Esophageal cancer: Outcome and potential benefit of esophagectomy in elderly patients

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Abstract
Background: This analysis evaluated the morbimortality and the potential benefit of esophagectomy for cancer in elderly patients.

Methods: Patients who underwent esophagectomy for EC were divided into elderly (≥70 years) and nonelderly (<70 years) groups. The groups were compared regarding patient and tumor characteristics, postoperative morbimortality, and disease-free, overall and cancer-specific survival.

Results: Sixty-one patients were classified into elderly, and 187 into nonelderly groups. The elderly were characterized by a higher rate of WHO score (p < 0.0001), higher cardiac (p < 0.004) and renal (p < 0.023) comorbidities. The rate of neoadjuvant therapy and especially of neoadjuvant CRT was significantly lower in elderly patients (p < 0.018 and p < 0.007). Operative morbidity was also higher in this group (p < 0.024).

The 30- and 90-day mortality was 8.2 and 11.5%, respectively in elderly patients and 0.5 and 3.2% in nonelderly patients (p < 0.004 and p < 0.012). This 90-day mortality decreased when specific surgery-related deaths were taken into consideration. OS and DFS were significantly better in the nonelderly group (p < 0.003 and p < 0.005) while no difference was observed for cancer-specific survival (CSS).

Conclusion: No difference in CSS was observed. Although elderly patients with EC had higher postoperative morbimortality, the age should not be a criterion whether to perform, or not to perform, esophagectomy. This decision must be based on the balance between the patient’s general condition and aggressive disease.

KEYWORDS
elderly, esophageal cancer, esophagectomy, outcomes

INTRODUCTION
Esophageal cancer is the eighth most common cancer and the sixth cause of cancer mortality. Unfortunately, treatment remains a therapeutic challenge, with most patients being diagnosed at a locally advanced stage. The approach is multimodal, and surgery constitutes the treatment’s key-stone and offers the best chance of cure. EC is more frequent in patients between 65 and 74 with a median age of 67 years. Longer life expectancy has increased the number of elderly patients referred for surgical treatment. In this group, comorbidities are more present and increase the operative risk.

The aim of our study was to evaluate the impact of age and associated comorbidities on postoperative morbidity and mortality and follow the long-term survival in patients
| Patient characteristics (N = 248) | Elderly: ≥70 years | Nonelderly: <70 years | p-value |
|----------------------------------|--------------------|-----------------------|---------|
|                                  | (N = 61)           | (N = 187)             |         |
| Gender - n (%)                   |                    |                       |         |
| Female (n = 48; 19.4%)           | 11                 | 37                    | 0.73    |
| Male (n = 200; 80.6%)            | 50                 | 150                   |         |
| Body mass index (kg/m²)          |                    |                       |         |
| Mean                             | 25.3               | 25.6                  |         |
| <22                              | 11                 | 44                    | 0.37    |
| ≥22                              | 50                 | 143                   |         |
| Weight loss                      |                    |                       |         |
| No or <10%                        | 29                 | 114                   | 0.09    |
| >10%                             | 32                 | 73                    |         |
| ASA score                        |                    |                       |         |
| 1                                | 0                  | 12                    | 0.037   |
| 2                                | 31                 | 109                   |         |
| 3                                | 30                 | 63                    |         |
| 4                                | 0                  | 3                     |         |
| 1–2                              | 31                 | 121                   | 0.075   |
| 3–4                              | 30                 | 66                    |         |
| Comorbidities                    |                    |                       |         |
| Cardiac                          | 44                 | 96                    | 0.004   |
| Pulmonary                        | 14                 | 48                    | 0.023   |
| Renal                            | 7                  | 7                     |         |
| Hepatic                          | 3                  | 14                    |         |
| Diabetes                         | 5                  | 27                    |         |
| Obliterating arteriopathy        | 2                  | 11                    |         |
| Surgical history                 |                    |                       |         |
| Yes                              | 49                 | 150                   | 0.985   |
| No                               | 12                 | 37                    |         |
| Alcohol                          |                    |                       |         |
| Yes                              | 50                 | 160                   | 0.499   |
| No                               | 11                 | 27                    |         |
| Smoking                          |                    |                       |         |
| Yes                              | 43                 | 140                   | 0.5     |
| No                               | 18                 | 47                    |         |
| WHO performance status           |                    |                       | <0.0001 |
| 0–1                              | 47                 | 185                   |         |
| 2–4                              | 14                 | 2                     |         |
| Nutritional before surgery       |                    |                       |         |
| Gastrotomy tube                  | 3                  | 5                     | 0.005   |
| Jejunostomy tube                 | 2                  | 14                    |         |
| Parenteral nutrition             | 7                  | 2                     |         |
| VEMS/CV                          |                    |                       |         |
| ≤70                              | 1                  | 6                     | 0.545   |
| >70                              | 53                 | 166                   |         |

Abbreviation: ASA score, American Society of Anesthesiologists score; CV, pulmonary vital capacity; VEMS, maximal expiratory volume per second; WHO, World Health Organization Performance Status.
undergoing esophagectomy for esophageal cancer. Patients of 70 years old and above were compared to those under 70.

