

Esophageal Cancer: Surgical Strategies



ARTIGO ORIGINAL

Cancro do Esófago: Estratégia de Abordagem Cirúrgica

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ABSTRACT

Introduction: Oesophagectomy for cancer is associated to a significant morbidity and mortality. The superiority of transthoracic vs transhiatal is still a matter of controversy. The aim of this paper is to discuss the results of a series of patients submitted to either a transthoracic or a transhiatal according to the anatomic location regarding the carina.

Material and Methods: Retrospective analysis of 52 consecutive patients, with oesophageal carcinoma, 7 female and 45 males, median age 64 [46-85] years. Location: cervical – 1; above carina - 22; below or at carina level - 19; cardia type I – 10. 19 adenocarcinoma, 32 squamous cells, 1 lymphoma. Twenty patients (40%) – neo-adjuvant therapy. Thoracoabdominal approach – 3, cervico-thoraco-abdominal – 20, transhiatal – 27, exploratory thoracotomy – 2.

Gastric pull-up 49 (cervical anastomosis – 46; thoracic - 3); cervical oesofagocoloplasty - 1.

Results: Pathologic staging: complete remission - 8; Ib – 3; IIa – 9; IIb - 4; IIa – 11; IIIb -2; IIIc – 10; IV – 1; non-stageable - 3. Major complications: 37%. Resectability: 96% (50/52). Mortality: 4th week - 6%; in-hospital - 14%. Median survival 18 months [3-80]. Survival Curves (Kaplan-Meier): 2 years - 47%; 5 years - 19% (transthoracic vs transhiatal $p > 0.05$).

Discussion: Selection of surgical approach based on the anatomic location of the tumour regarding the carina was safe, the resectability was high and similar when a transthoracic or a transhiatal was planned and carry-on.

Conclusions: In this series of oesophageal cancer patients, in advanced pathologic condition (52% p Stages III/IV) the overall survival was similar for transthoracic and transhiatal. Neo-adjuvant treatments definitively contributed to enhance resectability.

Keywords: Esophagectomy; Laparoscopy; Esophageal Neoplasms/surgery; Thoracotomy.

RESUMO

Introdução: A ressecção transmediastínica e a ressecção transtorácica têm mortalidade hospitalar (1,4% -14%) e sobrevivência (\pm 25% aos cinco anos) semelhantes. A terapêutica neo-adjuvante é opção em estádios avançados. A intenção deste trabalho é apresentar uma série consecutiva de 52 doentes - opção operatória baseada na localização anatómica: tumores infra-carinais e cervicais submetidos a ressecção transmediastínica e restantes ressecções transtorácicas.

Material e Métodos: O estudo incluiu 52 doentes consecutivos, sete mulheres e 45 homens, mediana de idade: 64 anos [46-85]. Localização: cervical – um; montante da carina - 22; jusante da carina -19; cárdia tipo I – 10. Histologia: 19 adenocarcinomas, 32 carcinomas pavimento-celulares, um linfoma. Vinte doentes (40%) - terapêutica neoadjuvante. Abordagem tóraco-abdominal – três, tóraco-abdómino-cervical – 20, transhiatal – 27, toracotomia exploradora – dois. Transposição gástrica 49 (anastomose cervical – 46; torácica - três); esofagocoloplastia cervical - um.

Resultados: Estadiamento patológico: regressão completa - 8; Ib – 3; IIa – 9; IIb - 4; IIa – 11; IIIb -2; IIIc – 10; IV – 1; linfoma - um; não classificáveis – três. Complicações maior: 37%. Ressecabilidade: 96% (50/52). Mortalidade: quatro semanas - 6%; hospitalar - 14%. Sobrevida mediana 18 meses [3-80]. Curvas de sobrevida (Kaplan-Meier): dois anos - 47%; cinco anos - 19%.

Discussão: Não tendo sido demonstrada vantagem oncológica para a ressecção transtorácica ou a ressecção transmediastínica, basear a opção operatória na localização do tumor permitiu-nos com segurança e eficácia, planejar e executar as ressecções esofágicas desta série.

Conclusão: As curvas de sobrevida foram sobreponíveis para ressecção transtorácica e ressecção transmediastínica e bastante favoráveis numa população com 52 % de estádios pIII/IV. A quimio-radioterapia contribuiu para aumentar a ressecabilidade.

Palavras-chave: Esófagectomia; Laparoscopia; Neoplasias Esofágicas/cirurgia; Toracotomia.

INTRODUCTION

Oesophageal tumours are currently treated following a multimodal multidisciplinary perspective, in line with what has been considered as standard in other gastrointestinal tumours. However, supported on scientific evidence, this is far from a consensual approach.

The approach to oesophageal tumours should be decided according to the patient, characteristics of the tumour, clinical experience and the availability of a multidisciplinary team, surgical team and life support unit.¹⁻⁴

Treatment is still based on oesophageal resection, when feasible, alone or combined, in order to improve other

therapy's outcomes.⁵⁻⁹

The main issue, which is still unclear, is based on the comparison between transthoracic (TTR) and transmediastinal resection (TMR). Pros and cons of each approach have been widely shown in individual and systematic reviews,¹⁰⁻¹⁵ although there is still insufficient evidence for definite recommendations to be established.

We have recently described our experience with gastric tube reconstruction upon oesophagectomy related to oesophageal cancer.¹⁶ Cervical oesophageal-gastric anastomosis was preferred, with excellent results and

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therefore considered as first-choice in most patients.¹⁵⁻¹⁷

Radiotherapy alone or following chemosensitization was our preferred approach to oesophageal cancer treatment, with interesting results despite some severe complications or requirements for a salvage surgical approach in a significant number of patients.¹⁸⁻²³

Our study aimed to show the results of a multimodal approach to treatment of oesophageal cancer and its surgical component, based on tumour location.

