

EXTENDED TRANSTHORACIC RESECTION COMPARED WITH LIMITED TRANSHIATAL RESECTION FOR ADENOCARCINOMA OF THE ESOPHAGUS

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ABSTRACT

Background Controversy exists about the best surgical treatment for esophageal carcinoma.

Methods We randomly assigned 220 patients with adenocarcinoma of the mid-to-distal esophagus or adenocarcinoma of the gastric cardia involving the distal esophagus either to transhiatal esophagectomy or to transthoracic esophagectomy with extended en bloc lymphadenectomy. Principal end points were overall survival and disease-free survival. Early morbidity and mortality, the number of quality-adjusted life-years gained, and cost effectiveness were also determined.

Results A total of 106 patients were assigned to undergo transhiatal esophagectomy, and 114 to undergo transthoracic esophagectomy. Demographic characteristics and characteristics of the tumor were similar in the two groups. Perioperative morbidity was higher after transthoracic esophagectomy, but there was no significant difference in in-hospital mortality ($P=0.45$). After a median follow-up of 4.7 years, 142 patients had died — 74 (70 percent) after transhiatal resection and 68 (60 percent) after transthoracic resection ($P=0.12$). Although the difference in survival was not statistically significant, there was a trend toward a survival benefit with the extended approach at five years: disease-free survival was 27 percent in the transhiatal-esophagectomy group, as compared with 39 percent in the transthoracic-esophagectomy group (95 percent confidence interval for the difference, -1 to 24 percent [the negative value indicates better survival with transhiatal resection]), whereas overall survival was 29 percent as compared with 39 percent (95 percent confidence interval for the difference, -3 to 23 percent).

Conclusions Transhiatal esophagectomy was associated with lower morbidity than transthoracic esophagectomy with extended en bloc lymphadenectomy. Although median overall, disease-free, and quality-adjusted survival did not differ statistically between the groups, there was a trend toward improved long-term survival at five years with the extended transthoracic approach. (N Engl J Med 2002;347:1662-9.)

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LONG-TERM survival after surgery with curative intent for adenocarcinoma of the distal esophagus and gastric cardia is only 20 percent.^{1,2} Surgery is generally considered to offer the best chance for cure, but opinions differ on how to improve survival by surgery. One strategy aims at decreasing early postoperative risk by the use of limited cervicoabdominal (transhiatal) esophagectomy without formal lymphadenectomy. Another is intended to improve long-term survival by performing a combined cervicothoracoabdominal resection, with wide excision of the tumor and peritumoral tissues and extended lymph-node dissection in the posterior mediastinum and the upper abdomen (transthoracic esophagectomy with extended en bloc lymphadenectomy).¹⁻⁵

We studied whether transthoracic esophagectomy with extended en bloc lymphadenectomy sufficiently improves overall, disease-free, and quality-adjusted survival over the rates with transhiatal esophagectomy to compensate for the possibly higher perioperative morbidity and mortality and the increased costs of the treatment.

METHODS

Study Design

The study was performed in two academic medical centers, each performing more than 50 esophagectomy procedures per year. The eligible patients had histologically confirmed adenocarcinoma of the mid-to-distal esophagus or adenocarcinoma of the gastric cardia involving the distal esophagus, had no evidence of distant metastases (including the absence of histologically confirmed tumor-positive cervical lymph nodes and unresectable celiac lymph nodes), and did not have unresectable local disease. These patients were randomly assigned to undergo transhiatal esophagectomy or transthoracic esophagectomy with extended en bloc lymphadenectomy between April 1994 and February 2000.

Patients had to be older than 18 years of age and in adequate physical condition to undergo surgery (as indicated by their assignment to American Society of Anesthesiologists class I or II⁶). Exclusion criteria were previous or coexisting cancer, previous gastric or esophageal surgery, receipt of neoadjuvant chemotherapy or ra-

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diation therapy, recurrent laryngeal-nerve palsy, and extension of the tumor that made it impossible for the surgeon to construct a gastric tube.

The preoperative diagnostic workup consisted of endoscopy with biopsy and histologic examination, endosonography, external ultrasonography of the abdomen and neck (with biopsy if indicated), chest radiography, indirect laryngoscopy, and bronchoscopy if tumor ingrowth in the upper airway was suspected. Computed tomography was performed only when indicated. Patients with carcinoma of the cardia underwent laparoscopy with laparoscopic ultrasonography.⁷ Positron-emission tomography was not performed. After giving written informed consent, the patients were randomly assigned to one of the surgical procedures two to four weeks before surgery. Randomization was stratified according to the hospital and tumor site (esophagus or cardia, as indicated by endoscopy). No blocking was used within each of the four strata. Patients were classified as having esophageal carcinoma if the bulk of the tumor was in the esophagus, Barrett's mucosa was present, or both; patients were classified as having carcinoma of the cardia if the bulk of the tumor was in the cardia and Barrett's mucosa was not present.