METHODS

Between January 2006 and December 2015, prospectively collected data from the medical records of patients who underwent esophagectomy for cancer in the Department of Digestive Surgery ULB-Erasme-Bordet were retrospectively reviewed. Patients were divided into two groups; elderly (age ≥70 years, elderly group) and nonelderly (age <70 years, nonelderly group) based on age at the time of surgery. Seventy-years is the age cutoff found in most of the esophageal literature. This study was approved by the ethical committee of Erasme and Bordet.

Variables including patient and tumor characteristics, neoadjuvant and adjuvant treatment, histology results,

| Tumor characteristics | Elderly: ≥70 years | Nonelderly: <70 years | p-value |
|------------------------|-------------------|-----------------------|---------|
|                        | (N = 61)          | (N = 187)             |         |
| **Histological classification** |                   |                       |         |
| Adenocarcinoma (n = 158; 63.7%) | 44 72.1 | 114 61.0 | 0.077  |
| Squamous cell carcinoma (n = 85; 34.3%) | 15 24.6 | 70 37.4 |         |
| Other (n = 5; 2%) | 2 3.3 | 3 1.6 |         |
| **Adenocarcinoma** |                   |                       |         |
| Well differentiated | 8 18.2 | 31 27.2 | 0.482  |
| Moderately differentiated | 19 43.2 | 46 40.4 |         |
| Poorly differentiated | 17 38.6 | 37 32.4 |         |
| **Squamous cell carcinoma** |                   |                       |         |
| Well differentiated | 5 33.3 | 16 22.9 | 0.488  |
| Moderately differentiated | 9 60.0 | 42 60.0 |         |
| Poorly differentiated | 1 6.7 | 12 17.1 |         |
| **Tumor location** |                   |                       |         |
| Upper | 3 4.9 | 19 10.1 | 0.25   |
| Middle | 8 13.1 | 39 20.9 |         |
| Lower | 50 82.0 | 143 70.0 |         |
| **Tumor response grade** |                   |                       |         |
| 0 | 0 0.0 | 1 1.7 |         |
| 1 | 3 25.0 | 26 44.8 |         |
| 2 | 3 25.0 | 13 22.4 |         |
| 3 | 0 0.0 | 9 15.5 |         |
| 4 | 5 41.7 | 8 13.8 |         |
| 5 | 1 8.3 | 1 1.7 |         |
| TRG 0–2 | 6 50.0 | 40 70.0 | 0.21   |
| TRG 3–5 | 6 50.0 | 18 30.0 |         |
| **Nodal status** |                   |                       |         |
| Negative | 36 59.0 | 115 61.5 | 0.73   |
| Positive | 25 41.0 | 72 38.5 |         |
| **C-stage** |                   |                       |         |
| IA | 8 13.1 | 27 14.5 | 0.69   |
| IB | 13 21.3 | 27 14.5 |         |
| IIA | 1 1.6 | 3 1.6 |         |
| IIB | 16 26.2 | 48 25.8 |         |
| IIIA | 16 26.2 | 63 33.9 |         |
| IIIB | 5 8.2 | 2 1.1 |         |
| IIC | 1 1.6 | 8 4.3 |         |
| IV | 1 1.6 | 8 4.3 |         |
operative morbimortality, and survival were collected and analyzed.

Before esophagectomy, a complete work-up including physical examination, blood test, esophagogram, upper GI endoscopy, endoscopic ultrasound, neck, chest and abdominal computed tomography (CT) scan, and finally positron-emission (PET)-CT, was mandatory to exclude distant metastasis and confirm local resectability. Laparoscopy was performed to rule out any liver metastases or peritoneal carcinosis suspected on CT or PET-CT.

Elderly patients benefit from an oncogeriatric evaluation based on performance status, comorbidity, medical and nutritional assessment, mental state, depression scale, geriatrics syndrome and socioeconomic state.

The American society of Anesthesiologists classification was used to assess the operative risk.

For tumors above the carina, a three-way approach (right anterolateral thoracotomy, laparotomy or laparoscopy, left cervicotomy) with total esophagectomy, manual anastomosis and three field lymphadenectomy was performed. A total pharyngo-laryngo-esophagectomy was achieved, in cases of recurrence or incomplete response after definitive chemoradiotherapy for cervical esophageal tumors, in cases of laryngeal or cervical recurrent nerve involvement, and/or insufficient margins. For tumors below the carina, a subtotal esophagectomy (aortic arch) with circular mechanical anastomosis and two-field lymphadenectomy was achieved (laparotomy or laparoscopy and right anterolateral thoracotomy).

