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Treatment and Complications of Patients with Oesophageal Cancer in Santiago de Cuba

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Abstract

Background: *Oesophageal cancer is considered one of the most lethal neoplasms with the worst prognosis and survival, with high mortality and morbidity. The incidence of OC has increased in recent years in Cuba as in the rest of the world, with more than 600,000 new cases diagnosed annually worldwide. In Cuba, in 2020 there were 852 deaths due to oesophageal cancer and the treatment of this cancer represents a challenge, mainly due to its late diagnosis. The biggest problem is that more than half of the patients have an unresectable tumour or have distant metastases at the time of diagnosis.*

Aims: *To describe the characteristics of surgical treatment in the reference population and to determine the number and type of complications, mortality at discharge, direct causes of death and hospital stay.*

Patients and Methods: *An observational, descriptive, cross-sectional study was conducted. For the population analysis, the period from January 2011–December 2020 was selected. The population consisted of 395 patients with oesophageal cancer, with a confirmatory histological diagnosis of the disease, aged ≥ 18 years and of both sexes. A simple random sample was selected using probability sampling techniques, with a confidence level of 95 % and a margin of error of 5 %, including 195 subjects.*

Results: *Surgeries with curative intent accounted for 16.4 % (29 cases; n=177) while palliative surgeries accounted for 83.6 % (148 cases; n=177). According to the total number of surgeries performed for each histological type, oesophagectomies in OSCC constituted 13.6 % (19; n=140) and in OAC 27.1 % (10; n=37), with a predominance of the Orringer technique. There were a total of 137 complications, with a predominance of surgical site infection of 32.8 % overall, 36.2 % for OSCC and 21.9 % for OAC.*

Conclusions: *In our environment transhiatal, oesophagectomy is the main technique to treat oesophageal cancer. Complications in these patients are frequent, either due to tumour progression or secondary to therapies, and mortality remains very high.*

Keywords: *adenocarcinoma of oesophagus, complications, oesophagus cancer, squamous cell carcinoma.*

Acronyms

Esophagectomy Complications Consensus Group (ECCG)

Gastro-oesophageal junction (GEJ)

Ivor-Lewis Oesophagectomy (ILO)

Oesophageal adenocarcinoma (OAC)

Oesophageal squamous cell carcinoma (OSCC)

Transhiatal oesophagectomy / Orringer oesophagectomy (THO)

Tri-incisional oesophagectomy / McKeown oesophagectomy (TIO)

Introduction

Oesophageal cancer (OC) is considered one of the most lethal neoplasms with the worst prognosis and survival, with high mortality and morbidity.[1,2] The incidence of OC has increased in recent years both in Cuba and in the rest of the world and each year approximately 600,000 new cases are diagnosed globally.[3–5] To give an idea, in 2020 alone, 604,100 new cases and 544,076 deaths due to OC were reported,[6] and in Cuba this same year there were 852 deaths (696 men and 156 women).[7]

The treatment of OC represents a challenge for any physician, mainly because of its late diagnosis. The biggest problem is that more than half of the patients have an unresectable tumour or have distant metastasis at the time of diagnosis, which makes this neoplasm one of those with the poorest survival rates.[8,9]

Anatomical and histological elements specific to the oesophagus[10] make its neoplasms some of the most aggressive. These include, for example, intrathoracic location, contiguity with vital organs, the absence of serosa to limit invasion and its unique lymphatic drainage. Once the obstruction of the oesophageal lumen is established, patients develop nutritional and immunological deficiencies, which in full catabolism limit the curative results expected with any therapeutic modality.[11]

Despite numerous advances in the treatment of OC, surgery remains the option that offers the best chance of cure and survival for patients with local, locally advanced, locoregional and even metastatic disease. It is worth noting that oesophageal surgery is the procedure on the digestive system with the

most complications. There are several alternatives for oesophageal resection, the choice of which is determined by the characteristics of the tumour, location, extent of lymphadenectomy and the expertise of the surgeons involved.**[**12–14**]**

Taking into account the above elements, we pose the following research questions: What is the magnitude of complications, mortality and hospital stay at discharge associated with the disease? What are the characteristics of surgical treatment that are distinctive in this population of patients?

To answer these questions, we set ourselves the following aims:

— To describe the characteristics of surgical treatment in the reference population.

— To determine the number and type of complications, mortality at discharge, direct causes of death and hospital stay.

Patients and Methods

Type of study

An observational, descriptive, cross-sectional study was conducted to identify treatment-related attributes and the magnitude of complications present in the study population. For the population analysis, the period from January 2011–December 2020 was selected.

Population and Sample

The population consisted of 395 patients with oesophageal cancer, with a confirmatory histological diagnosis of the disease, aged ≥ 18 years and of both sexes who were admitted to the Provincial Hospital Clinical-Surgical "Saturnino Lora" in Santiago de Cuba. A simple random sample was selected from this population using probability sampling techniques, with a confidence level of 95 % and a margin of error of 5 %, which included 195 subjects.

Sample size

The sample size has been calculated from the population estimates using the formula

$$n = \frac{z\hat{}2(p \times q)}{\frac{e\hat{}2 + [z\hat{}2(p \times q)]}{N}}$$

n= sample size

Z= desired confidence level (95 %)

p= proportion of the population with the desired characteristics (success)

q= proportion of the population without the desired characteristics (failure)

e= desired level of error (5 %)

N= population size

Once the sample, 195 subjects, was calculated from the finite population of 394 patients, the sample selection of subjects to be included was done by simple random probability sampling, using the computer programme "General Design Simulation System and Sample Applications (SIGESMU 2.0)".

Exclusion criteria

- Patients with a histological diagnosis other than squamous cell carcinoma and oesophageal adenocarcinoma.
- Patients with oesophagogastric junction cancer are categorized as Siewert-Stein II and III.

