COMPLEX SURGERY OESOPHAGUS

EVALUATION REPORT

[1/7/2019 – 30/6/2022]

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Belgian Cancer Registry

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Summary

Introduction

From 1 July 2019 onwards, complex surgical procedures of the oesophagus were concentrated in 10 acknowledged expert centres that acceded to a convention with the RIZIV-INAMI. The decision to centralize complex oesophageal surgeries in Belgium was supported by volume-outcome results delivered by the Belgian Cancer Registry. These results demonstrated that 30- and 90- day postoperative mortality after complex oesophageal surgery was significantly lower when the surgical procedure was carried out in a high-volume centre.

The aim of the convention is to improve overall quality of care that is delivered in the Belgian hospitals, and in particular to reduce postoperative mortality of complex oesophageal surgeries. All acceded expert centres were subjected to a mandatory registration of each patient that was discussed on a specialized multidisciplinary meeting and every complex surgical procedure that was carried out in the expert centre. A comprehensive evaluation of the centralization project was featured after a three-year period, i.e. based on collected data from 1 July 2019 until 30 June 2022. The results of this evaluation are consolidated in the current report. In addition, some first results for the fourth convention year are introduced.

Results

Volume criteria

An important pillar of the convention, aiming at quality-of-care improvement, was the structural condition of a minimal surgical volume for each individual expert centre. The imposed minimal volume after the three-year period was 75 procedures. This condition was not reached by three of the ten expert centres (individual volumes of 61, 63 and 68). Together with a minimal surgical volume, a minimal volume of specialized multidisciplinary meetings was determined in the convention, i.e. 150 discussions after three years. Only one out of the ten centres did not reach the minimal volume of discussions (individual volume of 138).

Evolution of outcome after complex oesophageal surgery

Data from the Belgian Cancer Registry from the most recent period before the start of centralization, i.e. the four year period 2015-2018, were used as reference ($T0_{2015\text{-}2018}$; N_{T0}=1.584) to compare the results for surgeries that were carried out for primary malignant oesophageal cancer before and after centralization ($N_{3Yconvention}$=1.184).

The ultimate interest is the comparison of the postoperative mortality before and after centralization. The overall unadjusted 30-day postoperative mortality during the $T0_{2015\text{-}2018}$ period was 4.2% 95%CI [3.3, 5.3] compared with the unadjusted result for the three year convention period of 2.8% 95%CI [1.9, 3.9]. When adjusting both results for case-mix characteristics (age group, sex, WHO performance score, clinical TNM-categories, primary tumour localisation), the adjusted odds ratio for the convention period - with the $T0_{2015\text{-}2018}$ period as the reference - was 0.69 95%CI [0.44-1.08]. Therefore, although a clinically relevant decreasing trend is observed in the overall 30-day postoperative mortality during the convention, the decrease is not statistically significant (p=0.105). The unadjusted 90-day postoperative

mortality during the $T0_{2015\text{-}2018}$ period was 9.5% 95%CI [8.1, 11.1], compared with 7.2% 95%CI [5.8, 8.8] in the convention. The adjusted odds ratio for the convention period was 0.8 95%CI [0.59, 1.07], therefore and similar to the 30-day postoperative mortality, although a clinically relevant decreasing trend is observed in the 90-day postoperative mortality, the decrease is not statistically significant (p=0.132).

The median time that passed between the histological confirmation of the malignancy and the start of any first treatment (options regarded as first treatment being chemotherapy, radiotherapy or surgery) for the patients treated in T0 was 39 days (IQR 28-55), compared to an identical result for the patients treated in the convention (39 days (IQR 28-50)). This finding is reassuring and refutes the hypothesis that concentrated care creates a longer time to treatment.

In general, when comparing T0 with the convention, some tendencies were observed in patient selection, surgical technique and the use of neoadjuvant treatment. A proportional decrease of patients with clinical stage I disease and an increase of clinical stage IV (mostly IVa), an increase of minimal invasive surgery, and an increase in use of neoadjuvant treatment were documented during the convention period.

Evaluation of 10 expert centres

The average age and male-female ratio of the surgically treated patients was very similar in the different centres. Patient selection for surgery varied between the centres as for tumour stage (proportion clinical stage 0-I and IV), tumour indication (proportion recurrence or salvage treatment after definitive chemoradiation), and the surgical technique (open versus minimally invasive surgery). The median time to treatment was independent from whether the patient was referred to the expert centre or not, nevertheless 4/10 expert centres had a median time that was at least 5 days longer than to the overall result. The overall 30-day postoperative mortality was higher in patients with 'non-standard' surgery (10.2%; 95%CI [3.8, 20.8]) compared to 'standard' surgery (2.4%; 95%CI [1.6, 3.4]) (non-standard surgery defined as emergency surgery, palliative surgery, total laryngectomy and recurrence surgery). As decided by the expert working group, assessment of the centre-specific results was based on statistical significance. The individual results, adjusted for the case mix of the different expert centres, showed a significantly higher 30-day mortality in 1 centre compared with the average, the same centre also performed significantly worse at 90-day mortality compared with the rest of the centres.

General commitment contributing to a continuous system of quality improvement

All expert centres attended to meetings that were organized by the RIZIV-INAMI to discuss the annual results. The centres also annually prepared an individual evaluation with the formulation of concrete action points for their own centre. Finally, the 10 expert centres united their scientific interests and created a new scientific group named the Audit of Belgian Esophageal Surgery (ABES). The ABES gathered at regular times to discuss specific surgery-related topics, to exchange experiences and to propose new research questions.

Important obstacles encountered during the convention

The COVID-19 crisis occurred in the middle of the 3-year period, creating diverse supplementary challenges for the expert centres. The possible impact of this healthcare crisis on the

individual development and the intended elaboration of the expert centres is an important factor when evaluating the convention.

As for the data collection, collected data on pathological resection margins appeared to be incomplete, with lack of information on the circumferential margin and the distal margin. The results regarding the removed lymph nodes were taken cautiously because of suspected differences in the examination method of the resection specimen. Finally, concerns were raised regarding the uniformity of the registration of the postoperative complications.

The different mentioned problems that were encountered each require specific actions in the future.

Other reflective findings

The directives of the convention didn't impose a compulsory discussion of every patient diagnosed with a new oesophageal cancer on a specialized multidisciplinary meeting in an expert centre. A first characterization of the cancer patients that were not discussed on a specialized consult demonstrated that they were on average older and that the stage of their cancer was proportionally more advanced (IV) compared to the patients that were included in the convention. When comparing the unadjusted observed survival 1 year after diagnosis, survival rates for the patients that were not discussed in the convention appeared to be consistently lower than for the patients included in the convention, also when comparing the results by clinical stage. Altogether these observations warrant further investigation and should be considered when evaluating the set-up of the convention and a possible extension to a specialized multidisciplinary consult for every patient with newly diagnosed oesophageal cancer.

First results of four years convention confirm decreasing mortality

With the addition of the fourth convention year, 90-day postoperative mortality was assessed for a total of $N_{4Yconvention}$=1.555, and compared with N_{T0}=1.584. The observed 90-day postoperative mortality for malignant oesophageal cancer during the subsequent convention years evolved from 6.3% (year 1), to 11.1% (year 2), 4.2% (year 3) and 3.2% in year 4. Thereby, the overall unadjusted 90-day postoperative mortality for four years of convention is 6.2% 95%CI [5.1, 7.6], and confirms the decreasing trend.

Conclusion

The evaluation of the first three years of concentration of complex oesophageal surgery in selected expert centres within the context of a convention with the RIZIV-INAMI shows that, notwithstanding the interference of the COVID-19 pandemic, the observed overall 30- and 90-day postoperative mortality decreased in Belgium. The first results of fourth year preserve the decreasing trend. The convention successfully installed a structure of quality control and induced consistent communication between clinical experts. Given the rather short period of evaluation time, continuation of the monitoring of process- and outcome results of the convention is highly recommended.

Definitions / abbreviations

MC expert = multidisciplinary consultation on complex oesophageal pathology organized in expert centre
Non-standard surgery = emergency surgery, palliative surgery, total laryngectomy and recurrence surgery
T0: period between 2015 and 2018

AAPC	Average Annual Percentage Change
AC	Adenocarcinoma
ASA	American Society of Anesthesiologists
BCR	Belgian Cancer Registry
CCI	Charlson Comorbidity Index
CD	Clavien-Dindo
CI	Confidence Interval
CRM	Circumferential Resection Margin
ECCG	Esophageal Complications Consensus Group
GOJ	Gastro-oesophageal Junction
IMA	Intermutualistic Agency
INSZ/NISS	Identificatienummer Sociale Zekerheid / Numéro d'Identification de la Sécurité Sociale (Social Security Number)
IQR	Interquartile Range
LN	lymph node
M/F	Male/Female
MIS	Minimal Invasieve Surgery
OD	Odds Ratio
PI	Prediction Interval
RIZIV/INAMI	Rijksinstituut voor Ziekte- en Invaliditeitsverzekering / Institut National d'Assurance Maladie-Invalidité (National Institute for Health and Disability Insurance)
SCC	Squamous cell carcinoma
SD	Standard Deviation
WHO	World Health Organisation
WSR	Age-standardised rate

Introduction

1. Background convention complex surgery RIZIV-INAMI

From 1 July 2019 onwards, complex surgical procedures of the oesophagus were concentrated in 10 acknowledged expert centres that acceded to a convention with the RIZIV-INAMI (see www.riziv.fgov.be).

CENTRA VOOR COMPLEXE SLOKDARMCHIRURGIE
CENTRES POUR CHIRURGIE COMPLEXE DE L'ŒSOPHAGE

ERKENNINGS-NUMMER	CENTRUM VOOR COMPLEXE SLOKDARMCHIRURGIE	ADRES	POST	GEMEENTE	SAMENWERKING MET [1]
NUMERO D'AGREMENT	CENTRE POUR CHIRURGIE COMPLEXE DE L'ŒSOPHAGE	ADRESSE	POST	COMMUNE	COLLABORATION AVEC [1]
710406-22-194	ULB HÔPITAL ERASME	ROUTE DE LENNIK 808	1070	ANDERLECHT	
710403-25-194	CLINIQUES UNIVERSITAIRES SAINT-LUC	AVENUE HIPPOCRATE 10	1200	BRUXELLES	
710300-31-194	UZ ANTWERPEN	WILRIJKSTRAAT 10	2650	EDEGEM	ZIEKENHUIS NETWERK ANTWERPEN
710322-09-194	UNIVERSITAIR ZIEKENHUIS LEUVEN	HERESTRAAT 49	3000	LEUVEN	
710371-57-194	ZIEKENHUIS OOST-LIMBURG – SITE ST. JAN	SCHIEPSE BOS 6	3600	GENK	JESSA ZIEKENHUIS - HASSELT
710707-12-194	CHU DE LIEGE – SITE SART TILMAN	AVENUE HIPPOCRATE 15, B 35	4000	LIEGE	
710039-01-194	CHU UCL NAMUR – SITE GODINNE	AVENUE DR. G. THERASSE 1	5530	YVOIR	CLINIQUE SAINT-LUC BOUGE
710534-88-194	CENTRE HOSPITALIER DE WALLONIE PICARDE – SITE UNION	AVENUE DELMEE 9	7500	TOURNAI	GRAND HOPITAL DE CHARLEROI
710117-20-194	AZ DELTA	RODE KRUISSTAAT 20	8800	ROESELAERE	AZ SINT-JAN BRUGGE OOSTENDE
710670-49-194	UNIVERSITAIR ZIEKENHUIS GENT	CORNEEL HEYMANSLAAN 10	9000	GENT	VZW ALGEMEEN ZIEKENHUIS SINT-LUKAS & VOLKSKLINIEK

[1] Vanaf 1/1/2020 worden de ingrepen niet meer vergoed in deze ziekenhuizen / A partir du 1/1/2020 les interventions ne seront plus remboursées dans ces hôpitaux

1.1. Why concentrate complex surgical procedures?

Population-based data from the Belgian Cancer Registry (BCR) pointed out that specialized care, in particular complex surgical procedures, can be safeguarded when care is delivered in appropriate circumstances. It was shown that, in the Belgian hospitals, 30- and 90- day postoperative mortality after complex oesophageal surgery was significantly lower when the surgical procedure was carried out in a high-volume centre (*Appendix B – T0 calculation*).[1]

1.2. Aim of the convention

The aim of the convention is to improve overall quality of care that is delivered in the Belgian hospitals, and in particular to reduce postoperative mortality of complex oesophageal surgeries *(see Appendix A – convention text)*. Therefore, the convention provides reimbursement of complex surgical procedures of the oesophagus carried

out for oesophageal cancer or non-oncological oesophageal pathology in expert centres. Reimbursement of complex surgical procedures of the oesophagus is to be requested by the expert centres using the following nomenclature codes:

- 228270-228281 Thoracic or thoraco-abdominal esophagectomy or gastroesophagectomy in one procedure with restorage of intestinal continuity
- 228292-228303 Subtotal esophagectomy up to the level of the arcus aortae with restorage of intestinal continuity
- 228314-228325 Thoracic or thoraco-abdominal esophagectomy or gastroesophagectomy in one procedure with restorage of intestinal continuity and extended lymphadenectomy
- 228336-228340 Subtotal esophagectomy up to the level of the arcus aortae with restorage of intestinal continuity and extended lymphadenectomy

1.3. Monitoring of the convention: article 7.6 and 8

All acceded expert centres were monitored by means of detailed registration of each discussed patient and every complex surgical procedure that was carried out in the expert centre. Every centre received annual feedback reports that were created by the BCR and contained an overview of all registered data and quality indicators that were decided by clinical experts and described in article 7.6 of the convention (see www.riziv.fgov.be). Global year reports for the first and second year of the convention, containing data of all expert centres combined, were published by the RIZIV-INAMI. After 3 years the final evaluation of the convention was planned, as described in article 8 of the convention. The BCR was appointed by the RIZIV-INAMI to create the final evaluation report.

1.4. Audit process performed by Audit ziekenhuizen RIZIV-FOD VVVL-FAGG

Independent from the final evaluation report, Audit ziekenhuizen RIZIV-FOD VVVL-FAGG is preparing an individual audit of each acceded expert centre.

1.5. Evaluation/validation by international experts

The RIZIV-INAMI invited international experts to review the final evaluation report of the convention *(see Appendix G)*. The national scientific group Audit Belgian Esophageal Surgery was asked to formulate recommendations *(see Appendix H)*.

2. Purpose of this final evaluation report

The final evaluation report is mentioned in article 8 of the convention and aims to answer the following research questions:

- Describe the epidemiology of oesophageal cancer in Belgium
- Compare overall outcome after complex oesophageal surgery before (T0) and during convention-period
- Evaluate the quality of the individual surgical expert centres

3. Information sources consulted for the final evaluation report

To build the final evaluation report, four different data sources were used.

3.1. Complex surgery database

The complex surgery database contains all the data registered at the BCR by the expert centres (*Appendix C – registration form*). Based on this database the individual feedback reports and the global year reports were created *(Appendix D – global 3-year report, Appendix E – case mix comparisons, Appendix F – centre specific results)*.

3.2. Cancer registration database

The cancer registration database holds information of every new malignancy that is diagnosed in Belgian residents. This database was used to create the T0 calculation for the convention.

3.3. IMA database

The BCR can link the cancer registration database with the administrative database of the InterMutualistic agency (IMA). The IMA database contains information on all medical procedures and pharmaceuticals reimbursed by national health insurance. The IMA database was also used to create the T0 calculation for the convention.

3.4. Crossroadsbank Social Security

The BCR can link the cancer registration database with the database of the Social Security to obtain information on the vital status of the patients.