MATERIAL AND METHODS

This was a retrospective study (2006-12) involving 52 consecutive patients with oesophageal carcinoma (seven female, median age 64 [46-85] years old). One of the authors (PC) participated as senior surgeon in all surgeries. Two patients were operated at *Hospital CUF Infante Santo (Lisboa)* and two other patients at *Hospital Beatriz Ângelo (Loures)*.

Tumor location - cervical ($n = 1$); supracarinal ($n = 22$); infracarinal ($n = 19$); type-I of the distal oesophagus ($n = 10$). One patient who underwent chemo-radiotherapy achieved complete remission and relapse occurred four years later with an indication for salvage surgery.

Histology: adenocarcinoma ($n = 19$), squamous-cell carcinoma ($n = 32$) and lymphoma ($n = 1$) (preoperatively characterised as undifferentiated carcinoma).

Twenty patients underwent neo-adjuvant therapy (chemo-radiotherapy [$n = 19$] and chemotherapy [$n = 1$]).

Surgical approach - thoracic-abdominal ($n = 3$); cervico-thoracic-abdominal ($n = 20$); transhiatal ($n = 27$) and exploratory thoracotomy ($n = 2$). A gastric transposition was performed in 49 patients (with cervical [$n = 3$] and thoracic anastomosis [$n = 46$]); oesophagocoloplasty was performed in one patient

- Diagnostic and resectability evaluation: endoscopy with biopsy; endoscopic ultrasound in selected patients; CT-scan of cervical, thoracic and abdominopelvic regions; bronchoscopy in retro-tracheobronchial tumours; PET-scan in suspected distant invasive disease.
- Oncological multidisciplinary decision for inclusion in neo-adjuvant therapy regimen, chemo-radiotherapy in most N+ tumours, adherent to non-resectable structures

(T IV-b) or bulky tumour masses.

- Preoperative risk assessment with summary testing including liver, renal and coagulation tests, cardiac (ECG; echocardiogram) and pulmonary evaluation (pulmonary function testing; arterial blood gases and chest X-ray) and optimization of nutritional status.^{24,25}
- Operative technique (TMR and TTR).

TMR – With the patient lying in dorsal decubitus, oesophageal surgery starts by abdominal approach aimed to determine surgical feasibility; a second surgical team uses a cervical approach to the oesophagus.

Upon median laparotomy incision, the rib cage is laterally retracted and raised with retractors; the section of the left coronary ligament allows for the mobilisation of the left lobe of the liver. In order to allow for an improved access to the oesophagus hiatus, an extensive phrenotomy is performed – Pinotti's technique.²⁶ The resection of the oesophagus and infracarinal/abdominal lymphadenectomy (lymph node regional stations 1, 2, 3, 7, 9, 11, 16, 19, 20, 108, 110, 111, 112)²⁷ is performed by abdominal approach, with adequate access and controlled dissection (Fig. 1). Mediastinal dissection is performed with adequate lighting from auto-adhesive strings containing optic fibres connected to a light generator or, more recently, with a videoscopic system providing intense lighting and wide vision of the structures almost up to the thoracic operculum. We prefer to use equipment allowing vascular section upon sealing. The elective ligation of the thoracic duct is performed in the last half series of patients.

Left cervicotomy is performed with the patient facing to the right, with the neck slightly hyperextended, by the left para-sternocleidomastoid approach. An extension is adjusted to patient's morphotype, in order to allow for a safe isolation of the oesophagus, keeping the vascular axis, recurrent nerves and trachea undamaged and to ensure adequate room for the anastomosis. In the absence of any oncological contraindication, the oesophagus is slightly moved from the thorax into the neck and incised with redundancy, ensuring enough room for a tensionless anastomosis and an implant in linear continuity with the patch.

Oesophago-gastric or oesophago-colic anastomosis

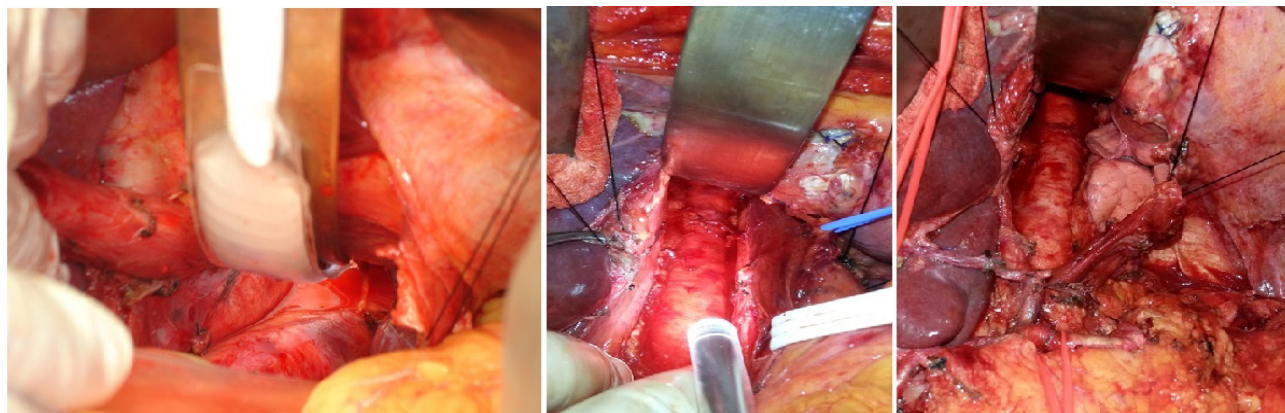


Figure 1 – Transhiatal resection procedure

is performed with manual terminolateral stitches, in a plane with separate stitches and reabsorbable sutures. Nasogastric (or nasocolic) tube is passed into the patch before completing the anastomosis, in order to make this manoeuvre easier and to ensure that it remains undamaged. The oesophagus, the anastomosis and the patch are repositioned close to the spine, usually at the level of the thoracic operculum. Cervicotomy is closed upon placement of aspiration drainage.