Obtaining bibliographic and statistical information

Relevant information on the disease under investigation was consulted in primary, secondary and tertiary sources. Articles related to the research topic published in the last 10 years in journals indexed in Index Medicus were reviewed. Other articles from previous years, with a specific interest in the topic, were also studied. A search for bibliographic information was carried out in the databases PubMed, ClinicalKey, ClinicalTrials.gov, Lilacs, EBSCO, Hinari and Scielo; and in search engines such as Google Academic. The strategy used was based on: a combination of keywords such as: "oesophageal adenocarcinoma", "oesophageal cancer", "squamous cell carcinoma", and their equivalents in Spanish; with no language limit and with free abstract or full text. Cuba's statistical data were obtained from the Cuban Medical Journals and the Cuban health portal Infomed. For the province of Santiago de Cuba, statistical information was obtained from the archives of the "Saturnino Lora" Provincial Hospital on the incidence of patients admitted to our centre for oesophageal cancer.

Statistical processing

Data analysis was carried out with the statistical programme SPSS for Windows version 20.0.

Descriptive statistics

Description of the population through the different variables, employing graphs and tables of frequency and percentages. The main variables analyzed: unresectability criteria, treatment, complications, direct death causes and stay in hospital. The analysis of postoperative complications was performed based on the elements provided by the Esophagectomy Complications Consensus Group (ECCG).[15]

Discussion and synthesis

The different points of view on the nosological entity analyzed were contrasted and the data were triangulated, using various sources of information and theoretical and researchers triangulation.

Bioethical considerations

This research was conducted in a GCP-certified centre, which provides an appropriate context for the research. It was also endorsed by the hospital's Ethics Committee and the hospital's Scientific Council.

The principles of bioethics, beneficence and non-maleficence were complied with, taking into account that the research aims were to adopt preventive measures that could reduce the incidence and prevalence of the disease, as well as increase survival.

Finally, the bioethical principle of justice is reflected in the context in which the study was conducted, characterised by a social system based on equity, in which each patient had the same opportunity to be included in the research according to defined criteria, and not by individual characteristics such as sex, race, creed, economic status or other aspects that could be discriminatory.

Discussion and Results

1. Surgical criteria for unresectability

The borderline for considering an OC as unresectable or not is very narrow and depends fundamentally on the diagnostic means available and whether or not they allow an adequate assessment of the T, N

and M categories. Based on clinical and paraclinical findings, it is clear that tumours that are categorised in earlier stages are more likely to be resected.

In this investigation, according to the data recorded in the medical records and the findings of the paraclinical studies, and adhering to the criteria for unresectability offered in the Clinical Guide of the Spanish Association of Surgeons,[16] we found the results shown in Table 1. We excluded 9 individuals who had presented invasion of the pleura, pericardium or diaphragm, who, having been staged according to the criteria of the Sixth Edition TNM (2002),[17] were considered unresectable, an element that, according to the Seventh Edition TNM (2009),[18] does not contraindicate curative surgery. Thus, of the sample, 81.0 % (158 individuals) did not qualify for curative therapy because they presented unresectability criteria, in addition to the 4.6 % represented by the 9 patients mentioned above.

Surgical criteria for unresectability	OSCC		OAC	
	No.	%	No.	%
T4b tumours with infiltration of the heart, great vessels and trachea.	9	6.9	2	7.1
Involvement of multiple lymph nodes in different lymph node territories.	3	2.3	1	3.6
UEG type 1 tumours with positive supraclavicular adenopathies.	0	0.0	0	0.0
Distant metastases (Stage IV), including as such non-regional adenopathies and positive peritoneal cytology, even in the absence of macroscopic carcinomatosis.	**114**	**87.7**	**25**	**89.3**
Cervical oesophageal tumours (< 5 cm from the cricopharyngeal muscle).	4	3.1	0	0.0
TOTAL	130	100	28	100

Table 1. Distribution according surgical criteria of unresectability and histological variants

In the series, the most important unresectability criteria were the presence of metastases (stage IV), which was similarly evident in both histological variants. Unresectability criteria for 5.6 % (11 subjects; n=195) were infiltration of the trachea, great vessels and heart, with 6.9 % (9; n=130) for OSCC and 7.1 % (2; n=28) for OAC. Only 29 patients presented resectability and operability criteria and underwent curative surgery using different techniques, predominantly transhiatal or Orringer.

Barrera Ortega et al.[19] state that 75.0 % of patients with oesophageal cancer and cancer of the GEJ, at the time of diagnosis, have an unresectable tumour, with locoregional lymph node metastases and locally advanced tumours, as well as deterioration of the general condition and severe malnutrition, which leaves palliation of dysphagia and improvement of quality of life as the only option.

2. Surgical treatment

Of the individuals diagnosed with OSCC and OAC studied in our series, 90.8 % (177 subjects) underwent some type of surgical procedure, either curative or palliative, and only 9.2 % (18 subjects) did not receive surgery, either because they refused it or because they died before the procedures were carried out. Patient refusal of surgery is reported by authors such as Cabrera and Caselli,[20] who report that a not insignificant number of patients in their study refused surgical treatment.

The various treatment modalities currently available for OC have the following fundamental objectives: control of dysphagia, recovery of the patient's quality of life and prolonged survival.[21] Oesophagectomy continues to be the treatment that offers the best chances of cure and disease-free survival, despite its complications and high morbidity and mortality. However, most patients diagnosed with OC are not candidates for this procedure due to their advanced stage and clinical deterioration. According to Clemente-Gutiérrez,[22] OC presents as a localised disease in 22.0 % of patients, and as a locoregional disease in 30.0 %, and he describes oesophagectomy as the only curative option for those who meet the criteria of resectability and operability.

The resectability of malignant oesophageal tumours is highly variable; in our series, we found a percentage volume of 14.9 % (n=195) and 16.4 % of all subjects undergoing surgical treatment are taken into account. Valladares et al.[23] report that the resectability rate in the Department of Surgery of the Clinical Hospital of the University of Chile is 61.0 % for all patients with surgical indications. The same author, in his study, shows different resectability rates obtained by various investigators in both hemispheres: for Liu, in China, it was 96.0 %; while for Puttawibull it was 36.1 % in patients undergoing oesophagectomy alone. In the West these rates were equally varied, the Belgian Nikadi reporting 97.0 % with the use of multimodal therapy and 84.0 % with surgery alone, and Dikken reporting 18.2 % in the UK; 28.5 % in the Netherlands and 41.5 % in Denmark

Currently, there are several techniques available for oesophageal resection, the selection of which depends on various criteria such as the location of the neoplasia, whether or not lymph node dissection is performed and, above all, the preference and expertise of the surgeons who will carry them out. Of these techniques, THO, ILO and TIO are performed in our hospital.

