UNIVERSITE DE NANTES

_____

FACULTE DE MEDECINE

_____

Année : 2019 N° 2019-174

THESE

pour le

DIPLOME D'ETAT DE DOCTEUR EN MEDECINE

Anesthésie Réanimation

par

MILLOUR Pierre

Né le 11/01/1990 à Fréjus (83)

_____

Présentée et soutenue publiquement le 09/10/2019

_____

Risk factors of severe postoperative complications following elective esophagectomy.

Facteurs de risques de complications post-opératoires graves après chirurgie de résection oesophagienne carcinologique.

_____

Président : Monsieur le Professeur Bertrand ROZEC

Directeur de thèse : Docteur Raphael CINOTTI

Remerciements :

- Au Docteur Raphael Cinotti, merci pour toute ton aide précieuse pour ce travail, le premier parmi d'autres je l'espère, aux parties d'échecs et aux BALC

- Au Professeur Bertrand Rozec, merci de présider ce jury de thèse et de me donner la possibilité de travailler en anesthésie-réanimation avec l'équipe du « bas »

- Au Professeur Karim Asehnoune, merci beaucoup de participer à ce jury de thèse, je sais maintenant « qu'en réa PTMC, on n'est pas au kebab » ☺

- Au Professeur Guillaume Meurette, merci beaucoup de participer à ce jury et d'y apporter votre expertise

- Aux services d'anesthésie et réanimation du CHU de Nantes qui m'ont permis d'apprendre ce formidable métier

- Aux services d'anesthésie et de réanimation du CHD de La Roche sur Yon, merci pour votre accueil chaleureux, j'ai énormément appris à vos côtés

- Au service de réanimation de Cholet, merci pour ce semestre formateur

- A ma famille qui m'a soutenu et encouragé depuis cette première année de médecine

- A mes amis du Sud, j'espère que ce post internat nous permettra de tous profiter à nouveau ensemble de grands moments

- A tous les nantais rencontrés depuis ce premier semestre en novembre 2014

- A Chrystelle, quel bonheur de vivre à tes côtés, tu me supportes et m'encourages depuis toutes ces années, entre Nice et Nantes et à notre famille qui va encore s'agrandir dans les mois à venir.

Table of contents

1. Abstract

Introduction. The incidence of postoperative complications after elective esophagectomy remains high. The risk factors of post-operative complications are poorly described.

Patients and Methods. We conducted a retrospective study in four centres in Nantes. Patients undergoing elective esophagectomy for tumour resection were eligible. The primary end point was a composite criterion including invasive mechanical ventilation duration ≥ 48h and/or surgical complication and/or mortality at day-90. Secondary endpoint was the prediction of invasive mechanical ventilation requirement, after surgery.

Results. Between 2012 and 2017, 215 patients were included. 77 (35.6%) patients displayed the primary endpoint. The day-90 mortality was 11 (5.2%). In multivariate analysis, Centre N°3 (OR 0.1 CI_{95} (0.02-0.3), $p < 10^{-5}$), preoperative renutrition (OR 0.3 (0.08-0.7), p=0.01) and neoadjuvant radiotherapy (OR 0.5 (0.2-0.9), p=0.02) were associated with less complications. Esophageal resection with triple approach (cervical, thoracic and abdominal) was associated with more complications (OR 18 (3.7-151), p=0.002). The leukocytes evolution in the first 5 days after surgery was associated with the need of invasive mechanical ventilation (p=0.001).

Discussion. Among modifiable risk factors, the promotion or early systematic renutrition seems mandatory. Specific bundles of care are to be promoted in order to improve outcome. Leukocytes monitoring could predict the need of invasive mechanical ventilation and thus prolonged in-ICU monitoring.

2. Abbreviations list

ASA: American Society of Anesthesiology
BMI : Body Mass Index
COPD: Chronic Obstructive Pulmonary Disease

3. Introduction

Oesophageal cancer is the 7th cause of cancer-related deaths in the world with almost 400,000 deaths per year in 2016. [1] The overall incidence is 3.8 / 100,000 inhabitants, with a male / female ratio of three to four times in adenocarcinoma and similar for squamous cell carcinoma.[2] Squamous cell carcinoma and adenocarcinoma represent nowadays the majority of cancer histology.[3] The 5-year prognosis is poor, with less than 15% survival without treatment. Oesophageal resection is the first line therapy, sometimes after neoadjuvant therapy for locally advanced disease [4] and improves prognosis up to 40-50% for R0 resection, and the 5-year survival reaches 74% in pT0 resection.[5] Ivor-Lewis technique consists of an abdominal followed by a thoracic approach for surgical anastomosis. Morbidity remains high despite surgical and anaesthetic improvements with a complication rate of 59% (including anastomotic leak (11.4%), atrial fibrillation (14.5%)), including 14.9% of health-care related pneumonia. [6] Respiratory and surgical complications are also present in 50% of patients. [7] Recently, hybrid minimally invasive esophagectomy showed a decrease of postoperative complications but remain significant (36%).[8] Recognition of high-risk patients for post-operative complication could be helpful to improve the outcome. There are little data in the current literature describing the risk-factors of post-operative major complications in the following of elective esophageal surgery. The aim of our study was to delineate the risk factors of severe complications in patients undergoing esophageal surgery.

4. Methods

We conducted a retrospective study from 2012 to 2017 in four centres in Nantes (France): one university hospital, one specialized cancer centre and 2 private clinics. The study was approved by the ethics committee (CERAR-Comité d'éthique en Anesthésie-Réanimation, Société Française d'Anesthésie-Réanimation, France, N°IRB 00010254 - 2018 - 030).

Inclusion criteria

The study included patients with squamous cell carcinoma and adenocarcinoma of the middle or lower third of the oesophagus who underwent a surgical resection. Inclusion criteria were: age over 18 years old, surgery with minimally or open abdominal and thoracic surgery, with or without cervical approach.

Exclusion criteria

Exclusion criteria were emergency surgery (caustic burn), surgery without thoracic approach (transhiatal approach), pregnancy, patients without health-insurance coverage. When the primary endpoint was not assessable because of missing data, patients were excluded.

Data collection

Demographic and clinical characteristics data collected were age, gender, height, weight, ASA class, tobacco and alcohol consumption, arterial hypertension, heart disease, dyslipidaemia, arteriopathy, chronic respiratory insufficiency, chronic obstructive pulmonary disease (COPD), previous cancer, diabetes, chronic kidney injury, denutrition (weight loss > 10-15% in the previous 6 months and/or body mass index < 18.5kg/m^2), preoperative renutrition management, cirrhosis, histological type, anatomical localisation, pTNM classification, resection margins. Preoperative biological data were collected: haemoglobin,

blood platelets, neutrophil and lymphocytes count, natremia, kalaemia, albumin, prothrombin ratio and partial thromboplastin time. Perioperative data collected were the duration of surgery, duration of abdominal and thoracic approach, duration of one-lung ventilation, tidal volume during abdominal and thoracic approach, bleeding, vascular expansion (cristalloids and colloids). Specific anaesthetic management was collected: central venous line placement, epidural analgesia, hemodynamic monitoring, minimal SpO2, alveolar recruitment, use of inhaled or intravenous anaesthetic agent, blood products transfusion, use of norepinephrine. We also reported the length of mechanical ventilation, intensive care unit length of stay. Postoperative clinical or biological data were collected at 8.00 am at day 1, 2, 3 and 5 after surgery: heart rate, respiratory rate, SpO2, arterial pressure, temperature, daily diuresis, norepinephrine, vascular expansion, invasive mechanical ventilation, non-invasive mechanical ventilation, high flow nasal cannula, face mask oxygen, blood products transfusion, amount of the drain, haemoglobin, platelets, natremia, kalaemia, urea, creatinine, calcemia, leucocytes, lactate, PaO2, PaCO2, FiO2, analgesia (epidural or/and intravenous), thromboprophylaxis, physiotherapy, enteral/parenteral feeding, central venous line, arterial catheter.