Surgery and Pathological Examination

Surgery was performed by or under the direct supervision of a surgeon-investigator with experience in esophageal surgery. During transhiatal esophagectomy, the esophagus was dissected under direct vision through the widened hiatus of the diaphragm, up to the inferior pulmonary vein. The tumor and its adjacent lymph nodes were dissected en bloc. A 3-cm-wide gastric tube was constructed. The left gastric artery was transected at its origin, with resection of local lymph nodes. Celiac lymph nodes were dissected only when there was clinical suspicion of involvement. After right-sided mobilization of the cervical esophagus, the intrathoracic, normal esophagus was bluntly resected from the neck to the abdomen with use of a vein stripper. Esophagogastrostomy was performed in the neck, without cervical lymphadenectomy.

Posterolateral thoracotomy was the first step in transthoracic resection with extended en bloc lymphadenectomy. The thoracic duct, azygos vein, ipsilateral pleura, and all periesophageal tissue in the mediastinum were dissected en bloc. The specimen included the lower and middle mediastinal, subcarinal, and right-sided paratracheal lymph nodes (dissected en bloc). The aortopulmonary-window nodes were dissected separately. Through a midline laparotomy, the paracardial, lesser-curvature, left-gastric-artery (along with lesser-curvature), celiac trunk, common-hepatic-artery, and splenic-artery nodes were dissected, and a gastric tube was constructed. The cervical phase of the transthoracic procedure was identical to the transhiatal procedure, but a left-sided approach was used.

In both procedures, the origin of the left gastric artery was marked. Subcarinal nodes were marked separately in case of a planned transthoracic resection. In the resection specimen, periesophageal tissue and the lesser omentum were palpated for the presence of lymph nodes and subsequently dissected. All lymph nodes identified by the pathologist were collected in separate boxes and marked according to location, then cut in two with both sides stained with hematoxylin and eosin. Pathological grading was performed by or under the supervision of an investigator who was a senior gastroenterologic pathologist. Tumors were assigned pathological tumor-node-metastasis (TNM) stages according to the Union Internationale contre le Cancer 1997 system. Carcinoma of the cardia and distal esophageal carcinoma were considered a single clinical entity.⁸⁻¹⁰

Early postoperative complications were prospectively scored by the study coordinators. Epidural anesthesia was used postoperatively to minimize pulmonary complications.

Follow-up and Assessment of End Points

All patients were seen at the outpatient clinic at intervals of three to four months during the first two years and every six months for

three more years. After five years, follow-up data were obtained by telephone from the patient or his or her family practitioner. Recurrence of disease was diagnosed on clinical grounds. However, whenever a relapse was suspected, radiologic, endoscopic, or histologic confirmation was sought. Recurrent disease was classified as local-regional (occurring in the upper abdomen or mediastinum) or distant (including cervical recurrences). Overall survival and disease-free survival were the main end points of the study.

Survival was adjusted for the quality of life by the calculation of quality-adjusted life-years.¹¹ For all 220 patients, the duration of survival in a certain state of health was obtained from the clinical data and multiplied by a factor representing the quality or "utility" of that state. Utilities range from 0 (death) to 1 (perfect health), and patients are typically asked to assign a value to their own current health state or to other potential outcomes of treatment. The following seven states of health were identified: hospitalization immediately after esophagectomy without complications, hospitalization immediately after esophagectomy with early postoperative pneumonia, early recovery at home, survival without recurrent disease, survival with recurrent local-regional disease, survival with recurrent distant disease, and survival after surgery for an unresectable tumor. In a single interview conducted 3 to 12 months after surgery, utilities for these seven hypothetical health states were obtained in a subsample of 48 of 59 consecutive eligible patients who were free of recurrence of disease and were interviewed between January 1997 and March 1998. The utilities were elicited with a standard-gamble method, in which the patients were asked to choose between a certain but imperfect health state and a gamble between a perfect health state with probability P and death with a probability 1-P. The value of P at which the participant is indifferent between the imperfect health state and the gamble is the utility.¹¹ The whole study cohort was subsequently included in the analysis of quality-adjusted survival.