### Table 3: Treatment modalities

|                      | Elderly: ≥70 years | Nonelderly: <70 years | p-value |
|----------------------|--------------------|-----------------------|---------|
|                      | (N = 61)           | (N = 187)             |         |
| Neoadjuvant treatment|                    |                       |         |
| Yes                  | 27 (44.3)          | 115 (61.5)            | 0.018   |
| No                   | 34 (55.7)          | 72 (38.5)             |         |
| Neoadjuvant chemotherapy|               |                       |         |
| Yes                  | 18 (29.5)          | 54 (28.9)             | 0.925   |
| No                   | 43 (70.5)          | 133 (71.1)            |         |
| Neoadjuvant chemoradiotherapy|           |                       |         |
| Yes                  | 9 (14.8)           | 61 (32.6)             | 0.007   |
| No                   | 52 (85.2)          | 126 (67.4)            |         |
| Adjuvant treatment   |                    |                       |         |
| Yes                  | 14 (23.0)          | 78 (41.7)             | 0.008   |
| No                   | 47 (77.0)          | 109 (58.3)            |         |
| Adjuvant chemotherapy|                    |                       |         |
| Yes                  | 11 (18.0)          | 61 (32.6)             | 0.029   |
| No                   | 50 (82.0)          | 126 (67.4)            |         |
| Adjuvant chemoradiotherapy|               |                       |         |
| Yes                  | 3 (4.9)            | 17 (9.1)              | 0.299   |
| No                   | 58 (95.1)          | 170 (90.9)            |         |
| Perioperative jejunostomy|               |                       |         |
| Yes                  | 15 (24.6)          | 54 (28.9)             | 0.516   |
| No                   | 46 (75.4)          | 133 (71.1)            |         |

### Table 4: Surgery modalities

|                      | Elderly: ≥70 years | Nonelderly: <70 years | p-value |
|----------------------|--------------------|-----------------------|---------|
|                      | (N = 61)           | (N = 187)             |         |
| Type of intervention |                    |                       |         |
| Total esophagectomy  | 9 (14.8)           | 42 (22.5)             | 0.111   |
| Partial esophagectomy| 52 (85.2)          | 138 (73.8)            |         |
| Pharyngo-laryngo-esophagectomy| | 0 (0.0) | 7 (3.7) |         |
| Procedure            |                    |                       |         |
| 1 way                | 1 (1.6)            | 4 (2.1)               | 0.172   |
| 2 ways               | 51 (83.6)          | 134 (71.7)            |         |
| 3 ways               | 9 (14.8)           | 49 (26.2)             |         |
| Resection            |                    |                       |         |
| R0                   | 54 (88.5)          | 182 (97.3)            | 0.011   |
| R1                   | 7 (11.5)           | 5 (2.7)               |         |
| Details R1           |                    |                       |         |
| Circumferential margin| 7 (100.0)          | 2 (40.0)              | 0.045   |
| Positive margin      | 4 (57.1)           | 1 (83.3)              |         |
| Margin <1 mm         | 3 (42.9)           | 1 (16.7)              |         |
| Proximal margin      | 0 (0.0)            | 3 (60.0)              |         |
| Conduit used         |                    |                       |         |
| Stomach              | 60 (98.4)          | 174 (93.0)            | 0.358   |
| Colon                | 1 (1.6)            | 8 (4.3)               |         |
| Jejunum              | 0 (0.0)            | 5 (2.7)               |         |
|                                         | Elderly: ≥70 years | Nonelderly: <70 years | p-value |
|-------------------------------|-------------------|-----------------------|---------|
| Length of in hospital stay (days) - mean | 18.31             | 18.28                 |         |
| Length of in hospital stay (days) - median | 14                | 14                    |         |
| Dindo–Clavien global score |                   |                       |         |
| 1                             | 23                | 112                   | 0.024   |
| 2                             | 21                | 45                    | 24.1    |
| 3a                            | 1                 | 5                     | 2.7     |
| 3b                            | 3                 | 9                     | 4.8     |
| 4a                            | 6                 | 9                     | 4.8     |
| 4b                            | 2                 | 4                     | 2.1     |
| 5                             | 5                 | 3                     | 1.6     |
| Anastomotic leakage excluding pharyngolaryngectomy |                   |                       |         |
| Yes                           | 3                 | 7                     | 3.9     | 0.73   |
| No                            | 58                | 180                   | 96.1    |
| Dindo–Clavien anastomotic leakage |                   |                       |         |
| 1                             | 0                 | 2                     | 18.2    |
| 2                             | 0                 | 1                     | 9.1     |
| 3a                            | 1                 | 1                     | 9.1     |
| 3b                            | 1                 | 5                     | 45.5    |
| 4a                            | 0                 | 1                     | 9.1     |
| 4b                            | 1                 | 0                     | 0.0     |
| 5                             | 0                 | 1                     | 9.1     |
| Intra-abdominal/thoracic abscess |                   |                       |         |
| Yes                           | 0                 | 2                     | 1.1     | 1      |
| No                            | 61                | 185                   | 98.9    |
| Mediastinitis |                   |                       |         |
| Yes                           | 2                 | 4                     | 2.1     | 0.638  |
| No                            | 59                | 183                   | 97.9    |
| Chylothorax |                   |                       |         |
| Yes                           | 1                 | 2                     | 1.1     | 0.573  |
| No                            | 60                | 185                   | 98.9    |
| Conduit ischemia |                   |                       |         |
| Yes                           | 1                 | 1                     | 0.5     | 0.402  |
| No                            | 60                | 186                   | 99.5    |
| Recurrent/phrenic nerve palsy |                   |                       |         |
| Yes                           | 0                 | 3                     | 1.6     | 1      |
| No                            | 61                | 184                   | 98.4    |
| Hemothorax/hematoma |                   |                       |         |
| Yes                           | 0                 | 0                     | 0.0     | 1      |
| No                            | 61                | 187                   | 100.0   |
| Splenectomy |                   |                       |         |
| Yes                           | 1                 | 3                     | 1.6     | 1      |
| No                            | 60                | 184                   | 98.4    |
| ARDS-ALI/ARI |                   |                       |         |
| Yes                           | 17                | 20                    | 10.7    | 0.001  |
| No                            | 44                | 167                   | 89.3    |