In the present research, surgeries with curative intent represented 16.4 % (29 cases, n=177) of all surgeries performed, while palliative surgeries were more frequent and were performed in 83.6 % (148 cases; n=177) of those who underwent surgery. According to the total number of surgeries performed for each histological type, resective surgeries in OSCC constituted 13.6 % (19; n=140) and in OAC 27.1 % (10; n=37), with a predominance of the Orringer technique.

Surgical technique	OSCC		OAC	
	No.	%	No.	%
Curative-intent techniques				
Orringer technique	**13**	**9.3**	**6**	**16.3**
McKeown technique	4	2.9	2	5.4
Ivor Lewis technique	2	1.4	2	5.4
TOTAL	19	13.6	10	27.1
Palliative-intent techniques				
Gastrostomy	**102**	**72.9**	12	32.4
Jejunostomy	13	9.2	15	40.5
Esophagostomy + Gastrostomy	6	4.3	0	0.0
TOTAL	121	86.4	27	72.9

Note: *Percentage is calculated based on the total number of surgeries according to histological types.*

Table 2. Distribution according to surgical treatment and histological variant

Table 2 shows the distribution of the different oesophagectomy techniques, the most commonly used for both histological types and overall was THO; 65.5 % (19 subjects; n=29) of the oesophageal resections were carried out by THO, this was performed in 13 patients with OSCC, representing 9.3 % (n=140) of all those who underwent surgical treatment with this histological type. 3.0 % (n=140) of all those submitted to surgical treatment with this histological type and if we analyse the percentage, taking as a reference the totality of the resective surgeries for OSCC (n=19), we find that it was performed in 68.4 % of the patients with this variety of OC. Of the OSCCs treated with this technique, 9 were located in the middle third and 4 in the lower segment.

For OAC, THO represented the most commonly used technique, performed in 6 patients (16.3 %; n=37), and evaluating only oesophagectomies for patients with OAC, the percentage was 60.0 % (n=10). The location of the OACs treated by THO was absolutely in the lower portion.

In the case of the remaining techniques, 20.7 % and 13.8 % were performed with the McKeown and Ivor Lewis techniques respectively, these being less frequent in our setting, both for OAC and OSCC. These results show a preference among surgeons at our institution for transhiatal oesophagectomy, a preference that is seen in the rest of Western countries, mainly in the USA and Europe. This technique saves time and reduces respiratory complications by avoiding thoracic access. Several authors[24–26] report that the surgical survival achieved with this technique and the quality of life obtained justify its use.

Seineldin[27] states that THO is essentially indicated for resectable tumours of the oesophageal endings, but that it can be used in tumours of any topography as long as there is no evidence of externalisation of the neoplasm. This technique has shown low morbidity and mortality, and good oncological results. Mark Orringer,[23] in his early work, published more than 2,000.00 THO, in which he obtained mortality of 1.0 %.

The ILO had the lowest percentage of resective techniques. It is indicated primarily for neoplasms located below the carinal plane. In recent years, according to reports by Zheng,[28] there has been an increase from 2007 to 2017 in the United States, from 37.0 % to 62.4 %, while THO has experienced a decrease, from 41.1 % to 21.5 %, and the latter was performed mainly in patients with high morbidity and a higher probability of mortality.

In other institutions in the country, there are reports such as that of Herrera et al.[29] where there is a predominance of ILOs over the rest of the techniques. This author reports that in his series, the most frequently used oesophagectomy was the ILO with 58.1 % compared to 37.1 % for THO and 4.8 % for TIO. This is indicative of the preferences and expertise of each hospital institution. Both ILO and TIO guarantee better access to the regional oesophageal lymph node chains and allow for better and more extensive lymph node dissection[30,31] in cases that warrant it.

Regarding the worldwide trend of these techniques, Haverkamp et al.[32] point out in their study that there is a high worldwide preference for transthoracic techniques. In their survey, they report that transthoracic oesophagectomy with two-field lymph node dissection and reconstruction with the stomach was the procedure preferred by the majority of surgeons, and they noted an increase in minimally invasive techniques. Of the oesophagogastric surgeons surveyed, 43.0 % preferred the minimally invasive transthoracic approach, 38.0 % the open transthoracic approach, 15.0 % the open transhiatal approach and 4.0 % the minimally invasive transhiatal approach. Among the open techniques, 93.0 % of respondents used the Ivor-Lewis approach.

The pyloroplasty was performed with a transmediastinal gastric ascent in the tubular form in all cases, which by requiring an anastomosis reduced the surgical time and therefore the perioperative and postoperative complications. Pyloroplasty was performed as standard using the Heineken technique with Corona modification,I except for one patient who underwent pyloromyotomy. A jejunostomy by feeding tube was also performed as a complementary procedure.

As far as lymphadenectomy is concerned, it is not performed in our setting, or at least not regularly. On the other hand, the option of neoadjuvant therapy has not been satisfactory in the few patients who have undergone it, and there are difficulties in performing it. It must be said that the arsenal available in our environment, both for diagnosis and treatment, is quite scarce, which, added to the aggressiveness of the tumour, its high lethality and late diagnosis, makes the prognosis exponentially more complex.

Gastrostomy, according to Gómez-España,**[**33**]** is a safe and effective solution for patients who are not candidates for surgical treatment and for whom the implantation of self-expanding oesophageal prostheses has failed or is not considered appropriate, and who have a life expectancy of more than three months. Furthermore, it is contraindicated cases of candidates for oesophagectomy with subsequent gastric ascent and in cases of stomach infiltration; in these cases, jejunostomy is suggested.