The laparotomy closure is performed by one team, while the anastomosis is performed by another. The diaphragm is partially closed avoiding narrowing of the gastric antrum.

TTR – This approach becomes part of a cervico-thoracic abdominal (three-way) or thoracic-abdominal (two-way) strategy.

Following the three-way approach, we perform a similar technique to the Brigham's procedure.²⁸ With the patient lying in left lateral decubitus position, right pulmonary exclusion is ensured with bronchoscopic control and oesophagectomy is performed by right thoracotomy (5th-6th intercostal space). Upon oesophagus mobilisation and adequate lymphadenectomy (lymph node regional stations 1, 2, 3, 7, 9, 11, 16, 19, 20, 106, 107, 108, 109, 110, 111, 112)²⁷ (Fig. 2), elective ligation of the thoracic duct is performed.

Upon placement of a silicone thoracic drainage tube, the thorax is closed and the patient re-positioned as for the transhiatal approach. In these cases, abdominal and cervical phases are performed with patients lying in dorsal decubitus position, followed by an anastomosis with the cervical oesophagus.

The Ivor-Lewis two-way procedure²⁹ starts with a median laparotomy that is closed at the end of abdominal phase for patch preparation and upon adequate lymphadenectomy. Patients are then re-positioned for thoracotomy and the procedure follows as previously described for oesophageal and lymphatic resection. Oesophago-gastric anastomosis is performed with a circular stapler introduced through the proximal portion of the patch that is removed with the

surgical sample. The preparation of the gastric tube was completed in the thorax in order to ensure an adequate patch dimension.

We will only describe some details regarding oesophagectomy technique. We recently published a study on gastric tube preparation technique¹⁶ considering in its design and mobilization the following: minimum manipulation of the stomach, careful sparing of vessels, Kocher manoeuvre aimed to allow for pyloric mobilisation up to the hiatus, pyloromyotomy and termino-lateral oesophago-gastric anastomosis. Sparing of right gastroepiploic and pyloric vessels that ensure patch's vascularization is a crucial surgical phase for gastric tube placement. As the coronary artery is ligated at its origin, which is a lymphadenectomy requirement, we are able to incise the lesser curvature vascular arcade at the most proximal level, still allowing for the excision of lymph nodes or regional stations 1, 2 and 3 together with those from 7, 8, 9 and 11, followed by the onset of gastric resection. The greater omentum is incised at 2-3cm from the greater curvature vascular arcade, from the origin of right gastroepiploic vessels to the origin of left gastroepiploic artery, close to the splenic artery. With this purpose, short vessels are sectioned close to splenic hilum and the venous plexus within the omentum between the left portion of the gastroepiploic arcade and the first short vessels are left undamaged whenever possible.

The technique proposed by DeMeester was used in patients who underwent a colon patch^{30,31} aimed to prepare an isoperistaltic anastomosis irrigated by the lower mesenteric artery, with ligation of the middle colic artery at its origin (before bifurcation).

Anesthesiology and Surgery teams should work in continuous interaction, mainly at the crucial phases of transmediastinal dissection and cervical transposition as sometimes there is the need to momentarily interrupt surgery in order to allow for the patient's haemodynamic recovery. The critical aspects of homeostasis include pulmonary exclusion during thoracotomy, monitoring volume losses and its adequate and timely replacement

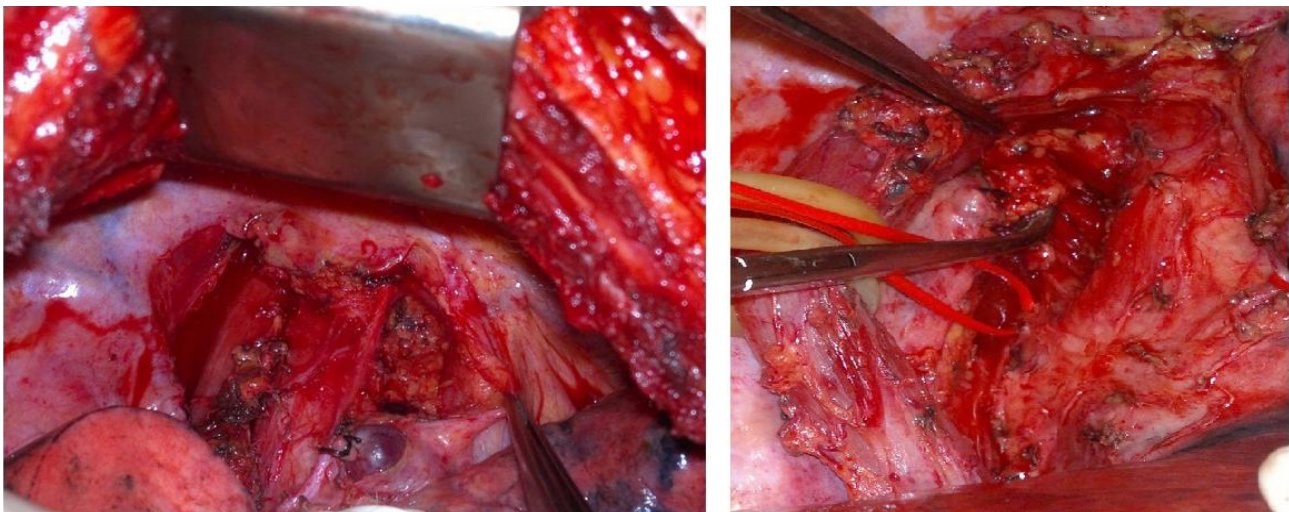


Figure 2 – Transthoracic resection procedure. Superior mediastinum.

aimed to prevent a 'wet lung' situation, minimal blood-loss surgery, lactic acidosis minimisation, blood pressure and arrhythmia monitoring.