Remark:

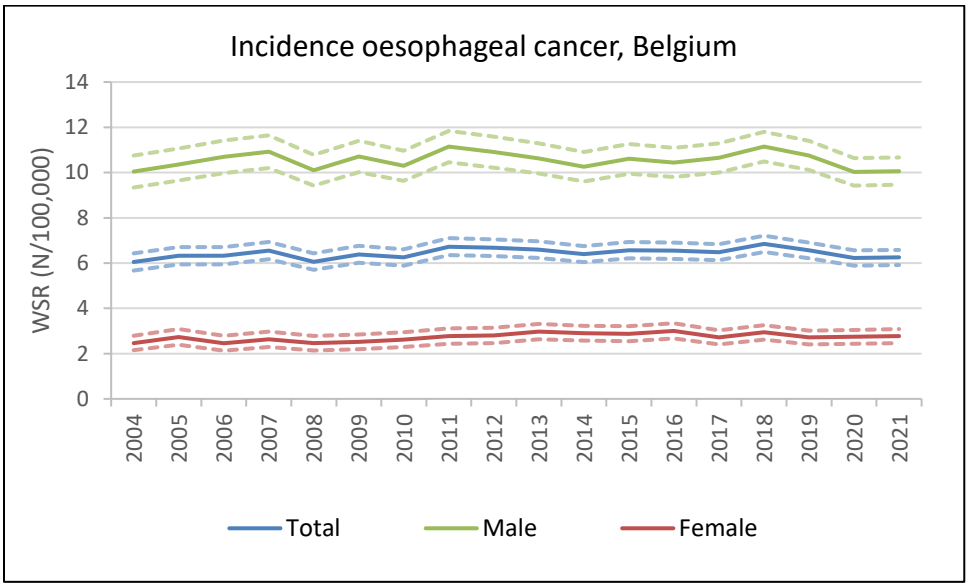
- Note that the T0 calculation published on the website of RIZIV-INAMI *(Appendix B)* applies to the time period 2008-2016, whereas for the comparison of overall outcome after complex oesophageal surgery before (T0) and during convention-period in the current report the time period 2015-2018 will be used for T0. Therefore, results for T0 in this report might differ from the results published in previous reports.
- As decided upon by the RIZIV-INAMI, only patients with official Belgian residence are included in the analyses, foreign patients are not included.
- The COVID-19 pandemic overwhelmed the Belgian health care system starting with its first wave in March 2020. During the convention years (1/7/2019 – 30/6/2022) concerns related to COVID-19 and the possible impact on surgical volumes and outcome after surgery were raised repeatedly by the clinical experts. To evaluate to some extent the impact of the crisis on surgical volumes, the BCR made predictions for the expected surgical volumes during the convention years based on incidence trends of the previous years. Based on these calculations, there was no evidence of a reduced surgical volume on the national scale. However, the BCR was not able to investigate whether there were important regional differences concerning the possible COVID-impact on individual hospital level. Also related to this topic, remarks were

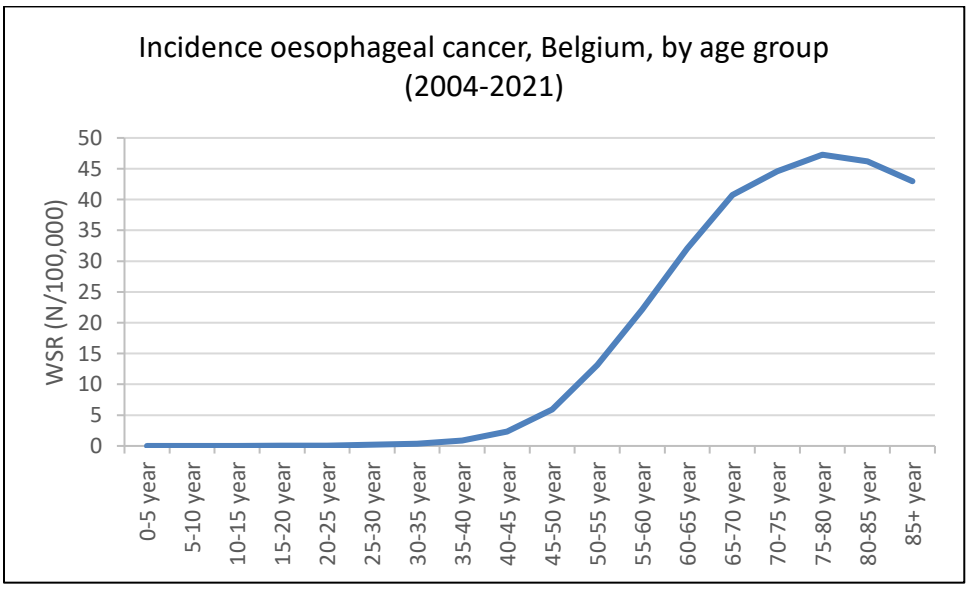
made to exclude mortality related to COVID-19 from the results. It was decided that based on international scientific standards, reported mortality should include all possible causes of death.

Epidemiology oesophageal cancer in Belgium

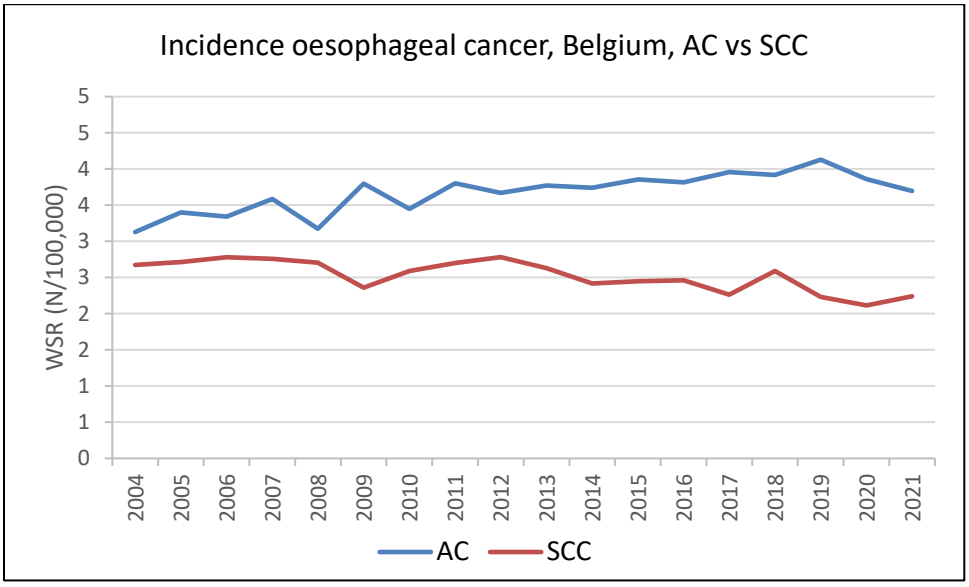
1. Incidence and trend over the years

In 2021, 1602 new diagnoses of oesophageal cancer (including the gastro-oesophageal junction (GOJ)) were notified in Belgium, of which 1207 (75%) in males and 395 (25%) in females (Male/Female (M/F) ratio 3.1). Oesophageal cancer risk is related with age, a peak in incidence is observed around the age of 75, the median age at diagnosis is 68 years. Between 2004 and 2021, the absolute number of new oesophageal cancer diagnoses increased with 40% (from 1143 to 1602 new diagnoses), corresponding to an increase of 42% in males and 35% in females. However, in essence, this increase can be explained by the growing and ageing population. When we take these elements into account and look at the age-standardized rates (WSR), we see that the overall risk of oesophageal cancer remained stable the last decades with an overall Average Annual Percentage Change (AAPC) of 0.2 (95% CI [0.0;0.5]; p>0.05) for the period 2004-2021.

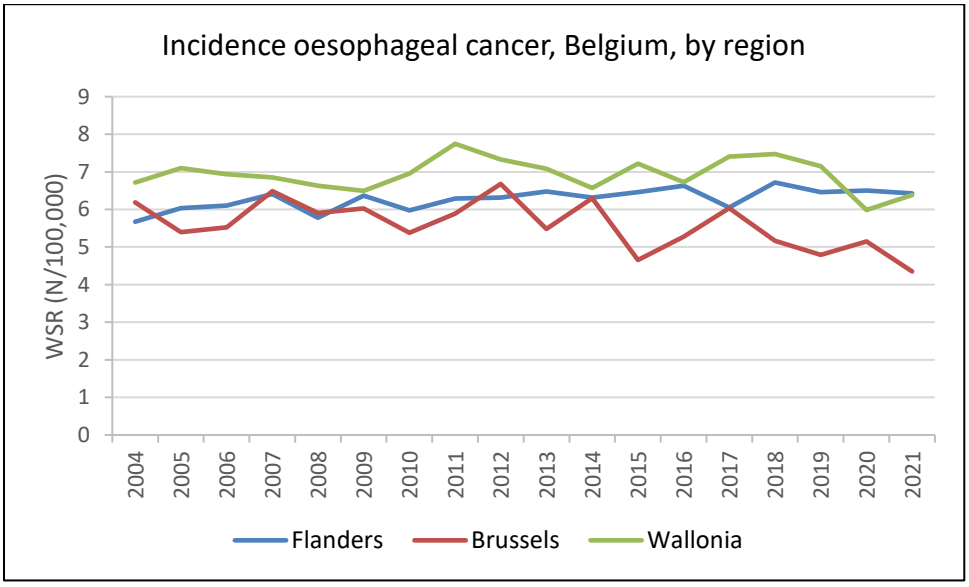




The 2 most common histological subtypes of oesophageal cancer are adenocarcinoma (AC) and squamous cell carcinoma (SCC). In 2021, 977 new diagnoses of AC and 548 of SCC were observed. Although between 2004 and 2021 the overall risk of oesophageal cancer remained stable, the risk of AC has increased (AAPC 1.1, 95% CI [0.7; 1.6], p<0.001) whereas the risk of SCC has decreased (AAPC -1.3, 95% CI [-1.8; -0.7], p<0.001).



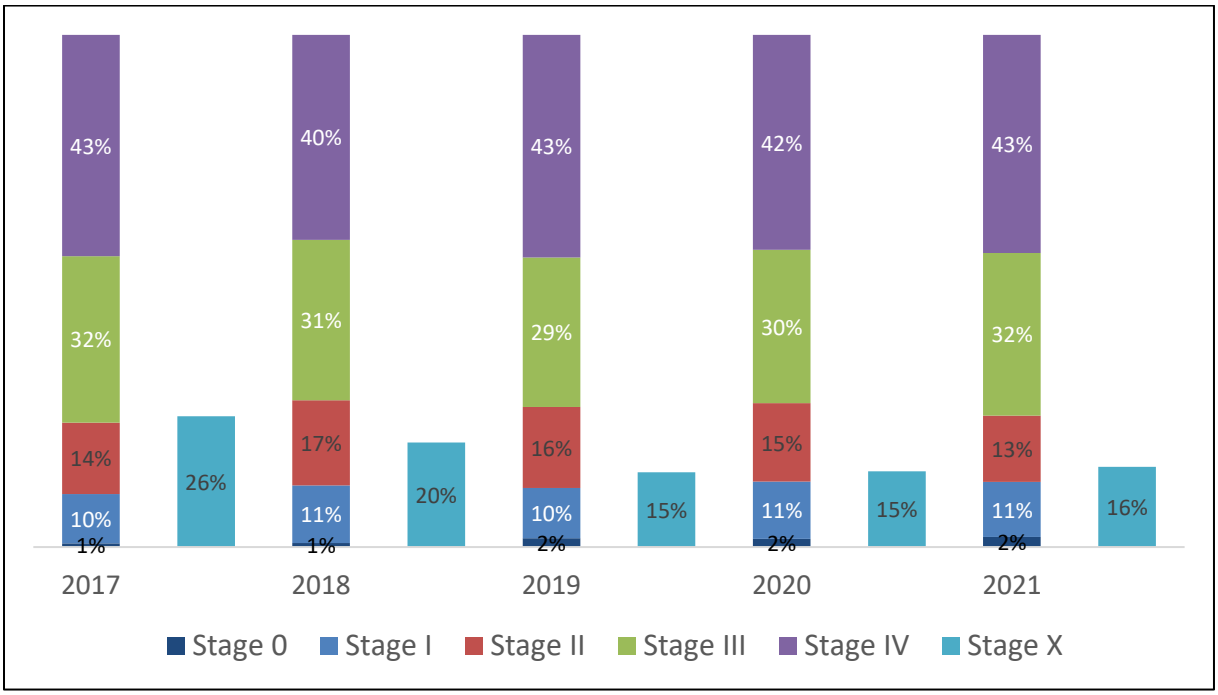
Regional oesophageal cancer risk (WSR) in Belgium is similar for Flandres and Wallonia, and a bit lower in Brussels. In 2021, 1018 diagnoses were observed in Flandres (WSR 6.4/100,000), 498 in Wallonia (WSR 6.4/100,000), and 86 in Brussels (WSR 4.4/100,000). Between 2004 and 2021, a slight increasing risk is noted in Flandres (AAPC 0.6, 95% CI [0.2; 0.9], p<0.01, a stable risk in Wallonia (AAPC -0.1, 95% CI [-0.7; 0.5], p>0.05), and a decreasing overall risk in Brussels (AAPC -1.3 95% CI [-2.2; -0.3], p=0.01).



In the year 2020, the COVID-19 pandemic caused a decrease of 6% in overall cancer incidence in Belgium compared to the year 2019.[2] In particular for oesophageal cancer, a decrease of 8% was noted in 2020 compared to 2019.

2. Stage at diagnosis

Oesophageal cancer is most often diagnosed in advanced stage. Of the diagnoses with known stage, 42% were clinical stage stage IV, 31% stage III, 15% stage II, 11% stage I and 1% stage 0 (period 2017-2021).[3]



3. Survival and trend over the years

Oesophageal cancer is known for its generally poor prognosis. Most recent CONCORD-survival data (CONCORD-3) report on the period 2010-2014, with 5-year age-standardized net survival rates for oesophageal cancer ranging between 10 and 30% in most countries.[4]

In Belgium, most up to date (period 2016-2021) 5-year relative survival (5yRS) rate of oesophageal cancer is 26.6% (95%CI [25.5; 27.7]). 5yRS in Belgium has improved slightly over the last decades, with 22.2% (95%CI [21.1; 23.2]) in 2004-2009, 24.6% (95%CI [23.6; 25.6]) in 2010-2015, and 26.6% (95%CI [25.5; 27.7]) in 2016-2021.

Survival rates vary substantially according to the stage at diagnosis, 5yRS (2016-2021) for stage I tumours is 54.6%, but decreases to 35.0% in stage II, 32.8% in stage III and 8.2% in stage IV. Also, the histological subtype influences survival, for AC only, overall 5yRS is 28.5% (95%CI [27.0; 30.0]) versus 23.2% (95%CI [21.4; 25.1]) for SCC only. Finally, survival decreases with the age at diagnosis.

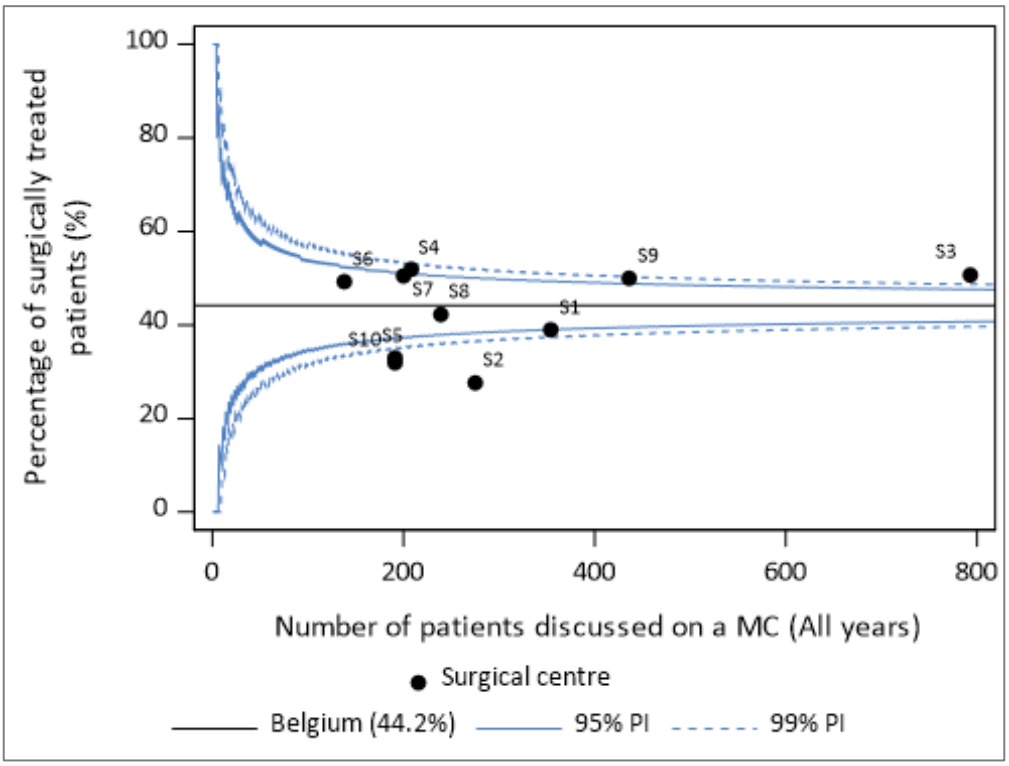
Overview convention data: numbers and volumes

As described in the convention text (article 8), each expert centre is required to achieve a minimal clinical activity after 3 years, which is defined as:

- discussion of at least 150 patients on a multidisciplinary consultation for complex oesophageal pathology (MC expert) AND
- performance of at least 75 surgical procedures (nomenclature 228270-228281, 228292-228303, 228314-228325, 228336-228340).

