

Treatment of Carcinoma of the Esophagus

Retrospective Study of 2,400 Patients

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A multicenter retrospective statistical study of 2,400 patients with tumors of the esophagus and cardia was undertaken. Study of individual sites revealed the operability of certain carcinomas of the upper third of the esophagus with a reasonable five-year survival rate despite macroscopic invasion seen in more than half the patients. For the middle third of the esophagus, intrathoracic colonic esophagoplasty with esophageal resection extending as high as possible appeared to offer the best long-term results, particularly if the anastomosis was performed in the neck. Tumors of the lower third of the esophagus were also associated with better results when the esophageal anastomosis was made at a level above the aortic arch, resulting in an improved survival rate for patients undergoing intrathoracic colonic esophagoplasties. For carcinomas of the cardia, use of total gastrectomy was superior to the use of upper polar gastrectomy, but the results were better when gastric excision was also associated with esophageal excision. The finding of normal lymph nodes did not preclude recurrence of the tumor in approximately one-fourth of the patients. Esophageal sections at a distance from the tumor was not necessarily synonymous with section in a healthy area, since the sites of sections studied were either invaded (29%) or areas of neoplastic repermeation (40%). Existence of a histologically normal esophageal section site did not preclude recurrences in 27% of patients with more than one-third in the esophagus. Undifferentiated or poorly differentiated squamous cell carcinomas paradoxically appeared to have a somewhat better long-term prognosis than well differentiated forms, but the increased number of metastases associated with them confirms their unfavorable prognosis. The importance of the T/N classification was confirmed for tumors in classes T1 and T2. From Stage T3, the N criterion was not important. Incidence of postoperative mortality from fistulas appeared to decrease progressively, chiefly due to appropriate medical treatment. Cervical fistulas were associated with a mortality rate of 21%. After esophageal anastomosis above the aortic arch was performed, more than 10% of the recurrences were seen in the neck, indicating the need for extension of the incision as high as possible. Metastases to the bone were present in 15% of the patients. Preoperative radiotherapy did not lessen the number of lymph nodes found to be invaded at the time of excision; the tumors considered to be histologically "sterilized" by

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irradiation were nevertheless associated with a high incidence of lymph node involvement (approximately one-third) and with more than a 40% rate of distant metastases. Excisions considered to be "palliative" by the surgeon nevertheless were of definite value. The mean survival rate at five years was 12%, and one-third of these patients showed no recurrence of neoplasm.

THIS STUDY IS BASED ON the records of 22 surgical teams* at the time of the meeting of the European Societies of Surgery in Paris in September 1979 under the joint chairmanship of Professors J. L. Lortat-Jacob and P. Maillet.

Materials and Methods

The study was performed by sending each surgeon a questionnaire for each patient operated on between January 1, 1970 and January 1, 1979. The form was divided into 44 sections, and a "dictionary" sent at the same time gave details about the questions (141 choices), using a scoring system which arithmetically defined cases of multiple responses to a single question. The long-term survival of patients was defined on the basis of the date that they were seen alive after operation, provided either from the case report or from information obtained from the civil authorities at the patients' place of birth. This provided the best information on the group of patients lost to follow-up.

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The data from the 2,400 case reports were transferred to perforated cards and then to a disk for computer analysis. For classification of results, division of the esophagus into thirds was retained and localization of carcinoma in the cardia was also studied. Identification of the site was verified by two types of numerical information; first, the upper limits of the lesion as recorded by endoscopy and second, the surgical site of the same lesion at the time of operation.

The results obtained were supplied in two forms. In addition to correlations for each section, survival curves on an actuarial basis were also drawn. The method used was the anniversary method, taking into account those patients in whom there was not sufficient follow-up information in terms of subsequent visits, those dying during the interval studied, and those considered as being lost to follow-up.

Intervals of confidence were calculated for each percentage value for the purpose of statistical interpretation in relation to the population involved. These graphs were drawn for each year during the five years following operation. Two different survival percentages calculated for each point are given in the results section: the first point concerned all patients undergoing operation and the second, which was higher, was related to only those patients surviving operation. When these results are cited, the upper and lower limits of the intervals of confidence are given each time after the principal percentage and are shown in parentheses.

In evaluation of the results, percentages are provided without a decimal. They were rounded off to the lower or upper unit according to their value in relation to the intermediate half percentage. For certain groups the values obtained could not respond numerically to the overall population studied because of the existence of a number of answers that were not completely usable in the section in question.

The mean age of all of the patients undergoing operation was 58 years, and the results of the mean survival must be interpreted in relation to the theoretical life expectancy of a healthy population of the same age.