Cost-Effectiveness Analysis

Costs were defined as the resources used multiplied by the price per unit of each resource. They consisted of direct medical costs, direct nonmedical costs, and indirect costs. Direct medical costs included preoperative costs, in-hospital costs of primary surgical treatment, and medical costs during follow-up. Direct nonmedical costs included expenses for the patient such as travel costs, special diets, or new clothes; indirect costs included time lost from work. Data on resource use during hospital treatment were collected prospectively from the information system at the hospitals. Other resource uses were assessed by means of a questionnaire completed by patients at base line and three months after surgery.

The 1998 costs of the operation per minute, the costs of a stay in the intensive care unit or medium care unit (ICU-MCU) per day, and the costs of a stay in the surgical ward per day were assessed in euros (€1 equals \$1) on the basis of real-cost calculations.¹² These real-cost calculations included personnel costs (surgeons, nurses, and anesthetists), costs of materials, costs of equipment, and overhead costs. Other costs were assessed according to the Netherlands guidelines for research on costs and included reimbursement fees (diagnostics and pathology), insurance charges (general-practitioner visits, outpatient visits, and medication), patient charges such as travel costs or aids, and costs of sick leave (based on the average national income).¹³ Finally, incremental costs per quality-adjusted life-year were computed.

Statistical Analysis

To detect an estimated improvement in median survival from 14 months to 22 months, corresponding to an increase in the 2-year survival rate from 30 percent to 45 percent, among patients undergoing transthoracic resection with extended en bloc lymphadenectomy, we calculated that 220 patients had to be enrolled. We assumed a two-sided significance level of 0.05 and a power of 0.90.

TABLE 1. CHARACTERISTICS OF 220 PATIENTS RANDOMLY ASSIGNED TO TRANSHIATAL ESOPHAGECTOMY OR TRANSTHORACIC ESOPHAGECTOMY WITH EXTENDED EN BLOC LYMPHADENECTOMY.*

| CHARACTERISTIC | TRANSHIATAL ESOPHAGECTOMY (N=106) | TRANSTHORACIC ESOPHAGECTOMY (N=114) |
|---|-----------------------------------|-------------------------------------|
| Age (yr) | | |
| Mean | 69 | 64 |
| Range | 23–79 | 35–78 |
| Sex (M/F) | 92/14 | 97/17 |
| Weight loss (kg) | | |
| Median | 4 | 4 |
| Range | 0–23 | 0–27 |
| American Society of Anesthesiologists class (no. of patients) | | |
| I | 39 | 40 |
| II | 67 | 74 |
| Location of tumor (no. of patients) | | |
| Esophagus | 87 | 93 |
| Cardia† | 19 | 21 |

*All differences between the groups were nonsignificant.

†Cancer of the gastric cardia was that in which the bulk of the tumor was at or distal from the gastroesophageal junction on endoscopy or endosonography, Barrett remnants were absent, and ingrowth in the esophagus was present.

Chi-square or Fisher's exact tests were used to compare categorical data; Student's t-test or the Mann-Whitney U test was used for continuous data. All reported P values are two-sided. P values below 0.05 were considered to indicate statistical significance. Survival curves were calculated from the time of randomization to death from any cause or to the time of the last follow-up visit (at which time data were censored). Disease-free survival was counted up to the time of a first relapse or death from any cause or the time of the last visit without a previous relapse (at which time data were censored). Survival curves were constructed by the Kaplan-Meier method, and the log-rank test was used to determine significance.

Patients with distant metastases, unresectable local tumor detected during the operation, or both were included in the analysis of disease-free survival even when the surgeon decided against resection or performed a different resection, on the intention-to-treat principle. In a separate analysis, the disease-free interval was studied only in patients who underwent resection with no residual tumor remaining and left the hospital alive, because in patients in whom there is no microscopical tumor residue after surgery, the benefit of extended lymphadenectomy might be greater than in other patients.

RESULTS

Between April 1994 and February 2000, 220 of 263 eligible patients were randomly assigned to treatment groups. There were no significant differences between the groups at base line in terms of demographic

TABLE 2. EARLY POSTOPERATIVE COURSE IN 220 PATIENTS RANDOMLY ASSIGNED TO TRANSHIATAL ESOPHAGECTOMY OR TRANSTHORACIC ESOPHAGECTOMY WITH EXTENDED EN BLOC LYMPHADENECTOMY.