The decision to define the minimal surgical volume of 75 procedures over three years was based upon statistical estimates. A minimal individual volume of 75 procedures was estimated to allow a statistical comparison of the postoperative mortality rates of the expert centres.

Patients discussed on MC in expert centre [1/7/2019 – 30/6/2022]

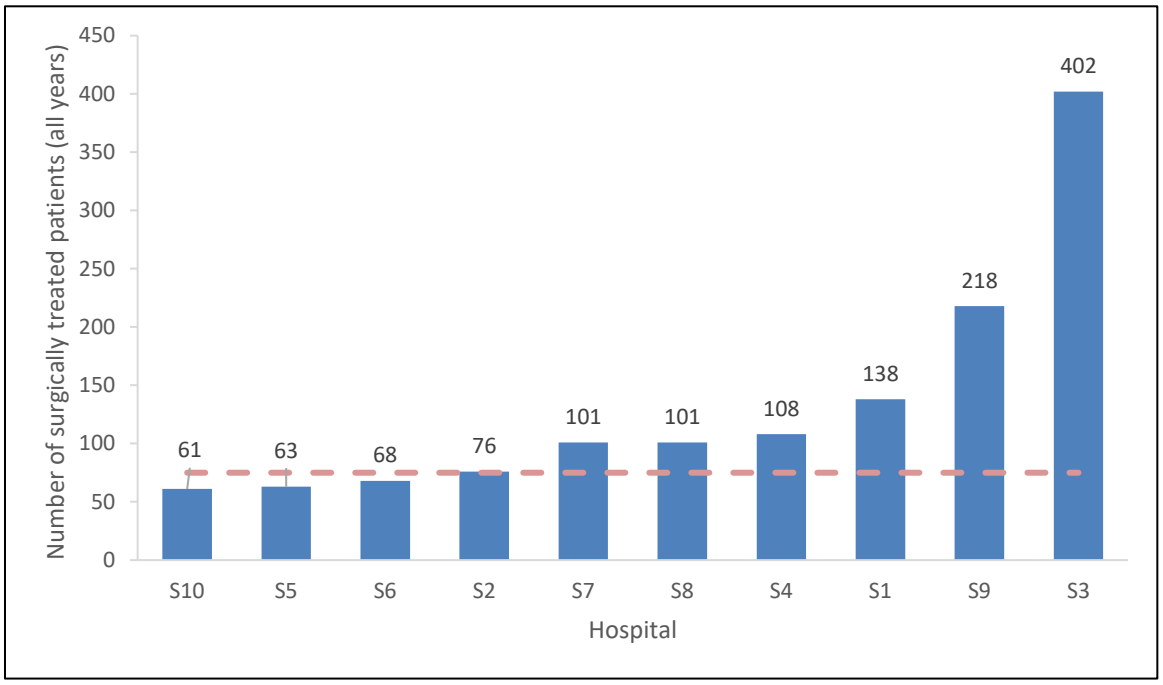


Funnel plot of the proportion of patients discussed on a MC that were treated surgically, by individual expert centre

In total, 3.025 patients were discussed on MC expert during the 3 convention years (2.869 malignant indications). On individual hospital level 1 hospital did not reach the minimum of 150 MC discussions over 3 years.

On average 44.2% of the discussed patients were subsequently selected for complex surgery. This proportion varied among the 10 centres between a minimum proportion of 27.6% and a maximum proportion of 51.9%.

Total surgical volume per expert centre [1/7/2019 – 30/6/2022]



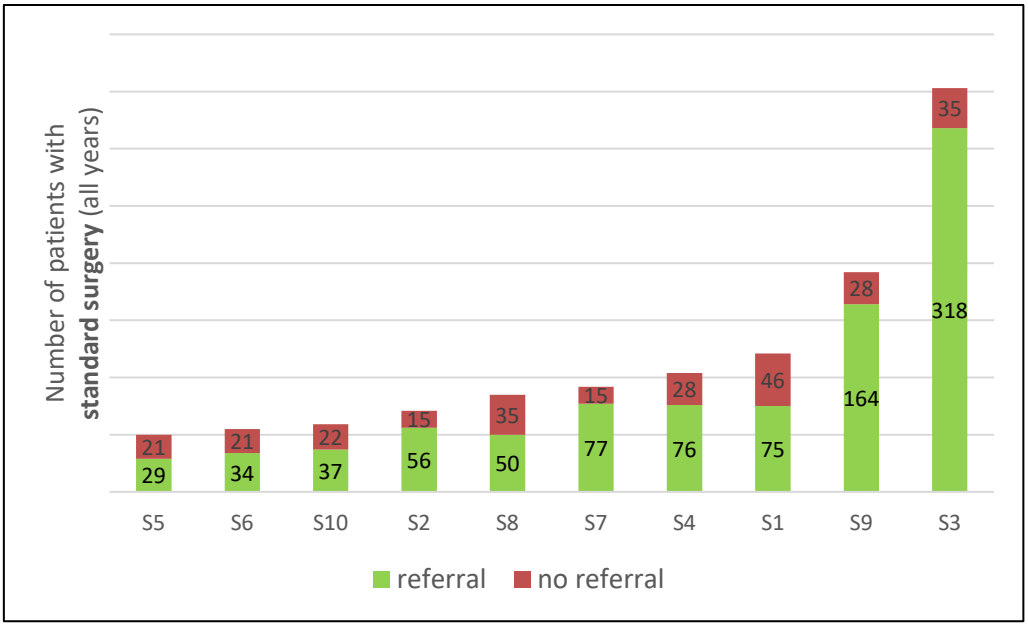
Absolute number of patients discussed on a MC expert that were treated surgically, by surgical centre

In total 1.336 complex surgical procedures were performed within the 3 convention years, 448 in year 1, 436 in year 2 and 452 in year 3. Out of the 10 expert centres, 3 centres did not reach the minimum surgical volume of 75 after 3 years. The respective centres had an individual volume of 61, 63 and 68.

The performed surgeries were carried out for malignant pathology in 93% (N=1.241).

Standard surgery versus non-standard surgery

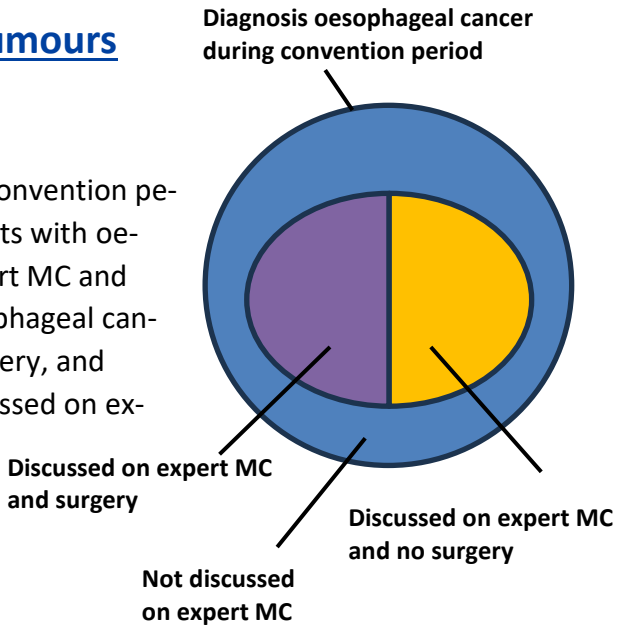
A selection of surgical procedures carried out for malignant indications were regarded as 'non-standard' surgery: emergency surgery, palliative surgery, total laryngectomy and recurrence surgery.
As such, in total 1.182 out of 1.241 surgeries for malignant pathology were considered 'standard' surgeries (=95%). At the individual centre level, the proportion of standard surgery varied among the 10 centres between 91% and 100%.



Absolute number of patients discussed on a MC expert that were treated with standard surgery, by surgical centre

Of the patients with a malignant tumour and undergoing standard surgery in an expert centre, 77% (N=916) were referred to the expert centre whereas the others (N=266) presented immediately at the expert centre. The proportion of referred patients treated with standard surgery varied among the 10 centres between 58% and 90%.

Delivered care for malignant oesophageal tumours



Description case-mix

To describe the patient and tumour characteristics for the convention period, 3 specific patient groups will be discussed. First, patients with oesophageal cancer who were discussed on a specialized expert MC and had surgery in an expert centre, second, patients with oesophageal cancer who were discussed on expert MC but did not have surgery, and third, patients with oesophageal cancer who were not discussed on expert MC. *See Appendix E – case mix comparisons*

1. Patients discussed on MC expert and selected for surgery

a) Description average case-mix of operated patients for the convention period (all patients) Appendix E, Table E1

During the convention period, 1.241 patients were operated, 980 (79%) males and 261 (21%) females (M/F ratio 3.8). The median age at the time of surgery was 66 years (IQR 60-72 years); the majority of the patients were 69 years or younger (64%) and only 5% were older than 80 years. 77% of the patients were referred to an expert centre, the remaining 23% immediately presented at the expert centre.

The patients were classified by 3 different scoring systems to describe their comorbidities, the Charlson Comorbidity Index (CCI), the American Society of Anesthesiologists (ASA) score, and the WHO performance status. The majority of the patients were in good condition at the time of surgery (WHO score 0 or 1 in 86%). 42% of the patients had no comorbidity (CCI 0). Patients that were registered with comorbidities most commonly had concomitant chronic pulmonary disease, diabetes without any damage to end-organs and peripheral vascular disease. 50% of the patients who had surgery had an ASA score of 3 (Serious systemic disease, limited activity).

For the surgically treated patients, 73% of the tumours were adenocarcinoma (AC), 25% were squamous cell carcinoma (SCC) and 2% had another histology. More than 95% of the patients were operated for a primary oesophageal tumour (N=1.184), 4.5% for an oesophageal tumour recurrence, and less than 0.5% for a metastasis. In terms of primary tumour localization, most of the tumours were located in the abdominal/lower third of the oesophagus (50%) followed by the GOJ (33%). In only 3% of the surgically treated patients, the tumour was located in the cervical or upper third of the oesophagus. The primary oesophageal tumours (N=1184) were clinically stage 0, I, II, III and IV in 1%, 10%, 18%, 49% and 21%,

respectively (for 1% the clinical stage was unknown). The tumours with clinical stage IV were subclassified as IVa (82%) and IVb (18%), i.e. locally advanced versus metastasized.

Surgeries were most commonly carried out after induction chemo(radio)therapy (70%), in 22% as primary treatment, in 5% as salvage treatment after definitive chemoradiation and the remainder were recurrences and palliative surgeries. Both for AC and SCC 77% of the patients received some type of neoadjuvant treatment (chemotherapy/radiotherapy/targeted therapy). According to the clinical stage, 0% of stage 0, 15% of stage I, 48% of stage II, 96% of stage III, and 94% of stage IV received neoadjuvant treatment.

The initial surgical technique was minimal invasive surgery (MIS) in 63% versus open surgery in 37%. The proportion of patients treated with MIS for esophageal cancer increased during the convention from 57% in year 1 to 67% in year 3.

b) Comparison of centre specific case-mix with average case-mix (all patients)

When comparing the expert centres regarding their case-mix, the age of the patients at surgery, M/F ratio and distribution between AC and SCC was comparable among all centres. As mentioned before, the patients were classified by 3 different scoring systems to describe their comorbidities, the CCI, the ASA score, and the WHO performance status. Differences in the distribution of these classifications between the centres were observed, but interpretation of the results is hampered by lack of consistency between the 3 different scoring systems within each centre.

Differences between the centres were observed regarding indications for surgical treatment. On average, 95% of the indications were primary tumours and 4.5% tumour recurrences, on centre-level, in 3 centres 100% of the indications were primary tumours without any surgical intervention for recurrence/metastasis. Also, the clinical stage of the selected patients was remarkably different from the average in some centres: on average 11% of the tumours were stage 0-I, in 1 centre the proportion of stage 0-I tumours was 17%; more pronounced were the differences in proportion of clinical stage IV tumours which on average was 21%, but ranged from 5% in one centre to 29% and even 32% in other centres. All the stage IV tumours were predominantly clinical stage IVa.

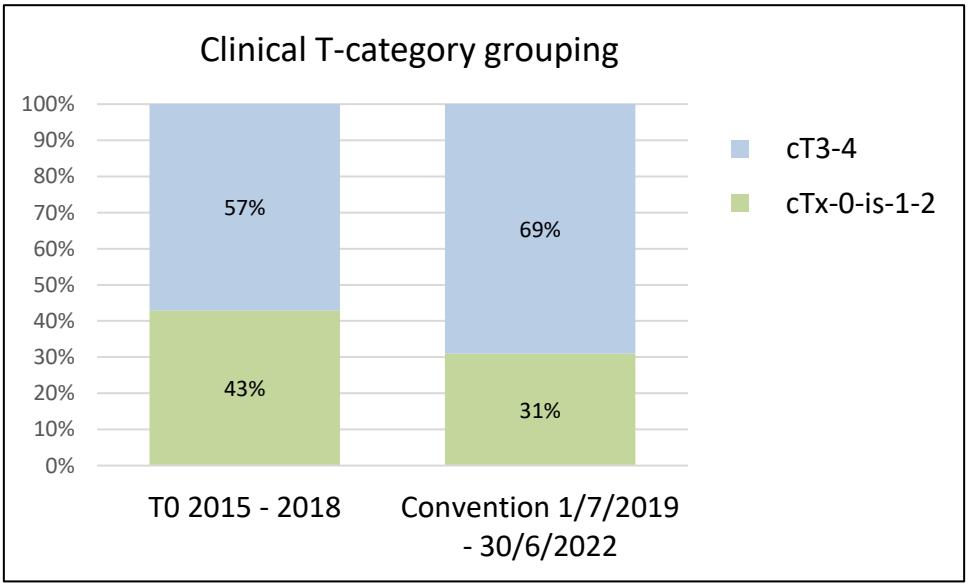
On average, neoadjuvant treatment was noted in 77% of the patients, in 2 centres the proportion rose to 84%, contrasting with 2 centres where the proportions were 66% and 67%. Also, on average 5% of the patients were treated within the convention as salvage treatment after definitive chemoradiation, in 1 centre this proportion was 17%. Finally, on average 63% of the surgeries were MIS and 37% open, in 3 centres the proportions of MIS were 90%, 93% and 99% respectively. In contrast, in 2 centres open surgery was offered to 52% and 59% of the patients, respectively.

c) *Comparison of average case-mix operated patients convention with average $T0_{(2015-2018)}$ results (only primary tumours) Appendix E, Table E2*

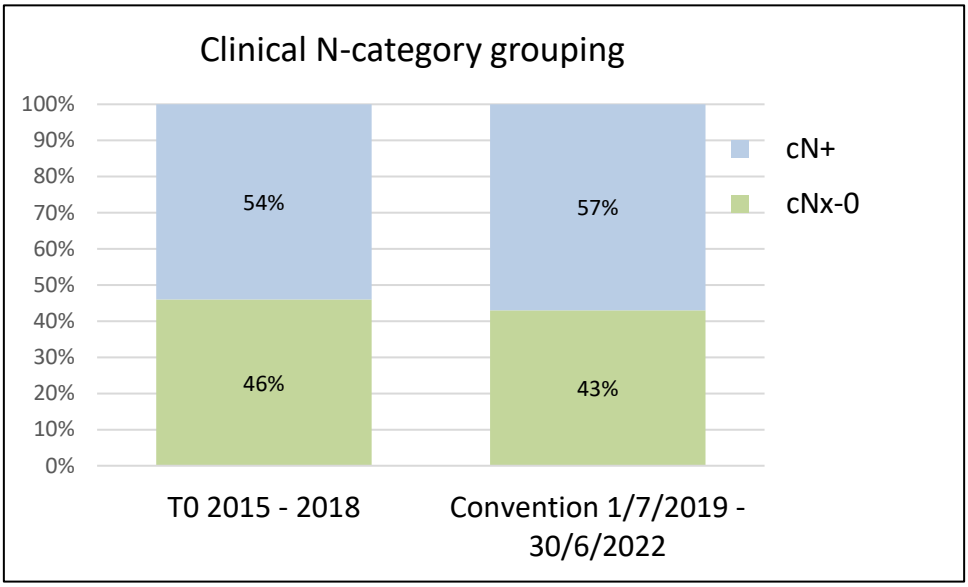
When comparing the average convention case-mix with the average $T0_{2015-2018}$ case-mix, only the primary tumours are selected in the convention, N=1.184, and compared with T0 (N_{T0}=1.584).
The age of the patients at surgery was comparable, as well as the M/F ratio and distribution between AC and SCC.

When comparing the localization of the primary tumour, there is a different distribution between the convention data and T0. In the convention, tumours more often originated in the abdominal/lower third of the oesophagus (51% vs 38% in T0) but less often in the GOJ (33% vs 39% in T0). In T0 however, 8% of the tumours had a not-specific location in the oesophagus.