(Continues)
**Table 5 (Continued)**

|                        | Elderly: ≥70 years (N = 61) | Nonelderly: <70 years (N = 187) | p-value |
|------------------------|------------------------------|---------------------------------|---------|
| **Infectious pneumopathy** |                              |                                 |         |
| Yes                    | 23                           | 47                              | 0.058   |
| No                     | 38                           | 140                             |         |
| **Dindo–Clavien pneumonia** |                            |                                 |         |
| 1–2                    | 14                           | 33                              | 0.434   |
| 3–5                    | 9                            | 14                              |         |
| **Atelectasis**        |                              |                                 |         |
| Yes                    | 2                            | 5                               | 0.804   |
| No                     | 59                           | 182                             |         |
| **Pleural effusion**   |                              |                                 |         |
| Yes                    | 5                            | 12                              | 0.633   |
| No                     | 56                           | 175                             |         |
| **Empyema**            |                              |                                 |         |
| Yes                    | 1                            | 4                               | 1       |
| No                     | 60                           | 183                             |         |
| **Intensive Care Unit readmission** |                        |                                 |         |
| Yes                    | 6                            | 14                              | 0.558   |
| No                     | 55                           | 173                             |         |
| **Length of stay in ICU readmission (days)** |                  |                                 |         |
| Mean                   | 0.5                          | 0.8                             |         |
| **Reintervention surgery** |                            |                                 |         |
| Yes                    | 4                            | 5                               | 0.159   |
| No                     | 57                           | 182                             |         |
| **Reintervention CT scan** |                          |                                 |         |
| Yes                    | 0                            | 2                               | 1.1     |
| No                     | 61                           | 185                             |         |
| **Reintervention endoscopy** |                        |                                 |         |
| Yes                    | 3                            | 9                               | 0.973   |
| No                     | 58                           | 178                             |         |
| **Reintervention prosthesis** |                      |                                 |         |
| Yes                    | 3                            | 7                               | 0.685   |
| No                     | 58                           | 180                             |         |

**Statistical considerations and analysis**

Patient characteristics were analyzed descriptively using frequency tables or summaries for continuous variable settings. The proportions of complications were estimated and the confidence intervals at 95% were accurately calculated.

Overall survival (OS) was measured as the time from the date of surgery to the time of last follow-up or death of any cause. Disease-free survival (DFS) was defined as the time from surgery to the first disease-free failure event (local or distant disease relapse or death). Cancer-specific survival (CSS) was calculated as the probability of survival, censoring noncancer causes of death. The cutoff date for analysis was February 02, 2021. Follow-up was calculated using the reverse Kaplan–Meier method. Distributions of time until an event were estimated using the Kaplan–Meier method. Median survival times as well as the 1-, 2- and 3-year survival rates (with confidence intervals at 95%) were calculated. Difference between the survival curves were assessed using the log-rank test. The X² test or Fisher’s test were used to compare proportion. The patients were managed and operated by the same surgeon, reinforcing the homogeneity of the populations.

Clinicopathological variables analyzed with a p-value <0.05 on log-rank test were entered into Cox proportional hazards multivariate analysis. All multivariate Cox models were built according to the rule of 10 events per variable.
All significant tests were two-sided, and all used a 5% level of significance. Statistical analyses were performed using SPSS software (version 22.0; SPSS).

RESULTS

Patient characteristics

The study population consisted of 248 consecutive patients; 200 males (80.6%) and 48 females (19.4%), who underwent esophagectomy for esophageal cancer between January 2006 and December 2015 (Table 1).