Results

For the 2,400 patients with carcinoma of the esophagus, the mean survival rate at five years was 14% (20%), with an overall operative mortality rate of 30%. Since the exact site of 49 tumors could not be defined on the basis of the responses, the relative proportion of carcinomas operated on according to site was 40% for the middle one-third of the esophagus (926), 33% for the lower one-third of the esophagus (789), 22% for the cardia (530) and 5% for the upper one-third of the esophagus (106). Sex distribution of the patients

operated on indicated a heavy predominance of males (2180) over females (187) (8%). The five-year survival rate among females was nevertheless notably higher [26% (38-15) and 19% (22-16)].

Of the tumors in the *upper third* of the esophagus, 106 were resected. The overall postoperative mortality rate for the operations performed was 31% and the five-year survival rate was 14% (24-4) and 21% (35-6). Sixty per cent of the patients had lymph node involvement and at the time of operation the majority had neither clinical evidence of metastases (97 of 106 patients) nor palpable cervical nodes (94 of 106 patients).

For 91 patients in whom the surgical procedure was defined precisely, the largest number (66 patients: 73%) underwent a one-stage procedure (21 esophagogastric resections and 31 intrathoracic esophagoplasties) and 25 patients (27%) had a two-stage operation (19 colonic esophagoplasties).

Survival rates according to the size of the tumor in its largest dimension indicated that while tumors larger than 5 cm (22 described) showed no survivors at three years, those patients with tumors between 4 and 5 cm (16 patients) were associated with a five-year survival rate of 56% (84-28). It is striking to note that beyond this limit the survival rate subsequently decreased with lesional diameter (29% smaller than 4 cm and 0% smaller than 3 cm).

Tumors located in the *middle third* of the esophagus in 926 patients were suitable for statistical evaluation for long-term survival. The overall postoperative mortality rate was 31% with a mean five-year survival rate of 10% (13-7) and of 15% (19-11). These levels varied according to certain features. When lymph nodes were involved (51% of the patients), the distant overall postoperative survival rate fell to 9% (14-4). Similarly, the existence of macroscopic tumor invasion at the time of operation (349 patients) was associated, at the price of a slightly higher operative mortality rate (34%), with a long-term overall survival rate of 4% (8-0).

Evaluation of the long-term survival rate in relation to the dimension of the tumor indicated, as above, that when the size was between 4 and 5 cm (128), the five-year survival rate was 10% (18-3) or 16%. In patients with small tumors, there were notable differences in survival rate between 55 carcinomas measuring 1-2 cm [18% (30-6)] and 17 tumors with a diameter of less than 1 cm (0%). The surgical approach used for resection of these tumors of the middle third was right thoracic in 60%, left thoracic in 22%, and mixed cervical and thoracic in 18%.

The incidence of this choice of surgical approach and uncomplicated postoperative course was identical (63 and 61%) in the case of supra- or infra-aortic anastomo-

TABLE 1. Proportion of Uncomplicated Postoperative Course (Middle One-third of the Esophagus)

	Supra-aortic Anastomosis	Subaortic Anastomosis	Cervical Anastomosis
Right approach	219 (63%)	136 (61%)	36 (50%)
Left approach	37 (57%)	94 (48%)	4 (50%)

sis, when performed through a right sided approach. In the left thoracic approach, the proportion was somewhat different being surprisingly in favor of supra-aortic anastomoses (Table 1). Anastomoses in the neck were associated with complications in almost half rates of half these patients.

Study of long-term survival rates showed that in patients with esophagogastric resections, the overall survival rate was the same with a right [9% (13-6)] or a left approach [7% (13-1)], and the upper limit of the two intervals of confidence were the same. The operative mortality rate was, nevertheless, higher following excision via a left-sided approach (42%) than right (26%), but the upper and lower limits of the two intervals were very similar (34 and 30%). After this type of resection, long-term results varied markedly according to the extent of the esophageal excision performed.

In 177 patients who had a limited resection with anastomosis below the aortic arch, the survival rate did not exceed 8% at five years (16-0) and in this group the operative mortality rate was higher (36%). Among 736 patients in whom the anastomosis was performed above the aortic arch, the operative mortality rate was lower (27%) and the overall survival at five years higher [13% (16-10)]. When the resection was even more extensive and the anastomosis was performed in the neck (84 patients), the operative mortality rate was similar (31%) but the long-term survival rate appeared better [24% (40-8)]. By comparison with all esophagogastric resections performed, the survival rates of the 58 patients having undergone extensive resection of the esophagus, an intrathoracic esophagoplasty with a high anastomosis showed a mean five-year survival rate of 21% (39-2).

Study of the results of two-stage operations for tumors of the middle third of the esophagus was performed after precise evaluation of the operative risk for each phase, the number of patients not having undergone the second operation having been recorded on the questionnaire. The number of postoperative deaths (56/199, *i.e.* 28%) was less than that for esophagogastric resections. Thus dissociated, overall operative mortality with all operative stages mixed of these operations completed by anastomosis in the neck was 16% with a survival rate at five years of 24% (36-11) or 28% (43-13).