Antibiotic prophylactic therapy is performed and whenever any suspected or diagnosed infectious event occurs.

Patients remain at the ICU during the immediate post-operative period. Homeostasis monitoring is ensured by resident Intensive Care physicians, aimed to obtain the earliest orotracheal extubation and to ensure, in situations when longer ventilatory support is needed, the earliest weaning of assisted ventilation. Timely diagnostic and therapeutic action in any haemodynamic and metabolic change is essential for the vitality of the patch. Vasopressor agents are carefully used with dosing titration at short intervals in order to allow for its cessation. Systematic monitoring of inflammatory parameters is ensured. Any post-operative pleural effusion is drained. Diagnostic and therapeutic bronchoscopy is generously used. Haemofiltration and haemodialysis are carried out whenever needed. Prophylactic low-molecular-weight heparin is used in all patients from the first post-operative day.

The Lerut classification is used in anastomotic fistula diagnosis and treatment³² as well as in the procedures that we recently presented.¹⁶

Descriptive statistics and Kaplan-Meier curves to calculate the actuarial survival were used in the presentation of our results.

RESULTS

- The indication for blood transfusion from the day before surgery, intra-operatively and up to a 48-hour postoperative time period of patients who underwent oesophagectomy was as follows: a) No RBC transfusion ($n = 23$); b) One RBC unit ($n = 6$); c) Two RBC units ($n = 14$) and d) Three or more RBC units ($n = 7$).
- Resectability rate: 96% (50/52).
- Postoperative staging: complete remission ($n = 8$) (TTR: $n = 5$; TMR: $n = 3$); Ib ($n = 3$) (TTR: $n = 0$; TMR: $n = 3$); IIa ($n = 9$) (TTR: $n = 6$; TMR: $n = 3$); IIb ($n = 4$) (TTR: $n = 2$; TMR: $n = 2$); IIIa ($n = 11$) (TTR: $n = 5$; TMR: $n = 6$); IIIb ($n = 2$) (TTR: $n = 1$; TMR: $n = 1$); IIIc ($n = 10$) (TTR: $n = 2$; TMR: $n = 8$); IV ($n = 1$) (TTR: $n = 0$; TMR: $n = 1$); lymphoma ($n = 1$); undetermined staging ($n = 3$).
- Stage III and IV ($n = 26$; 52%).
- There was microscopic involvement of distal margins in five patients (10%) and R0 resection was obtained in 90%.
- Number of resected lymph nodes (average) – 16.
- Median of hospital stay - 24 days [9 -129].
- Significant complications in 37% of the patients: Anastomotic fistula ($n = 3$ – two patients with clinical grade II fistula + one patient with radiological grade I fistula); recurrent lesion ($n = 2$); lesion to the thoracic duct ($n = 1$); pleural effusion ($n = 2$); nosocomial pneumonia ($n = 4$); ARDS (acute respiratory distress syndrome) ($n = 4$); broncho-pleural fistula ($n = 1$);

haemothorax with haemopericardium ($n = 1$); AMI (acute myocardial infarction) ($n = 1$); bone marrow aplasia ($n = 1$); cervical seroma ($n = 1$); endoscopically-controlled gastric haemorrhage ($n = 1$); gastric stasis controlled with prokinetics drugs (30% of the patients).

- No patch necrosis occurred.
- Four-week mortality - 6% and in-patient hospital mortality - 14%.

TMR ($n = 3$) and TTR mortality ($n = 4$). From these seven deceased patients, five followed neoadjuvant therapy regimens.

- Causes of death at eight weeks: broncho-pleural fistula + nosocomial pneumonia ($n = 1$); acute bone marrow aplasia ($n = 1$); undetermined ($n = 1$). Hospital mortality: ARDS ($n = 2$); AMI ($n = 1$); undetermined ($n = 1$).
- All patients were discharged with no dysphagia, autonomous nutrition capability, indication to progressive volume increase and food diversification according to Dietitian's recommendation.
- Post-operative dysphagia occurred in eleven patients. When radiological control showed stenosis of the anastomosis, endoscopic dilation was performed. More than one dilation procedure was generally necessary and occurred almost always on the first postoperative year.
- Median survival of 18 [3-80] months. Over this timeframe, no surgical procedure related to gastric tube functioning was necessary.
- Kaplan-Meier survival curves: 47% two-year and 19% five-year survival (Fig. 3).

No significant differences were found related to survival of TMR-operated when compared to TTR-operated patients: $p > 0.05$ (Fig. 4).

No significant differences were found regarding survival neither in patients with adenocarcinoma vs. squamous-cell carcinoma ($p > 0.05$) nor in patients in complete remission ($p > 0.05$).