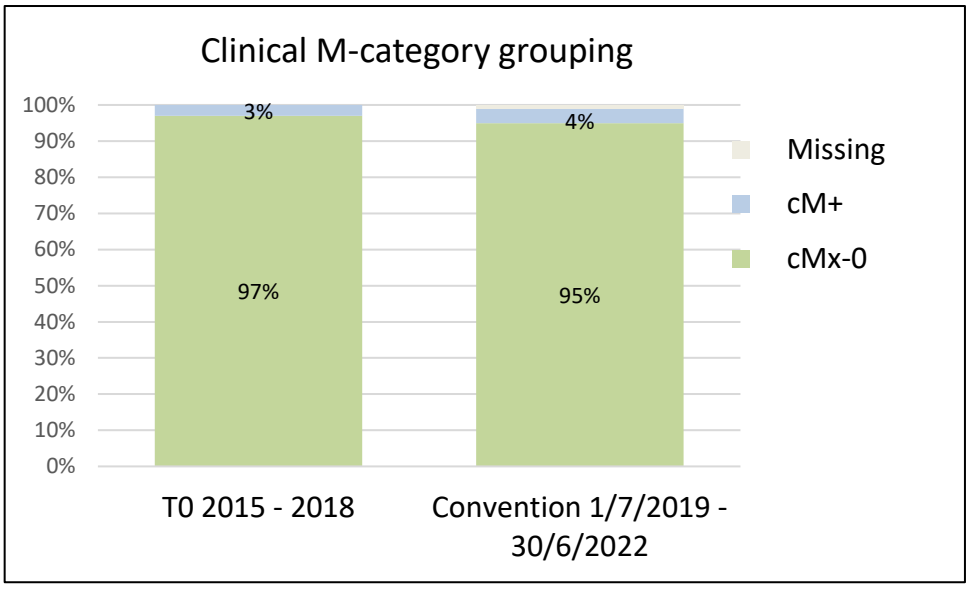
As for the comparison of the clinical stage of the patients that were selected for surgery in the 2 periods, the implementation of TNM8 in 2017 hampers the direct comparison of the clinical stage distribution in both periods of interest. Therefore the comparison is made based on the 3 TNM categories separately.[2,4]



As for clinical T, the proportion of more advanced primary tumours (cT3-4) was larger during the convention (69%) compared to $T0_{2015-2018}$ (57%). Or vice-versa, the proportion of smaller tumours decreased during the convention period.



As for clinical N status, a small increase in the proportion of positive nodes (cN1/2/3) was observed during the convention (57%) compared to $T0_{2015\text{-}2018}$ (54%).

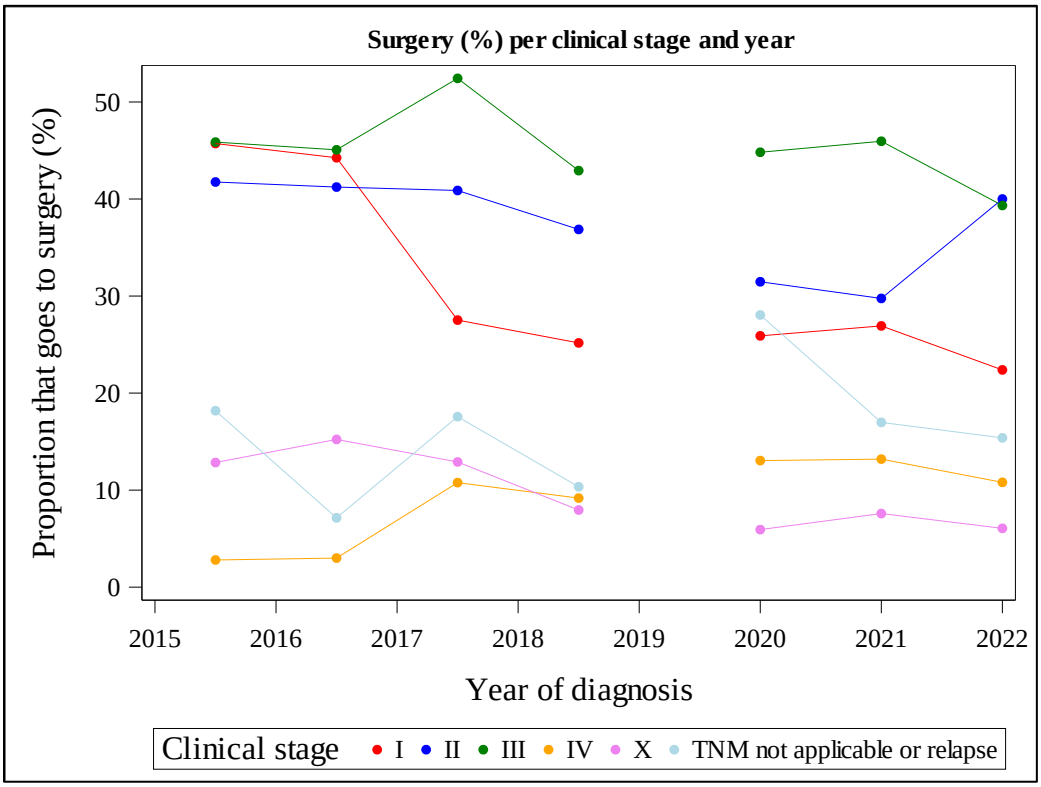


As for clinical M status, no differences were observed between both periods.

Finally, the proportion of the patients that received neoadjuvant treatment increased in the convention period (N=910; 77%) compared to $T0_{2015\text{-}2018}$ (N=1.088; 69%), the main choice of neoadjuvant treatment was chemoradiotherapy and remained proportionally comparable.

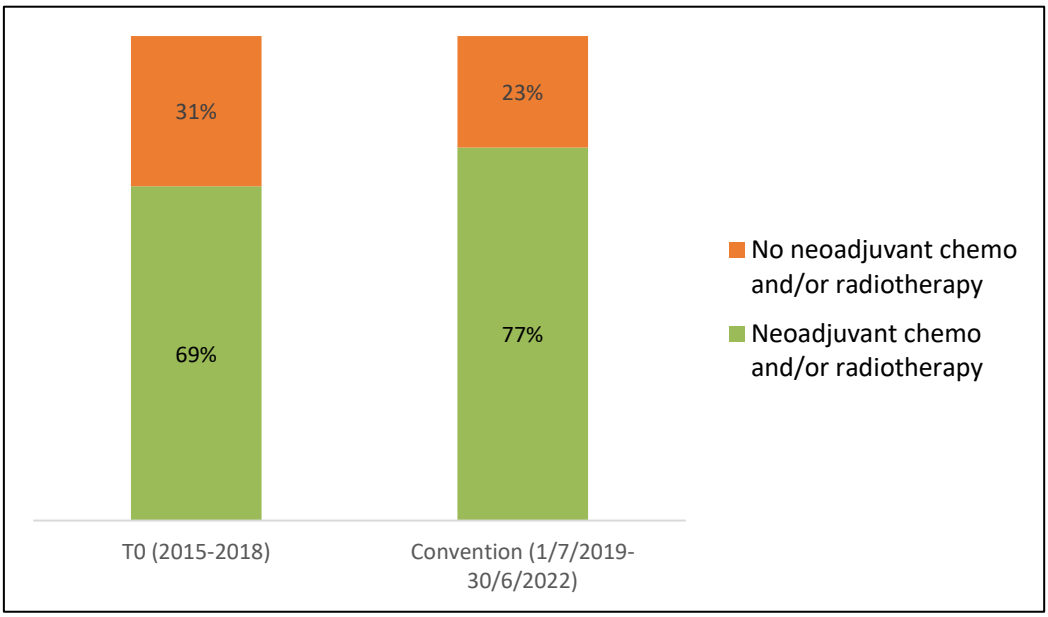
d) Observed trends in time

- *Clinical stage of tumours that are selected for surgery*



A decrease in clinical stage I tumours that are selected for surgery is observed, opposed to an increasing proportion of clinical stage IV tumours; both trends are already observed during the $T0_{2015\text{-}2018}$ period. Also remark that in 2017 the 8th edition of TNM classification was implemented, where tumours with clinical T4b or N3 no longer fall in clinical stage III but in stage IV. This can also explain (part of) the increasing proportion of stage IV in time.

- *Use of neoadjuvant treatment*



The proportion of the patients that received neoadjuvant treatment increased in the convention period (N=910; 77%) compared to $T0_{2015\text{-}2018}$ (N=1.088; 69%).

- *Surgical technique during convention years*
  During the convention period, the proportion of patients with oesophageal cancer that were treated with MIS has increased from 57% in the first year to 67% in the third year. Nevertheless, an important variation of these proportions exists between the individual centres.

2. Patients discussed on MC expert but not selected for surgery

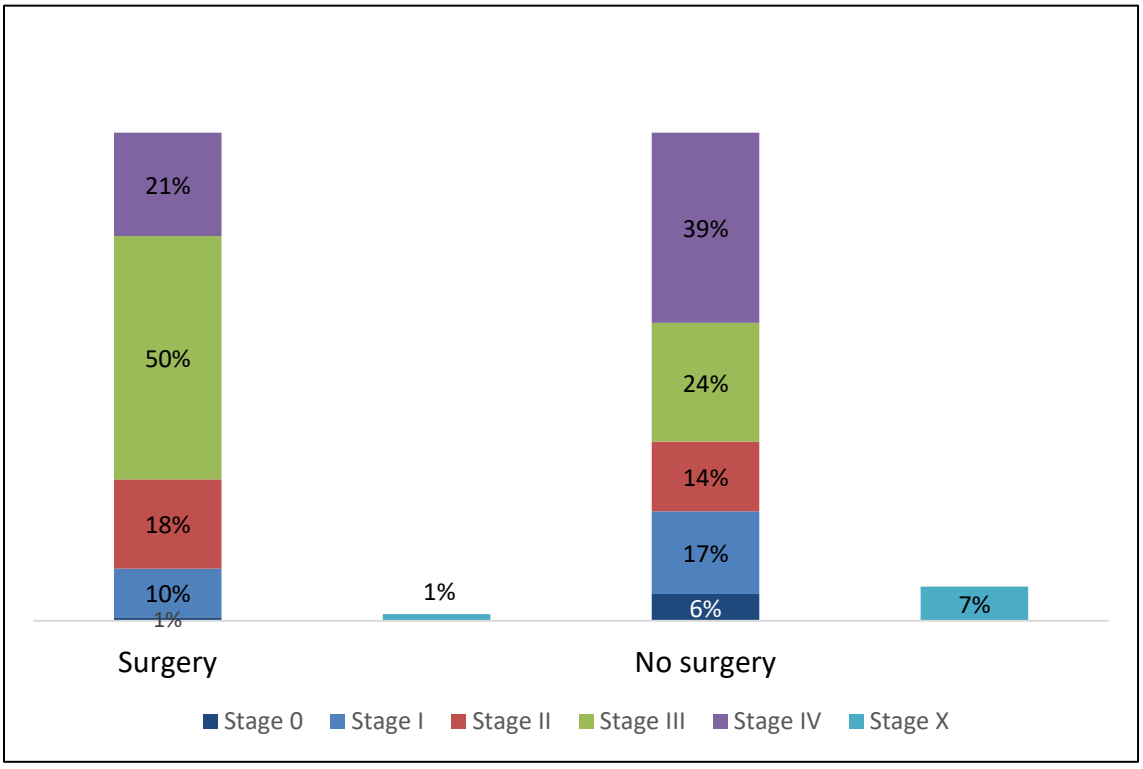
a) Description average case-mix of patients discussed on MC but not selected for surgery for the convention period (all patients)

During the convention period, 1.628 patients were discussed on MC expert for whom it was decided not to perform surgery. Of these patients there were 1.239 males (76%) and 389 females (24%). The median age at the time of surgery was 69 (IQR 62-76 years) years. The majority of the patients were in good condition at the time of surgery (WHO score 0 or 1 in 63%), 5% was scored WHO 2, and for 31% there was no information available for the WHO score. 95% of the patients were discussed because of a primary oesophageal tumour (N=1.540), 5% because of an oesophageal tumour recurrence, and 4 patients because of a metastasis. The main histological subtypes of the tumours were AC (55%) and SCC (42%).

b) Comparison of characteristics of patients discussed on MC expert that were selected for surgery versus patients that were not selected for surgery (all patients) Appendix E, Table E3

When comparing the average convention case-mix of patients selected for surgery (N=1.241; surgery group) with the average convention case-mix of patients not selected for surgery (N=1.628; no surgery group), there were no differences as for the type of lesion to treat: 95% primary tumours, 5% tumour recurrences, very few metastases. The age distribution of the patients was different, with a younger median age in the surgery group (66 years) versus the no surgery group (69 years), in the surgery group only 5% was 80 or older versus 16% in the no surgery group. M/F ratios were slightly different with 3.8 for surgery versus 3.2 in the no surgery population.

Also, the distribution between AC and SCC was different, with a remarkably larger proportion of SCC in the no surgery group (42%) compared to the surgery group (25%). The tumour localization differed between both groups, particularly for proximal/cervical tumours that were more present in the no surgery group (13% versus 3% in the surgery group) and contrarily junctional tumours that were less present in the no surgery group (17% versus 33% in the surgery group).



Remarkable differences were observed as for the clinical stage of the patients that were selected for surgery versus no surgery. In the no surgery group, a larger proportion is seen of both early-stage tumours (stage 0 and I; 21% versus 11%) and very advanced stage tumours (stage IV; 36% versus 21%), on the contrary a smaller proportion of stage II and II tumours is

observed (36% versus 67%). Also, subclassification of the stage IV tumours is, as expected, clearly different, in the no surgery group 27% tumours stage IVa and 73% IVb versus 82% IVa and 18% IVb in the surgery group. Finally, the patients that were selected for surgery were referred to the expert centre in 77%, whereas the patients for which it was decided not to offer surgery were referred to the expert centre in 62%.

3. Patients not discussed on MC expert (period 1/7/2019 – 31/12/2021)

The convention didn't impose a discussion of every patient diagnosed with a new oesophageal cancer on an MC in an expert centre. Therefore, a part of the oesophageal cancer incidence is not captured within the convention. The following results describe this specific population.

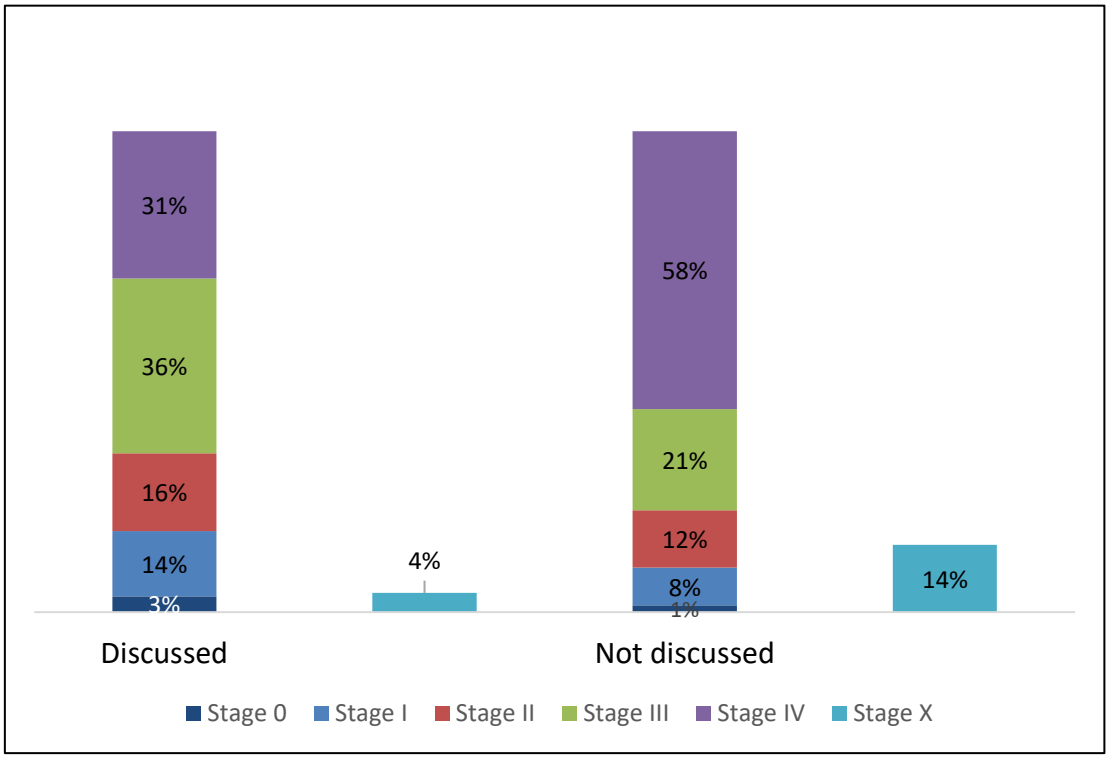
a) *Description average case-mix of patients that were not discussed on MC expert for the convention period 1/7/2019 – 31/12/2021 (only primary tumours)*