The median age of the patients was 62 years. There was 61 patients (age ≥70 years) in the elderly group and 187 patients (age <70 years) in the nonelderly group.

Patient characteristics were almost similar except for significant higher cardiac and renal comorbidities in the elderly group ($p < 0.004$ and $p < 0.023$ respectively). The elderly group was characterized by a higher rate of WHO PS 2–4 ($p < 0.0001$). Almost 65% of nonelderly group patients presented a lower ASA score: 1 or 2. The malnutrition rate was similar in the two groups.

Tumor characteristics

A total of 158 patients presented with an adenocarcinoma (64%) and 85 with a squamous cell carcinoma (34%). The repartition was the same in both groups. Most of the tumors were located below the carina (78.6%) and were classified as stage III (38.3%) according to UICC 2009. No significant

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### Table 6: Recurrence and mortality

|                      | Elderly: ≥70 years | Nonelderly: <70 years | p-value |
|----------------------|--------------------|-----------------------|---------|
|                      | (N = 61)           | (N = 187)             |         |
| Recurrence           |                    |                       |         |
| Yes                  | 21                 | 87                    | 0.098   |
| No                   | 40                 | 100                   |         |
| Follow-up (mean days)| 1438.6             | 2041.2                |         |
| Follow-up (mean months)| 48.0           | 68.0                  |         |
| Salvage              |                    |                       |         |
| Yes                  | 4                  | 17                    | 0.791   |
| No                   | 57                 | 170                   |         |
| Mortality            |                    |                       |         |
| Yes                  | 41                 | 99                    | 0.051   |
| No                   | 20                 | 88                    |         |
| Operative mortality ≤30 days |              |                       |         |
| Yes                  | 5                  | 1                     | 0.004   |
| No                   | 56                 | 186                   |         |
| Mortality ≤90 days   |                    |                       |         |
| Yes                  | 7                  | 6                     | 0.012   |
| No                   | 54                 | 181                   |         |
| Causes of death      |                    |                       |         |
| Surgery related      | 4                  | 3                     | 0.003   |
| Cancer recurrence related | 16              | 68                    |         |
| Other                | 21                 | 28                    |         |
| Causes of death ≤90 days |                |                       |         |
| Surgery related      | 2                  | 2                     | 1       |
| Cancer recurrence related | 2               | 1                     |         |
| Other                | 3                  | 3                     |         |
| Survival             |                    |                       |         |
| 1 year               | 41                 | 162                   | 0.001   |
| 2 years              | 32                 | 131                   | 0.02    |
| 3 years              | 26                 | 115                   | 0.01    |
| 4 years              | 24                 | 104                   | 0.04    |
| 5 years              | 22                 | 96                    | 0.04    |
difference was observed in the clinical stages of the tumor (Table 2).

**T able 7  Multivariate analysis overall survival**

| Variables          | HR   | 95% CI    | P-value |
|--------------------|------|-----------|---------|
| Age <70            | 1    | 1.29–2.85 | 0.001   |
| Age ≥70            | 1.91 |           |         |
| ASA 1–2            | 1    | 0.39–0.79 | 0.001   |
| ASA 3–4            | 0.56 |           |         |
| Weight loss >10% before surgery | Yes | 1 | 0.55–1.12 | 0.188 |
| No                 | 0.78 |           |         |
| Neoadjuvant treatment | No  | 1 | 0.58–1.27 | 0.439 |
| Yes                | 0.86 |           |         |
| Adjuvant treatment | Yes  | 1 | 1.29–2.80 | 0.001 |
| No                 | 1.90 |           |         |
| Histological differentiation | Well | 1 |     | 0.098 |
| Moderate           | 1.72 | 1.03–2.88 |         |
| Poor               | 1.37 | 1.02–2.05 |         |
| Resection margins  | R0   | 1 | 0.19–0.73 | 0.004 |
| R1                 | 0.37 |           |         |
| Nodal status       | N1   | 1 | 0.50–1.08 | 0.114 |
| N0                 | 0.73 |           |         |
| Nodal ratio        | <0.2 | 1 | 1.04–2.74 | 0.033 |
| ≥0.2               | 1.69 |           |         |
| pT stage           | T1–T2 | 1 | 1.03–2.20 | 0.039 |
| T3–T4              | 1.50 |           |         |

Note: HR >1 denotes higher risk of death.
Abbreviations: CI, confidence interval; HR, hazard ratio.