Montiel Roa,**[**34**]** in his series, reports that the greatest number of interventions performed were palliative, mainly gastrostomies for Stamm, Witzel or percutaneous feeding, with 40.6 %, and in the case of jejunostomies for feeding, he only reports their use in 1 case. Our report, regarding gastrostomies, agrees with this author; we report 114 gastrostomies (64.4 %; n=177), this technique being the most frequent among OSCC patients who underwent surgery (72.9 %), while in subjects operated with OAC, jejunostomy was the most frequent, with 40.5 %. A total of 28 palliative jejunostomies were performed, representing 18.9 % (n=148) of all palliative surgeries performed.

Table 2 shows the different surgical modalities performed. It shows the prevalence of gastrostomy as a palliative technique, as mentioned above, and also shows that 3.9 % of patients with OC underwent oesophagostomy + gastrostomy, in all cases involving tumours located in the upper third of the oesophagus.

Ostomas for palliative purposes is not considered the first option for the treatment of unresectable OC. For Barrera Ortega et al.**[**19**]** —who agree with international protocols— abdominal ostomies should be a procedure of the last choice, given the ethical issues involved. Currently, the most commonly used strategies to treat dysphagia and ensure feeding are laser therapy, implantation of self-expanding prostheses and derivative techniques such as Graviliu and Postlethwait; other therapies such as argon

plasma coagulation, photodynamic therapy, cryoablation and oesophageal dilatations are also mentioned.[35,36]

In our hospital we do not have the necessary resources to develop these techniques and experience in performing bypass techniques is quite limited, so we limit ourselves in these cases to performing abdominal ostomies. It should also be noted that a large number of authors suggest oesophageal resection as the best treatment option, since removing the tumour guarantees nutrition and avoids complications such as haemorrhage, perforation and fistulisation due to invasion of adjacent structures. Mederos Trujillo,[33] in an interview with experts, concludes that they suggest that patients should always be offered a surgical option that guarantees normal physiological functions and condemns ostomies for feeding, considering them a last resort.

Liaño et al.[36] advocate surgical resection in patients with unresectable oesophageal tumours and consider that patients with locally very advanced diseases would benefit from this type of procedure. They suggest that resection should be attempted provided the following conditions are met: absence of distant metastases, low surgical risk and skilled surgeons.

In this study, it was difficult to evaluate the use of other palliative therapies for OC in the patients in the series, as most of them were in advanced stages of the disease, with deteriorating general, immunological and nutritional status, and could not undergo radiotherapy or chemotherapy.

3. Clinical and surgical complications

The clinical complications are reflected in table 3, which includes all the complications presented by patients who underwent some type of surgical treatment (palliative or curative), before surgery and those after surgery that were not related to surgery, as well as the complications developed by patients who did not receive any type of surgical therapy.

Clinical complications	OSCC		OAC	
	No.	%	No.	%
Pneumonia	**52**	**32.3**	**9**	**20.9**
Severe anaemia	27	16.8	6	14.0
Acute respiratory distress syndrome	26	16.1	7	16.3
Pulmonary thromboembolism	19	11.8	3	7.0

Tracheoesophageal fistula	11	6.8	0	0.0
Deep vein thrombosis	9	5.6	5	11.6
Upper gastrointestinal bleeding	6	3.7	**9**	**20.9**
Pneumothorax	6	3.7	0	0.0
Urinary tract infection	3	1.9	4	9,3
Atelectasis	2	1.2	0	0.0
TOTAL	161	100	43	100

Note: *Percentage is calculated based on total complications.*

Table 3. Distribution according to clinical complications and histological variant

The number of clinical complications was highest in patients undergoing palliative treatment, as would be expected given the advanced stage of the disease. During follow-up, a significant number were admitted more than once to our institution for complications related to their neoplastic disease. Meanwhile, patients who underwent curative surgery presented few preoperative complications, 2 developed nosocomial pneumonia, which they overcame, and 1 presented severe anaemia.

Of the clinical complications, pneumonia stood out for both histological subtypes, with 32.3 % for squamous cell carcinoma and 20.9 % for OAC. Pneumonia occurred in patients with advanced disease, mainly with Karnofsky index < 50, but 4 patients who underwent curative surgery developed pneumonia postoperatively. Bed rest and poor mobilisation, as well as the existence of regurgitations leading to bronchoaspiration, and the presence of tracheobronchial fistulas, associated with the poor nutritional and clinical condition of these patients, are responsible for respiratory infectious processes. Respiratory distress syndrome was present in 16.1 % of OSCC and 16.3 % of OAC.

Upper gastrointestinal bleeding occurred in 3.7 % of OSCC and 20.9 % of OAC, both in the form of melena and haematemesis, not only as a consequence of ulceration and bleeding from the primary tumour lesion but also as a result of gastric infiltration. After pneumonia and upper gastrointestinal haemorrhage, Acute Respiratory Distress Syndrome (16.3 %) and severe anaemia (14.0 %) were the most frequent complications of OAC. These complications accounted for 16.1 % and 16.8 % respectively for OSCC.

Tracheoesophageal fistulas were present in 11 (6.0 %; n=195) cases with OSCC and conditioned a poor prognosis for the patients, who died within 12 weeks of admission to our institution as a result of respiratory complications. Shamji[37] as well as other authors[38,39] point out that tracheoesophageal fistula occurs in 5.0 %–15.0 % of patients with untreated OC and that respiratory complication, mainly pneumonia, are the most frequent effects of this disease. In our series, we found that all 11 patients developed pneumonia.

In OAC, there were no complications such as tracheoesophageal fistula, atelectasis and pneumothorax, which did appear in OSCC, due to the more distal location of the lesion in the oesophagus, although we present 4 reports of middle third location that did not develop these complications.

Table 4 shows the trans-operative and post-operative surgical complications (early and late) that were demonstrated in the 137 patients who underwent surgery, either for curative or palliative purposes. There were a total of 137 complications with a predominance of operative site infection (OSI) 32.8 % overall with 36.2 % for OSCC and 21.9 % for OAC.