During the convention period 1/7/2019 – 31/12/2021, 1.874 patients diagnosed with oesophageal cancer and notified through the classical cancer registration were not discussed on a MC expert. Of these patients there were 1.377 (73%) males and 497 (27%) females. The mean age at the time of surgery was 73 years, 39% of the patients were 69 or younger, 32% between 70 and 79 and 29% was 80 or older. Most of the patients were in good condition at the time of diagnosis (WHO score 0 or 1 in 71%), 21% was scored WHO 2 or 3, and 1% WHO 4. The main histological subtypes of the tumours were AC (62%) and SCC (32%). The primary oesophageal tumours were clinically stage 0, I, II, III and IV in 1%, 7%, 10%, 18% and 50% (for 14% the clinical stage was unknown). The tumours with clinical stage IV, were subclassified as IVa and IVb in 13% and 87%.

b) *Comparison of case-mix characteristics of patients **discussed on MC expert** (period 1/7/2019 – 30/6/2022) versus patients **not discussed on MC expert** (period 1/7/2019 – 31/12/2021) (only primary tumours) Appendix E, Table E4*

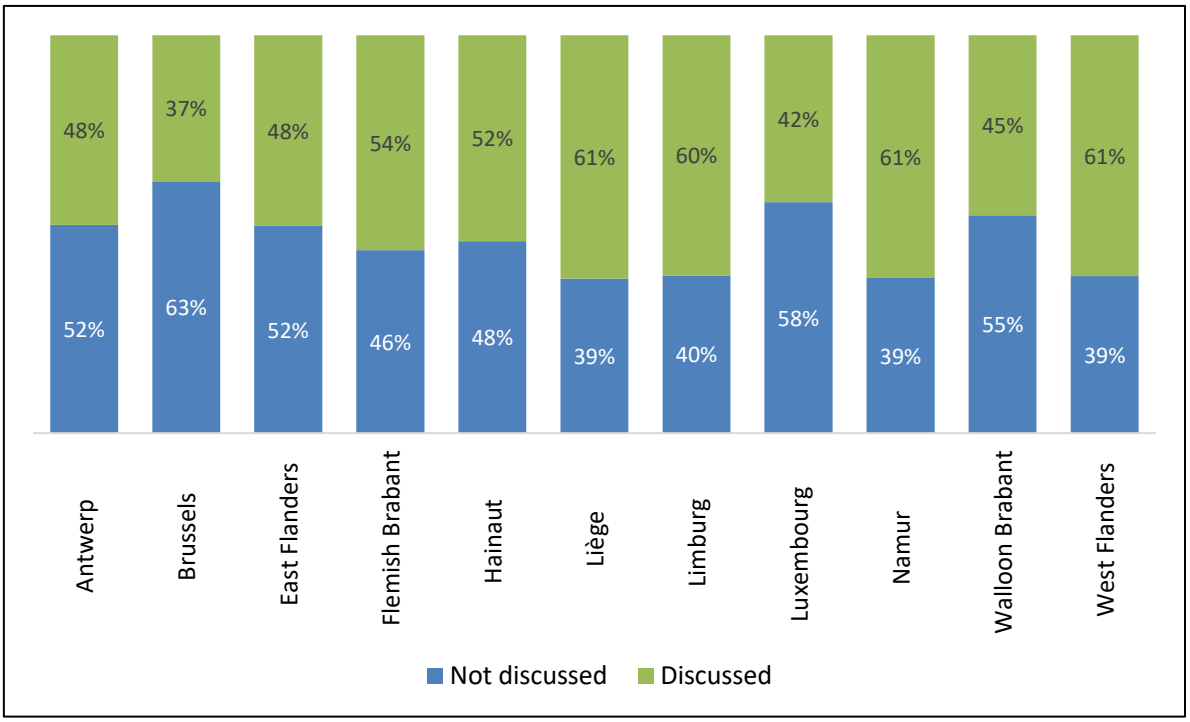
During the convention period 1/7/2019 – 30/6/2022, 2.724 patients diagnosed with primary oesophageal cancer were discussed on MC expert, whereas 1.874 newly diagnosed patients in the period 1/7/2019 – 31/12/2021 were not discussed on expert MC (=population not discussed). The patients that were discussed on MC expert were statistically significantly younger than those who were not discussed on MC expert ($p<0.0001$), 11% of the convention population was 80 years or older compared to 29% of the population not discussed. M/F ratio was 3.4 in the convention, versus 2.8 in the population not discussed.

Remarkable differences were observed as for the clinical stage of the patients.



In the convention population, a larger proportion is seen of stage 0, I, II and III tumours (66% compared to 36% in population not discussed) and conversely the proportion of stage IV tumours and unknown stage tumours is smaller (29% stage IV and 4% stage unknown compared to 50% and 14% in the population not discussed). Also, the subclassification of the stage IV tumours is clearly different in the convention population (44% stage IVa and 54% IVb) versus the population not discussed (13% IVa and 87% IVb).

Furthermore, there are differences between the 11 provinces in Belgium in terms of the proportion of the patients with newly diagnosed esophageal cancer residing in a particular province that are (not) discussed on an expert MC.

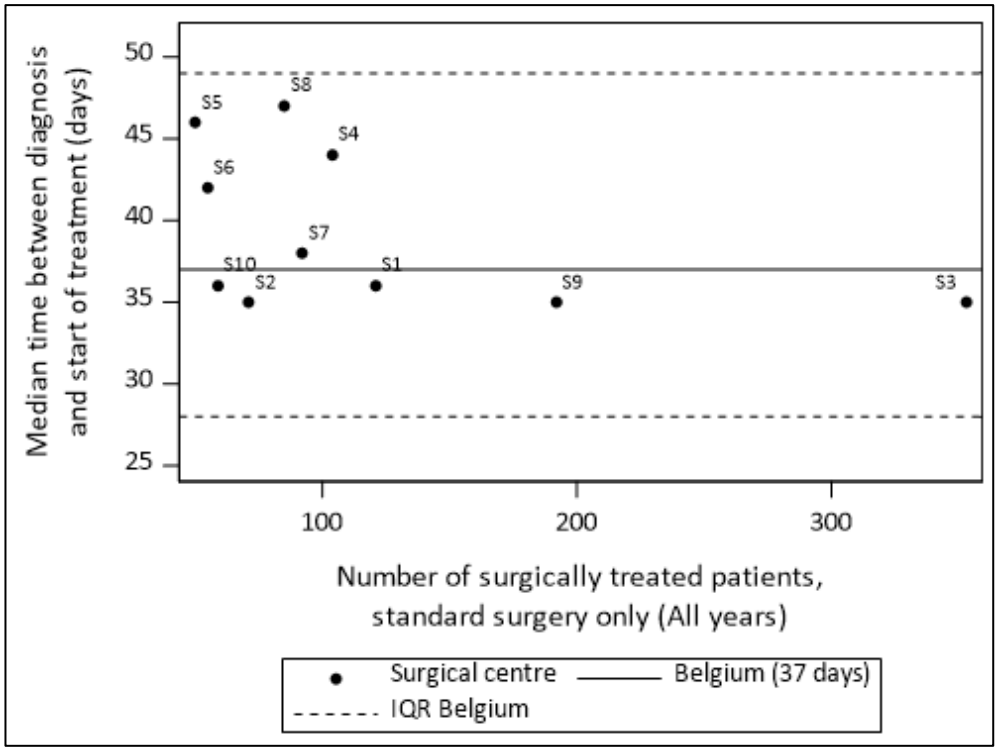


Percentage of the total incidence of oesophageal malignancies in a specific province that was discussed or not discussed on a specialized expert MC

The figure demonstrates for each province the total number of patients with newly diagnosed esophageal cancer (100%), and shows the proportion of patients that was discussed or was not discussed on an expert MC. A higher % of patiënts residing in Brussels (63%) and Luxembourg (58%) were not discussed on an expert MC, whereas in Liège (39%), Namur (39%), West Flanders (39%) and Limburg (40%) the proportion of not discussed patients was lower.

Median time between anatomopathologically confirmed diagnosis and start of any treatment (for standard surgery/for all operated patients with primary tumours)

a) Description average results for the convention and centre specific results, *standard surgery (Appendix F)*



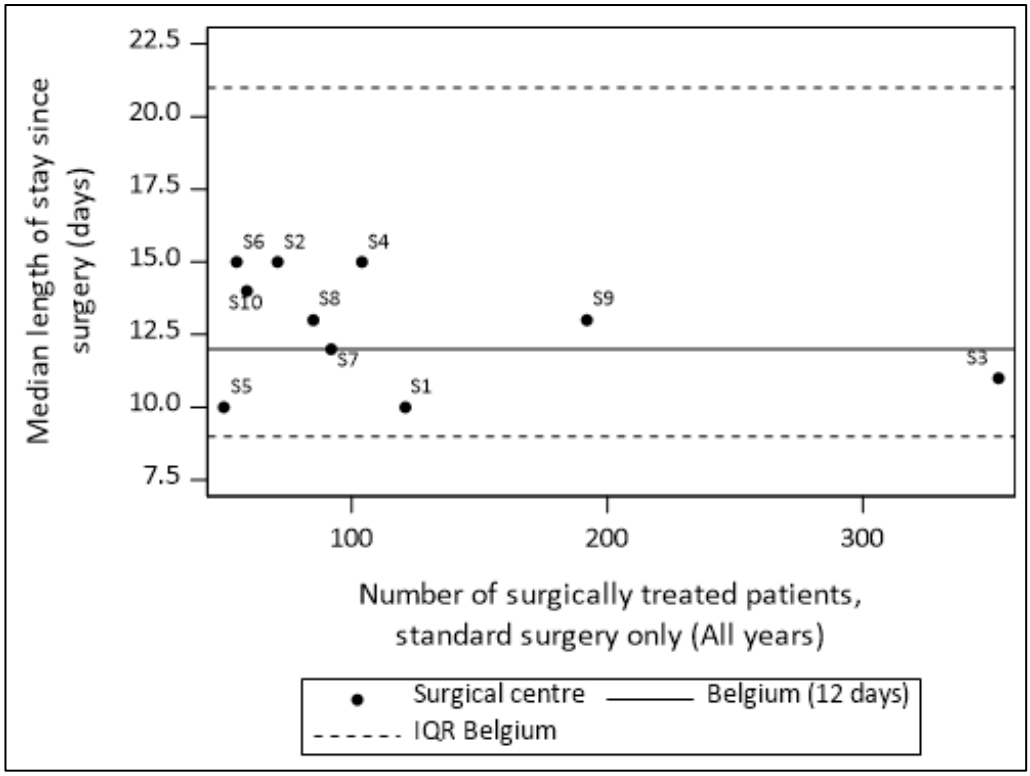
Patients with oesophageal cancer that underwent standard surgery had a median time between confirmed diagnosis and start of *any first* treatment of 37 days (interquartile range (IQR) 28-49). The median time to first treatment was similar for patients who presented immediately at the expert centre and those who were referred to an expert centre, namely 36 days (IQR 27-49) versus 38 days (IQR 28-49), no statistically significant difference (p=0.9132). On individual expert centre level, median time to first treatment was comparable for 6/10 centres, 4 centres had a longer median time to first treatment of 42 days (IQR 26-56) to the maximum median time of 47 days (IQR 29-57).

b) Comparison of average convention results for *all operated primary tumours* with average $T0_{(2015\text{-}2018)}$ results

The median time between confirmed diagnosis and start of any first treatment (options regarded as first treatment being chemotherapy, radiotherapy or surgery) for the patients in $T0_{2015\text{-}2018}$ (N=1.584) was 39 days (IQR 28-55), compared to an identical result for the convention for primary malignant tumours with surgery (N=1.184) of 39 days (IQR 28-50).

Length of stay in the expert centre (for standard surgery)

a) Description average results for the convention and centre specific results, *standard surgery (Appendix F)*



Patients with oesophageal cancer that underwent standard surgery had a median length of hospital stay of 12 days (IQR 9-21). In 4 expert centres the median length of stay was equal to or shorter than the overall result, with a minimum of 10 days (IQR 8-14), the longest median length of hospital stay was noted in 3 expert centres and was 15 days for the 3 centres. In these 3 centres, the proportions of open surgical approach were 11%, 24% and 46% respectively (compared to an overall average of 37% open surgical approach). As such, the prolonged hospital stay cannot clearly be linked with the surgical approach.

b) Comparison of average convention results with average $T0_{(2015\text{-}2018)}$ results

Data on length of hospital stay are not available for the T0 period.

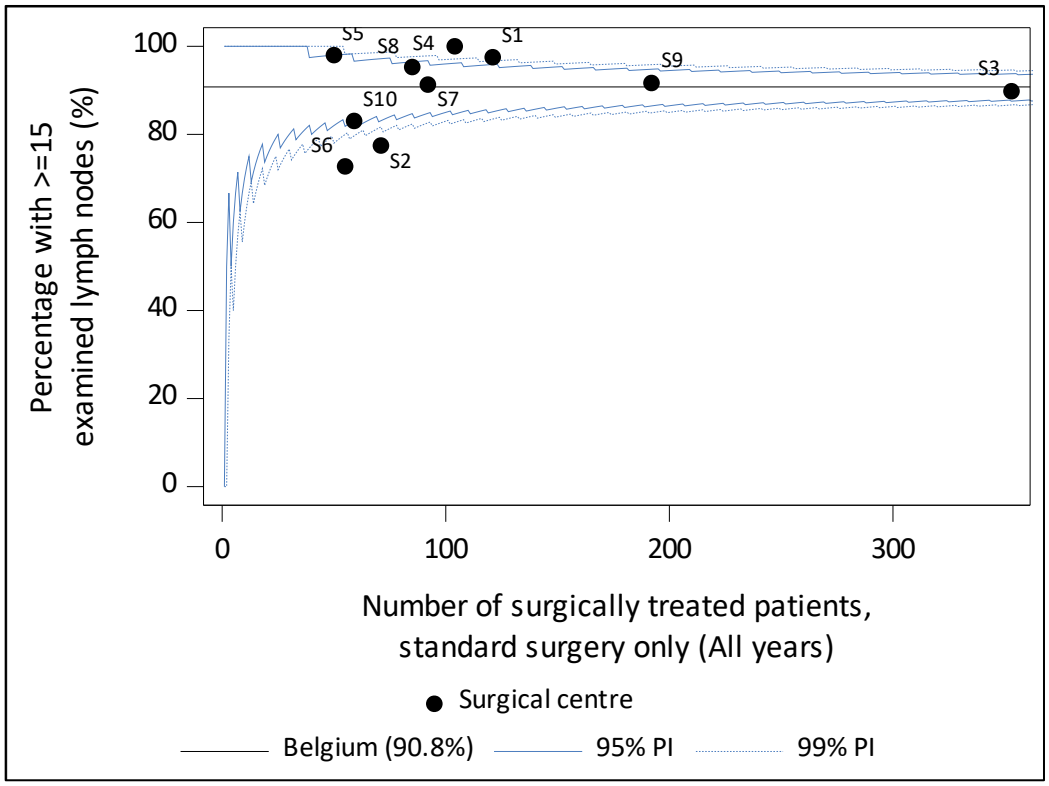
Proportion of surgically treated patients with >= 15 LN examined (for standard surgery)

The number of resected lymph nodes has been identified as independent predictor of survival after esophagectomy.[6-8] Unfortunately, concerns were raised by the clinical experts as for the reporting of the number of resected lymph nodes. It was said that there was no clear

standard as for which lymph nodes needed to be counted, and that therefore important variation in the way of reporting exists between the different expert centres.

a) Description average results for the convention and centre specific results, *standard surgery (Appendix F)*

On average, in 91% of the patients with standard surgery ≥15 LN were examined. When the surgery intention was primary surgery, ≥15 LN were examined in 94% of the patients, compared to 90% when the surgery was performed after induction therapy, and in 85% when surgery was performed as salvage post-radical chemo- and/or radiotherapy.