**T able 8  Multivariate analysis DFS**

| Variables          | HR   | 95% CI    | P-value |
|--------------------|------|-----------|---------|
| Age <70            | 1    | 1.29–2.85 | 0.001   |
| Age ≥70            | 1.81 |           |         |
| ASA 1–2            | 0.64 | 0.46–0.90 | 0.01    |
| ASA 3–4            | 1    |           |         |
| Weight loss >10% before surgery | Yes | 1.14 | 0.80–1.63 | 0.46 |
| No                 | 1    |           |         |
| Neoadjuvant treatment | No  | 1 | 0.53–1.24 | 0.89  |
| Yes                | 0.81 |           |         |
| Adjuvant treatment | Yes  | 0.54 | 0.36–0.81 | 0.003 |
| No                 | 1.0  |           |         |
| Histological differentiation | Well | 1 |     | 0.28 |
| Moderate           | 1.29 | 0.81–2.04 |         |
| Poor               | 1.75 | 1.07–2.86 |         |
| Resection margins  | R0   | 1 | 1.23–5.06 | 0.01  |
| R1                 | 2.49 |           |         |
| Nodal status       | N1   | 1 | 0.87–2.05 | 0.18  |
| N0                 | 1.94 |           |         |
| Nodal ratio        | <0.2 | 1 | 0.71–2.10 | 0.47  |
| ≥0.2               | 1.22 |           |         |
| pT stage           | T1–T2 | 1 | 1.09–2.31 | 0.015 |
| T3–T4              | 1.59 |           |         |

Note: HR >1 denotes higher risk of death.
Abbreviations: CI, confidence interval; DFS, disease-free survival; HR, hazard ratio.

**Treatment modalities**

Unfortunately, neoadjuvant therapy was significantly less recommended in the elderly group (44.3%/61.5%; p < 0.018) and especially CRT (14.8%/32.6%; p < 0.007). Elderly patients received less adjuvant chemotherapy (18%/32.6%; p = 0.029) (Table 3).

**Surgery and postoperative complications**

A subtotal esophagectomy was performed in most of the cases (n = 190; 76.6%). A total of 51 patients underwent total esophagectomy and seven patients from the noneelderly group a pharyngo-laryngo-esophagectomy. Tubulized stomach was used for reconstruction in most of the cases (94.35%). Only 14 patients had a jejunal (n = 5) or colon (n = 9) interposition. No difference in the mean number of harvested lymph nodes was observed (18 lymph nodes) and the positive nodes on total node ratio was 39% (Table 4–5).

According to the European pathological classification, the R1 resection was significantly higher in the elderly group (7/61 [11.48%] vs. 5/187 [2.67%], p = 0.011). Indeed, seven patients had a positive circumferential margin (<1 mm) compared to two in the younger group. In the nonelderly group, three patients had a positive proximal margin, and two were missed on frozen section. In one patient in the elderly group and two in the nonelderly group the resection was considered R1 following a salvage surgery.
The length of hospital stay was comparable in both groups (mean: elderly group: 18.31 days; nonelderly group: 18.28 days. median: 14 in both groups).

Considering the Dindo–Clavien general score, operative morbidity was higher in the elderly group ($p = 0.024$). In this group, patients experienced more respiratory infectious complications and acute respiratory distress syndrome (ARDS).

Fourteen patients presented an anastomotic leak (14/248; 5.6%); two cervical, eight thoracic and four following pharyngo-laryngo-esophagectomy. This number decreased to 10 patients if the four patients from the nonelderly group who underwent a salvage pharyngo-laryngo-esophagectomy (10/241; 4.1%) are excluded. No significant difference in anastomotic leak rate was observed between the two groups (4.9%/3.9%; $p = 0.73$).

The rate of ICU readmission and reintervention for complications were not significantly different.

**TABLE 9**  Multivariate analysis cancer specific survival

| Variables                                | HR   | 95% CI        | p-value |
|------------------------------------------|------|---------------|---------|
| Age <70                                  | 1    | 0.63–2.03     | 0.67    |
| Age ≥70                                  | 1.13 |               |         |
| ASA 1–2                                  | 1    | 0.91–2.23     | 0.12    |
| ASA 3–4                                  | 1.42 |               |         |
| Weight loss >10% before surgery          |      |               |         |
| Yes                                      | 1    | 0.86–2.21     | 0.18    |
| No                                       | 1.38 |               |         |
| Neoadjuvant treatment                    |      |               |         |
| No                                       | 1    | 0.52–1.51     | 0.65    |
| Yes                                      | 0.88 |               |         |
| Adjuvant treatment                       |      |               |         |
| Yes                                      | 1    | 1.58–4.45     | <0.001  |
| No                                       | 2.65 |               |         |
| Histological differentiation            |      |               |         |
| Well                                     | 1    |               | 0.14    |
| Moderate                                 | 1.43 | 0.73–2.77     |         |
| Poor                                     | 1.97 | 0.98–3.96     |         |
| Resection margins                        |      |               |         |
| R0                                       | 1    | 1.72–7.97     | 0.001   |
| R1                                       | 3.70 |               |         |
| Nodal status                             |      |               |         |
| N0                                       | 1    | 0.84–2.24     | 0.201   |
| N1                                       | 1376 |               |         |
| Nodal ratio                              |      |               |         |
| <0.2                                     | 1    | 1.15–3.76     | 0.016   |
| ≥0.2                                     | 2.07 |               |         |
| pT stage                                 |      |               |         |
| T1–T2                                    | 1    | 1.18–3.62     | 0.009   |
| T3–T4                                    | 1.96 |               |         |

Note: HR >1 denotes higher risk of death.
Abbreviations: CI, confidence interval; HR, hazard ratio.