Such an evaluation, involving only 12% of operated patients should be interpreted only with caution but would appear to reflect at least a certain tendency of concept among the surgeons questioned since in 62% of cases, moderately sized tumors were present with a diameter of 1 to less than 4 cm. By extrapolating these findings an estimation of the recurrence rate reveals a marked dissociation between the results in favor of several stage operations (20%) and those performed in one stage (40%).

Examination of 789 tumors of the *lower third* of the esophagus revealed that the mean operative mortality rate (30%) was the same for those of previous sites. The survival curve was slightly above that of the middle third of the esophagus with a five-year survival of 17% (21-13) or 24% (29-18). This latter percentage, in the case of excision with invaded lymph nodes (465 patients, *i.e.* 59%) fell to 21% (27-14).

The poor prognosis of patients with small tumors emerged from comparative survival rates, with carcinomas 4–5 cm in diameter (109) once again having an apparently better survival rate [26% (37-14) and 36%] and those between 1 and 2 cm in diameter (27) having by contrast the worst prognosis (41%) with no survivors at five years.

When attempting to define long-term results in accordance with the extent of the resection performed, it may be noted that in relation to all of the 605 esophagogastric resections performed [overall survival: 16% (21-12)]; the large number of patients (230) in whom the anastomosis was high, patients who had anastomosis above the aortic arch, had a greater life expectancy at five years [20% (27-13)].

In comparison with this group, the 61 patients who had extensive resection with intrathoracic replacement esophagoplasty rate for the same lesion had a higher operative mortality rate (36%) but a long-term survival rate [32% (49-14)] twice as high as that of all esophagogastric resections taken together. It is of interest to note that the lower limits of the intervals of confidence for these three types of operation were identical.

Study of carcinomas of the *cardia* was associated with that of the sites already discussed in view of the necessary and extensive esophageal resection which must be envisaged at the time of surgical resection of such tumors. The survival rate of the 530 patients undergoing operation was apparently the highest: the operative mortality rate was 28% and the five-year survival rate was 19% (24-14) or 26% (33-19). It may be noted that this latter figure corresponds exactly to the upper limit of the postoperative interval of confidence for patients undergoing surgery for a carcinoma of the middle third of the esophagus.

Two types of operation (upper polar and total gastrectomy) were compared for long-term results.

Their distribution according to tumor size (Table 2) indicated that almost three-fourths of small tumors of the cardia were treated by partial resection while among 109 total gastrectomies almost 9/10 were performed, undoubtedly because of necessity, for large tumors with a diameter of at least 4 cm.

The results obtained favored excision, the overall survival of which doubles [36% (50-22)] that of upper polar gastrectomy [18% (24-12)]. The upper limit of the interval of confidence for partial gastrectomies scarcely reached the lower limit for total gastrectomy.

In the group of operations limited to the upper pole of the stomach, resections with high esophageal anastomoses above the aortic arch had a survival rate which was apparently somewhat higher than those mentioned previously [23% (41-5)]. It was, again, twice as low as that of total gastrectomy in which a long segment of esophagus (more than 4 cm) had been resected [46% (64-28)].

The operative mortality rate following total excision (24%) was less than that of partial excision (27%), possibly because of the number of fistulas (12%) which was less than half of that following partial gastrectomy (24). The long-term recurrence rate (6%) was about three times less than that noted after partial gastrectomy (17%).

In this comparison between the results of two types of operation, we did not notice the same spread which we had seen in the statistics of one single department only,¹ with nil survival following upper polar excision at four years but the differences seen in the present study were statistically perfectly significant.

They were current once again in study alone of the postoperative survival of the patients with a level once again twice as high in favor of total gastrectomy [49% (67-31)] in comparison with the partial operation [25% (33-16)], the same remark as above applying to the upper and lower limits of the respective intervals of confidence.

Determination of the influence of tumor size on the long-term survival rate indicated that for tumors of the cardia the same phenomenon applied as for other sites in the esophagus. When less than 3 cm in diameter five-year survival was the lowest [15% (39-9)], while the outlook was the best for tumors with a diameter between 4 and 5 cm [35% (53-17)].