Borráez Segura et al., in their classic text Fundamentals of Surgery,[40] emphasise that infections are one of the complications most feared by the surgeon, a precept that agrees with our series, where surgical site infection predominated in both groups. This event is to be expected in most of these patients, whose healing process is delayed and who present a significant risk of infection due to their poor nutritional status and the immunological deterioration in which they face the surgical procedure.

Surgical complications	OSCC		OAC	
	No.	%	No.	%
Intraoperative				
Arrhythmia	3	2.9	1	3.1
Haemorrhage	2	1.9	0	0.0
Postoperative				
Operative site infection	**38**	**36.2**	7	21.9
Pneumonia	16	15.2	5	15.6
Urinary tract infection	13	12.4	**9**	**28.1**
Anastomotic leakage	9	8.6	2	6.3

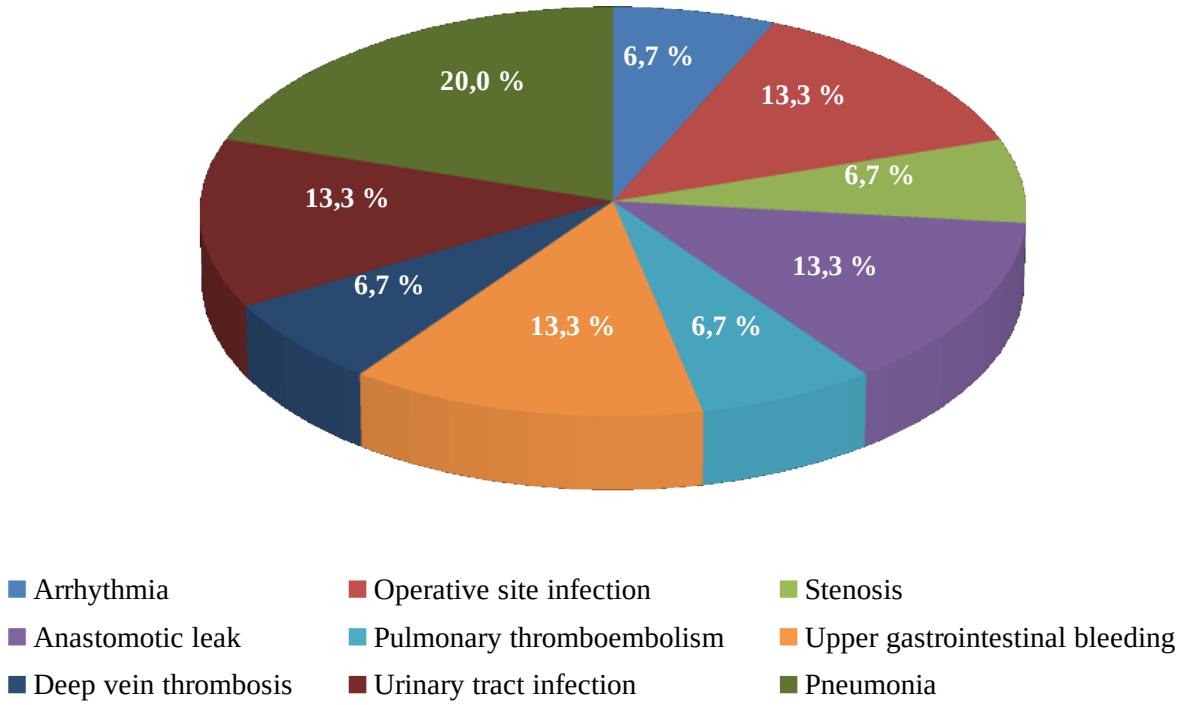
Deep vein thrombosis	8	7.6	1	3.1
Pulmonary thromboembolism	7	6.7	2	6.3
Mediastinitis	4	3.8	0	0.0
Anastomotic stenosis	2	1.9	1	3.1
Upper gastrointestinal bleeding	0	0.0	3	9.4
Peritonitis (ostomy failure)	2	1.9	1	3.1
Empyema	1	1.0	0	0.0
TOTAL	105	100	32	100

Note: *Percentage is calculated based on total complications.*

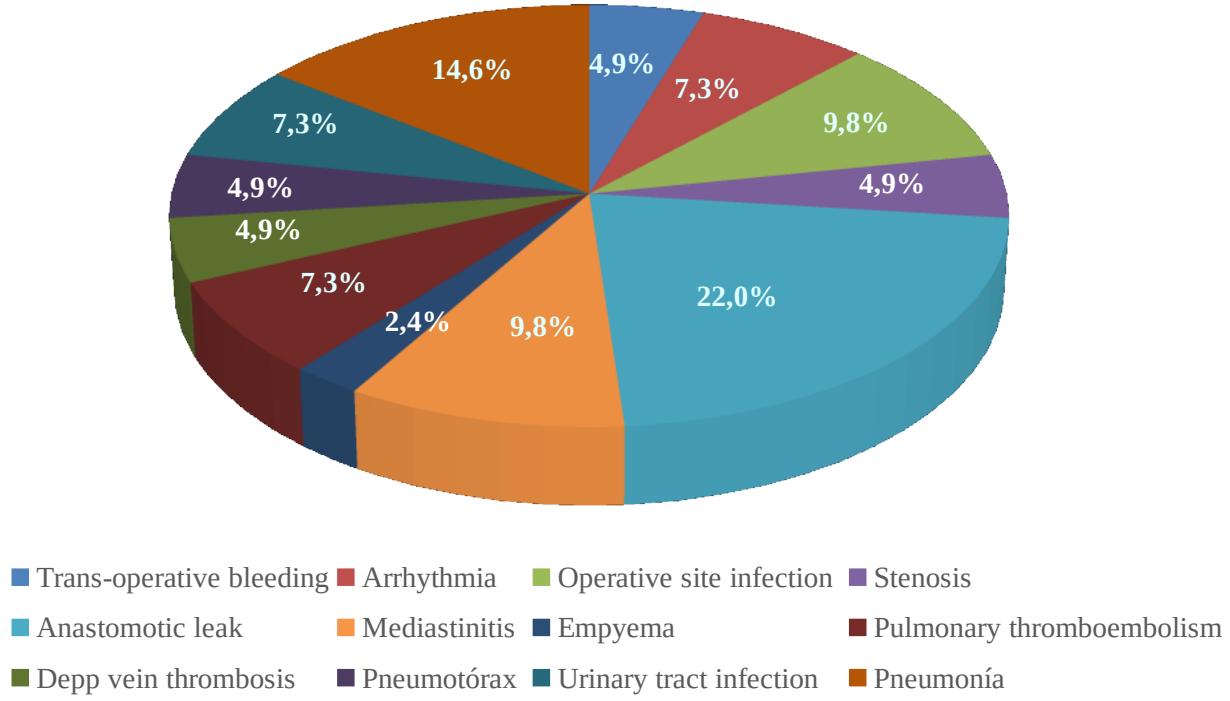
Table 4. Distribution according to surgical complications and histological variant