DISCUSSION

Biological and oncological aggressiveness of oesophageal tumours is responsible for the less favourable results usually published. Several lines of research were based on this assumption, aimed to minimize the risks of therapy, improving patients' life quality and survival. Over the last few decades, tumour resectability, morbidity and mortality of surgical procedures improved, but no similar advances were achieved as far as patient survival, related to local or distant metastatic disease.^{2,10,12,13,23}

Surgery has currently a well-defined role in major oesophageal cancer therapeutic regimens, both in squamous-cell or adenocarcinoma.^{5-9;17}

Oncological issues related to radical aspects of procedures were not clearly shown in well-designed trials carried out by experienced groups, nor were the meta-analysis crucial in the selection of surgical extension and radicality.¹⁰⁻¹⁴

The issue regarding the determination of equivalence

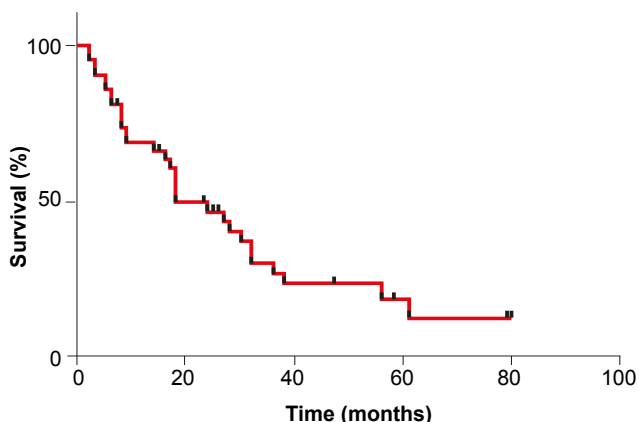


Figure 3 – Global Survival

or superiority of TMR compared to TTR, allowing for more extensive radicality in high mediastinal resection has not yet been solved. TMR and TTR both have currently in-patient hospital mortality rates between 1 - 20%³² (which tends to be higher in TTR with more extensive resections) and in most of best series survivals are equivalent between both techniques (approximately 25% at five years).^{1,2,12-15,34-36}

Pros and cons of each option were largely shown in individual experiences and systematic previously referred reviews.

In the absence of a clear oncological superiority for any of the approaches to oesophagectomy (TMR or TTR)^{2,10-15} we proposed an approach oriented by the patient and tumour location. Therefore, the tumours located in a lower plan to the carina were operated by TMR, with extensive phrenotomy, directed lighting and direct view to the tumour, surrounding tissues and infracarinal and lower mediastinal lymphatic drainage²⁷ allowing for safe resection. Cervical tumours may also be approached by TMR although they hardly ever have a surgical indication. High thoracic tumours were operated by TTR with the already referred lymphadenectomy.²⁷

The standardisation of the surgical approach to oesophageal tumours has contributed to the results that we obtained on the last 50 patients that were treated in our Department, following a multidisciplinary strategy. For that purpose, one of the authors participated in all the operations as a senior surgeon. In medium-volume oesophagectomy centres such as our Department, the differentiation in digestive oncology related to referral and training of the involved surgeons have been referred as factors that allow for equivalent results to be obtained when compared to other centres with higher volume of such pathology.^{3,37,38}

Our results are in line with those found by other groups, with an 18-month median global survival and no significant differences ($p > 0.05$) regarding both approaches (TMR and TTR). The 47% two-year survival with a significant reduction at five years (19%) has been described.^{2,11,12-15,34,35}

Some recent prospective studies³⁹⁻⁴¹ showed similar survivals for both techniques despite higher disease-free

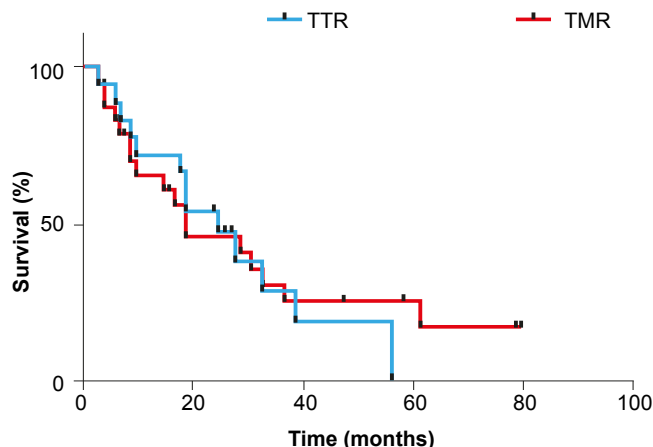


Figure 4 – TTR vs. TMR survival

time with TTR.

In such a complex surgical procedure as oesophagectomy, the operative technique may affect immediate and delayed outcomes. Immediate outcomes are mainly assessed by resectability, morbidity and mortality. These significantly influence delayed outcomes of cancer-related oesophagectomy (survival).

The reduced need for perioperative blood transfusions (zero units in 46% of the patients) is related to the surgical approach (TMR vs. TTR) allowing for visual and adequate access to anatomical regions place a higher technical demand on the surgical team's training and on lighting and vessel sealing available resources. Mainly with TMR, a well-rehearsed phrenotomy together with the already described technological resources changed this type of surgery from being generally based on tactile sensitivity into a procedure currently performed almost completely under visual control and direct access. In TMR, we initially used a lighting source based on bands adhered to surgical instruments, generally to a retractor. We only recently started using the videoscopic approach.