| VARIABLE | TRANSHIATAL ESOPHAGECTOMY (N=106) | TRANSTHORACIC ESOPHAGECTOMY (N=114) | P VALUE |
|---------------------------------------|-----------------------------------|-------------------------------------|---------|
| Postoperative complications — no. (%) | | | |
| Pulmonary complications* | 29 (27) | 65 (57) | <0.001 |
| Cardiac complications | 17 (16) | 30 (26) | 0.10 |
| Anastomotic leakage† | 15 (14) | 18 (16) | 0.85 |
| Subclinical | 9 (8) | 8 (7) | |
| Clinical | 6 (6) | 10 (9) | |
| Vocal-cord paralysis‡ | 14 (13) | 24 (21) | 0.15 |
| Chylous leakage | 2 (2) | 11 (10) | 0.02 |
| Wound infection | 8 (8) | 11 (10) | 0.53 |
| Ventilation time — days | | | <0.001 |
| Median | 1 | 2 | |
| Range | 0–19 | 0–76 | |
| ICU-MCU stay — days§ | | | <0.001 |
| Median | 2 | 6 | |
| Range | 0–38 | 0–79 | |
| Hospital stay — days¶ | | | <0.001 |
| Median | 15 | 19 | |
| Range | 4–63 | 7–154 | |
| In-hospital mortality — no. (%) | 2 (2) | 5 (4) | 0.45 |

*Pulmonary complications include pneumonia (indicated by the isolation of a pathogen from a sputum culture and a new or progressive infiltrate on a chest x-ray film) and atelectasis (indicated by lobar collapse on a chest x-ray film).

†Subclinical anastomotic leakage was defined as anastomotic leakage seen only on contrast radiography, and clinical anastomotic leakage as anastomotic leakage resulting in a cervical salivary fistula. Reintervention was needed in two patients with anastomotic leakage, both after transthoracic esophagectomy.

‡In most cases, vocal-cord paralysis was temporary.

§ICU denotes intensive care unit, and MCU medium care unit.

¶The hospital stay was defined as the number of days from the day of operation to discharge. Patients were generally admitted two days before surgery.

characteristics or characteristics of the tumor (Table 1). Complete endosonography was possible in 88 percent of patients. The mean time between randomization and surgery was three weeks in both groups.

Ninety-three of the 106 patients in the transhiatal-esophagectomy group (88 percent) and 109 of the 114 patients in the transthoracic-esophagectomy group (96 percent) underwent the planned procedure (P=0.08). One patient did not undergo resection after massive aspiration, whereas the presence of unresectable local tumor, distant metastases, or both (detected during the operation) precluded resection in 11 patients. Total gastrectomy was performed in three patients, and conversion to either unplanned transthoracic or unplanned transhiatal resection took place in another three. Transhiatal resection was associated with a shorter median duration of surgery (3.5 hours, as compared with 6.0 hours for transthoracic resection; P<0.001) and a lower median blood loss per procedure (1.0 vs. 1.9 liters, P<0.001). There were no perioperative deaths. Transhiatal resection was associated with fewer pulmonary complications, less chylous leakage, a shorter duration of mechanical ventilation, and shorter stays in the ICU-MCU and in the hospital

(Table 2). Overall in-hospital mortality was 3 percent; two patients (2 percent) in the transhiatal group and five patients (4 percent) in the transthoracic group died.

Four patients in each group did not have evidence of adenocarcinoma in the resection specimen. These patients were included in all analyses. Tumor stages were similar in the two groups, with a tendency toward more stage IV tumors in the transthoracic-esophagectomy group (15 percent, as compared with 7 percent in the transhiatal-esophagectomy group) (Table 3). A mean (\pm SD) of 16 ± 9 nodes were identified in the resection specimen after transhiatal resection, and 31 ± 14 after transthoracic resection. One hundred patients undergoing transthoracic resection (88 percent) had 15 or more lymph nodes identified in the resected specimen. There was no difference in the radicality of surgery, as indicated by the residual-tumor classification, between the two groups.

Follow-up continued until July 2002, ensuring a minimal follow-up of two and a half years. Follow-up was complete for all patients. The median follow-up was 4.7 years (range, 2.5 to 8.3). Recurrent disease developed in 62 patients after transhiatal resection (58