Braghetto et al.**[**41**]** a study conducted in Chile reports 23.2 % of respiratory complications, although they do not specify whether it is exactly pneumonia or acute respiratory distress syndrome, making a comparison with our series difficult. In the Chilean study, 8.6 % of pulmonary thromboembolism is reported, a complication that we found with practically similar figures, although with a lower percentage, in the case of OSCC with 6.7 % and 6.3 % in the OAC, and globally represented 6.6 % (n=137) of all post- and trans-operative complications.

Of cardiovascular complications, Braghetto**[**41**]** reports 14.5 % in his casuistry, while in our casuistry there were 4 (2.9 %; n=137) reports of arrhythmias in patients operated by THO and ILO, which occurred trans-operatively. Urinary tract infection (UTI) was the second most frequent complication among surgically operated subjects, accounting for 16.1 % of all cases; it was followed in frequency by postoperative pneumonia which was diagnosed in 21 cases (15.3 %, n=137), occurring in 16 patients with OSCC and 5 with OAC.



Graph 1. Complications in OSCC patients operated with curative-intent techniques



Graph 2. Complications in OAC patients operated with curative-intent techniques

Although the above table shows surgical complications in both palliative and curative surgery patients, we consider it necessary to evaluate the incidence of these complications independently in patients undergoing oesophagectomy, which will allow us to better understand the results of the technique and the evolution of patients after resection surgery for curative purposes. Graphs 1 and 2 show the main complications that generally occur in patients undergoing curative treatment, based on the criteria of ECCG.[15]

The number of complications in the oesophagectomised patients was high, with 41 reported in patients with OSCC and 15 in those who developed OAC. In the previous graphs, the percentage of complications was calculated based on the number of complications. Anastomotic leaks accounted for 20.0 % of all complications among patients operated with curative intent, these were categorized, following ECCG criteria,[15] into type I (5); type II (1) and type III (5), the five patients included in type III underwent surgical treatment, with mediastinitis in 4 patients who had undergone oesophagectomy for OSCC and one with the same histological type developed empyema. Anastomotic leaks for OSCC accounted for 22.0 % and 13.0 % for OAC of all complications in both histological forms. If we calculate the percentage based on the total number of operated patients, we have that globally anastomotic leaks occurred in 38.0 % (11 subjects; n=29), for OSCC it was 47.3 % (9 subjects; n=19) and in OAC it was 20.0 % (2 patients; n=10).

Authors such as Braghetto et al.[41] report that anastomotic leaks represent the main complication after oesophagectomy. In their series, out of 69 cases operated by minimally invasive surgery, they reported that 63.7 % presented anastomotic dehiscence, 60.8 % were type I and type II, and only 2.8 % required reoperation. Ferreira and Saavedra, in Brazil,[42] when analysed OC treatment in three periods 1987–1997, 1998–2003 and 2007–2015, and showed the following percentages of anastomotic leaks: 9.5 %; 6.8 % and 20.7 % respectively. Moral Moral et al.,[43] analysing 318 OC cases with 81 oesophagectomies between 2007–2015, reported 13.5 % fistulae in the first period and 7.0 % in the second.

For the series of Borráez Segura et al.,[44] anastomotic leakage was also more frequent at 30.0 % when comparing their results with Hulscher (15.0 %), and Atkins (14.0 %) and Merrit (12.3 %), showed higher figures. In this same series, it was noted that complications were higher in women, which is not consistent with our results, as the highest frequency of complications in patients who underwent oesophagectomy was in the male sex.

Herrera et al.[29] report that in their study, anastomotic strictures prevailed with 34.8 %, followed by haemopneumothorax. In our study, no haemopneumothorax was found, and we only presented 2

patients with postoperative pneumothorax in those who underwent oesophagectomy using the Ivor-Lewis and McKeown technique. The second most frequent complication in this group of patients in our series, unlike Herrera's, was pneumonia with an overall percentage of 16.4 %.

We found 3 cases with stenosis of the anastomosis, 2 of which occurred 6 months after surgery and one during admission; they received endoscopic treatment by dilatation with a resolution of the stenosis. One of the patients had previously presented with a type II anastomotic leak.

Clavien-Dindo	OSCC		OAC	
	No.	%	No.	%
Type I	4	8,3	2	13,3
Type II	**20**	**41,7**	**11**	**73,3**
Type IIIa	2	4,2	1	6,7
Type IIIb	12	25,0	0	0,0
Type IV	3	6,3	1	6,7
Type V	**7**	**14,6**	0	0,0
TOTAL	48	100	15	100

Table 5. Distribution of complications according to Clavien-Dindo classification in patients undergoing oesophagectomy according to histological variant.

The Clavien-Dindo Classification plays an important role in categorising postoperative complications,**[**45,46**]** and its use is of great value in assessing the quality of surgical interventions and documenting complications. Applying it to this study, we found the results shown in table 5. As can be seen, patients with OSCC presented more complications than those who developed OAC; in both histological varieties, type II complications were more frequent, representing 31.1 % in OSCC and 60.0 % in OAC. More cases of OSCC were confirmed in the following groups, which are more complex and have a worse prognosis, as shown in the tables above. Perioperative mortality (Clavien-Dindo type V classifier) was present in 7 subjects (14.6 %) with OSCC.