The average number of 16 resected lymph nodes and negative margins in 45 R0 patients (90%) are in line with what has been generally described.⁴²

We analysed our experience with the use of the gastric tube in digestive reconstruction upon gastric cancer-related oesophagectomy. We mainly performed the cervical oesophago-gastric anastomosis with excellent results¹⁶ when compared to recent literature.^{15,17,33} There was a very low graft-related complication rate, including anastomotic fistula ($n = 3$)³² (two patients with Grade II clinical fistula and one patient with Grade I radiological fistula), endoscopically-controlled gastric haemorrhage and gastric stasis, controlled with prokinetic drugs, in approximately 30% of the patients. The prevalence of fistula related to this anastomosis varied between 9.6 and 16%.^{2,10,11,33} We did not find any patch necrosis, unlike what has been described in other studies.^{33,43,44}

The 22% stenosis rate of cervical anastomosis with an indication to endoscopic dilation is lower than other

reference clinical series.¹⁵

Data from a recent meta-analysis¹⁵ involving cervical vs. thoracic anastomosis did not allow for a determination of strong evidence in favour of any of the options. These data confirm the results of other studies^{2,10-14,23} showing a slightly higher fistula and stenosis rate with cervical anastomosis. However, the 'benignity' of these complications when compared to similar complications occurring in the thorax was considered as a strongly positive factor in favour of cervical anastomosis. When we use the posterior mediastinum and the oesophagus and the tube are well positioned, tension-less and with a vertical continuity, this seems to be an acceptable alternative. However, we should note that cervical anastomosis may relate to a higher risk of pulmonary complications.^{10,12,15,16}

Oesophagectomy's morbidity and mortality in patients with esophageal cancer has improved over the last few decades, despite remaining high (morbidity: 38 – 60%; mortality at 30 days: 0-22%).^{2,23,33,34}

Our results reflect this reality, with significant complications in 37% of the patients with a 6% four-week mortality and a 14% in-patient mortality.

Many authors aimed to obtain decision algorithms related to the operative risk, in order to reduce morbidity and mortality, based on a better selection of patients, in other words, narrowing the indication for surgery.^{24,25,34,45-52} Fitness for surgery is intended to relate more to probability calculations and less to clinical impression. The lung and the heart were mainly affected by complications. A standard pattern has not yet been found and in our group of patients we carried out similar functional evaluations aimed at personalizing therapeutic individual decision which would have been difficult to base on a normogram.^{51,53}

Neoadjuvant therapy (chemotherapy, radiotherapy or mainly chemo-radiotherapy) may improve resectability, patient's survival and/or disease-free time, without significantly increasing morbidity and mortality, when radiotherapy is focused to reduce lung exposure.^{6,7,23,54,55}

The high resectability rate (96%) that was obtained in our group of consecutive patients proposed for oesophagectomy derived from a careful preoperative evaluation and from the inclusion of patients in neoadjuvant therapy programs.

Chemo-radiotherapy was prescribed to N+ and T3-4 patients to reduce tumour mass and allowed for a good resection rate in patients selected to surgery.

Patient's inclusion in neoadjuvant therapy regimens increased over the last few years, due to a better multidisciplinary integration at our hospital, an objective that we have longed aimed to achieve. In 1983 we presented the preliminary results of the evaluation methodology of preoperative chemotherapy in esophageal carcinoma [Costa P, Costa B, Silveira JC, Camilo E, Guerreiro D, Veiga Fernandes F. *Metodologia da avaliação da quimioterapia*

pré-operatória no carcinoma do esófago (dados pessoais, III Congresso Nacional de Cirurgia, 1983)]. At the time, we aimed to reduce tumour mass and burden, to increase resectability, granting time to achieve a biological optimisation to improve patient's risk and selection assessment and therefore to reduce mortality. These objectives remain the basis for the underlying therapy we currently call neoadjuvant.^{2,6,7,22,23}

We did not find any significant differences regarding neither survival of patients with adenocarcinoma vs. squamous-cell carcinoma ($p > 0.05$) nor in patients in complete remission ($p > 0.05$).

The real meaning of a 20-40% complete tumour regression is still undetermined, regarding its influence on global and disease-free survival, on local and distant recurrence [Tato Costa J, Costa L, Casimiro S. *Effects of chemotherapy and radiotherapy in rectal cancer: significance of different cellular outcomes in tumour behaviour (personal data – PhD thesis project – IMM/FMUL, under way)]. The presence of senescent tumour cells having lost their division capability, even when mitogen-triggered, has been described in complete remissions. These cells remain metabolic and synthetically active (PDGF, VEGF, EGF, TGF- α , etc.) and may cooperate in local relapse development. These relapses have been managed by salvage surgery with good results.*

CONCLUSION

Regarding TMR and TTR, although we were not able to show any significant oncological advantage of one technique over the other, we believe each has a place as the optimal surgical option, based on tumour location, safely and efficiently allowing for oesophageal resection to be planned and carried out in our group of patients.

TMR and TTR survival curves overlapped and the results found were quite favourable in a group where 26.5% of the patients were in a III/IV stage.

Chemo-radiotherapy has contributed to increase tumour resectability and complete remission was induced in 42% of the patients.

OBSERVATIONS

This study was partially presented at the XXXIII Congresso Nacional de Cirurgia, 2013.

CONFLICTS OF INTEREST

There were no conflicts of interest in writing this manuscript.

FINANCIAL SOURCES

There was no financial gain for writing this manuscript.