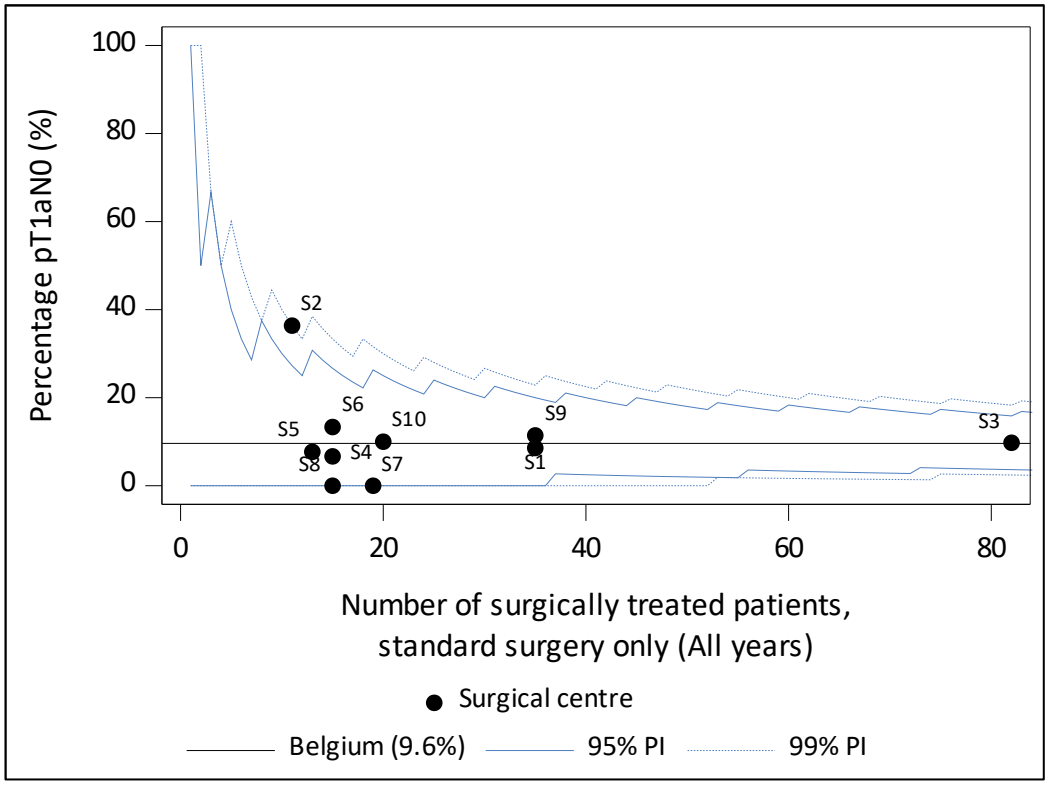
In 3 expert centres, ≥15 LN were examined in less than the average of 91% of the patients (with the minimal centre result being 73%). In 1 centre, all patients with standard surgery had ≥15 LN examined.

b) Comparison of average convention results with average $T0_{(2015\text{-}2018)}$ results

Data on number of examined lymph nodes are not available for the T0 period.

Proportion of surgically treated patients that were pT1aN0 (standard surgery)

a) Description average results for the convention and centre specific results, *standard surgery (Appendix F)*



Ten percent of all patients without neoadjuvant treatment who had standard surgery were pT1aN0 (N=25/260). In 2 centres, the proportion was larger than the average, with a maximum centre result of 36% (N=4/11).

As for the oesophageal tumours that concerned pT1aN0 (N=25), in 64% of the cases the tumour was clinically staged as I, and in 28% as clinical stage II. In addition, the majority of the pT1aN0 tumours were adenocarcinoma (N=18; 72%). The type of performed surgery was mainly MIS (N=18; 72%).

b) Comparison of average convention results with average $T0_{(2015\text{-}2018)}$ results

Data are not available for the T0 period.

Mortality

1. 30-day postoperative mortality

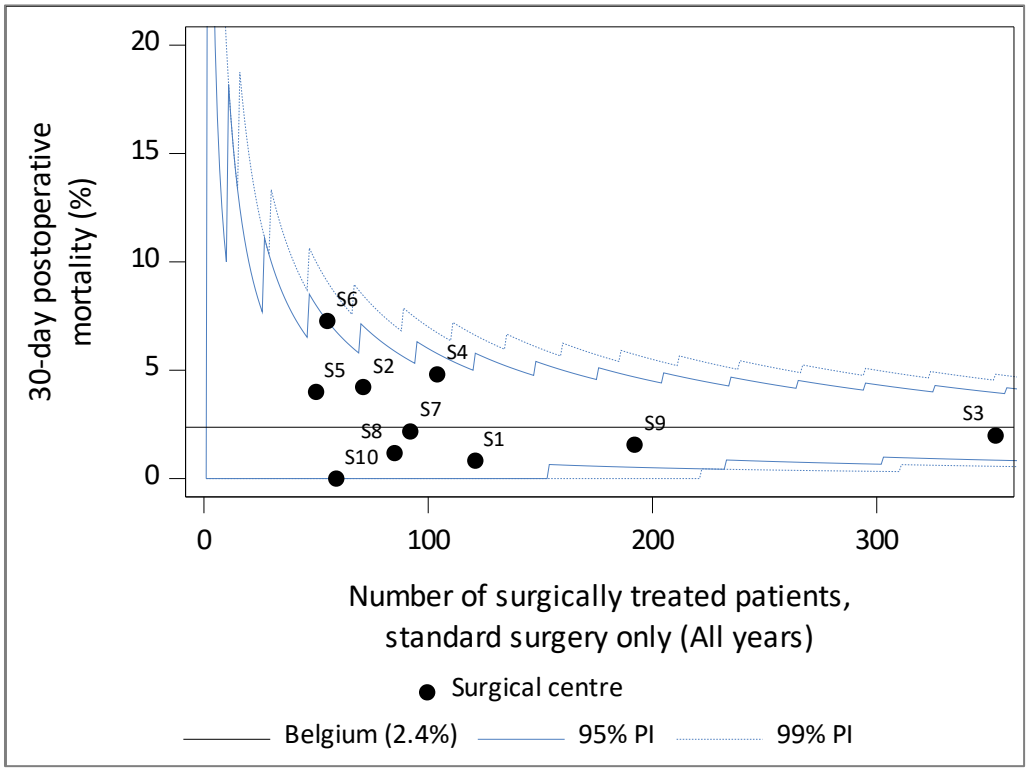
The overall observed 30-day postoperative mortality over the 3 years is 2.7% (95%CI [1.9, 3.8]), with an absolute number of deaths of 34. During the 3 years, 30-day postoperative mortality fluctuated, namely 3.1% in the first year, 4.0% in the second year, and 1.2% in the third year. The overall 30-day postoperative mortality was higher in patients with 'non-standard' surgery (10.2%; 95%CI [3.8, 20.8]) compared to 'standard' surgery (2.4%; 95%CI [1.6, 3.4]).

Remark: COVID-19 crisis
Remarks were made by clinicians to exclude mortality cases related to COVID-19 from the results. It was decided that based on international scientific standards, reported mortality should include all possible causes of death. For information, in 2 cases (2/34) COVID-19 was mentioned in the description of the cause of death for the 30-day mortality.

a. Description average results for the convention and centre specific results

Unadjusted 30-day postoperative mortality, standard surgery (Appendix F)

In patients who received standard surgery, the average 30-day postoperative mortality was 2.4% 95%CI [1.6, 3.4] (28 deaths over 1182 surgeries), with 2.5% in the first year, 3.4% in the second, and 1.2% in the third year.



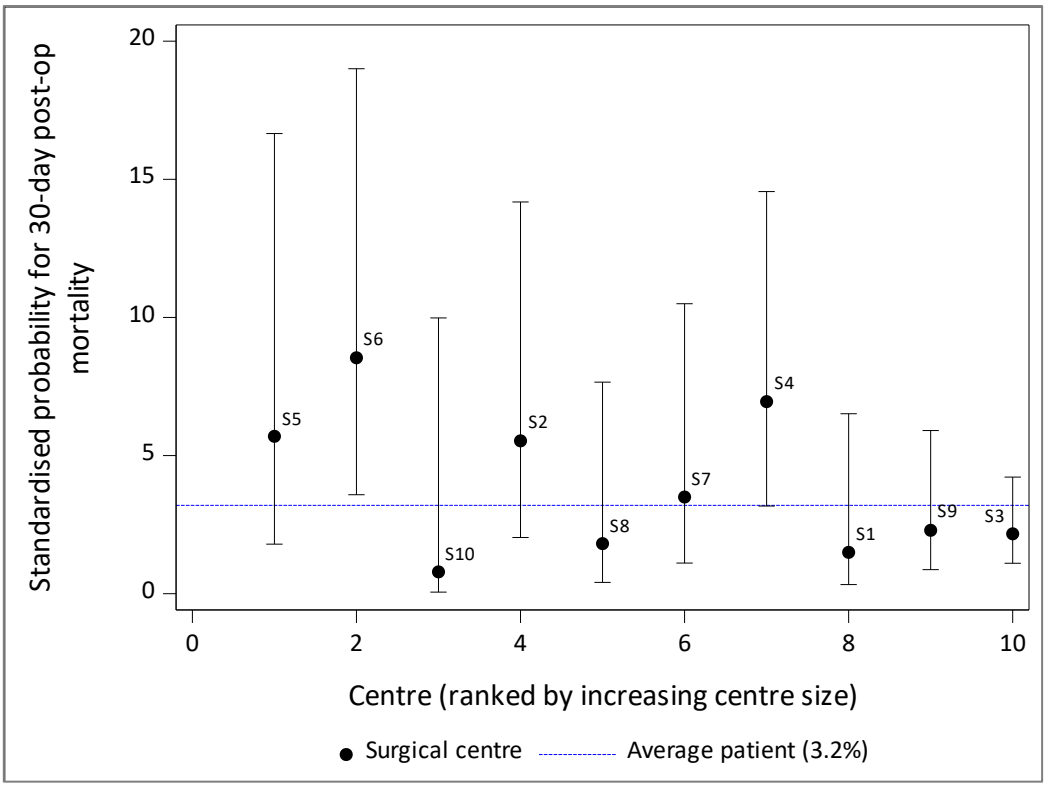
The average centre specific results for 30-day postoperative mortality ranged between 0% up to 7.3%, in 4 centres the 30-day postoperative mortality was higher than the Belgian average, but all the results remained within the 95% prediction interval (PI).

Adjusted 30-day postoperative mortality, standard surgery

To enable comparison of the centre-specific results, case-mix adjusted odds ratios (OR) for postoperative mortality within 30 days and the centre specific direct standardized 30-day mortality rates (%), together with their accompanying 95%CI, are calculated. The adjustment factors were selected by the Audit Belgian Oesophageal Surgery (ABES). The 'average patient' OR and direct standardized result are weighted averages of the individual centre results with the fraction of patients per centre as weights. The 'average patient' results for the case-mix adjusted OR and the direct standardized mortality serve as references and enable comparison of the individual centre results with the reference. An individual centre result is significantly different from the average result if the average result is not included in the centre specific confidence interval.

	Adjusted Odds Ratio			Standardised probability (%)		
Expert centres	Estimate	95% CI	Average patient	Estimate	95% CI	Average patient
S5	1.94	[0.58, 6.50]	1.06	5.7	[1.8, 16.7]	3.2
S6	3.07	[1.15, 8.25]	1.06	8.5	[3.6, 19.0]	3.2
S10	0.24	[0.02, 2.73]	1.06	0.8	[0.1, 10.0]	3.2
S2	1.88	[0.65, 5.45]	1.06	5.5	[2.0, 14.2]	3.2
S8	0.57	[0.13, 2.41]	1.06	1.8	[0.4, 7.7]	3.2
S7	1.14	[0.35, 3.68]	1.06	3.5	[1.1, 10.5]	3.2
S4	2.43	[0.99, 5.94]	1.06	7.0	[3.2, 14.6]	3.2
S1	0.47	[0.11, 1.99]	1.06	1.5	[0.3, 6.5]	3.2
S9	0.73	[0.27, 1.98]	1.06	2.3	[0.9, 5.9]	3.2
S3	0.69	[0.32, 1.49]	1.06	2.2	[1.1, 4.2]	3.2

Adjusted for surgery intention, primary tumour location, CCI and clinical stage (as proposed by Audit Belgian Esophageal Surgery).



The postoperative mortality probability was modelled using a logistic regression model. All the possible two-way interaction terms between the case-mix variables were evaluated during the model building procedure. The quality of the regression was assessed considering the deviance as well as Pearson goodness-of-fit and the Hosmer and Lemeshow goodness-of-fit test, and the residual plots were examined for potential influential points and resolved when needed.

The average direct standardized 30-day postoperative mortality for standard surgery was 3.2%. One centre had a significantly higher postoperative mortality than the average, namely 8.5% 95%CI [3.6, 19.0], 1 centre performed borderline with 7.0% 95%CI [3.2, 14.6], all other centres performed statistically not different from the average result.

b. Comparison of average convention results for *all operated primary tumours* with average $T0_{(2015\text{-}2018)}$ results

The overall unadjusted 30-day postoperative mortality during the $T0_{2015\text{-}2018}$ period (N=1.584) was 4.2% 95%CI [3.3, 5.3]. During the convention period the unadjusted result including *all operated primary* tumours was 2.8% 95%CI [1.9, 3.9].

When adjusting both results for case-mix characteristics (age group, sex, WHO performance score, clinical TNM-categories, primary tumour localisation), the adjusted OR for the convention period - with the $T0_{2015\text{-}2018}$ period as the reference - was 0.688 95%CI [0.438-1.081]. Therefore, although a decreasing trend is observed in the unadjusted overall 30-day postoperative mortality during the convention in comparison to the $T0_{2015\text{-}2018}$ period, the decrease is not significantly significant (p=0.1051).

2. 90-day postoperative mortality

Currently, the international standard for 90-day mortality after oesophageal surgery in high-volume centres is 4.5%.[9,10] The Belgian results for 90-day mortality after oesophageal surgery that were provided by the BCR for the period 2008-2018 revealed significant differences according to the annual hospital volume.[1] It was shown that in the only 2 Belgian hospitals having an annual volume of at least 40 surgeries in this time period, 90-day postoperative mortality was significantly lower compared to all the other hospitals, with an adjusted OR of 0.4 which can be translated in a direct standardised probability of 5% versus 12% 90-day mortality in high versus low volume hospitals respectively.

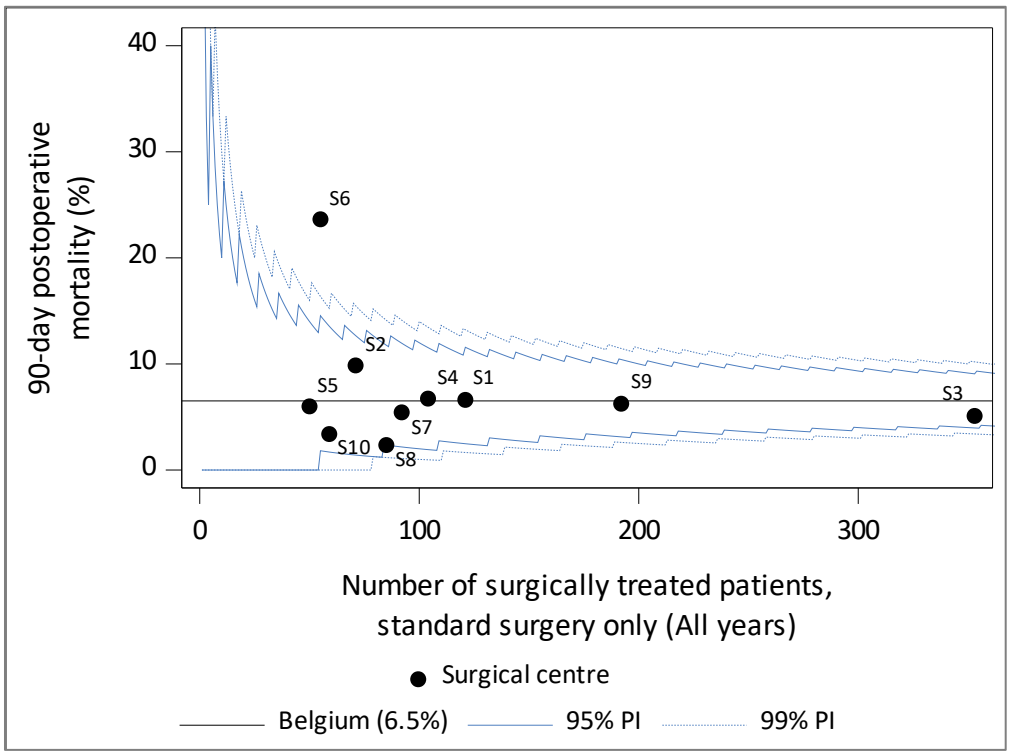
a. Description average results for the convention and centre specific results

The overall observed 90-day postoperative mortality over the 3 convention years is 7.1% (95%CI [5.7, 8.7]), with an absolute number of deaths of 88. During the 3 years, 90-day postoperative mortality fluctuated, namely 6.5% in the first year, 10.9% in the second year, and 4.1% in the third year. The overall 90-day postoperative mortality was higher in patients with non-standard surgery (18.6%; 95%CI [9.7, 30.9]) compared to standard surgery (6.5%; 95%CI [5.2, 8.1]).