TABLE 3. CHARACTERISTICS OF THE TUMOR AND OF SURGERY IN PATIENTS WHO UNDERWENT TRANSHIATAL ESOPHAGECTOMY OR TRANSTHORACIC RESECTION WITH EXTENDED EN BLOC LYMPHADENECTOMY.*

| CHARACTERISTIC | TRANSHIATAL ESOPHAGECTOMY (N=94) | TRANSTHORACIC ESOPHAGECTOMY (N=111) | P VALUE |
|--|----------------------------------|-------------------------------------|---------|
| Histologic type — no. (%) | | | 0.99 |
| Adenocarcinoma | 90 (96) | 107 (96) | |
| Other† | 4 (4) | 4 (4) | |
| TNM stage — no. (%)‡ | | | 0.15 |
| 0 | 2 (2) | 2 (2) | |
| I | 10 (11) | 15 (14) | |
| IIa | 18 (19) | 10 (9) | |
| IIb | 10 (11) | 7 (6) | |
| III | 47 (50) | 60 (54) | |
| IV | 7 (7) | 17 (15) | |
| Radicality of surgery — no. (%)§ | | | 0.28 |
| R0 | 68 (72) | 79 (71) | |
| R1 | 23 (24) | 28 (25) | |
| R2 | 1 (1) | 4 (4) | |
| Uncertain | 2 (2) | 0 | |
| No. of lymph nodes dissected — mean \pm SD | 16 ± 9 | 31 ± 14 | <0.001 |

*Patients who underwent total gastrectomy or had unresectable tumor were excluded from this analysis; patients in whom the operation was converted from the assigned procedure to the other were included as part of the assigned group. P values are for the comparison of all stages combined and all resections achieved.

†Two patients with high-grade dysplasia (stage 0), one with squamous-cell carcinoma, and one with adenocarcinoma were erroneously assigned to each group.

‡In three of the four patients who underwent R2 resections (i.e., resections with macroscopical residual tumor) after assignment to transthoracic esophagectomy, distant metastases were found during the abdominal phase of surgery.

§R0 denotes no residual tumor, R1 microscopic residual tumor, and R2 macroscopical residual tumor.

percent) and 57 after transthoracic resection (50 percent). Local–regional recurrence occurred in 14 percent and 12 percent of patients, respectively; distant recurrence in 25 percent and 18 percent; and both in 18 percent and 19 percent ($P=0.60$). For the transhiatal and transthoracic procedures, the median disease-free interval was 1.4 years (95 percent confidence interval, 0.8 to 2.0) and 1.7 years (95 percent confidence interval, 0.7 to 2.7), respectively ($P=0.15$) (Fig. 1). The estimated rate of disease-free survival at five years was 27 percent (95 percent confidence interval, 19 to 38 percent) after transhiatal resection, as compared with 39 percent (95 percent confidence interval, 30 to 48 percent) after transthoracic resection. The 95 percent confidence interval for the difference in the rates was -1 percent to 24 percent (the negative value indicates that survival was better with transhiatal resection).

At the end of follow-up, 142 patients had died —

74 in the transhiatal-esophagectomy group (70 percent) and 68 in the transthoracic group (60 percent; $P=0.12$). Thirteen patients died of causes unrelated to cancer. The median overall survival was 1.8 years (95 percent confidence interval, 1.2 to 2.4) after transhiatal resection and 2.0 years (95 percent confidence interval, 1.1 to 2.8) after transthoracic resection with extended en bloc lymphadenectomy ($P=0.38$) (Fig. 2). The estimated rate of overall survival at five years was 29 percent (95 percent confidence interval, 20 to 38 percent) after transhiatal resection, as compared with 39 percent (95 percent confidence interval, 30 to 48 percent) after transthoracic resection. The 95 percent confidence interval for the difference was -3 percent to 23 percent. The median number of quality-adjusted life-years after transhiatal resection was 1.5 (95 percent confidence interval, 0.8 to 2.1), as compared with 1.8 (95 percent confidence interval, 1.1 to 2.4) after