Histologic examination of surgically removed lymph nodes indicated that the level of invasion (75%) was the highest of the various sites of carcinoma involved in the esophagus (lower third: 68%, middle third: 58%, upper third: 60%). More than one-quarter (26%) were in the mediastinal nodes. Involving this parameter with the results of the two principal types of operation performed, the superiority of the results of total gastrectomy was even more marked than in the overall

TABLE 2. Gastric Excision in Relation to Tumor Size (Cardia)

Size of Tumor	Upper Polar Gastrectomy	Total Gastrectomy
1-3 cm	34	12
4-≥5 cm	194	97

assessment. The postoperative five-year survival rate of 52 patients undergoing total gastrectomy with concomitant lymph node invasion was 48% (74-22) compared with 70 patients in whom an upper polar gastrectomy was performed without involvement of the lymph nodes examined was much lower [36% (55-16)]. This percentage fell to 17% (25-9) when evidence of lymph node involvement was found at the time of partial excision.

Discussion

Among the different parameters examined in patients with carcinoma of the esophagus, *age* did not appear to have any influence (with the exception of patients over the age of 80 years) on either operative mortality or long-term survival. The four largest groups of patients (884, 727, 418, and 263) were situated respectively in the age groups less than 69, 59, 49, and 79 years, with survival rates of 13, 13, 15, and 12% respectively. The extent of relative *weight loss* before the operation, whether less than 5% of the patient's body weight, between 5 and 10% or greater than 10% had no significant influence on either more operative mortality rates (30%, 39%, 32%) or the five-year survival rate (18%, 19% and 14%).

The observation made at the different sites of the poorest prognosis for *small tumors* in comparison with large lesions may initially be surprising. This same feature has nevertheless emerged when combining tumors of equivalent size according to histological type. For those tumors with a diameter of between 1 and 3 cm there were no postoperative survivors at five years regardless of type. As the size increased, long-term survival rates also increased up to tumors reaching 4 cm with a figure invariably higher for adenocarcinomas [21% (30-12) and 53% (75-32)]. For tumors larger than 5 cm in diameter the prognosis regularly decreased with the same distinction in favor of adenocarcinomas, but the long-term survival rate remained markedly greater than that of small tumors [(44-20) and 13% (19-7)].

This becomes easier to explain when considering the long-term results of excision of these tumors in relation to the *T/N classification*. In this comparison, which involves not the size of the tumor but its spread in terms of depth into the esophageal wall, it may be noted that while for stage T3 the influence of the criterion N was negligible [13% (19-6) if N+ and 15% (19-11) if

TABLE 3. Length of Esophageal Excision According to Tumor Site

Site of Tumor	Esophageal Excision <1 cm (%)	Esophageal Excision >4 cm (%)
Upper one-third	12	29
Middle one-third	10	48
Lower one-third	13	50
Cardia	7	55

N-], it became dominant for the other types of tumor. The difference was already marked for T2 class tumors [25% (33-17) if N+ and 36% (47-26) if N-]. This was even more so for tumors scored T1: 0% at 4 years if N+ and 39% (64-14) if N-.

The *macroscopic appearance* of the tumor had virtually no influence on the extent of the esophageal excision performed, an extensive esophagectomy at least 4 cm from the lesion being performed almost as frequently in the case of infiltrating carcinoma (44%), ulcerated carcinoma (47%), multifocal or fungating (55%) lesion.

Long-term overall prognosis nevertheless appeared to vary in accordance with the appearance of the tumor, being the most favorable when fungating [22% (30-15)], intermediate in the case of ulcerated tumor [19% (24-14)] and the poorest when the tumor was infiltrating [12% (18-7)].

The results were obtained respectively in 543, 818, and 564 patients having received no radiotherapy showed little variation after irradiation. In the first group (165 patients), the rate was in fact less [19% (31-7)] and the same applied with ulcerated tumors [17% (24-10)]. Infiltrating tumors were those in which radiotherapy was given the most frequently (270 patients). They were also the only lesions in which the favorable effect of such treatment could be detected [21% (29-13)].

Overall assessment of long-term survival rates confirmed the more favorable prognosis of *adenocarcinomas* (518 cases) with a rate of 27% (34-20) at five years. By comparison, evaluation of the long-term survival rate of *squamous cell carcinomas* of the esophagus revealed a rather special result: well differentiated squamous cell lesions being the most numerous (1155) were associated with the lowest long-term life expectancy [16% (19-12)]. For relatively undifferentiated squamous cell carcinomas (425) the survival rate was higher [17% (22-12)], and similar to that of nondifferentiated squamous cell carcinomas (163) reaching 25% at five years (39-11).

In this series of estimations based on histologic type, the highest long-term survival was found in the group of tumors considered histologically to be "sterilized" by preoperative radiotherapy, being 41% at five years for a small group of 47 patients, with an obviously high range of intervals of confidence (65-16), the lower limit being markedly below that of adenocarcinomas.

For glandular carcinomas of the lower third of the

esophagus (137 patients), the survival rate was identical to that of patients with lesions situated in the cardia. The marked differences in prognosis seen in this latter case according to the type of operation would indeed appear to be due, in relation to this site, to the extent of gastric and esophageal excision and the lymph node dissection performed.