Cause of death between 30 and 90 days after surgery
When reviewing all the reported causes of death that occurred between 30 and 90 days after surgery (N=54), 50/54 were specified. 11/50 deaths (22%) were related to progressive disease. For 7/50 (14%) deaths palliative care or euthanasia was mentioned. In 3/50 (6%) reported causes of death a relation with COVID-19 was mentioned.

Unadjusted 90-day postoperative mortality, standard surgery (Appendix F)

In patients who received standard surgery, the average 90-day postoperative mortality was 6.5% 95%CI [5.2, 8.1] (77 deaths over 1182 surgeries), with 5.8% in the first year, 9.7% in the second, and 4.2% in the third year.



The average centre specific results for 90-day postoperative mortality ranged between 2.4% up to 23.6%. In 2 centres the 90-day postoperative mortality was higher than the Belgian average, with one result outside the 95% PI.

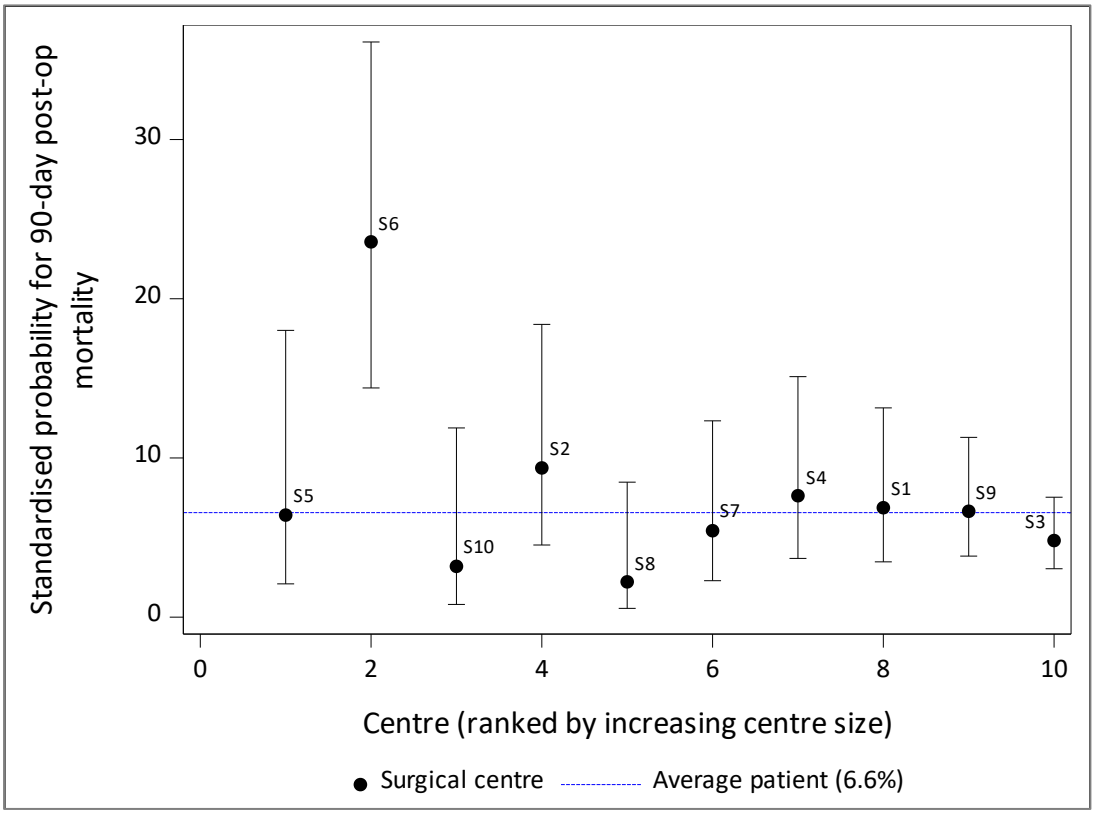
Adjusted 90-day postoperative mortality, standard surgery

The adjustment factors were selected by the Audit Belgian Oesophageal Surgery (ABES).

	Adjusted Odds Ratio			Standardised probability (%)		
Expert centres	Estimate	95% CI	Average patient	Estimate	95% CI	Average patient
S5	1.01	[0.33, 3.05]	1.08	6.4	[2.1, 18.0]	6.6
S6	4.80	[2.50, 9.22]	1.08	23.6	[14.4, 36.1]	6.6
S10	0.48	[0.13, 1.78]	1.08	3.2	[0.8, 11.9]	6.6
S2	1.54	[0.71, 3.34]	1.08	9.4	[4.5, 18.4]	6.6
S8	0.33	[0.09, 1.21]	1.08	2.2	[0.6, 8.5]	6.6
S7	0.84	[0.35, 2.01]	1.08	5.4	[2.3, 12.3]	6.6

	Adjusted Odds Ratio			Standardised probability (%)		
Expert centres	Estimate	95% CI	Average patient	Estimate	95% CI	Average patient
S4	1.22	[0.57, 2.62]	1.08	7.6	[3.7, 15.1]	6.6
S1	1.09	[0.53, 2.24]	1.08	6.9	[3.5, 13.1]	6.6
S9	1.05	[0.57, 1.93]	1.08	6.7	[3.8, 11.3]	6.6
S3	0.74	[0.43, 1.26]	1.08	4.8	[3.0, 7.5]	6.6

Adjusted for surgery intention, primary tumour location, CCI and clinical stage (as proposed by Audit Belgian Esophageal Surgery).



This table and figure show the case-mix adjusted odds ratio for postoperative mortality within 90 days and the centre specific direct standardized 90-day mortality (%), together with their accompanying 95% confidence intervals. Interpretation and modelling are similar to results for the 30-day postoperative mortality (cfr supra).

The average direct standardized 90-day postoperative mortality for standard surgery was 6.6%. One centre had a significantly higher postoperative mortality than the average, namely 23.6% 95%CI [14.4, 36.1], all other centres performed statistically not different from the average result.

b. Comparison of average convention results for *all operated primary tumours* with average $T0_{(2015-2018)}$ results

The overall unadjusted 90-day postoperative mortality during the $T0_{2015-2018}$ period (N=1.584) was 9.5% 95%CI [8.1, 11.1]. During the convention period the unadjusted result including *all operated primary* tumours was 7.2% 95%CI [5.8, 8.8].

When adjusting both results for case-mix characteristics (age group, sex, WHO performance score, clinical TNM-categories, primary tumour localisation), the adjusted OR for the convention period - with the $T0_{2015-2018}$ period as the reference - was 0.797 95%CI [0.593, 1.071]. Therefore, although a decreasing trend is observed in the unadjusted overall 90-day postoperative mortality during the convention in comparison to the $T0_{2015-2018}$ period, the decrease is not statistically significant (p=0.132).

Survival

In Belgium, overall 5yRS of oesophageal cancer is 26.6% (period 2016-2021). Survival rates vary substantially according to the stage at diagnosis, for clinical stage I tumours 5yRS is 55%, but decreases to 35% in stage II, 33% in stage III and 8% in stage IV.

For the convention period 1/7/2019 – **31/12/2021** (last 6 months of 3-year convention not yet available), 3.930 patients were diagnosed with oesophageal cancer and notified through the cancer registration in the BCR database. Because of the limited follow-up time, survival results are limited to 1 year survival.

For the total Belgian malignant oesophageal cancer cohort, overall observed 1 year survival (1yOS) was 57.1% 95%CI [55.5, 58.6]. According to the stage at diagnosis, for clinical stage I tumours 1yOS was 82%, but decreases to 67% in stage II, 68% in stage III and 42% in stage IV (see Table 1 below).

Remark: death *by all causes* is reported.

1. Unadjusted observed survival 1 year after surgery for patients discussed on MC expert and **selected for surgery**

For the following analyses, 1yOS will be assessed after the *date of surgery* (not after date of diagnosis).

a. Description average results for surgery during the convention (all patients)

Overall 1yOS for the convention (N=1.241, all surgeries) was 79.9% 95%CI [77.5, 82.2]. According to the stage at diagnosis, for clinical stage I tumours 1yOS was 92%, and decreases to 86% in stage II, 79% in stage III and 73% in stage IV.

b. Comparison of average convention results for *all operated primary tumours* with average $T0_{(2015-2018)}$ results

Overall 1yOS for the convention (N=1.184, all surgeries for primary tumours) was 80.3% 95%CI [77.8, 82.6]. Overall 1yOS for the $T0_{2015-2018}$period (N=1.584) was 75.9% 95%CI [73.7, 77.9] (Table 1 below).

According to the stage at diagnosis, in $T0_{2015-2018}$ 1yOS for clinical stage I tumours was 89%, and decreased to 76% in stage II and 71% in stage III and IV. For the convention, 1yOS for clinical stage I tumours was 92%, and decreased to 86% in stage II, 79% in stage III and 73% in stage IV.

2. Unadjusted observed survival 1 year after diagnosis of patients discussed on MC expert but **not selected for surgery**

For the following analyses, 1yOS will be assessed after the *date of diagnosis*.

Description average results during the convention (all patients discussed on MC expert and no surgery)
Overall 1yOS for the convention (N=1.574) was 64.9% 95%CI [62.3, 67.3]. According to the stage at diagnosis, for clinical stage I tumours 1yOS was 84%, and decreases to 67% in stage II, 53% in stage III and 48% in stage IV (Table 1 below).

3. Unadjusted observed survival 1 year after diagnosis of patients that were **not discussed on MC expert**

For the following analyses, 1yOS will be assessed after the *date of diagnosis*.

Description average results during the convention period (all patients not discussed on MC expert)
Overall 1yOS for the convention period [1/7/2019 – 31/12/2021] (N=1.874) was 40.2% 95%CI [38.0, 42.4]. According to the stage at diagnosis, for clinical stage I tumours 1yOS was 69%, and decreases to 48% in stage II, 53% in stage III and 31% in stage IV (Table 1 below).

Table 1 - Overview of the unadjusted 1-year OS for the different subgroups of patients with oesophageal cancer; all calculated after date of diagnosis

	Convention period				**$T0_{2015-2018}$ period**	
	[1/7/2019 – 31/12/2021] All primary oesophageal cancers	**[1/7/2019 - 30/06/2022]** With surgery*	**[1/7/2019 - 30/06/2022]** No surgery	**[1/7/2019 – 31/12/2021]** Not discussed on MC	**$T0_{2015-2018}$** All primary oesophageal cancers	**$T0_{2015-2018}$** With surgery*
Overall 1yOS	57% (N=3930)	87% (N=1184)	64% (N=1536)	40% (N=1874)	55% (N=6129)	82% (N=1584)
cStage I	82% (N=362)	92% (N=113)	84% (N=214)	69% (N=117)	77% (N=605)	89% (N=227)
cStage II	67% (N=482)	90% (N=208)	67% (N=180)	48% (N=178)	68% (N=781)	82% (N=326)
cStage III	68% (N=1017)	85% (N=563)	53% (N=308)	53% (N=313)	64% (N=1532)	80% (N=714)
cStage IV	42% (N=1438)	84% (N=214)	48% (N=491)	31% (N=861)	36% (N=1737)	81% (N=112)
cStage IVA	59% (N=348)	85% (N=195)	45% (N=130)	37% (N=113)	57% (N=245)	83% (N=66)
cStage IVB	37% (N=1090)	81% (N=44)	49% (N=353)	31% (N=748)	35% (N=767)	_ (N=19)

* Calculated from date of diagnosis

1yOS by clinical stage is only provided if clinical stage information is available (so not provided for clinical stage unknown or not applicable).

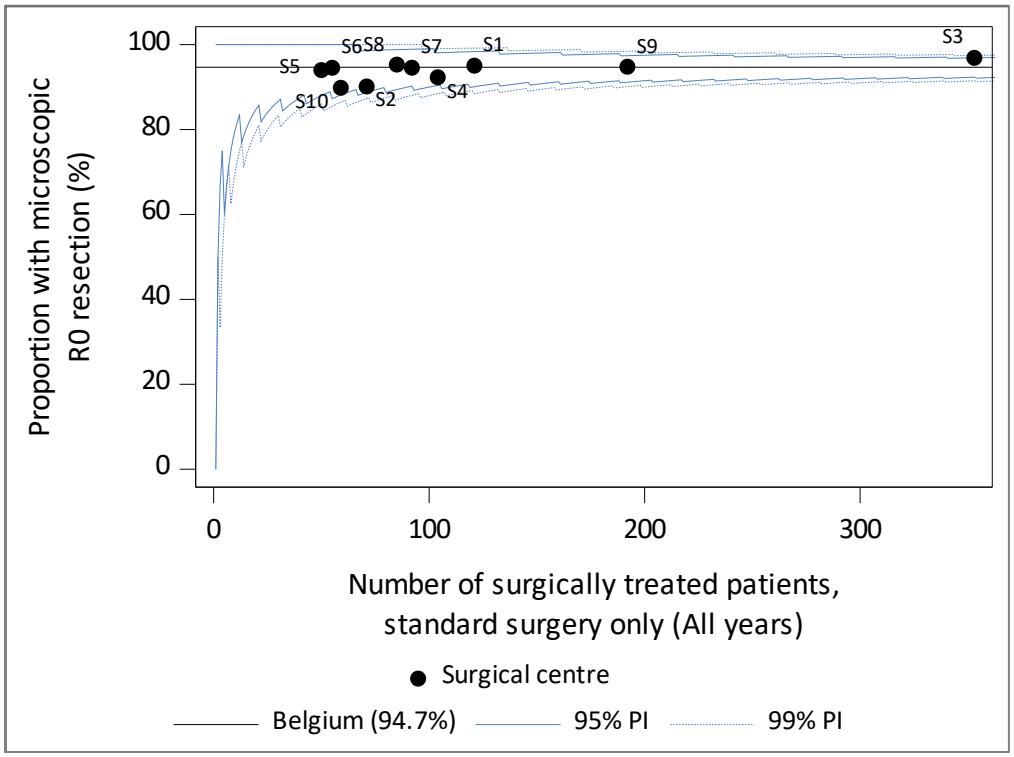
Proportion of surgically treated patients with a R0 resection (standard surgery)

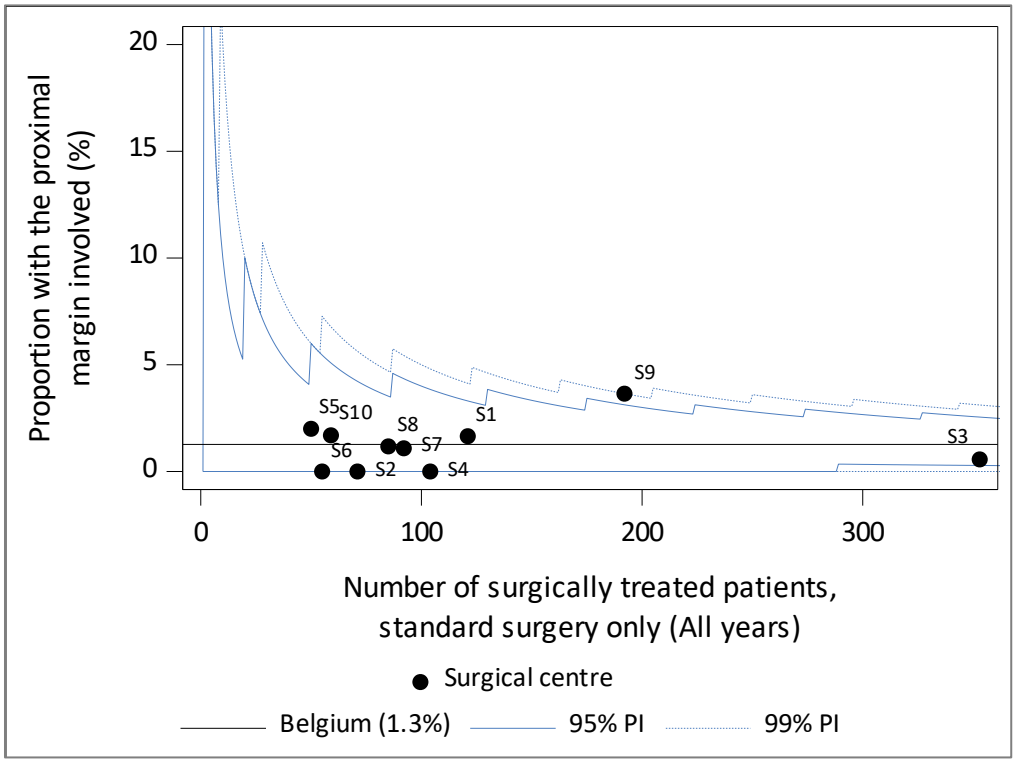
The radicality of resection (R0 versus R1 versus R2 resection) has been identified as independent predictor of survival after esophagectomy.[11-13] R0 resection of the proximal margin can be conclusively confirmed on intraoperative frozen section analysis, in contrast with the circumferential resection margin (CRM) where the neighbouring structures of the oesophagus may limit the radicality or the resection and therefore more often lead to R1 resection.