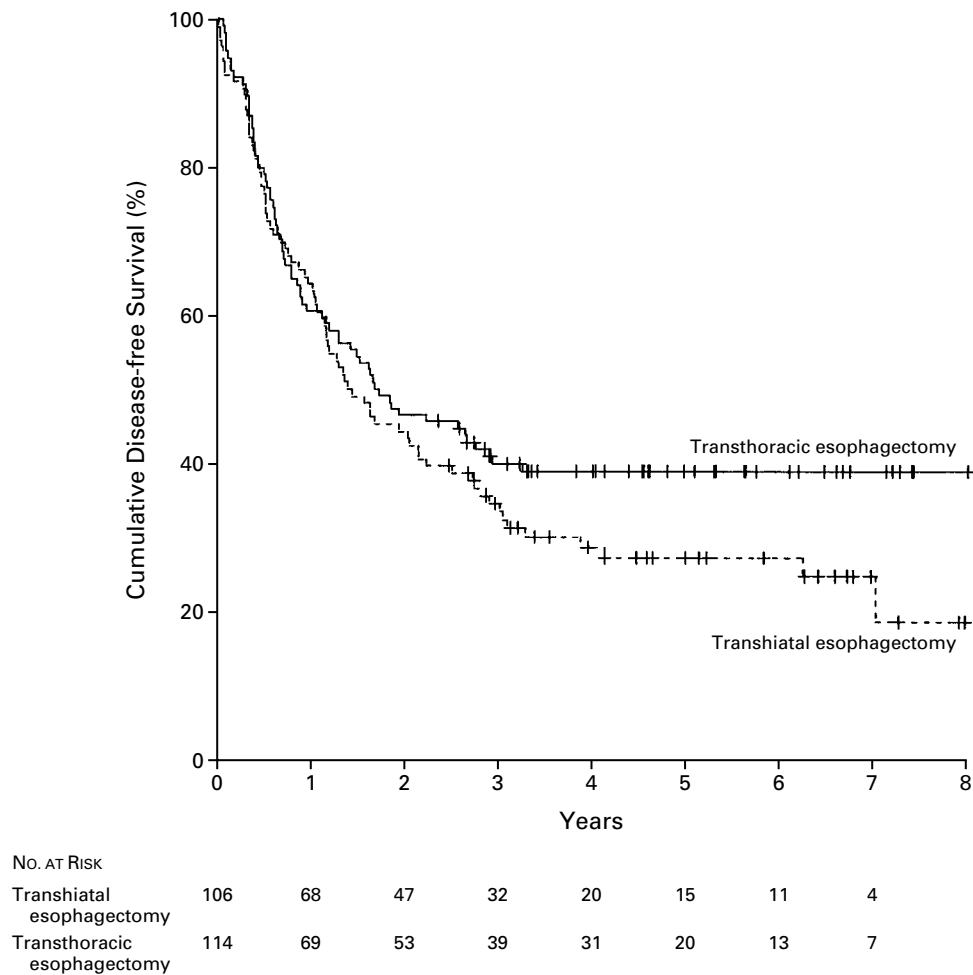


Figure 1. Kaplan–Meier Curves Showing Disease-free Survival among Patients Randomly Assigned to Transhiatal Esophagectomy or Transthoracic Esophagectomy with Extended en Bloc Lymphadenectomy.

transthoracic resection with extended en bloc lymphadenectomy (P=0.26) (Fig. 3).

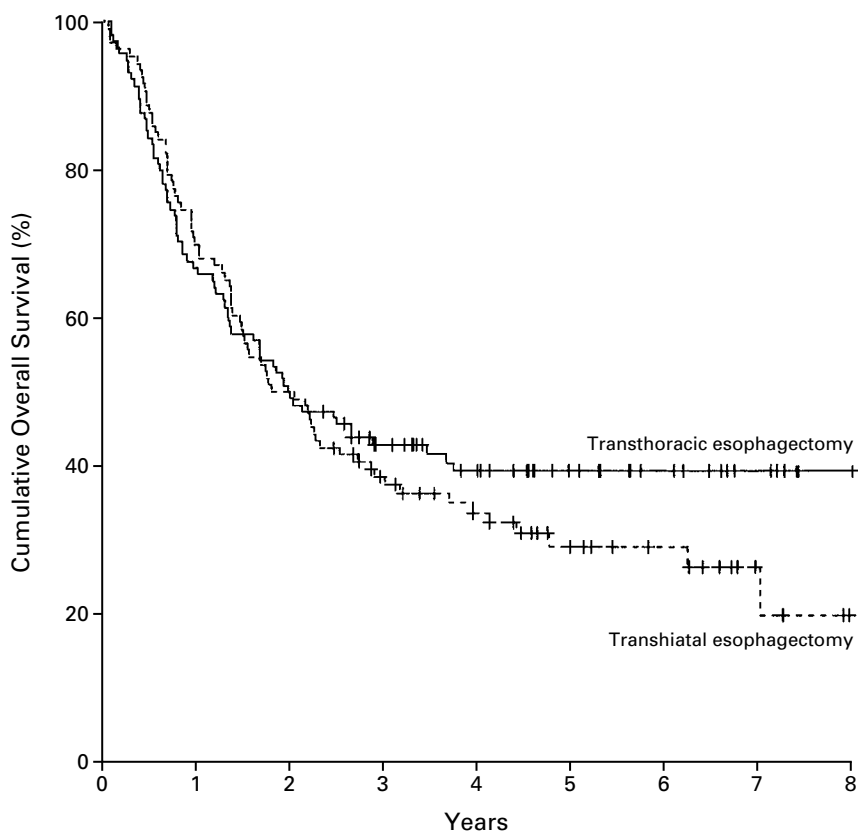
The mean total direct and indirect costs of the procedure were €23,809 for transhiatal resection and €37,099 for transthoracic resection with extended en bloc lymphadenectomy (Table 4). Therefore, the cost of treatment with transthoracic resection was 56 percent higher. The costs of surgery, of the stay in the ICU–MCU, and of the stay in the regular hospital surgical ward were the largest contributors to overall costs (Table 4). The incremental cost of transthoracic esophagectomy was €41,531 per quality-adjusted life-year gained.