If available, chest X-rays and electrocardiogram were analysed on day 1, 2, 3 and 5.

Surgical complications were recorded: anastomotic leak, conduit necrosis, chylothorax, recurrent paralysis, new thoracic intervention. Respiratory complications included: health-care associated pneumonia, respiratory failure, atelectasis, pleural effusion, acute respiratory distress syndrome, pulmonary embolism and the need of invasive mechanical ventilation. The other complications recorded during hospital stay were: cardiac arrhythmia, mediastinitis, deep vein thrombosis, the need of renal replacement therapy. The in-intensive care unit length-of-stay, in-hospital length of stay, in-hospital mortality and day-30, day-90 mortality were also recorded.

Primary Outcome

The primary end point was a composite criterion including invasive mechanical ventilation duration ≥ 48h and/or surgical complication in the first 90 days and/or mortality at day-90. The primary outcome was to delineate the risk factors associated with the primary endpoint.

Secondary Outcomes

Secondary outcomes were the epidemiology of patients undergoing elective esophagectomy in these institutions, the description of perioperative management. Another secondary endpoint was to underline the clinical and biological features predictive of invasive mechanical ventilation patients after surgery.

Statistical analysis

Continuous data are expressed as mean (±standard deviation) or median [quantile] and compared with the Student t-test or Mann-Whitney test whenever appropriate. Nominal data are expressed as N(%) and compared with the χ^2 or Fisher exact test whenever appropriate. Variables identified as potential risk factors for severe post-operative complications by the univariate analysis with a cut-off at 0.15, were included in a multivariable logistic regression model and backward selection was applied. The final model was presented with the crude odds ratio (OR) and 95 % confident interval (CI). The outcomes of patients in the group with complications and those in the group without were compared with the χ^2 or Fisher's exact test for qualitative variable. In order to predict the need of invasive mechanical ventilation after surgery, we selected patients with invasive mechanical ventilation at day-2 and/or day-3 and/or day-5. Patients still under mechanical ventilation at day-1 after surgery were removed. A one-way ANOVA analysis was performed to predict the need of mechanical ventilation with the evolution of the following parameters in the first 5 days after surgery: heart rate,

mean arterial pressure, systolic arterial pressure, haemoglobin, leucocytes, platelets, natremia, chest X-ray (atelectasis, pleural effusion, infiltrate). All statistical tests were two-sided. A p value <0.05 was considered statistically significant. Statistical analyses were performed with R Studio version 1.0.136 (The "R" Foundation for Statistical Computing, Vienna, Austria).

5. Results

From January 2012 to December 2017, 225 patients underwent esophagectomy and ten patients were excluded because of missing data. Seventy-seven (35.8%) patients displayed the primary endpoint. The day-90 mortality was seen in 11 (5.2%) patients. The median age was 63 years [56-69], 180 (85%) patients were male and the median ASA class was 2 [2-3]. Thirty-three (15%) patients were operated in Centre 1, 51 (24%) in Centre 2, 50 (23 %) in Centre 3 and 81 (38%) in Centre 4. One hundred and forty (65%) patients had adenocarcinoma, 66 (31%) had squamous cell carcinoma. Two hundred and two (94%) patients underwent an Ivor Lewis intervention, the abdominal approach was the first choice (151 (69.6%) patients). Neoadjuvant therapy was performed in 156 (72.6%) patients who received chemotherapy and 89 (41.4%) patients who received radiotherapy. Postoperative complications are displayed in Table S1 in supplemental data.

Regarding the primary end-point, more patients displayed an ASA class of 3 (39 (50.6%) versus 41 (30.8%), p=0.013), alcohol consumption (20 (27.8%) versus 20 (14.9%), p=0.026), arteriopathy (13 (16.9%) versus 9 (6.6%), p= 0.018). Neoadjuvant therapy with radiotherapy was significantly more frequent in the group with the primary end point (38 (52.8%) versus 51 (37.8%) p=0.038). Complete demographic and clinical data are displayed in Table 1. There was no difference between the two groups regarding the preoperative biological data (Table 2). There was no significant difference regarding the TNM classification between the two groups (Table 3).

Regarding peri-operative data, there were more complications when inhaled anaesthetic agents were used (52 (80%) versus 69 (57%), p=0.001). Epidural analgesia was more frequent in the group without complication (115 (87.8%) versus 53 (70.7%), p=0.02). Complete peri-operative data are displayed in Table 4.

Complete clinical, biological, radiological data about the primary end point on day 1, 2, 3 and 5 are displayed in table S5, S6, S7 and S8 in supplemental data, respectively.

Multivariable analysis

In multivariate analysis, three factors were significantly associated with less complications: Centre N°3 (OR 0.1 CI_{95} (0.02-0.3), $p < 10^{-5}$), preoperative renutrition (OR 0.3 CI_{95} (0.08-0.7), p=0.01), and neoadjuvant radiotherapy (OR 0.5 CI_{95} (0.2-0.9) p=0.02).

Because of the obvious centre effect, we compared demographical and clinical characteristics between centres. There were significantly less ASA 3 patients in Centre N°3 (10 (20.4%) patients versus 70 (42.2%) p=0.001). In Centre N°3, patients had significantly less chronic hypertension (24 (48%) versus 114 (68.7%), p=0.008) and dyslipidaemia (22 (44%) versus 101 (60.8%), p=0.035). There was an unbalance between centres regarding the TNM classification (Table S3 in supplemental data). In Centre N°3, 50 (100%) patients received epidural analgesia versus 119 (75.3%) in others (p<0.05), complete perioperative data between Centre 3 and others are displayed in Table S4 in supplemental data.

Secondary outcomes

The in-intensive care unit and in-hospital length of stay were both longer in the group with the primary endpoint, 9 (7-11) days versus 15 (10-20) days and 16 (14-18) versus 28 (18-39.5), respectively). Four (5%) patients received extrarenal replacement therapy in the group with complications (p=0.007).

We aimed at predicting the patient's need for invasive mechanical ventilation after surgery. Fifteen patients received mechanical ventilation between day 2 and day 5, without mechanical ventilation at day 1. We found no statistically significant results for heart rate, mean arterial pressure, systolic arterial pressure, haemoglobin, platelets, natremia, chest X-ray (atelectasis,

pleural effusion, infiltrate). The leukocytes evolution during the first five days was associated with the need of invasive mechanical ventilation (Figure 1).