In the convention database, data were collected on radicality of the resection (Appendix C). Unfortunately, in case of R1 resection, only involvement of the proximal margin was documented, and no information concerning CRM involvement or distal margin involvement. This limitation of the data was stressed by the clinical experts and it was therefore also decided that the results for the indicators on the resection margin status could not be used to evaluate the quality of the surgical procedures or compare the results of the different centres.

Description average results for the convention and centre specific results

99% of all surgically treated patients had a macroscopic R0 resection (1171/1182) and 95% had a microscopic R0 resection (1119/1182). In only 1% of the cases (15/1182), the proximal margin was involved.





On centre level, the microscopic R0 resection rate ranged from 89.8% to 99.7%. Three centres had a % lower than the average of 95%. As for proximal margin involvement, the maximal rate noted was 3.6% (7/192).

Postoperative complications (standard surgery)

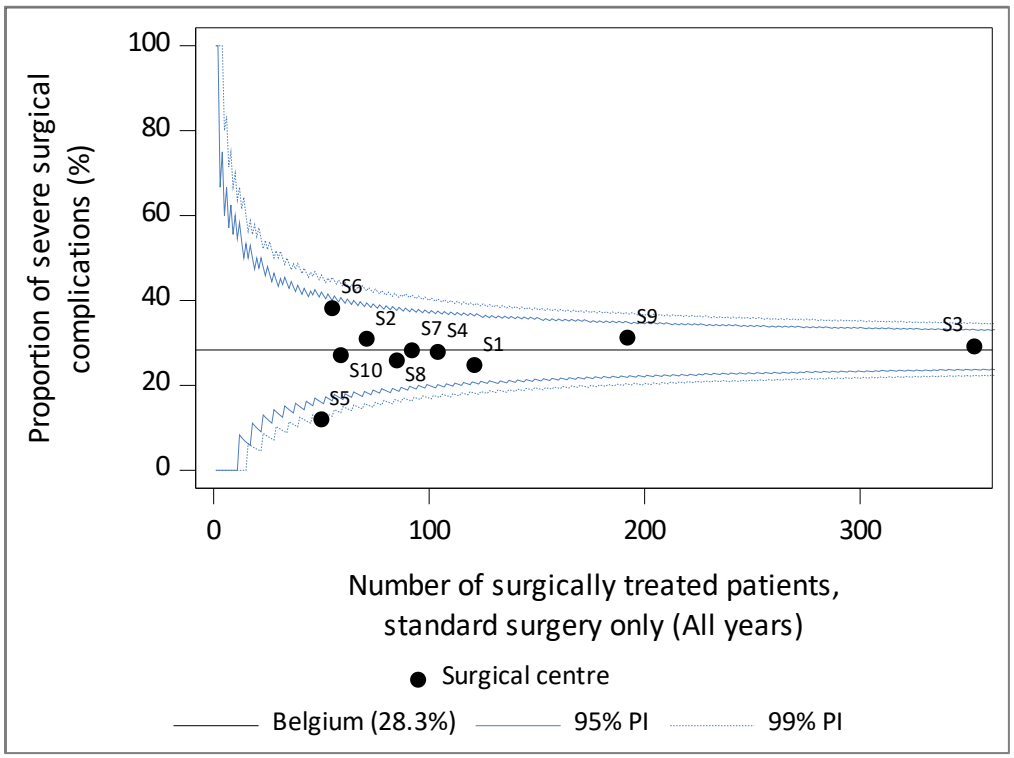
Oncologic esophagectomy is a demanding procedure that is associated with significant morbidity and mortality. The complication rate after esophagectomy is generally high, and results reported by experienced centres range from 30 – 50%. The Oesophageal Complications Consensus Group (ECCG) developed a standardized platform for reporting mortality, complications and quality measures associated with esophagectomy.[14] Results from this initiative were published and documented an overall incidence of complications of 59%.[15] The most common complication was pneumonia (14.6%), anastomotic leak was documented in 11.4%, chyle leak in 4.7%. Severe complications Clavien-Dindo (CD) ≥IIIb were recorded in 17.2%.

Description average results for the convention and centre specific results *(Appendix F)*

Complications were rated using the Clavien-Dindo (CD) classification system. The most common type of complication during the convention period was pneumonia (N=246; 21%), followed by esophago-enteric leak (N=173; 15%) and chyle leak (N=89; 8%) *(Appendix D – global 3-year report)*.

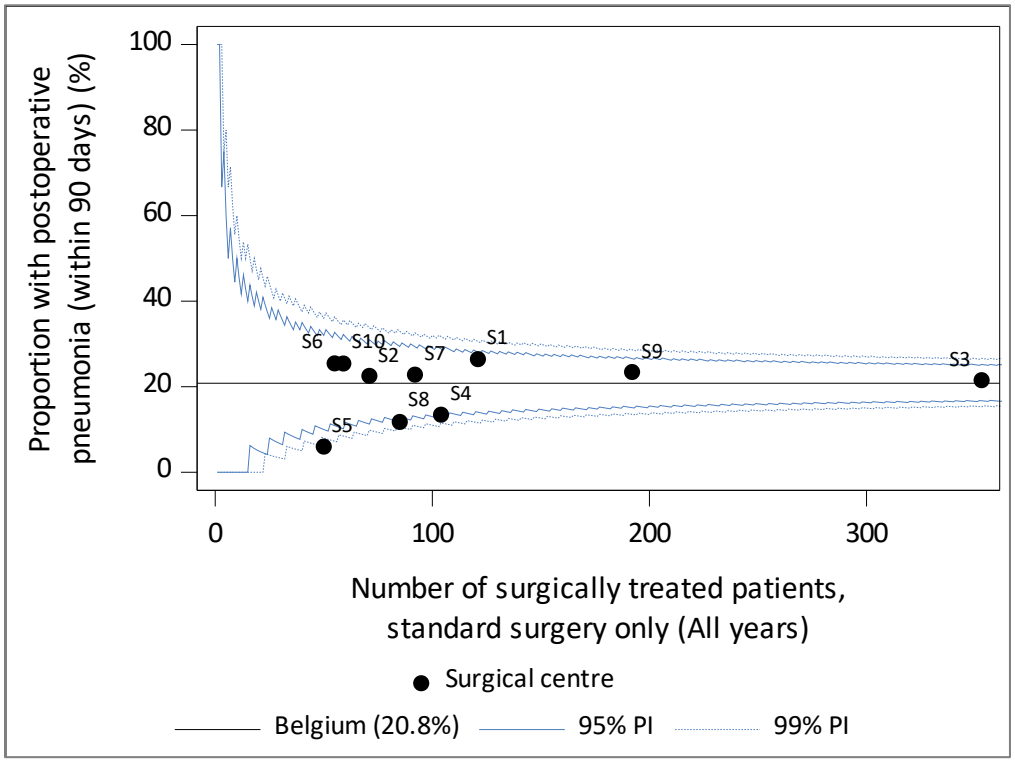
Remark: Although it was defined which classifications systems were to be used to rate the complications, concerns were raised by the clinical experts as for the reliability of the registration of complications within the convention.

a) Severe surgical complications



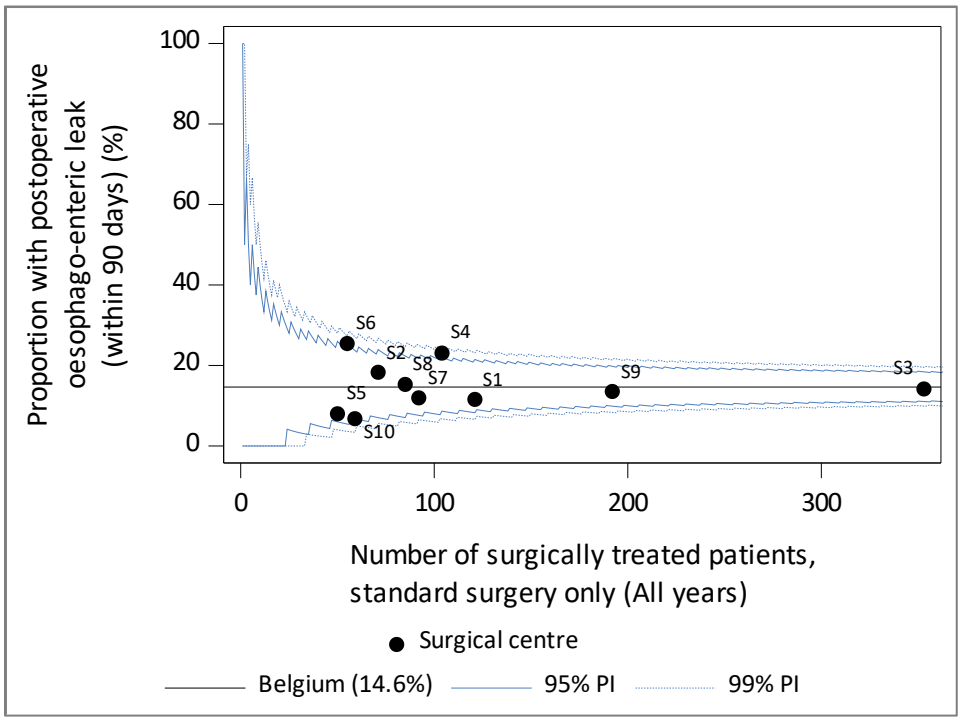
Severe surgical complications were defined CD ≥IIIb. On average, in about 28% of the cases, severe surgical complications were documented. Appendix D provides more details on the patient/tumour/treatment characteristics associated with severe complications. The % of severe complications ranged between 12% and 38% among the different centres.

b) Postoperative pneumonia



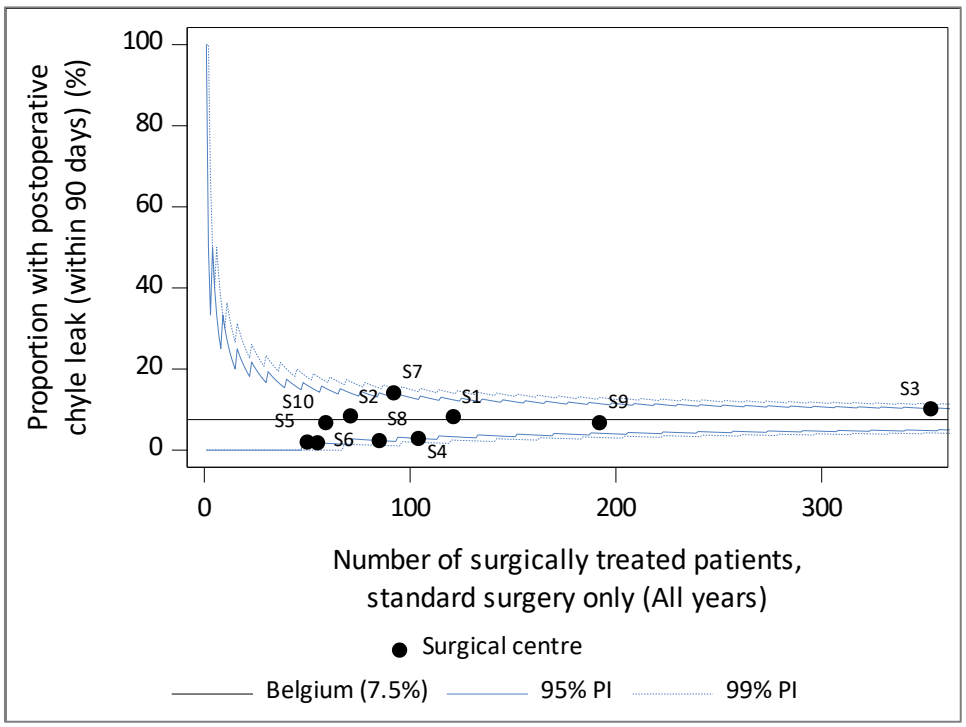
Pneumonia (CD I-V) was noted in 21%, although remaining the most common documented complication, its rate has declined over the 3 years of the convention from 24% in Y1 to 20% in Y2 and 18% in Y3. Documented pneumonia rates differed between the centres between 6% and 26%.

c) Postoperative anastomotic leak



Esophago-enteric or anastomotic leak (CD I-V) was noted in 15%, consistently throughout the 3-year period. Centre-specific rates range between 7% and 25%.

d) Postoperative chyle-leak



Chyle leak (CD I-V) was noted in 8%, consistently over the 3 years. Centre-specific rates range between 2% and 14%.

Evaluation individual organization of care in expert centres

Appendix F provides an overview of several results **on hospital level**.

Volume criteria

An important pillar of the convention, aiming at quality-of-care improvement, was the structural condition of a minimal surgical volume for each individual expert centre. The imposed minimal volume after the three-year period was 75 procedures. This condition was not reached by three of the ten expert centres (individual volumes of 61, 63 and 68). Together with a minimal surgical volume, a minimal volume of specialized multidisciplinary meetings was determined in the convention, i.e. 150 discussions after three years. Only one out of the ten centres did not reach the minimal volume of discussions (individual volume of 138).

Time to treatment

The median time that passed between the histological confirmation of the malignancy and the start of any first treatment (options regarded as first treatment being chemotherapy, radiotherapy or surgery) for the patients treated in T0 was 39 days (IQR 28-55), compared to an identical result for the patients treated in the convention (39 days (IQR 28-50)). This finding reassures that concentrated care did not create a longer time to treatment, however, further exploration of the delay between diagnosis and first treatment is recommended. The median time to treatment was independent from whether the patient was referred to the expert centre or not, nevertheless 4/10 expert centres had a median time that was at least 5 days longer than to the overall result.

Differences in individual performance between the 10 expert centres

The average age and sex of the surgically treated patients was very similar in the different centres. Patient selection for surgery varied between the centres as for tumour stage (proportion clinical stage 0-I and IV), tumour indication (proportion recurrence or salvage treatment after definitive chemoradiation), and the surgical technique (open versus minimally invasive surgery). The overall 30-day postoperative mortality was higher in patients with 'non-standard' surgery (10.2%; 95%CI [3.8, 20.8]) compared to 'standard' surgery (2.4%; 95%CI [1.6, 3.4]) (non-standard surgery defined as emergency surgery, palliative surgery, total laryngectomy and recurrence surgery). The individual results, adjusted for the case mix of the different expert centres, showed a significantly higher 30-day mortality in 1 centre compared with the average, the same centre also performed significantly worse at 90-day mortality. Based on the adjusted mortality results, all other 9 centres performed comparable.

General commitment contributing to a continuous system of quality improvement

All expert centres attended to meetings that were organized by the RIZIV-INAMI to discuss the annual results. The centres also annually prepared an individual evaluation with the formulation of concrete action points for their own centre. Finally, the 10 expert centres united their scientific interests and created a new scientific group named the Audit of Belgian Esophageal Surgery (ABES). The ABES gathered at regular times to discuss specific surgery-related topics, to exchange experiences and to propose new research questions. For the

continuation of the convention, the ABES can play an important role in the process of continuous quality improvement.

Reflections and recommendations based on evaluation after 3 years

- The collected data on resection margin status were incomplete and lacked information of the distal and circumferential margin. It is recommended to include these parameters to the registration form.
- Uniform guidelines on the evaluation of removed lymph nodes during surgery are necessary to allow comparison of these data.
- The evaluation of postoperative complications by registrars needs to be trained to achieve uniform interpretation.
- A substantial proportion of the patients diagnosed with oesophageal cancer during the 3-year period was not discussed on a specialized MC in an expert centre (more than 40%). For the continuation of the convention, this population needs to be characterized further to evaluate whether it is recommended to organize a specialized MC for every patient with newly diagnosed oesophageal cancer.
- Data regarding patient experience and quality of life were not collected, this should be considered for the continuation of the convention.
- Data regarding recurrences were not collected, this should be included in the future.

Addendum: observed mortality year 4 of the convention

The evaluation report is based on collected data from 1 July 2019 until 30 June 2022. Awaiting the in depth-analysis of the subsequent year (1/7/2022 until 30/6/2023), the observed 90-day mortality results of the fourth year were already computed.

The observed 90-day postoperative mortality for malignant oesophageal cancer during the subsequent convention years evolved from 6.3% (year 1), to 11.1% (year 2), 4.2% (year 3) and finally 3.2% in year 4. With the addition of the fourth convention year, the 90-day postoperative mortality was assessed for a total of $N_{4Yconvention}$=1.555 and compared with N_{T0}=1.584. Thereby, the overall unadjusted 90-day postoperative mortality for four years of convention is 6.2% 95%CI [5.1, 7.6] compared to 9.5% 95%CI [8.1, 11.1] for the four years preceding the centralization of oesophageal surgery, and confirms the decreasing trend.

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