In the evaluation of long-term survival rates, it was of interest to determine whether the *length of esophagus* resected above the tumor had a marked influence. This parameter was recorded in centimeters up to 4 cm from the lesion. The number of high excisions decreased proportionately with the height of the carcinoma (Table 3) but nevertheless involved only 55% of the resections for carcinoma of the cardia.

Histologic study of the *site of esophageal section* led to the following observations: a totally healthy appearance was seen most often (53%) following section of the esophagus at a great distance from the tumor (more than 4 cm), but this appearance was subsequently found to be equally distributed for all sections of the esophagus ranging from 4 cm from the tumor to less than 1 cm from the lesion. When histologic examination revealed complete invasion of the section, in a large percentage (29%) the section had nevertheless been made in an apparently healthy area, at more than 4 cm from the tumor. This level was scarcely greater than that of invasion seen after section of the esophagus immediately adjacent to the carcinoma (24%). Intermediate cases of isolated areas of neoplastic repermeation led to the finding of similar differences (40% at more than 4 cm, 18% at less than 1 cm).

Actuarial curves of postoperative survival corroborated these findings. The five-year survival rate of 734 patients in whom esophageal section was made at more than 4 cm from the tumor showed very little difference [24% (30-19)] from that of patients where the excision was made immediately adjacent to the lesion [20% (30-10)].

Recurrence of the tumor in relation to the histologic findings at the site of section revealed that while it was more than 36% when the area of section showed isolated areas of tumor repermeation or was the site of complete invasion, it was still 27% in apparently favorable cases where the line of section had been considered to be healthy by the histopathologist. The site of the recurrence was distributed between the esophagus (36%), mediastinum (40%) or the otolaryngologic area (10%). The proportion of esophageal recurrences rose to 54% when the section site showed evidence of invasion.

Estimation of the onset of recurrence in relation to the length of esophagus resected above the tumor gives similar results for all resections performed between 1 and 4 cm (34-39%). Only the most extensive resections were associated with a lower recurrence rate (26%),

distributed between the esophagus (36%), mediastinum (46%), cervical regions (14%) and the otolaryngologic area (9%). The number of metastases in relation to the length of esophagus resected and the appearance of the site of section led to similar conclusions. They were markedly less in number of extensive resections (19%) than for very limited operations (35%), the same applying to a healthy section site (18%) or invaded section site (25%).

An attempt was made to determine the overall influence of *surgical technique* used on the results. We noted (Table 4) the large number of patients in whom for a low lesion of the esophagus attempts at resection with high extension had been carried out. It was felt to be of interest to determine whether the possibility of a completely uncomplicated postoperative course was the same as subaortic anastomosis (1028: 62%) or supra-aortic anastomosis (716: 60%). It was in this latter group that the fistula complications were the lowest (10% vs. 13%). When the suture line was in the cervical region (351 patients), the rate of uncomplicated postoperative course was the lowest (50%) and the fistula rate the highest (25%).

We verified findings from a previous study performed in a single department² concerning the absence of statistical influence of the technical type of anastomoses on the subsequent development of breakdown (12% for 1071 single layer anastomoses, 14% for 871 anastomoses in two layers, 14% for 43 anastomoses with a continent valve and 8% for 85 mechanical anastomoses). The proportion of fistula closure was the highest after continent anastomosis (50%) or mechanical anastomosis (43%). It was the lowest, though similar, for sutures in one or two layers (38 and 27%). The site of the anastomosis within the thorax had no more influence than its type on possible breakdown. Excluding resections involving the upper third of the esophagus (36%), this complication occurred in 14% of patients for all other types of tumor site.

A number of distinctions may nevertheless be drawn on the basis of the type of surgery performed: following esophagogastric resection, regardless of its level (595 patients) the mean fistula rate was 12% with a paradoxical increase from the middle third to the cardia (11%, 13% and 14%). This figure was slightly higher (16%) following intrathoracic colonic esophagoplasty (241

TABLE 5. *Type of Operation According to Tumor Site*

Site of Tumor	Esophagogastric Resection	Intrathoracic Esophagoplasty
Upper one-third	21	31
Middle one-third	600	58
Lower one-third	605	61
Cardia	349	79
Not defined	8	11

patients) but the mortality rate of the complication was less (51%) than in the previous group (68%) due to a longer mean period elapsing before development of the fistula. When the latter developed in the neck, in an area where despite its frequency it has a better reputation, the fistula was nevertheless associated with a high mortality rate of 21%. The precise site of the fistulous collection undoubtedly offers a partial explanation, since in 12% of patients the latter was situated in the mediastinum or pleura.