6. Discussion

In this retrospective study, we found three factors significantly protective of severe post-operative complications after elective esophagectomy (Centre N°3, preoperative renutrition, neoadjuvant radiotherapy) and one factor (three-incision approach/McKeown esophagectomy) associated with more complications.

Oesophageal resection has been routinely performed for many years and still bears significant morbidity (up to 50%), with frequent respiratory complications, anastomotic leak, cardiac arrhythmia, leading to an increased hospital and intensive care unit stay. Pneumonia has been largely reported: Asaka et al [9] reported an incidence of postoperative pneumonia of 24.5% in a retrospective cohort between 2008 and 2015 in Japan.
Two randomized-controlled studies in Europe in 2012 and 2019 found an interest in the mini invasive approach, with fewer postoperative pneumonia (14.6% and 12% respectively). [10] [8] Recently, Low et al. in an international retrospective cohort reported up to 59% of perioperative complications with 15% of pneumonia and 11.4% of anastomotic leak. [6] In a retrospective cohort in North America Seesing et al. [11] found an incidence of pneumonia of 10.9%. Moreover in the 2000's, Hulscher and al [9] found an in-hospital mortality of 3% and a 5-years survival of 39% after Ivor Lewis. Recently, Mariette and al [8] found a day-30 and a day-90 mortality of 1 and 5% respectively. There are few French cohorts on this topic. Our results are in-line with previously published data regarding morbidity and mortality. These results advocate for urgent specific management to improve the outcome.

There is a major centre effect in our study, in spite of similar volume. Demographical and clinical characteristic before surgery were comparable between centres, except ASA classification, hypertension and dyslipidaemia. This classification from 1941 discriminates

patients in 6 groups, according to the anaesthetic risk. Despite criticisms, it's always used nowadays. Recently, a large retrospective study found a correlation between morbidity/mortality and the ASA classification [12]. In spite of its oversimplification, the ASA classification remains thus useful. However, the ASA classification should be cautiously interpreted, since it could be used for billing services information and could be therefore utilized by institutions by overclassifying patients. [12] There were no statistically significant differences regarding other comorbidities between centres, except the TNM classification. Pathological tumour-node-metastasis stage is poorly associated with 5-year survival [13] and quality of life, but not with postoperative complications. [14] Since this histology is gathered after surgery, this imbalance between centres cannot be accounted for.

Some specific bundle of care in Centre N°3 are noteworthy. First, epidural analgesia was systematic. It's recommended in first line postoperative pain management. [15] Postoperative analgesia is better in esophagectomy with epidural analgesia during the first 5 days after surgery in comparison with intravenous analgesia [16]. Popping et al. [17] in a meta-analysis including 5904 patients found also less pneumonia in abdominal and thoracic surgery and epidural analgesia was associated with less mortality and morbidity in another one including 9044 patients. [18] Others effects like decreased anastomotic leak and decreased recurrence of cancer have conflicting results. [19] In the recent Mariette's cohort [8], epidural analgesia was performed in all patients. Thus, we believe that epidural should be systematically performed in these patients.

The surgeon's experience is important on perioperative complications. The rate of anastomotic leak decreases when he/she has performed at least 100 procedures: van Workum

[20] found that 119 cases of minimally Ivor Lewis were requested to reach the plateau of the learning curve. However, this parameter was not available in our study.

Nutritional support was a protective factor against complication. Oesophageal cancer is the cancer associated with the greatest weight loss before diagnosis. Malnutrition is diagnosed in up to 80% patients [21] and is associated with increased morbidity and mortality after surgery [22]. A prognostic score including the body mass index and scanographic evaluation of the psoas thickness, is able to predict outcomes after surgery and identifies patients requiring preoperative rehabilitation [23]. Intensive nutritional support before surgery decreases short-term postoperative complications and greater neoadjuvant therapy completion rates [24]. This nutritional rehabilitation can be performed orally or with a nasogastric tube or jejunostomy when oral intake is not sufficient, 4-5 weeks before surgery in patients with low physical reserves. [25] We didn't identify renutrition modalities in our cohort, but achieving optimal nutrition status before oesophageal surgery seems of paramount importance.

Three-field surgical approach, described in 1976 by McKeown, is performed in middle of inferior oesophageal cancer. This approach is currently less utilized, compared to the two-field approach in Europe and North America, [22], due to a possible increase in anastomotic leak and nerve injury. [23] A retrospective study found less respiratory complications, anastomotic leakage and nerve injury in the minimally Ivor-Lewis approach. [24]. Another study didn't find any difference in the incidence of anastomotic leakage between minimally or hybrid two or three field approach. [26] A randomized trial comparing double versus triple approach is currently performed (N°NCT 2333). Our results suggest the superiority of the 2-field approach.

The prediction of in-hospital complications after esophagectomy is challenging, and some markers have been most studied. Park and al. [26] found day-3 CRP was a predictive marker of anastomotic leak. Shao and al. [27] pointed out that the CRP/albumin ratio at day-3, could predict anastomotic leak. Hoeber et al. in a study of 45 patients [28] suggested that elevated day-2 and day-3 CRP and elevated day-3 PCT could predict infectious and surgical complications. Leukocytes increase is common after surgery, with a maximum level at day-2 after surgery. [27] However, our study is the first to establish a relationship between the evolution of leukocytes and the need of invasive mechanical in the first five days after this surgical procedure. Thus, this easy-to-use biomarker could be helpful in screening patients requiring extra-monitoring after surgery.

Our study bears limitations. Although this study is retrospective, this is one of the largest French cohort on this topic including to the best of our knowledge, patients from several public and private structures. In spite of a recruitment period of more than 5 years, the number of patients included can seem low. In comparison, during a similar period, Hayoung Choi et al. performed a cohort of 1132 patients in Seoul (10 millions inhabitants), whereas our city covers an area of less than 1 million inhabitants, which could explain the modest number of patients. [28] Because of the retrospective nature of the study, there are missing data and we did not perform multiple imputation analysis.

Between day 1 and day 5, few complications requiring mechanical ventilation occurred in patients. Only eleven patients required mechanical ventilation during screening period. In comparison, 46 (21.8%) patients required mechanical ventilation for more than 24 hours, so 36 patients after day 5, complications occurred later.

We couldn’t study the association between several markers like PCT, CRP or albumin and complications either because of lacking data or because they were not dosed. The centre effect was also important in our study. Specific surgical and anaesthetic bundle of cares should be promoted in order to facilitate high-quality management. Finally, our analysis suggest association and not causation. Nonetheless, easy and potentially important management such as preoperative nutrition, epidural analgesia should be encouraged.

7. Conclusion

Esophagectomy with abdominal and thoracic approach is the gold standard procedure to treat oesophageal cancer of the middle or lower oesophagus. Perioperative morbidity and mortality remain high despite improvements in surgical and anaesthetic procedures. Leukocytes monitoring on the first 5-days after surgery could be interesting to detect early major complications. In order to improve the outcome of these patients, nationwide research networks are urgently needed.

