heart rate and heart rate variability during operation were associated with postoperative arrhythmias in patients undergoing pulmonary surgery.<sup>11</sup> Theoretically, thoracic epidural anesthesia could have effects on the heart function via modulation of autonomic function.<sup>15-16</sup> How-

ever, a previous study showed that thoracic epidural anesthesia does not affect the occurrence of arrhythmia in esophagectomy patients.<sup>17</sup> Further studies will be required to ascertain the clinical effects of thoracic epidural anesthesia on arrhythmias.

In our study, patients with arrhythmias on preoperative EKG showed a 45.6% incidence of arrhythmia during operation. The preoperative arrhythmias included both chronic arrhythmias and newly developed arrhythmias on preoperative EKG. If we had excluded chronic arrhythmias, we could have better delineated the significance of preoperative arrhythmias. This study has several limitations: previous patient cardiac medications were unknown, and the specific types and duration of intraoperative arrhythmia were also unavailable, due to the retrospective study design. However, the 37.2% rate of reoccurrence of the arrhythmia after an operation is outstanding. The mechanism of arrhythmia reoccurrence is uncertain, but it may be related to the extent of trauma during the dissection, or to the limited cardiopulmonary reserve of the patient. Anesthetic management of those with the risk factors for intraoperative arrhythmia will need to account for the possibility of arrhythmia during and after the operation.

In conclusion, cardiac disease, poor PFTs, cervical anastomosis, elevated CVP, and higher ephedrine doses were factors predicting the occurrence of an arrhythmia during an esophagectomy.

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