**FIGURE 1**  Disease free-survival stratified by age.

**FIGURE 2**  Overall survival stratified by age.

**Recurrence and mortality**

The median follow-up was 54.9 months for all patients at the time of data cutoff (Tables 6–9, Figures 1–3).

The 30 and 90-day postoperative mortality was 8.2% (5/61) and 11.5% (7/61), respectively in the elderly group and 0.5% (1/187) and 3.2% (6/187) in the nonelderly group ($p = 0.004$ and $p = 0.012$). This 90-day mortality rate decreased to 3.3% (2/61), and 1.1% (2/187) ($p = 0.59$), respectively when we consider specific surgery-related deaths.

In the elderly group, two patients died from cancer spread, three of aspiration and arrhythmia and two of surgically-related complications. On the other hand, in the
From the analysis of the National Cancer Database (NCDB), Vlachic et al.\textsuperscript{4} pointed out the survival benefit from any tumor-directed therapy and even palliative treatment in elderly patients with locally advanced esophageal cancer. The trimodal approach offered the best survival benefit and its use increased over time. The authors identified different factors impacting the treatment results and advised caution and care in the choice of the most appropriate approach.

Little data exists regarding the feasibility of neoadjuvant therapy in elderly patients, especially chemoradiotherapy (CRT). In our experience, despite no significant difference in the cTNM classification between the two groups, elderly patients received significantly less neoadjuvant treatment ($p = 0.018$), in particular less CRT ($p = 0.007$), probably due to the reluctance of our oncologists and the associated comorbidities in this group. In a series of 312 consecutive patients who underwent esophagectomy for esophageal cancer, Rice et al. compared the outcome of $\geq$70 year old patients who received neoadjuvant therapy with those who did not, and those younger than 70 years who received preoperative treatment. No increase in major postoperative complications in the elderly was observed, but postoperative atrial arrhythmias were more likely to develop.\textsuperscript{7}

Even in the presence of medical risk factors, resection is still preferred for the elderly unless the risk is prohibitively high. Cardiopulmonary diseases are the main risk factors in these patients. In a study by Poon et al., 13\% of patients were deemed unresectable because of poor physical condition or cardiopulmonary status.\textsuperscript{3} Our elderly patients presented a higher rate of cardiac ($p = 0.004$) and renal ($p = 0.023$) comorbidities as compared to their younger counterparts. Moreover, the rate of WHO PS 2–4 showed a significant difference between the two groups ($p < 0.0001$). These findings were shared by other authors.\textsuperscript{8}

The Dindo–Clavien score was significantly higher in elderly patients ($p = 0.024$). More recent reviews and pooled analysis pointed out this higher incidence of postoperative morbidity.\textsuperscript{1,8,9} Similarly, Cjs et al. observed a greater rate of nonsurgical complications in elderly patients.\textsuperscript{10} For others, the postoperative morbidity seemed comparable to younger patients with a cutoff for elderly patients at 80 years or greater.\textsuperscript{11}

Pulmonary complications were found to be the most common cause of postoperative death in both young and elderly patients.\textsuperscript{3,5,8,12,13} They represent 33\% of postoperative cause of mortality in our series. In Sunpaweravong et al., pneumonia was observed in 22.8\% of their patients.\textsuperscript{14} In a pooled analysis, the rate of pulmonary complications varied from 4\% to 56\% in elderly patients.\textsuperscript{15} These results strongly suggest that greater preoperative precautions must be taken to manage cardiopulmonary complications, particularly in elderly patients. We are in agreement that the primary aim of postoperative esophagectomy care should be the prevention of pulmonary complications such as aspiration and pneumonia by preoperative rehabilitation and also checking the swallow function before resuming oral intake.

Nonelderly group, one patient died from cancer spread, one of massive aspiration, one of bronchomalacia, one in a traffic accident and two of surgically-related complications.

The overall 1- and 3-year survival rate was 67 and 43\%, respectively in the elderly group versus 87 and 61\% in the nonelderly group ($p = 0.001$ and $p = 0.01$). The DFS was longer in younger patients (58.4 months [95\% CI: 28.7–88.2]) as compared with elderly patients (20.2 months [95\% CI: 8.1–32.2]), $p = 0.005$ (Figure 1). When considering overall survival, patients <70 years have a significantly longer OS (median: 88.0 months [95\% CI: 52.1–123.8]) as compared with $\geq$70 years patients (median:44.8 months [95\% CI:12.4–96.8], Figure 2). In the multivariate model adjusted for potential prognostic factors, age was an independent prognostic factor for both DFS (Table 8) and OS (Table 7).