8. Tables and Figures

Table 1: Demographic and clinical characteristics of patients between two groups.

	No complication N= 138 (64.2%)	Complication N=77 (35.8 %)	P-value
Age	63 [57-68]	62 [56-68]	0.7
Male	111 (81%)	63 (81.8%)	0.9
BMI	25 [22-28]	24.9 [21.2-27.3]	0.7
ASA 1	12 (8.9%)	4 (5.19%)	0.01
ASA 2	82 (60.7%)	34 (44.2%)	
ASA 3	41 (30.4%)	39 (50.7%)	
Arterial hypertension	85 (62.5%)	52 (67.5%)	0.5
Dyslipidaemia	72 (53%)	50 (65%)	0.09
Cardiopathy	24 (17.8%)	20 (26%)	0.2
Arteriopathy	9 (6.6%)	13 (16.9%)	0.02
Smoking	84 (62.7%)	50 (66.7%)	0.6
Alcohol	14 (10.2%)	13 (17.3%)	0.1
Previous cancer	26 (19.4%)	12 (15.8%)	0.5
Denutrition	75 (56.4%)	47 (61.8%)	0.4

Legend: BMI Body Mass Index, ASA American Society of Anesthesiology

Table 2: Biological characteristics between two groups.

	No complication N= 138 (64.2%)	Complication N= 77 (35.8 %)	P-value
Haemoglobin (g/dl)	13 [11.8-14]	12.9 [11.9-14]	0.9
Platelets (G/L)	229.5 [190-291.3]	219.5 [186.75-271.5]	0.1
Neutrophils (G/L)	3751 [3062 -5137]	4133 [3420-5226]	0.5
Lymphocytes (G/L)	1371 [728-1874]	1210 [733-1880]	0.5
PT	98 [94-100]	99 [87.8-106.3]	0.7
Urea (mmol/L)	5.7 [4.5-6.9]	5.7 [4.2-7.1]	0.9
Creatinin (μmol/L)	65 [49.5-84.8]	67 [54.5-88.3]	0.3
Albumin (g/L)	43 [41-45]	42 [40-45]	0.9

Legend: PT = prothrombin time

Table 3: Oncologic data between groups

	No complication N= 138 (64.2%)	Complication N=77 (35.8 %)	P-value
Histological type			
-Adenocarcinoma	97 (71.3%)	43 (57.3%)	0.1
-Squamous cell carcinoma	36 (26.5%)	30 (40%)	0.1
-Other	3 (2.2%)	2 (2.7%)	0.1
pTNM classification			
-T0Nx	20 (15.5%)	9 (13.2%)	0.8
-T1Nx	31 (24%)	15 (22.1%)	
-T2Nx	20 (15.5%)	12 (17.7%)	
-T3Nx	56 (43.4%)	32 (47.1%)	
-T4Nx	2 (1.6%)	0 (0%)	
R0 resection	123 (93.9%)	70 (94.6%)	0.8
Neoadjuvant therapy			
-Radiotherapy	51 (37.8%)	38 (52.8%)	0.04
-Chemotherapy	99 (75%)	57 (78.1%)	0.6
Adjuvant chemotherapy	41 (31.8%)	14 (20%)	0.08

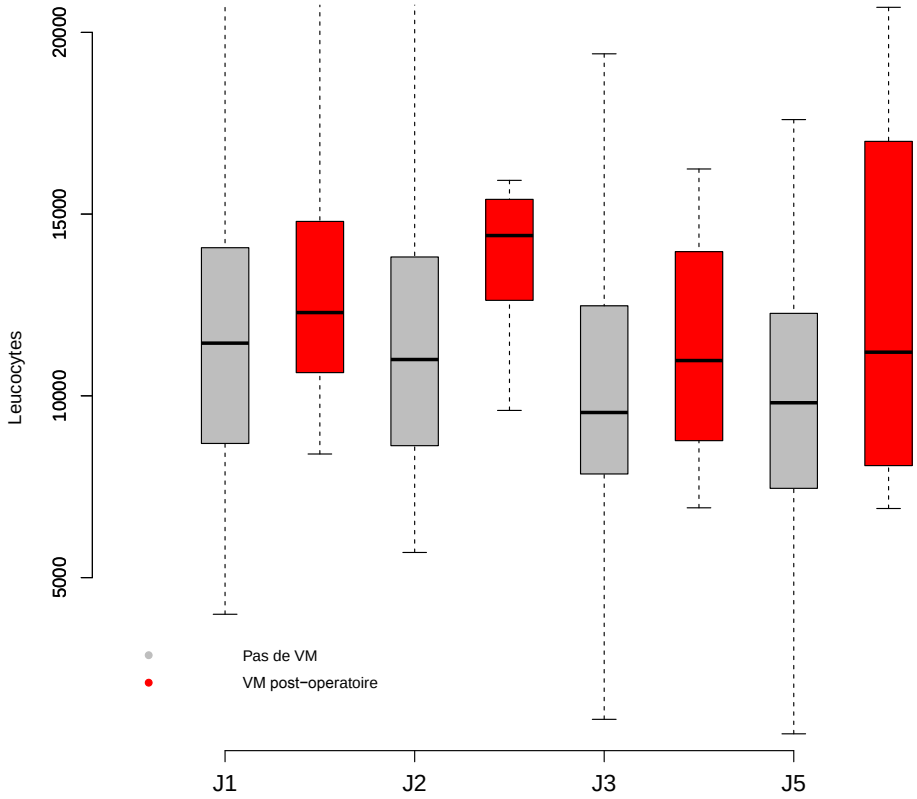
Table 4: Perioperative data between two groups

Variable	No complication N= 138 (64.2%)	Complication N=77 (35.8 %)	P.value
Central venous line	75 (56%)	41 (54.7%)	0.9
Central venous line complication	0 (0%)	1 (1.5%)	0.2
Supine (mn)	180 [150-221.5]	180 [120-238]	0.2
Left lateral position (mn)	159 [120-193]	130 [120-190]	0.5
Median tidal volume (ml)	513 [482-529]	494 [470-502]	0.1
Minimal SpO2 (%)	93 [90-95]	94 [90-95]	0.7
Intravenous anaesthetic agent	57 (46.7%)	15 (23.1%)	0.002
Volatile anaesthetic agent	69 (56.6%)	52 (80%)	0.001
Epidural analgesia	115 (87.8%)	53 (70.7%)	0.002
Epidural analgesia complication	2 (1.6%)	0 (0%)	0.3
Lidocaine	13 (9.7%)	10 (13.2%)	0.4
Ketamine	129 (96.3%)	65 (85.5%)	0.005
Duration of surgery (mn)	338 [250-386]	300 [240-400]	0.4
Bleeding (ml)	200 [100-300]	200 [200-300]	0.5
Crystalloid (ml)	2500 [2000-3000]	2500 [1625-3000]	0.3
Colloid (ml)	0 [0-500]	125 [0-1000]	0.2
Volume expansion (ml)	2600 [2000-3500]	3000 [2000-3500]	0.1
Blood transfusion	0 [0-0]	0 [0-0]	0.4
Fresh frozen plasma	0 [0-0]	0 [0-0]	0.2
Platelets transfusion	0 [0-0]	0 [0-0]	0.7
Norepinephrine	23 (17%)	9 (11.7%)	0.3
Jejunostomy	93 (68.4%)	44 (57.1%)	0.1
Nasogastric tube	133 (97.8%)	76 (98.7%)	0.6
Mechanical ventilation in operating room (h)	4 [3-5]	6 [4-12]	0.06