REFERENCES

- Pennathur A, Zhang J, Chen H, Luketich J. The "Best operation" for esophageal cancer? *Ann Thorac Surg.* 2010;89:S2163-7.
- Lagarde SM, Vrouenraets BC, Stassen LP, Van Lanschot JJ. Evidence-based surgical treatment of esophageal cancer: overview of high-quality studies. *Ann Thorac Surg.* 2010;89:1319-26.
- Dikken JL, Wouters MW, Lemmens VE, Putter H, Van der Geest LG, Verheij M, et al. Influence of hospital type on outcomes after oesophageal and gastric cancer surgery. *Br J Surg.* 2012;99:954-63.
- Boddy AP, Williamson JML, Vipond MN. The effect of centralization on the outcomes of oesophagogastric surgery – a fifteen years audit. *Int J Surg.* 2012;10:360-3.
- Worni M, Martin J, Gloor B, Pietrobon R, D'Amico TA, Akushevich I, et al. Does surgery improve outcomes for esophageal squamous cell carcinoma? An analysis using the surveillance epidemiology and end results registry from 1998 to 2008. *J Am Coll Surg.* 2012;215:643-51.
- Werutsky G, Ducreux M, Lutz M, Mauer M, Van Clutsem E, Ruers T, et al. The EORTC gastrointestinal tract cancer group: 50 years of research contributing to improved gastrointestinal cancer management. *EJC supplements IO.* 2012;1:51-7.
- Gebski V, Burmeister B, Smithers BM, Foo K, Zalberg J, Simes J. Survival benefits from neoadjuvant chemo radiotherapy or chemotherapy in oesophageal carcinoma: a meta-analysis. *Lancet Oncol.* 2007;8:226-34.
- Abrams JA, Buono DL, Strauss J, McBride RB, Hershman DL, Neugut AI. Esophagectomy compared with chemoradiation for early stage esophageal cancer in the elderly. *Cancer.* 2009;115:4924-33.
- NCCN Guidelines Version 1. 2013 Sub-Committees Esophageal and Esophagogastric Junction Cancers; [Consultado 2013 Abr 7]. Disponível em: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp#site.
- Hulscher JB, Tijssen JG, Obertop H, van Lanschot JJ. Transthoracic versus transhiatal resection for carcinoma of the esophagus: a meta-analysis. *Ann Thorac Surg.* 2001;72:306-13.
- Orringer MB. Transhiatal esophagectomy without thoracotomy. In: Cohn LH, Patterson A editors. *Operative Techniques in Thoracic and Cardiovascular Surgery.* Philadelphia: Elsevier Spring; 2005. p. 63-83.
- Yang K, Chen H, Chen XZ, Lu QJ, Pan L, Liu J, et al. Transthoracic resection versus non-transthoracic resection for gastroesophageal junction cancer: a meta-analysis. *Plos one.* 2007;6:e37698.
- Chang AC, Ji H, Birkmeyer NJ, Orringer MB, Birkmeyer JD. Outcomes after transhiatal and transthoracic esophagectomy for cancer. *Ann Thorac Surg.* 2008;85:424-9.
- Barreto JC, Posner MC. Transhiatal *versus* transthoracic esophagectomy for esophageal cancer. *World J Gastroenterol.* 2010;16:3804-10.
- Bierre SS, Maas KW, Cuesta MA, van der Peet DL. Cervical or thoracic anastomosis after esophagectomy for cancer: a systematic review and meta-analysis. *Dig Surg.* 2011;28:29-35.
- Costa P, Esteves R, Lages P, Ferreira F. Transposição cervical de tubo gástrico na reconstrução digestiva após esofagectomia por cancro do esófago – detalhes técnicos. *Rev Port Cirurgia.* 2013;25:9-21.
- Oezcelik A, Kaiser GM, Niebel W, Sleyman C, Treckmann JW, Sotiropulos GC, et al. Ten-year survival of esophageal cancer after an en-bloc esophagectomy. *J Surg Oncol.* 2012;105:284-7.
- Wong RK, Malthaner RA, Zuraw L, Rumble RB. Combined modality radiotherapy and chemotherapy in nonsurgical management of localized carcinoma of the esophagus: a practice guideline. *Int J Radiat Oncol Biol Phys.* 2003;55:930-42.
- Yamada S, Nemoto K, Ariga H, Jingu K. Radiotherapy for esophageal cancer in Japan. *Esophagus.* 2012;9:66-74.
- Atsumi K, Shioyama Y, Arimura H, Terashima K, Matsuki T, Ohga S, et al. Esophageal stenosis associated with tumor regression in radiotherapy for esophageal cancer: frequency and prediction. *Int J Radiation Oncol Biol Phys.* 2012;85:1973-80.
- Nishimura Y, Koike R, Ogawa K, Sasamoto R, Murakami Y, Itoh Y, et al. Clinical practice and outcome of radiotherapy for esophageal cancer between 1999 and 2003: the Japanese Radiation Oncology Study Group (JROSG) survey. *Int J Clin Oncol.* 2012;17:48-54.
- Xu Y, Yu X, Chen Q, Mao W. Neoadjuvant versus adjuvant treatment: which one is better for resectable esophageal squamous cell carcinoma? *World J Surg Oncol.* 2012;10:173-80.
- Merrit RE, Whyte RI, D'Arcy NT, Hoang CD, Shrager JB. Morbidity and mortality after esophagectomy following neo adjuvant chemoradiation. *Ann Thorac Surg.* 2011;92:2034-40.
- Hashimi S, Smith M. Medical evaluation of patients preparing for an esophagectomy. *Surg Clin N Am.* 2012;92:1127-33.
- Grotenhuis BA, Wijnhoven BP, Grune F, Van Bommel J, Tilanus HW, Van Lanschot JJ. Preoperative risk assessment and prevention of complications in patients with esophageal cancer. *J Surg Oncol.* 2010;101:270-8.
- Pinotti HV. *Acesso ao esófago torácico por transecção mediana do diafragma.* São Paulo: Atheneu; 1999.
- Japan Esophageal Society. *Japanese Classification of Esophageal Cancer, Tenth Edition: Parts II and III.* Esophagus. 2009;6:71-94.
- Swanson SJ, Batirel HF, Bueno R. Transthoracic esophagectomy with radical mediastinal and abdominal lymph node dissection and cervical esophagogastrostomy for esophageal carcinoma. *Ann Thorac Surg.* 2001;72:1918-25.
- Lewis I. The surgical treatment of carcinoma of the esophagus, with special reference to a new operation for growths of the middle third. *Br J Surg.* 1946;34:18-31.
- DeMeester TR, Johansson KE, Franze J, Eypasch E, Lu CT, McGill JE, et al. Indications, surgical technique, and long-term functional results of colon interposition or bypass. *Ann Surg.* 1988;208:460-74.
- DeMeester TR. Esophageal replacement with colon interposition. *Oper Tech Cardiac Thorac Surg.* 1997;2:73-86.
- Lerut T, Coosemans W, De Leyn P, Nafteux P, van Raemdonck D. Anastomotic complications after esophagectomy. *Dig Surg.* 2002;19:92-8.
- Raymond D. Complications of esophagectomy. *Surg Clin N Am.* 2012;92:1299-313.
- Gockel I, Exner C, Junginger T. Morbidity and mortality after esophagectomy for esophageal carcinoma: a risk analysis. *World J Surg Oncol.* 2005;3:37-44.
- Tachibana M, Kinugasa S, Yoshimura H, Shibakita M, Tomomoto Y, Dhar DK, et al. En-bloc esophagectomy for esophageal cancer. *Am J Surg.* 2004;188:254-60.
- Rentz J, Bull D, Harpole D, Bailey S, Neumayer L, Pappas T, et al. Transthoracic versus transhiatal esophagectomy: a prospective study of 945 patients. *J Thorac Cardiovasc Surg.* 2003;125:1114-20.
- Rouvelas I, Lindblad M, Zeng W, Viklund P, Ye W, Lagerland J. Impact of hospital volume on long-term survival after esophageal cancer surgery. *Arch Surg.* 2007;142:113-7.
- Kozower BD, Stukenborg GJ. Hospital esophageal cancer resection volume does not predict patient mortality risk. *Ann Thorac Surg.* 2012;93:1690-8.
- Stiles BM, Altorki NK. Traditional techniques of esophagectomy. *Surg Clin N Am.* 2012;92:1249-63.
- Hulscher JB, Sandick JW, De Boer AG, Wijnhoven BP, Tijssen JG, Fockens JG, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus. *N Engl J Med.* 2002;347:1662-9.
- Schröder W, Schneider PM, Hölscher AH. Transthoracic en-bloc esophagectomy. *The Chinese-German J Clin Oncol.* 2004;3:229-32.
- Herrera JL. Extent of lymphadenectomy in esophageal cancer: how many lymph nodes is enough? *Ann Surg Oncol.* 2010;17:676-8.
- Schweigert M, Solymosi N, Dubecz A, Stadlhuber RJ, Muschweck H, Ofner D, et al. Endoscopic stent insertion for anastomotic leakage following oesophagectomy. *Ann R Coll Surg Engl.* 2013;95:43-7.
- Briel JW, Tamhankar AP, Hagen JA, DeMeester SR, Johansson J, Choustoulakis E, et al. Prevalence and risk factors for ischemia, leak, and stricture of esophageal anastomosis: gastric pull-up versus colon interposition. *J Am Coll Surg.* 2004;198:536-42.
- Bailey SH, Harpole DH, Rentz JJ, Neumayer LA, Pappas TN, Daley J, et al. Outcomes after esophagectomy: a ten-year prospective cohort. *Ann Thorac Surg.* 2003;75:217-22.
- Law S, Wong KH, Kwok KF, Chu KM, Wong J. Predictive factors for postoperative pulmonary complications and mortality after esophagectomy for cancer. *Ann Surg.* 2004;240:791-800.
- Ferguson MK, Celauro AD, Prachand V. Prediction of major pulmonary complications after esophagectomy. *Ann Thorac Surg.* 2011;91:1494-501.
- Bakhos CT, Fabian T, Oyasiji TO, Gautam S, Gangadharan SP, Kent MS, et al. Impact of surgical technique on pulmonary morbidity after esophagectomy. *Ann Thorac Surg.* 2012;93:221-7.
- Togo S, Ligang L, Wei X, Tiechang P, Chen T, Ouattara MA, et al. Complications and mortality after esophagectomy for esophageal carcinoma: risk factor analysis in a series of 378 patients. *Chir Thorac Cardio-Vasc.* 2010;14:25-8.