The combined study of 339 fistulas gave an overall indication of the fall in the mortality rate as the period between the time of operation and development of the fistula increased [93% before two days (15 patients) and 41% between ten and 14 days (59 patients)]. The greatest number of fistulas (131 patients, *i.e.* 57%) occurred between the fifth and seventh days, with a mortality rate of 57%.

With the exception of the hypothesis of an alimentary jejunostomy (25 patients) or mediastinal drainage (30 patients), as a general rule these patients received purely medical treatment for an overall mortality rate of 47%. However, long-term survival of 49 patients who survived such a complication was greater than the average [35% (50-20)], without any particular immunologic relationship between healing of the fistula and long-term survival being demonstrated.

Whether performed by a right (756) or left (814) approach, *esophagogastric resections* had a similar overall mean mortality rate (25 and 30%) and were associated with a strictly identical five-year survival rate of 18% with the same intervals of confidence (16-9).

Among the entire group of resections studies (1583), and separating those in whom there was macroscopic evidence of extratumoral involvement (489), the operative mortality rate rose from 28 to 32% and the five-year survival rate decreased by half from 13% (15-10) to 7% (10-3). In comparison with esophagogastric resection, estimation of the results of 240 intrathoracic colonic *esophagoplasties* indicated that for a similar operative mortality rate the long-term survival rate was virtually double with a mean rate of 24% (33-15). Furthermore, it is of interest (Table 5) that among the total group of intrathoracic esophagoplasties performed, more than one-third (79) were performed for lesions of the cardia. [survival: 30% (44-15) and 38% (56-20)]. The respective percentages of these

TABLE 4. *Level of Anastomosis According to Tumor Site*

Site of Tumor	Cervical Anastomosis (%)	Supra-aortic Anastomosis (%)	Subaortic Anastomosis (%)
Upper one-third	80	20	
Middle one-third	23	55	22
Lower one-third	10	31	58
Cardia	5	5	90

TABLE 6. Rate and Site of Recurrences According to Tumor Site

Site of Tumor	Overall Recurrence Rate (%)	Esophagus	Site of Recurrence (%)		
			Mediastinum	Neck	ENT
Upper one-third	41	32	45	18	4
Middle one-third	46	28	50	12	9
Lower one-third	49	46	37	13	4
Cardia	33	73	21	5	2

operations were all the more suitable for statistical interpretations since the limits of their intervals of confidence never overlapped.

Overall evaluation of the results of surgical treatment of the esophagus in *one or several stages* indicated, with the same precautions concerning interpretation as already mentioned above for the treatment of lesions of the middle third, a better long-term survival for the 234 patients undergoing two-stage treatment [19% (27-11)] and for the much greater number (2022) undergoing a single stage procedure [14% (16-14)], the lower limit of the two intervals of confidence being virtually the same. Recurrence rates also appeared to be in favor of multistage operations (21%). In the case of esophageal reconstruction from the onset (recurrences: 30%), the more favorable outlook for extensive resections was found with an intermittent recurrence rate markedly greater in the case of esophagogastric resection (32% in 1105 patients) than in the case of intrathoracic esophagoplasty (23% of 115 patients). It is, no doubt, useful to define that in this case recurrences were more frequent in the esophagus (47%) but also in the mediastinum (20%), neck (28%) or otolaryngologic area (9%).

Analysis of the conditions surrounding the onset of a recurrence or metastasis following esophageal resection was performed separately in the study. These possibilities were sought among the patient populations from which had been previously eliminated, in addition to those dying during the immediate or subsequent postoperative course, all who had subsequently been lost to follow-up.

The possibility of tumor *recurrence* appeared to increase progressively from the upper third (41%) down to the lower third of the esophagus (49%) to subsequently decrease notably after resection of the cardia (39%—Table 6). In the latter situation, the very high percentage of esophageal (73%) and mediastinal (21%) recurrences should be noted. Such findings, corroborated by those already made with regard to histologic study of the level of section in accordance with the length of esophagus resected represent a justification for a concept of even more extensive surgery of the cardia, with extension of the excision

not only to the whole of the stomach but also very high in the thoracic esophagus.

For all sites, the frequency of cervical (5–18%) or otolaryngologic (2–9%) recurrences would appear to be worthy of emphasis.

The histologic type of tumor appeared to have a marked influence on the possibility of a recurrence. The figure for the latter was on average 33% for 1229 squamous cell carcinomas, individual rates being the same (32% and 31%) for well or poorly differentiated carcinomas, but higher (42%) for undifferentiated lesions. For these tumors, often associated with wide excision because of their site, recurrence in the esophagus itself was relatively low (29%) but that of secondary involvement of the mediastinum, cervical or otolaryngologic areas was by contrast very high (40%, 12% and 6%). In comparison, recurrences in 389 adenocarcinomas resected were less frequent (23%) but as in the case of tumors of the cardia a very high proportion (56%) of esophageal recurrences was found.