Table 5: Multivariate analysis of predictive factors of complications

	OR IC 95%	P value
Centre N°3	0.1 [0.02-0.3]	$<10^{-5}$
Preoperative renutrition	0.3 [0.08-0.7]	0.01
Neoadjuvant radiotherapy	0.5 [0.2-0.9]	0.02
Surgery with cervical approach	18 [3.7-151]	0.002

Figure 1: Leukocytes evolution during first five days after surgery



9. Supplemental data

Table S1: Postoperative complications (N = 77)

Arrhythmia	44 (20.3%)
Surgical complication	
-Surgical revision	22 (10.1%)
-Anastomotic leakage	35 (16.1%)
-Chylothorax	12 (5.5%)
-Scar disunity	15 (6.9%)
-Transplant necrosis	10 (4.6%)
Respiratory complications	
-Pneumonia	71 (32.7%)
-ARDS	20 (9.2%)
-Pulmonary embolism	2 (0.9%)
Mediastinitis	15 (6.9%)
Renal replacement therapy	4 (1.8%)

Legend: ARDS Acute Respiratory Distress Syndrome.

Table S2: length of stay in hospital, length of stay in intensive care units, mortality on day-30 and day-90 (N = 215)

Length of stay in hospital (day)	10 (7-14)
Length of stay in intensive care unit (day)	17 (14-24)
In hospital mortality	11 (5.1%)
Mortality on day-30	11 (5.1%)
Mortality on day-90	11 (5.1%)

Table S3: preoperative data between Centre 3 and others (N = 215)

	Others N= 165 (64.2%)	Centre 3 N= 50 (35.8 %)	P value
Age	63 [57-69]	61 [51.5-66.8]	0.05
Male	137 (82%)	38 (76%)	0.3
BMI	25 [22-27]	26 [22-29]	0.6
ASA 1	8 (4.8%)	9 (18.4%)	0.001
ASA 2	88 (53%)	30 (61.2%)	
ASA 3	70 (42.2%)	10 (20.4%)	
Alcohol	33 (20.6%)	9 (18.4%)	0.7
AH	114 (68.7%)	24 (48%)	0.01
Dyslipidaemia	101 (60.8%)	22 (44%)	0.04
Cardiopathy	33 (20%)	11 (22%)	0.6
Arteriopathy	20 (12%)	2 (4%)	0.1
Previous thoracic surgery	7 (4.2%)	6 (12%)	0.04
Aortic aneurysm surgery	1 (0.6%)	0 (0%)	0.6
Respiratory failure	1 (0.6%)	1 (2%)	0.4
Smoking	101 (62.4%)	34 (68%)	0.5
COPD	22 (13.4%)	6 (12%)	0.8
VEMS (L)	0.93 [0.7-1]	0.96 [0.9-1.1]	0.07
CVF (L)	1.04 [0.9-1.1]	1.02 [0.98-1.1]	0.4
Tiffeneau Index	0.78 [0.7-0.8]	0.84 [0.8-0.9]	0.2
Previous cancer	31 (18.9%)	8 (16.3%)	0.7
Diabetes	17 (10.2%)	5 (10%)	0.96
Cirrhosis	2 (1.2%)	0 (0%)	0.4
Chronic kidney injury	1 (0.6%)	0 (0%)	0.6
Denutrition	99 (61.1%)	25 (50%)	0.1
Renutrition	125 (81.7%)	47 (97.9%)	0.005
Adenocarcinoma	105 (64%)	36 (72%)	0.3
Other histological type	6 (3.7%)	0 (0%)	0.3
Squamous cell carcinoma	53 (32.3%)	14 (28%)	0.3
Tumour’s size (mm)	30 [19-40]	30 [22-44]	0.7
Location			
Cardia	40 (24.1%)	12 (24%)	0.3
Lower third	90 (54.2%)	24 (48%)	0.3

Middle third	22 (13.3%)	12 (24%)	0.3
Upper third	14 (8.4%)	2 (4%)	0.3
TNM classification			0.03
T0	21 (14.1%)	8 (16.7%)	
T1	35 (23.5%)	11 (22.9%)	
T2	18 (12.1%)	14 (29.2%)	
T3	74 (49.7%)	14 (29.2%)	
T4	1 (0.7%)	1 (2.08%)	
R0 resection	147 (93.6%)	48 (96%)	0.5
Radiotherapy	72 (45%)	19 (38%)	0.4
Neoadjuvant chemotherapy	123 (77.9%)	35 (70%)	0.3
Adjuvant chemotherapy	44 (28.6%)	12 (25%)	0.6
Haemoglobin (g/dl)	12.9 [11.8-13.9]	13.3 [11.9-14.3]	0.3
Platelets (G/ml)	226 [189-271]	230 [18-311]	0.2
Neutrophils (G/L)	4186 [3131-5660]	3690 [3062-4341]	0.07
Lymphocytes (G/L)	1403 [726-1932]	1249 [751-1772]	0.6
PT (%)	98 [92.5-104.5]	100 [91-100]	0.2
aPTT	0.99 [0.9-1.04]	1 [0.9-1.03]	0.3
Urea (mmol/L)	5.85 [4.5-7]	5.2 [4.4-6.9]	0.3
Creatinin (μmol/L)	69 [53.3-88.8]	63 [10-66]	0.03
Natremia (mmol/L)	140 [138-141]	140 [139-141]	0.9
Kalaemia (mmol/L)	4.1 [3.9-4.2]	4.3 [4.1-4.5]	0.3
Albumin (g/L)	42 [39.7-45]	43 [41-45]	0.07

Legend: AH Arterial Hypertension, aPTT activated partial thromboplastin time, COPD Chronic Pulmonary Obstructive Disease

Table S4: perioperative data between Centre 3 and others (N = 215)

	Others N = 165 (64.2%)	Centre N°3 N= 50 (35.8 %)	P-value
Central venous line	93 (57.4%)	25 (50%)	0.4
Central venous line complication	1 (0.7%)	0 (0%)	0.7
Duration of surgery (mn)	161 [120-213]	208 [180-239.5]	0
Duration of left lateral position (mn)	128 [118-153]	202.5 [182-225]	0
SpO2min (%)	94 [91.2-96]	92 [88-94]	0
Intravenous anaesthetic agent	35 (25.2%)	37 (74%)	0
Volatile anaesthetic agent	108 (77.7%)	15 (30%)	0
Epidural analgesia	119 (75.3%)	50 (100%)	0
Epidural analgesia complication	3 (2.1%)	0 (0%)	0.3
Lidocain	23 (14.2%)	1 (2%)	0.02
Ketamin	146 (90.1%)	50 (100%)	0.02
Duration of surgery (mn)	285 [235-360]	378 [355-416]	0
Bleeding (ml)	200 [200-368]	100 [27.5-200]	0
Crystalloid (ml)	2500 [1750-3000]	2500 [2000-3000]	0.2
Colloid (ml)	175 [0-1000]	0 [0-500]	0.04
Volume expansion (ml)	3000 [2000-3500]	2500 [2000-3000]	0.04
Transfusion :			
Blood transfusion	0 [0-0]	0 [0-0]	0.9
Fresh frozen plasma	0 [0-0]	0 [0-0]	0.9
Platelets	0 [0-0]	0 [0-0]	0.2
Norepinephrine	27 (16.4%)	6 (12%)	0.5
Jejunostomy	93 (56%)	47 (94%)	0
Nasogastric tube	162 (97.6%)	50 (100%)	0.3