50. Bosch DJ, Pultrum BB, Bock GH, Oosterhuis JK, Rodgers MG, Plukker JT. Comparison of different risk-adjustment models in assessing short-term surgical outcome after transthoracic esophagectomy in patients with esophageal cancer. *Am J Surg.* 2011;202:303-9.
51. Moyes LH, McCaffer CJ, Carter RC, Fullarton GM, Mackay CK, Forshaw MJ. Cardiopulmonary exercise testing as a predictive of complications in oesophagogastric cancer surgery. *Ann R Coll Surg Engl.* 2013;95:125-30.
52. Hashimi S, Smith M. Medical evaluation of patients preparing for an esophagectomy. *Surg Clin N Am.* 2012;92:1127-33.
53. Grotenhuis BA, Van Hagen P, Reitsma JB, Lagarde SM, Wijnhoven BP, van Berge Henegouwen, et al. Validation of a normogram predicting complications after esophagectomy for cancer. *Ann Thorac Surg.* 2010;90:920-6.
54. Reynolds JV, Ravi N, Hollywood D, Kennedy MJ, Rowley S, et al. Neo adjuvant chemoradiation may increase the risk of respiratory complications and sepsis after transthoracic esophagectomy. *J Thorac Cardiovasc Surg.* 2006;132:549-55.
55. Reim D, Gertier R, Novotny A, Becker K, zum Buschenfelde CM, Ebert M, et al. Adenocarcinomas of the esophagogastric junction are more likely to respond to preoperative chemotherapy than distal gastric cancer. *Ann Surg Oncol.* 2012;19:2108-18.

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