DISCUSSION

Our study was performed to determine whether transthoracic esophagectomy with extended en bloc lymphadenectomy could sufficiently improve overall,

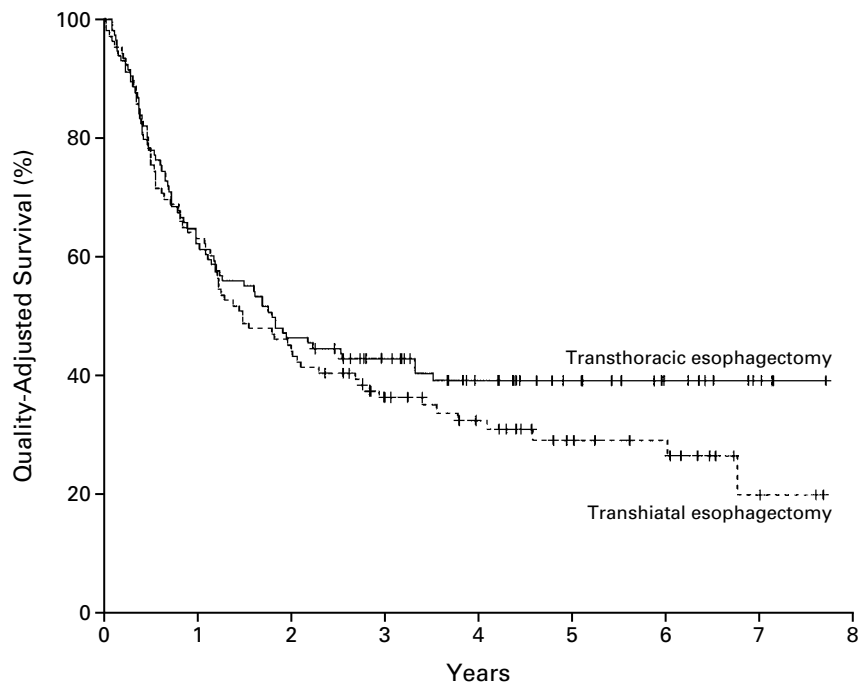
disease-free, and quality-adjusted survival over the rates with transhiatal esophagectomy to compensate for a possible increase in perioperative morbidity and mortality and in the costs of treatment. The significantly higher in-hospital morbidity (but not mortality) after transthoracic resection led to longer ICU–MCU and hospital stays and higher costs. The curves for disease-free and overall survival were similar early after surgery but diverged (without the difference reaching statistical significance) after three years, with the difference favoring the extended resection.

Almost 90 percent of the patients who underwent extended en bloc lymphadenectomy after transthoracic esophagectomy had 15 or more lymph nodes removed and identified in the section by the pathologist, indicating that the extent of lymphadenectomy had been adequate.¹⁴ Posterolateral thoracotomy gives wide access to the mediastinum, thus offering



| No. AT RISK | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|-----------------------------|-----|----|----|----|----|----|----|---|---|
| Transhiatal esophagectomy | 106 | 74 | 53 | 35 | 25 | 16 | 11 | 4 | |
| Transthoracic esophagectomy | 114 | 76 | 57 | 42 | 31 | 20 | 14 | 7 | |

Figure 2. Kaplan–Meier Curves Showing Overall Survival among Patients Randomly Assigned to Transhiatal Esophagectomy or Transthoracic Esophagectomy with Extended en Bloc Lymphadenectomy.



| NO. AT RISK | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|-----------------------------|-----|----|----|----|----|----|----|---|---|
| Transhiatal esophagectomy | 106 | 68 | 47 | 32 | 20 | 15 | 11 | 4 | |
| Transthoracic esophagectomy | 114 | 69 | 53 | 39 | 31 | 20 | 13 | 7 | |