Table S5: clinical, radiological and biological data on day 1 (N = 215)

	No complication N= 138 (64.2%)	Complication N= 77 (35.8 %)	P value
Systolic blood pressure (mmHg)	115 [105-128.5]	117 [104-126.3]	0.6
Diastolic blood pressure (mmHg)	67 [60-71.5]	65.5 [56.3-70.8]	0.6
Mean blood pressure	79 [75-94]	75 [65.5-80]	0.04
Heart rate	85 [80-93]	87 [80-98.8]	0.5
Temperature (°C)	36.8 [36.5-37.2]	37.1 [36.7-37.5]	0.9
Diuresis (L)	1300 [1000-1600]	950 [800-1200]	0.06
Norepinephrine	11 (8.2%)	8 (11%)	0.5
Crystalloid (ml)	0 [0-500]	0 [0-500]	0.3
Colloid (ml)	0 [0-0]	0 [0-0]	0.97
Volume expansion (ml)	0 [0-500]	0 [0-500]	0.4
Transfusion :			
Blood transfusion	1 (0%)	2 (1.3%)	0.2
Fresh frozen plasma	3 (0.7%)	2 (1.3%)	0.7
Platelets transfusion	3 (0.7%)	1 (0%)	0.5
Respiratory rate	19 [16-20]	20 [18-22]	0.1
SpO2 (%)	96 [94-98]	95 [94-97]	0.07
Invasive mechanical ventilation	3 (2.2%)	11 (14.3%)	0.001
Oxygenotherapy	109 (83.9%)	59 (78.7%)	0.4
Non-invasive ventilation	22 (16.4%)	21 (27.6%)	0.05
HFNC	3 (2.2%)	4 (5.2%)	0.2
Colloid (ml)	0 [0-500]	125 [0-1000]	0.2
Chest X-ray infiltrate	75 (62.5%)	46 (68.7%)	0.4
Chest X-ray	3 (2.5%)	4 (6.06%)	0.2
Epidural analgesia	112 (83.6%)	52 (68.4%)	0.01
Intravenous analgesia	31 (23.1%)	30 (39.5%)	0.01
Thromboprophylaxis	128 (95.5%)	75 (98.7%)	0.2
Enteral nutrition	13 (9.7%)	13 (17.3%)	0.1
Parenteral nutrition	61 (46.2%)	34 (45.3%)	0.9
Haemoglobin (g/dl)	12.3 [11.3-13.5]	12.2 [10.8-13.4]	0.7
Platelets (G/L)	200 [172-247]	189.5 [167.3-242.5]	0.9
Leucocytes (G/L)	11610 [8537.5-14280]	11560 [9295-14200]	0.8

Natremia (mmol/L)	138 [136-139]	137 [135-138]	0.1
Kalaemia (mmol/L)	4.4 [4.1-4.7]	4.3 [3.9-4.8]	0.2
Urea (mmol/L)	6 [5-9]	7 [5-8]	0.6
Creatinin (μmol/L)	68 [55.4-79.1]	66 [59-81.8]	0.3
Lactate (mmol/L)	1.6 [1.3-2.3]	1.75 [1.4-2.3]	0.6
PaO2 (kPa)	12.1 [10.5-12.7]	12.55 [9.9-16.9]	0.8
PaCO2 (kPa)	5.5 [5.1-6]	5.25 [4.75-6.5]	0.4
FiO2	0.2 [0.2-0.2]	0.2 [0.2-0.3]	0.001

Legend: HFNC = High Flow Nasal Cannula

Table S6: clinical, radiological and biological data on day 2 (N = 215)

Variable	No complication N= 138 (64.2%)	Complication N= 77 (35.8 %)	P value
Systolic blood pressure (mmHg)	120 [110-130]	125.5 [112-135]	0.3
Diastolic blood pressure (mmHg)	70 [60-75]	64 [59-70]	0.3
Mean blood pressure (mmHg)	92 [81-98.8]	81 [75-86]	0.06
Heart rate	88 [80-96]	89 [82-96]	0.6
Temperature (°C)	36.8 [36.5-37.2]	37 [36.6-37.5]	0.3
Diuresis (ml)	1500 [1250-1900]	1250 [863-1483]	0.02
Norepinephrine	7 (5.2%)	8 (10.5%)	0.2
Crystalloid (ml)	0 [0-0]	0 [0-500]	0.09
Colloid (ml)	0 [0-0]	0 [0-0]	0.4
Volume expansion (ml)	0 [0-0]	0 [0-500]	0.06
Transfusion			
Blood transfusion	124 (91.9%)	72 (96%)	0.3
Fresh frozen plasma	128 (95%)	73 (97%)	0.4
Platelets	127 (94%)	73 (97%)	0.3
Respiratory rate	20 [17-21]	20 [18-22]	0.06
SpO2 (%)	95 [94 -97]	95 [94-96]	0.1
Invasive mechanical ventilation	0 (0%)	6 (8%)	0.001
Non-invasive ventilation	25 (18.7%)	23 (31.1%)	0.04
HFNC	4 (3%)	5 (6.8%)	0.2
Colloid (ml)	0 [0-500]	125 [0-1000]	0.2
Chest X-ray infiltrate	81 (73%)	61 (88.4%)	0.01
Chest X-ray	5 (4.4%)	7 (10.1%)	0.1
Epidural analgesia	112 (84.2%)	50 (66.7%)	0.003
Intravenous analgesia	30 (22.6%)	28 (37.3%)	0.02
Thromboprophylaxis	134 (99.3%)	75 (100%)	0.5
Enteral nutrition	25 (19.5%)	14 (19.2%)	0.95
Parenteral nutrition	69 (54.8%)	32 (43.8%)	0.1
Haemoglobin (g/dl)	11.6 [10.5-12.4]	11.55 [10.6-12.3]	0.7

Platelets (G/L)	191 [157-225]	186 [152-225]	0.8
Leucocytes (G/L)	10840 [8635-13910]	12300 [9700-14853]	0.2
Natremia (mmol/L)	136 [135-139]	137 [135-138.5]	0.6
Kalaemia (mmol/L)	4 [4-5]	4 [4-4]	0.3
Calcemia (mmol/l)	2.09 [2-2.2]	2.04 [1.9-2.1]	0.2
Urea (mmol/L)	6 [5-7]	4 [3.5-6]	0.3
Creatinin (µmol/L)	61.6 [52.8-70.8]	61.8 [54.3-77.9]	0.1
PaO2 (kPa)	40.1 [7.6-76.3]	12.4 [10-15.2]	0.4
PaCO2 (kPa)	23.95 [7.5-40.5]	5.4 [5-6.4]	0.3
FiO2	0.21 [0.21-0.21]	0.21 [0.21-0.21]	0.02