Recent publications**[**47–49**]** on surgical complications show indicators between 23.0 % and 27.0 %, figures that are above almost all of our results. Oesophagectomy remains the option that offers the best chance of survival for patients with OC, but it is also the elective gastrointestinal surgical intervention with the highest morbidity and mortality**[**12,50,51**]** and entails multiple technical and functional complications.**[**52**]**

Reynold et al. [53] report that from January 2015–December 2016, 2,704 oesophageal resections were entered in the ESODATA.org database of the ECCG, and 95.6 % of the surgeries were performed by EC; the overall incidence of complications was 59. 0 % and the most frequent complications were: pneumonia (14.6 %), atrial arrhythmia (14.5 %), anastomotic leak (11.4 %), conduit necrosis (1.3 %), chyle leak (4.7 %) and recurrent injury (4.2 %).

From the results obtained when analysing the complications in patients undergoing OC oesophagectomy in our series, we can see that this surgery results in high morbidity and mortality. In the series of oesophagectomised patients, all of whom underwent primary surgery, i.e. did not receive neoadjuvant treatment, we found overall morbidity of 72.0 % (21; n=29). All patients diagnosed with OAC had complications to one extent or another, accounting for 24.1 %, while those diagnosed with OSCC constituted 47.9 %.

Patil et al.,[54] in an analysis of 238 patients undergoing oesophagectomy, determining overall morbidity of 37.4 % (89/238) and reported pneumonia, pleural effusion and arrhythmias as the main complications, with respiratory complications being the main causes of morbidity; and reported anastomotic leakage in 14 cases. On the other hand, a multicentre study by Geller et al.[55] reported morbidity of 56.0 %, i.e. 428 patients of the 761 patients studied experienced at least one complication. These same authors reported that factors associated with a higher likelihood of complications included age (p=.001), female sex (p=.005), and pack-years of cigarettes (p=.006) among others.

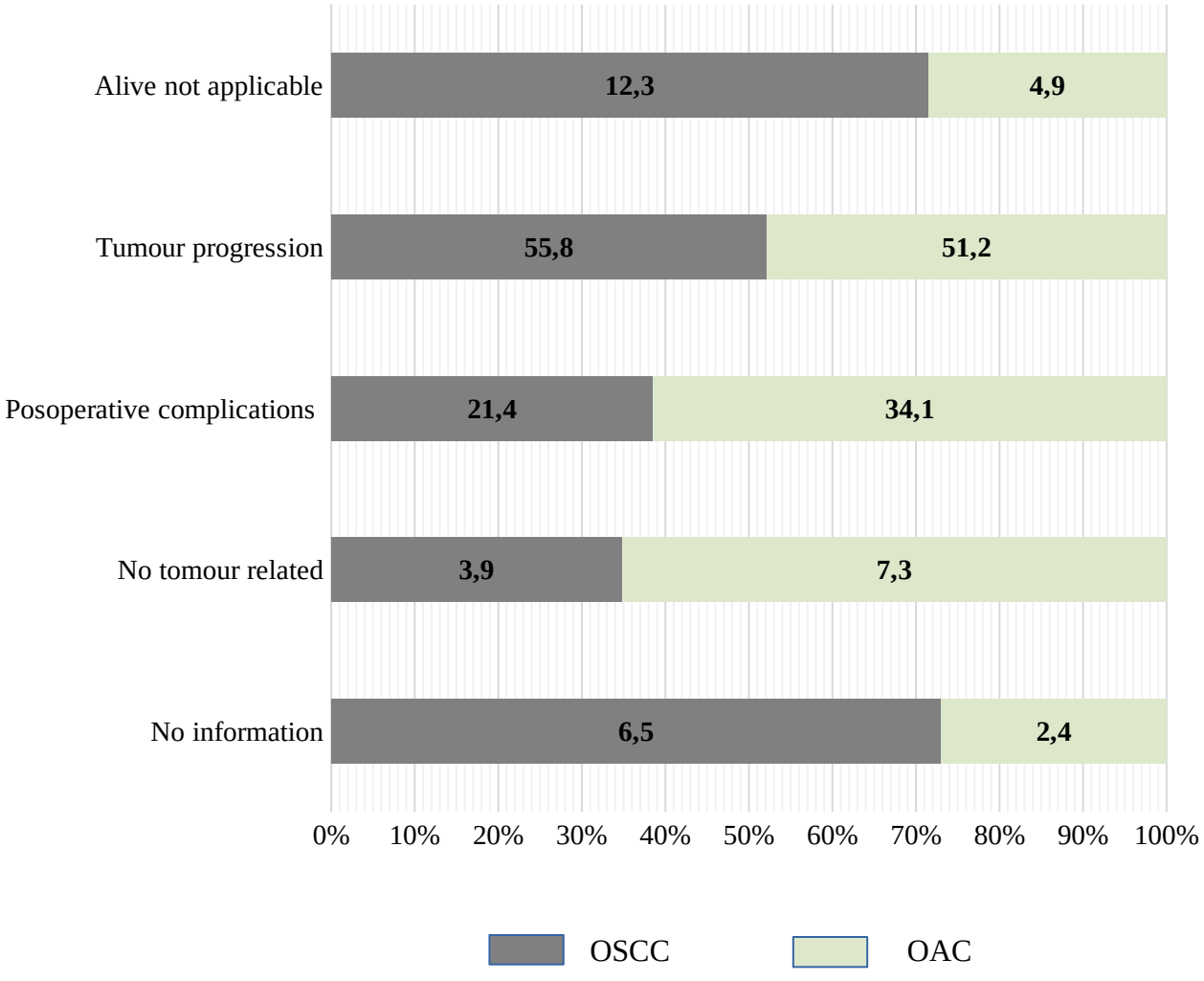
4. Mortality

At the time this study was completed, 173 patients had died, representing overall mortality of 88.7 %, i.e. only 11.3 % of the sample was alive. This is evidence that mortality from OC is high, a fact that most national and international publications agree with. The national statistics provided by the Ministry of Public Health in the health yearbooks[5,56] show that the number of patients dying from oesophageal cancer has been increasing significantly in our country. In 1970, mortality from OC was 272 subjects with an adjusted rate of 3.2, at the beginning of this century it was 393 cases and, according to the 2020 statistical yearbook, deaths amounted to 852 (adjusted rate of 7.6) for the same year.