Figure 3. Kaplan–Meier Curves for Quality-Adjusted Survival among Patients Randomly Assigned to Transhiatal Esophagectomy or Transthoracic Esophagectomy with Extended en Bloc Lymphadenectomy. Survival was expressed in quality-adjusted life-years as calculated with the standard-gamble method.

both the possibility of extended lymphadenectomy and the theoretical advantage of improving control by extended en bloc dissection of all peritumoral tissues. However, the radicality of the surgery was similar in the two groups, reflecting the possibility of achieving adequate local control by transhiatal resection. The distribution of TNM stages was also similar. There were slightly more patients with celiac-node involvement (M1) in the transthoracic-esophagectomy group, probably because of the lymphadenectomy in the upper abdomen, which led to upgrading of the tumor when positive nodes were found. Tumor staging was therefore improved by the increase in the number of dissected lymph nodes in the upper abdomen after an extended en bloc lymphadenectomy, as has been shown for gastric cancer.^{15,16} Such “stage migration” might slightly influence the stage-by-stage comparison, since positive nodes were found in the extended fields in roughly 20 percent of the patients.¹⁵ However, this phenomenon did not affect the difference in overall survival rates.

Extended resection is believed to reduce the rate of local–regional recurrence, thereby increasing the quality of life and prolonging disease-free and overall survival. In this series, the patterns of recurrence were similar after both types of resection. Disease-free and overall survival curves were virtually identical in the first two years of follow-up. Later during follow-up, both disease-free and overall survival curves diverged, showing a trend in favor of the extended transthoracic approach. Estimated five-year disease-free survival rates were 27 percent and 39 percent, respectively, whereas five-year overall survival rates were 29 percent and 39 percent.

Early morbidity, but not mortality, was significantly higher after extended transthoracic resection, leading to longer stays in the ICU–MCU and the hospital and to higher costs. However, improvement of perioperative care might lower these early rates of complications, thereby decreasing the early benefits of a limited transhiatal resection. At present, the choice for patients with adenocarcinoma of the mid-to-distal esophagus

TABLE 4. MEAN TOTAL COSTS OF TREATMENT PER PATIENT FOR PATIENTS ASSIGNED TO TRANSHIATAL ESOPHAGECTOMY OR TRANSTHORACIC ESOPHAGECTOMY WITH EXTENDED EN BLOC LYMPHADENECTOMY.*

| VARIABLE | TRANSHIATAL ESOPHAGECTOMY (N=106) | TRANSTHORACIC ESOPHAGECTOMY (N=114)† |
|---------------------------------------|---|--|
| | euros | |
| Preoperative costs | | |
| Outpatient visits | 419 | 382 |
| Diagnostic tests | 1,206 | 1,345 |
| Visits to general practitioner | 37 | 42 |
| Subtotal | 1,662 | 1,768 |
| In-hospital treatment costs | | |
| Esophagectomy | 3,551 | 5,389 |
| ICU-MCU stay | 5,563 | 13,459 |
| Stay in surgical ward | 5,934 | 7,409 |
| Reintervention | 101 | 340 |
| Pathological examinations | 473 | 633 |
| Diagnostic tests | 1,114 | 1,688 |
| Subtotal | 16,736 | 28,918 |
| Medical costs during follow-up | | |
| Outpatient visits | 754 | 737 |
| Readmission | 839 | 1,399 |
| Visits to general practitioner | 46 | 57 |
| Aids | 439 | 438 |
| Other | 18 | 15 |
| Subtotal | 2,096 | 2,646 |
| Nonmedical costs | | |
| Travel | 143 | 124 |
| Other costs to patient | 78 | 116 |
| Subtotal | 221 | 240 |
| Indirect costs | | |
| Absenteeism from work | 3,094 | 3,527 |
| Total costs | 23,809 | 37,099 |

*All costs are given in euros (€1 equals \$1). ICU denotes intensive care unit, and MCU medium care unit. Costs were derived from the hospital information systems and postal questionnaires.

†Items may not sum to the subtotals because of rounding.

or of the gastric cardia is between increased early morbidity and the hope of better long-term benefit with transthoracic resection and extended en bloc lymphadenectomy, on the one hand, and lower early morbidity but apparently decreased long-term survival with the transhiatal approach, on the other. Our data do not permit us to make a clear recommendation of one treatment over the other. Further follow-up of the patients in this study may clarify whether the long-term benefits of the extended approach, in terms of survival, outweigh the increase in early morbidity and associated costs. Further follow-up may therefore elucidate the role of transthoracic resection with extended en

bloc lymphadenectomy in the treatment of this group of patients.

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