Legend: HFNC = High Flow Nasal Cannula,

Table S7: clinical, radiological and biological data on day 3 (N = 215)

	No complication N= 138 (64.2%)	Complication N = 77 (35.8 %)	P value
Systolic blood pressure (mmHg)	120 [110-132]	123 [113-136]	0.6
Diastolic blood pressure (mmHg)	70 [60-78]	67 [58-72]	0.2
Mean blood pressure (mmHg)	92 [86-94]	84 [78-86]	0.07
Heart rate	88 [80-96]	92 [80-103]	0.5
Temperature (T°C)	36.8 [36.3-37.1]	37 [36.7-37.4]	0.04
Diuresis (ml)	1600 [1250-2000]	1078 [864-1313]	0
Norepinephrine	3 (2.2%)	13 (17.1%)	0
Crystalloid (ml)	0 [0-0]	0 [0-0]	0.03
Colloid (ml)	0 [0-0]	0 [0-0]	0.7
Volume expansion (ml)	0 [0-0]	0 [0-1]	0.04
Blood transfusion	3 (2.2%)	2 (2.6%)	0.9

Table S8: clinical, radiological and biological data on day 5

Variable	No complication N = 138 (64.2%)	Complication N= 77 (35.8 %)	P value
Systolic blood pressure (mmHg)	125 [112.5-130]	122 [114.3-140]	0.7
Diastolic blood pressure (mmHg)	70 [63-80]	63 [59-73]	0.09
Mean blood pressure (mmHg)	92 [91-93]	78 [70-82]	0.002
Heart rate	88 [80-96]	90 [84-95]	0.4
Temperature (°C)	36.8 [36.2-37.2]	36.9 [36.6-37.4]	0.3
Diuresis (ml)	1750 [1375-2325]	1400 [1200-1950]	0.2
Norepinephrine	1 (0.7%)	12 (15.8%)	0
Crystalloid (ml)	0 [0-0]	0 [0-0]	0.08
Colloid (ml)	0 [0-0]	0 [0-0]	0.2
Volume expansion (ml)	0 [0-0]	0 [0-0]	0.04
Blood transfusion	131 (97%)	75 (100%)	0.1

10. References

[1] Global Burden of Disease Cancer Collaboration, Fitzmaurice C, Akinyemiju TF, Lami Al FH, Alam T, Alizadeh-Navaei R, et al. Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-Years for 29 Cancer Groups, 1990 to 2016. JAMA Oncol 2018;4:1553–16. doi:10.1001/jamaoncol.2018.2706.

[2] Ingelfinger JR, Rustgi AK, El-Serag HB. Esophageal Carcinoma. N Engl J Med 2014;371:2499–509. doi:10.1056/NEJMra1314530.

[3] G. Lledo, C. Mariette, J.-L. Raoul, L. Dahan, B. Landi, T. Conroy, G. Piessen, D. Tougeron, G. Créhange, V. Lepillez, P. Artru, A. Drouillard, J.-F. Bosset. «Cancer de l'œsophage». Thésaurus National de Cancérologie Digestive, http://www.tncd.org; 09-2016, [accessed 28 august 2019]

[4] Lordick F, Mariette C, Haustermans K, Obermannová R, Arnold D. Oesophageal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†. Annals of Oncology 2016;27:v50–7. doi:10.1093/annonc/mdw329.

[5] Mariette C, Piessen G, Briez N, Gronnier C, Triboulet JP. Oesophagogastric junction adenocarcinoma: which therapeutic approach? The Lancet Oncology 2011;12:296–305. doi:10.1016/S1470-2045(10)70125-X.

[6] Low DE, Kuppusamy MK, Alderson D, Cecconello I, Chang AC, Darling G, et al. Benchmarking Complications Associated with Esophagectomy. Annals of Surgery 2017;269:291–8. doi:10.1097/SLA.0000000000002611.

[7] Raymond DP, Seder CW, Wright CD, Magee MJ, Kosinski AS, Cassivi SD, et al. Predictors of Major Morbidity or Mortality After Resection for Esophageal Cancer: A Society of Thoracic Surgeons General Thoracic Surgery Database Risk Adjustment Model. The Annals of Thoracic Surgery 2016;102:207–14. doi:10.1016/j.athoracsur.2016.04.055.

[8] Mariette C, Markar SR, Dabakuyo-Yonli TS, Meunier B, Pezet D, Collet D, et al. Hybrid Minimally Invasive Esophagectomy for Esophageal Cancer. N Engl J Med 2019;380:152–62. doi:10.1056/NEJMoa1805101.

[9] Hulscher JBF. Extended Transthoracic Resection Compared with Limited Transhiatal Resection for Adenocarcinoma of the Esophagus. N Engl J Med 2002:1–8.

[10] Biere SS, van Berge Henegouwen MI, Maas KW, Bonavina L, Rosman C, Garcia JR, et al. Minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomised controlled trial. The Lancet 2012;379:1887–92. doi:10.1016/S0140-6736(12)60516-9.

[11] Seesing MFJ, Wirsching A, van Rossum PSN, Weijs TJ, Ruurda TJ, van Hillegersberg R, et al. Defining pneumonia after esophagectomy for cancer: validation of the Uniform Pneumonia Score in a high volume center in North America. Dis Esophagus 2018:1–8. doi:10.1093/dote/doy002.

[12] Hackett NJ, De Oliveira GS, Jain UK, Kim JYS. ASA class is a reliable independent predictor of medical complications and mortality following surgery. International Journal of Surgery 2015;18:184–90. doi:10.1016/j.ijsu.2015.04.079.

[13] Qi W, Zixiang W, Tianwei Z, Shuai F, Sai Z, Gang S, et al. Long-term outcomes of 530 esophageal squamous cell carcinoma patients with minimally invasive Ivor Lewis esophagectomy. J Surg Oncol 2018;117:957–69. doi:10.1002/jso.24997.