Study of the development of *metastases* leads to similar conclusions, confirming the commonly described gravity of undifferentiated squamous cell carcinomas which were associated with the highest rate (47%/102 patients). Such findings certainly attenuate the supposition of the apparently slightly more favorable survival of such undifferentiated tumors as described above.

For other squamous cell carcinomas (164 well differentiated and 268 poorly differentiated), the metastasis rate was half as high (23 and 24%) and strictly identical to that of 240 adenocarcinomas (24%). It is felt important to emphasize that in 37 patients in whom histologic examination indicated excision of a tumor apparently “sterilized” by preoperative radiotherapy, an early or distant metastasis occurred in only 40% of cases.

Neoplastic involvement of *lymph node chains* removed at operation was not without influence on the possibility of development of a recurrence or metastasis. Respective rates were similar in the case of mediastinal or coeliac lymph node involvement (32% and 30%). The rate increased in the presence of cervical node involvement (47% and 21%). It is remarkable to note that when lymph nodes were healthy, a recurrence nevertheless developed in more than a quarter of patients (27%) and metastasis in 21%. These recurrences were most often mediastinal (52%) or esophageal (35%) and freedom from node involvement did not exclude the possibility of a secondary tumor localization in the neck (6%) or otolaryngologic area (7%). Similarly, preoperative discovery of a supraclavicular node did not necessarily have the extremely unfavorable prognosis which is commonly associated. For 62 patients in such a situation having survived

TABLE 7. Influence of Radiotherapy on Recurrences and Metastases

	Overall Recurrence Rate (%)	Overall Metastasis Rate (%)
Preoperative Radiotherapy		
<1000 r		17
<3000 r	50	25
>3000 r	58	25
Postoperative Radiotherapy		
<1000 r	87	
<3000 r	50	40
>3000 r	36	30

the operation (upper third: 19%, middle third: 40%, lower third: 24%, cardia: 16%), one third were alive after five years [33% (52-14)].

The influence of pre- or postoperative radiotherapy on the course of the neoplastic disease (Table 7) was assessed after prior determination of the size of the tumors to which treatment had been given (Table 8). Both before as well as after operation it was small and medium size tumors of less than 4 cm diameter (164/207 and 72/100) which were irradiated, with the apparent aim of perfecting if possible the results of complete surgical treatment. When less than 3,000r pre- or postoperative radiotherapy was of no value, and the recurrence rate and metastases under such circumstances even showed values not seen in other assessments (87%), though no conclusions may be drawn from this latter figure. By contrast, beyond 3,000r and in particular when given after surgery, radiotherapy appeared to have some influence on recurrence rate (36%) and metastasis rate (30%). In this context, study of reoperations led to no particular conclusion concerning recurrences (Table 9). Such secondary procedures consisted above all of alimentary gastrostomies or pyloroplasties. The number of repeated resections was very small and corresponded to only approximately 4% of reoperations after esophago-gastric resection. The long-term survival of these patients was 9% at five years (15-3).

Comparison was made of the histologic appearance of resected lymph nodes, for all of the patients and secondly for those who had undergone preoperative radiotherapy. As mentioned above, adenocarcinomas were associated with the highest lymph node involvement (74% of 585 patients). In approximately one quarter of patients these lymph nodes were situated in the mediastinum. It was in such patients, despite the poor theoretical response of these tumors to irradiation, that a relative fall, which must be interpreted with caution, was seen in lymph node involvement after treatment (64% of 28 patients treated). By contrast, while the overall invasion rate in squamous cell carcinomas was somewhat lower (63% in 1882

TABLE 8. Proportions of Tumors Treated by Radiotherapy in Relation to Size

Tumor Size	Preoperative Radiotherapy (%)	Postoperative Radiotherapy (%)
1 cm (29)	38	27
2 cm (112)	51	18
3 cm (332)	40	13
4 cm (340)	35	14
<5 cm (315)	25	17
>5 cm (718)	18	11

patients), preoperative radiation did not give rise to any detectable notable improvement (61% for 589 patients).

The effects of radiotherapy were studied according to other surgical parameters. When given before surgery, this did not appear to imply any modification in its course, the percentage of excisions with macroscopic invasion being the same as in those cases which had not undergone radiotherapy (44% for 254 patients). In attempting to define the influence of irradiation on the carcinoma according to its site, the following conclusions may be drawn: it was in the upper third of the esophagus that radiotherapy, widely used (72 patients), appeared to be associated with a certain degree of efficacy. Such a possibility was nevertheless tangible only in a very small number of patients (14%) in whom a preoperative and postoperative treatment was given and where the five-year survival rate was 46% (84-8). In other cases, preoperative [25% (49-0)] or postoperative [35% (63-6)] given in isolation had no evident effect.