Interestingly, age failed to influence CSS in the univariate (Figure 3) and multivariate analyses (Table 9).

**DISCUSSION**

Esophageal cancer is the eighth most common cancer and the sixth cause of cancer mortality worldwide.\textsuperscript{1} The diagnosis is more frequent in patients between 65 and 74 with a median age of 67 years.\textsuperscript{2}

Not so long ago, advanced age was considered as a relative contraindication to major surgery such as esophagectomy. Indeed, this surgery has been associated with higher rates of perioperative mortality.\textsuperscript{3–5}

In recent years, there has been an increase in the number of elderly patients undergoing surgery for esophageal cancer. Whether the prognosis of this group of patients is more unfavorable than that in younger patients remains controversial.

In the study by Finlayson et al.,\textsuperscript{6} operations for esophageal cancer were found to present the highest mortality rate in octogenarian compared to lung or pancreatic cancer.
with fiberoptic endoscopy or cineradiography, our preference being the latter. In our experience, despite careful patient selection and preoperative rehabilitation, including smoking and alcohol cessation, preoperative physical exercises, and respiratory physiotherapy, we reached an overall rate of 28% of pulmonary infections and 15% of acute respiratory distress syndrome (ARDS). Major respiratory complications occurred much more in elderly patients ($p < 0.058$) with a significant higher ARDS rate ($p = 0.001$).

The overall anastomotic leak rate was 5.6% (14/248). This rate dropped to 4.1% if we exclude four patients from the nonelderly who underwent a salvage pharyngo-laryngo-esophagectomy (10/241); indeed the risk of such complication is higher after these procedures. No significant difference was observed in the leak rate between the two groups (elderly: 4.9%, nonelderly: 3.9%). Unfortunately, despite this low rate, leak remains a severe surgical complication. Similarly, Ruol et al. obtained a 7.5% leak rate in elderly patients compared to 10.2% in the other group. Sunpaweravong et al. reported a leak incidence of 15.9% in patients with locally advanced stage of disease.

The hospital length of stay was similar in both groups (median: 14 days). No significant difference was observed in the literature.

In esophageal cancer surgery, the primary objective is to perform an R0 resection and the status of resection is not affected by patient age. In our series, the rate of circumferential R1 resection, defined by the European pathologists was significantly higher in elderly patients, which is probably due to the lower rate of neoadjuvant CRT in this group.

The 30 ($p < 0.004$) and 90 day ($p < 0.036$) operative mortality rate was significantly higher in the elderly group. When we consider the specific surgery-related postoperative mortality, the 90-day rates drop to 3.3 and 1.1%, respectively. In the elderly group, two patients died of cancer spread, three of arrhythmia and aspiration and two of surgically-related complications. Many of these patients refused therapeutic relentlessness. Our mortality rate is comparable to other studies.

In our series, the 5-year survival rate was significantly higher in the nonelderly group ($p < 0.04$). In the study by Lagergren et al., patients aged 75 and over was an independent risk factor for higher short-term mortality and lower long-term survival. Few studies suggest that there is no correlation between age and long-term survival in cases of appropriate patient selection for surgery, which emphasize that age should not be a barrier to surgery.

In the present study, the age impacted the OS and DFS but not the CSS. Indeed, the DFS and OS curves were significantly in favor of nonelderly patients ($p = 0.005$ and $p = 0.003$) but no significant difference between the two groups was observed in the CSS. CSS is probably a better endpoint for comparing the two groups of patients because independently of esophageal cancer, elderly patients have a higher risk of death. Our multivariate analyses confirmed that older age was an independent risk factor for OS and DFS but not for CSS, which indicated that older patients had poorer survival but were not at greater risk of cancer-specific death. This suggests that noncancer-specific mortality was an important competing risk event in this group. Similarly, Aoyama et al. found a significant difference between the two groups in OS and DFS.

Although chronological age should not be a sole criterion for recommending esophagectomy, Schlottmann et al. suggest that the increased rate of mortality in elderly patients is not only explained by the higher incidence of comorbidities in those patients. We share some authors’ opinions that selected elderly patients with esophageal or gastroesophageal junction cancer should not be denied surgery.

In conclusion, the rate of esophageal and gastroesophageal cancer in the elderly went with an increase in life expectancy. Elderly patients may be at increased anesthetic risk and consequently a lower rate of operability. An accurate preoperative assessment and intensive perioperative preparation and care are mandatory for the selection of surgical candidates and may increase the operability rate and decrease postoperative morbidity and mortality. Elderly patients might present a higher morbimortality rate but might present a survival benefit and a better quality of life no matter the type of treatment. We conclude from our data that despite the poorer DFS and OS, elderly patients were not at greater risk of cancer specific death and the noncancer specific mortality was a competing risk event in this group. We believe as do many other authors that selected elderly patients with this disease should not be denied surgery.

**CONFLICT OF INTEREST**

The authors have no conflicts of interest to declare.

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LAURENT ET AL.

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