[14] Baba Y, Yoshida N, Shigaki H, Iwatsuki M, Miyamoto Y, Sakamoto Y, et al. Prognostic Impact of Postoperative Complications in 502 Patients With Surgically Resected

Esophageal Squamous Cell Carcinoma. Annals of Surgery 2016;264:305–11. doi:10.1097/SLA.0000000000001510.
[15] Low DE, Allum W, De Manzoni G, Ferri L, Immanuel A, Kuppusamy M, et al. Guidelines for Perioperative Care in Esophagectomy: Enhanced Recovery After Surgery (ERAS®) Society Recommendations. World J Surg 2018:1–32. doi:10.1007/s00268-018-4786-4.
[16] Flisberg P, Törnebrandt K, Walther B, Lundberg J. Pain relief after esophagectomy: Thoracic epidural analgesia is better than parenteral opioids. Journal of Cardiothoracic and Vascular Anesthesia 2001;15:282–7. doi:10.1053/jcan.2001.23270.
[17] Popping DM, Elia N, Marret E, Remy C, Tramer MR. Protective effects of epidural analgesia on pulmonary complications after abdominal and thoracic surgery: a meta-analysis. Arch Surg 2008;143:990–9–discussion1000. doi:10.1001/archsurg.143.10.990.
[18] Popping DM, Elia N, Van Aken HK, Marret E, Schug SA, Kranke P, et al. Impact of Epidural Analgesia on Mortality and Morbidity After Surgery. Annals of Surgery 2014;259:1056–67. doi:10.1097/SLA.0000000000000237.
[19] Cummings KC III, Kou TD, Chak A, Schluchter MD, Margevicius S, Cooper GS, et al. Surgical approach and the impact of epidural analgesia on survival after esophagectomy for cancer: A population-based retrospective cohort study. PLoS ONE 2019;14:e0211125–18. doi:10.1371/journal.pone.0211125.
[20] van Workum F, Stenstra MHBC, Berkelmans GHK, Slaman AE, van Berge Henegouwen MI, Gisbertz SS, et al. Learning Curve and Associated Morbidity of Minimally Invasive Esophagectomy. Annals of Surgery 2017;269:88–94. doi:10.1097/SLA.0000000000002469.
[21] Weimann A, Braga M, Harsanyi L, Laviano A, Ljungqvist O, Soeters P, et al. ESPEN Guidelines on Enteral Nutrition: Surgery including Organ Transplantation. Clinical Nutrition 2006;25:224–44. doi:10.1016/j.clnu.2006.01.015.
[22] Bower MR, Martin RCG II. Nutritional management during neoadjuvant therapy for esophageal cancer. J Surg Oncol 2009;100:82–7. doi:10.1002/jso.21289.
[23] Shichinohe T, Uemura S, Hirano S, Hosokawa M. Impact of Preoperative Skeletal Muscle Mass and Nutritional Status on Short-and Long-Term Outcomes After Esophagectomy for Esophageal Cancer: A Retrospective Observational Study. Ann Surg Oncol 2019:1–10. doi:10.1245/s10434-019-07188-z.
[24] Ligthart-Melis GC, Weijs PJM, Boveldt te ND, Buskermolen S, Earthman CP, Verheul HMW, et al. Dietician-delivered intensive nutritional support is associated with a decrease in severe postoperative complications after surgery in patients with esophageal cancer. Dis Esophagus 2012;26:587–93. doi:10.1111/dote.12008.
[25] Weimann A, Braga M, Carli F, Higashiguchi T, Hübner M, Klek S, et al. ESPEN guideline: Clinical nutrition in surgery. Clinical Nutrition 2017;36:623–50. doi:10.1016/j.clnu.2017.02.013.
[26] Boles J-M, Bion J, Connors A, Herridge M, Marsh B, Melot C, et al. Weaning from mechanical ventilation. European Respiratory Journal 2007;29:1033–56. doi:10.1183/09031936.00010206.
[27] Tsujimoto H, Ono S, Takahata R, Hiraki S, Yaguchi Y, Kumano I, et al. Systemic inflammatory response syndrome as a predictor of anastomotic leakage after esophagectomy. Surgery Today 2011;42:141–6. doi:10.1007/s00595-011-0049-9.
[28] Choi H, Cho JH, Kim HK, Choi YS, Kim J, Zo JI, et al. Prevalence and clinical course of postoperative acute lung injury after esophagectomy for esophageal cancer. J Thorac Dis 2019;11:200–5. doi:10.21037/jtd.2018.12.102.

Vu, le Président du Jury,

Professeur Bertrand Rozec

Vu, le Directeur de Thèse,

Docteur Raphael Cinotti

Vu, le Doyen de la Faculté,

Professeur Pascale JOLLIET

NOM : MILLOUR PRENOM : Pierre

Titre de Thèse : Risk factors of severe postoperative complications following elective esophagectomy.

RESUME

Esophagectomy resection improves prognosis up to 40-50% for R0 cancer. The incidence of postoperative complications remains high, up to 50%. We conducted a retrospective study in four centres in Nantes. The trial included patients with oesophageal cancer undergoing surgery. The primary end point was composite criteria including invasive mechanical ventilation duration ≥ 48h and/or surgical complication and/or mortality at day-90. Between 2012 and 2017, 215 patients were included in the study. 77 (35.6%) patients displayed the primary endpoint. Day-90 mortality was 11 (5.2%). In multivariate analysis, three factors were significantly associated with less complications: Centre N°3 (OR 0.1 CI_{95} (0.02-0.3), $p < 10^{-5}$), preoperative renutrition (OR 0.3 (0.08-0.7), p=0.01), neoadjuvant radiotherapy (OR 0.5 (0.2-0.9), p=0.02). Oesophageal resection with triple approach was associated with more complications (OR 18 (3.7-151), p=0.002). There was a statistically significant association between leukocytes evolution in the first 5-days and the need of invasive mechanical ventilation (p=0.001). Leukocytes monitoring on the first 5-days after surgery could be interesting to improve monitoring in high-risk patients.

MOTS-CLES

ESOPHAGEAL CANCER, ESOPHAGECTOMY, IVOR-LEWIS, POSTOPERATIVE COMPLICATIONS, LEUKOCYTES.

NOM : MILLOUR PRENOM : Pierre

Titre de Thèse : Facteurs de risques de complications post opératoires graves après chirurgie de résection oesophagienne carcinologique.

RESUME

La chirurgie de résection oesophagienne pour cancer améliore le pronostic de 40-50% pour une résection R0. L'incidence des complications graves post-opératoires demeure élevée (plus de 50%). Nous avons mené une étude rétrospective dans 4 centres à Nantes. Nous avons inclus des patients présentant un cancer de l'oesophage avec chirurgie de résection. Le critère de jugement principal était composite : ventilation mécanique invasive ≥ 48h et/ou complication chirurgicale et/ou mortalité à J-90. Entre 2012 et 2017, 215 patients ont été inclus. 77 (35,6%) patients ont présenté le critère principal. En analyse multivariée, 3 facteurs sont associés significativement à moins de complications: Centre N°3 (OR 0.1 CI_{95} (0.02-0.3), $p < 10^{-5}$), renutrition pré-opératoire (OR 0,3 (0,08-0,7), p= 0,01), radiothérapie néoadjuvante (OR 0,5 (0,2-0,9) p= 0,02). La chirurgie avec triple abord (cervical, thoracique et abdominal) est associée à plus de complications (OR 18 (3,7-151) p= 0,002). Il y avait une association significative entre l'évolution des leucocytes et le recours à une ventilation mécanique invasive dans les 5 premiers jours post-opératoires. La surveillance de l'évolution des leucocytes opératoires pourrait être intéressante pour le monitorage prolongé des patients.

MOTS-CLES

CANCER DE L'OESOPHAGE, CHIRURGIE OESOPHAGIENNE, LEWIS-SANTY/IVOR-LEWIS, COMPLICATIONS POST OPERATOIRES, LEUCOCYTES