Five hundred ninety-four tumors of the middle one-third were irradiated, and in the majority of cases (62%) before surgery. Long-term results, evaluated only in those patients who had survived, failed to reveal any particular improvement [20% (26-13)].

Postoperative irradiation only [13% (21-6)] or in association with preoperative treatment [16% (27-6)], undoubtedly reserved for the most advanced tumors, was apparently even less effective.

TABLE 9. Reoperation After One-Stage Surgery

Initial Operation	Reoperation			
	Pyloro- plasty	Gastros- tomy	Resec- tion	Other
Esophagogastric resection (1157)	36	56	6	39
Intrathoracic Esophago- plasty (174)		5	1	7
Prethoracic Esophago- plasty (11)			1	
Total Gastrectomy (83)		4		4
Extended excision (59)		2	2	3
Other operation (70)		1		3

Numbers in parentheses indicate number of patients.

For the lower third of the esophagus, radiotherapy once again failed to be associated with any improvement in the long-term prognosis in the 306 patients treated in this way. Once again there was predominance of preoperative irradiation (57% of patients) with the best long-term survival rate [29% (40-18)]. A progressive fall in this rate was seen for postoperative irradiation alone [24% (40-9)], then mixed irradiation [21% (31-9)].

Reflecting the more frequent use at present of high energy sources, 48 patients with a tumor of the cardia were irradiated, but only in very poor patients. The majority (64%) underwent radiotherapy before operation with no survivors at four years. Following operation, irradiation (52%) did not yield a better result [10% (29-0)], the level remaining markedly lower than the mean rate for postoperative survival in all tumors of the cardia together (27%). None of the few patients who had undergone pre- and postoperative treatment (4%) survived longer than two years.

An unfavorable impression is given by examination of postoperative survival curves of patients grouped according to the histologic type of their tumor. Preoperative irradiation of squamous cell carcinomas (547 of 666) failed to indicate any increase in survival in comparison with patients not receiving such treatment [20% (26-15) and 18% (22-13)]. Quite similar rates were seen with pre- or postoperative irradiation.

When lymph node involvement was present, radiotherapy failed to be associated with any improvement in long-term prognosis. In the presence of mediastinal lymph nodes, pre- or postoperative irradiation, with a mean rate of 15% (25-6) was not associated with any particular benefit in comparison with nonirradiated patients [14% (19-9)]. The same applied to coeliac nodes: in comparison with group of nonirradiated patients [22% (29-16)], the long-term postoperative survival rate of treated patients was poorer, whether treatment was preoperative [12% (23-1)] or postoperative [11% (23-0)].

Such findings in the case of tumors which, as mentioned above, were rather of small or medium size, corroborated the results seen in terms of recurrences or metastases and essentially confirmed the lack of efficacy of this type of treatment in our series.

This study also involved a subjective and purely surgical criterion, concerning the "overall impression of the surgeon" once resection was completed. When the latter was considered to be "curative", there was a relatively good hope of long-term patient survival [29% (35-29)], this applying to 859 patients. A "palliative" (770 patients) impression, although significantly justified by a much poorer survival, was nevertheless

associated with a survival rate of 12% at five years (16-8). It may be noted that in these unfavorable cases, the addition of complementary radiotherapy (304 patients) had no effect on the long-term survival rate [8% (13-3)]. The impression of the surgeon, when favorable, was unrelated to the development to any possible recurrence. The latter occurred in 60% of patients (including 43% in the esophagus itself). By contrast, when the impression was one of a palliative operation, it may be noted that the anticipated recurrence occurred in only 30% of patients. When the latter did occur it was in the mediastinum (43%) more often than in the esophagus (26%).

This retrospective study offers certain data concerning tendencies among surgeons questioned in relation to the treatment of various sites of carcinoma of the esophagus, which logically must include carcinomas of the cardia of the stomach. The justification of increasingly high resections would appear to emerge progressively from the overall studies made. Furthermore, it would no longer appear to be justified to abstain from treatment in the presence of preoperative macroscopic invasion or the existence of a lymphadenopathy.

The essential criteria of curative excision could not yet be formally defined on the basis of the conclusion drawn from these 2,400 patients. Certain indications nevertheless merge from the results and make it possible to envisage the development of a prospective study using the same teams. This may offer the hope of more useful results in the future.

Addendum

Since the writing of this paper, the representative members of surgical Societies from eight different countries (Austria, Belgium, France, West Germany, Italy, Netherlands, Spain, Switzerland) decided, in the aim of a prospective study in the field of esophageal cancer surgery, to join together to form an Association named O.E.S.O. (Organisation Européenne d'études Statistiques pour les maladies de l'Oesophage) European Organization for Statistical studies on Esophageal diseases.

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