On the other hand, it should be noted that 30-day postoperative mortality in our series was 24.1 % (7; n=29) and occurred in 6 patients who underwent transhiatal oesophagectomy and 1 with tri-incisional or McKeown oesophagectomy. This result is consistent with those of Herrera et al.[29] who reported postoperative mortality of 6 cases, representing 9.7 % of the casuistry. However, these same authors

report that in Cuba the best known and most reported series have mortality between 10.0 % and 25.0 %.

Graph 3 shows the data obtained concerning the direct causes of death of the patients, grouped according to the criteria set out by Romera Garrido in his doctoral thesis,**[**8**]** which we believe allows a better understanding of this variable. As can be seen in the graph, information on the direct cause of death is not available for 11 patients, either because they were lost to follow-up or because the information was not available in any registry; and 22 are still alive. The main causes of death were related to conditions expected from the presence and progression of the tumour, representing 66.4 % of the 162 patients with a known cause of death; for OSCC there were 86 cases with this cause and for OAC 21 subjects.

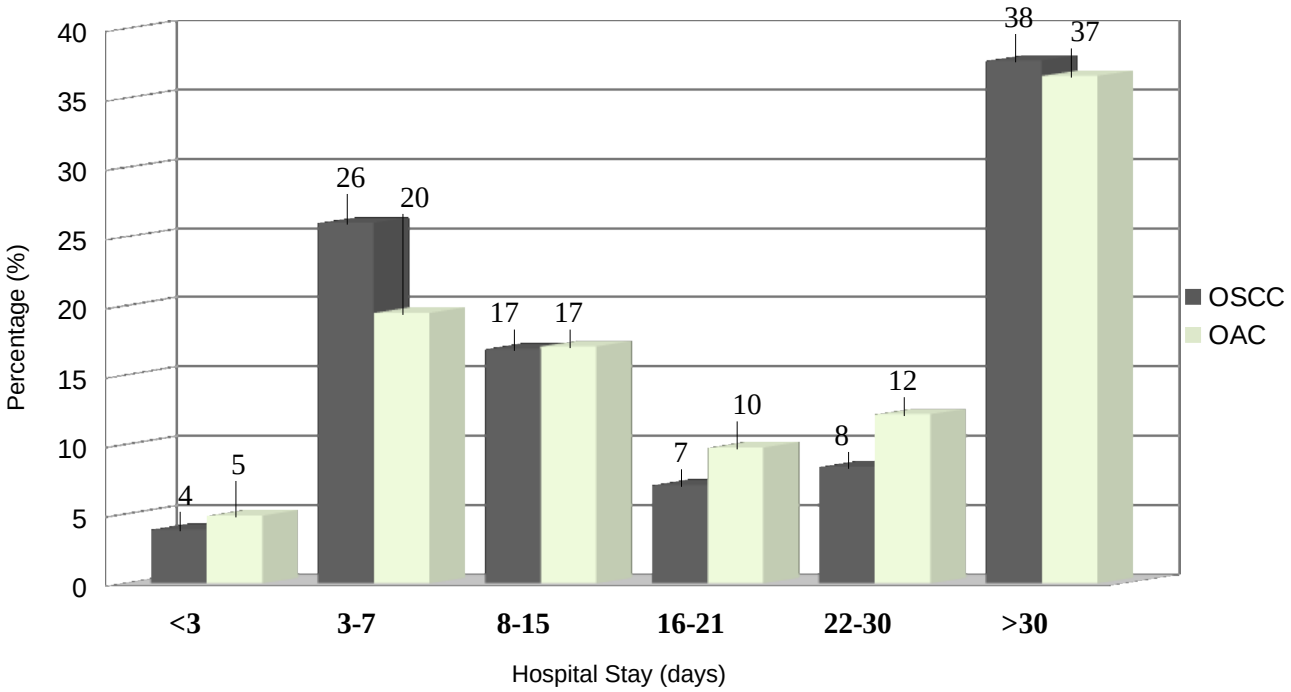


Graph 3. Distribution according to cause of death

Clinical complications were reported in 33 and 14 subjects with OSCC and OAC respectively and were mainly represented by pulmonary thromboembolism, multiple organ dysfunction and septic shock. In his casuistry, Romera Garrido**[**8**]** reports that 69.1 % (501; n=725) of the causes of death were due to tumour progression followed by clinical complications.

5. Hospital Stay

Hospital stay in our series ranged from 1 to 66 days with a range of 65 days. The average length of stay was 23,9 days **[**18.4; CI 95 %: 21.3-26.5**]**, being higher in patients undergoing oesophagectomy, mainly among those who developed some kind of postoperative complication. As shown in graph 4. 37,4 % (73 patients; n=195) had a hospital stay of more than 30 days; 58 patients (37,7 %; n=154) for OSCC and 15 patients (36,6 %; n=41) for OAC. Within this group of patients, there were 6 cases (3.1 %; n=195) where the length of stay was over 60 days.



Graph 4. Distribution according to hospital stay and histological variants

A not insignificant number of patients were admitted more than once to our institution after their first admission, mainly due to complications related to disease progression or issues related to palliative procedures such as ostomies. Forty patients (2.1 %) were found in this situation, of whom 32 were admitted on two occasions, seven on three occasions and one patient was admitted on six occasions. The mean time between the intervals of each admission was 102.8 days **[** 203.8; CI 95 %: 39.6-166.0**]**.

Conclusion

The therapy that offers the best chances for OC patients, regardless of histological type, remains surgical, although it is not free of complications, and in our setting the transhiatal technique remains the main one.

Complications are frequent, whether due to disease progression or secondary to palliative therapy or oesophagectomy.

Mortality in these patients is very high and is closely related to tumour progression and complications.

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