

# Disparity in oesophageal cancer management in South Africa: a comparison between two tertiary centres with special focus on the palliation of dysphagia

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**Background:** For most patients with oesophageal cancer worldwide, palliation of dysphagia is the goal which is most commonly achieved with self-expanding metal stents (SEMS). The aim of this study was to assess the profile and management of oesophageal cancer patients at Frere Hospital in the Eastern Cape, and compare this to a similar cohort from Groote Schuur Hospital (GSH) in the Western Cape Province.

**Methods:** This study is a retrospective comparative cohort which reviewed all patients diagnosed with oesophageal cancer by the Frere Hospital and GSH endoscopy units from January to December 2015. Independent prospective electronic databases for the two hospitals were merged for comparative analysis.

**Results:** During the study period, 346 and 108 patients were diagnosed with oesophageal cancer at Frere Hospital and GSH respectively. The rate of curative intended intervention was similarly low, with 3% of cases at Frere Hospital undergoing oesophagectomy or definitive radiotherapy as compared to 5% at GSH ( $p=0.48$ ). In terms of palliation, significantly more patients received palliative oncological therapy at GSH as compared to Frere Hospital (21% vs 8%,  $p < 0.001$ ). At Frere Hospital, 281 patients (81%) were treated primarily with serial dilatations. At GSH, 9 patients received a single dilatation, all as a bridge to radiotherapy or stenting. At Frere Hospital, 28 patients (8%) were stented, as compared to GSH where 69 patients (64%) were managed with a stent ( $p < 0.001$ ).

**Conclusion:** This study shows significant differences in the oncological and endoscopic palliation of patients between the two institutions, highlighting a gross disparity in healthcare provision between them. The reasons for these disparities should be investigated and equipoise addressed by national health policy makers.

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## Introduction

Global epidemiological studies have shown that oesophageal cancer is both more common and deadly in the developing world, where it ranks eighth for cancer incidence and fifth for cancer mortality.<sup>1-3</sup> Whereas adenocarcinoma is more prevalent in Western societies, squamous cancer of the oesophagus predominates in the developing world.<sup>3</sup> South Africa has a high incidence of oesophageal cancer, in particular in the Eastern Cape where epidemiologists in the 1950s discovered an especially high incidence and it remains the cancer with the highest incidence and mortality rate in the region.<sup>4-8</sup>

Despite improvement in treatment outcomes in the last few decades, the prognosis of oesophageal cancer remains poor, with an overall 5-year survival of 14%.<sup>9,10</sup> In a first world setting, 40% of patients present with metastatic disease and less than half of patients will be candidates for potential curative resection.<sup>9</sup> In Africa, patients have a greater delay in presentation, present at a more advanced stage, are less often candidates for resection, and have a poorer overall outcome.<sup>11-17</sup> For most patients, cure is not an option and best supportive care (BSC) with palliation of dysphagia is the goal.<sup>18</sup> Dysphagia relief can be achieved with placement of self-expanding metal stents (SEMS), radiotherapy (brachytherapy or external beam radiotherapy (EBRT))

or oesophageal dilatation. SEMs are the most commonly used method and have been shown to offer rapid, safe and effective relief of dysphagia with low procedure-related morbidity and mortality rates.<sup>19-24</sup> Brachytherapy and EBRT, although effective, have a delay in symptom relief, making it unsuitable in patients with < 3 estimated survival months.<sup>25-29</sup> Oesophageal dilatation is easy and cheap, with a complication rate (mainly perforation) of 2.5–10%. Unfortunately, the effect is short lived and necessitates a serial dilatation policy.<sup>30-33</sup> Older guidelines have recommended dilatation alone for patients with an expected life span of less than 4 weeks, but more recent guidelines recommend SEMs as primary intervention, reserving dilatation only for the management of post-radiotherapy strictures and very high lesions that are not stentable.<sup>34,35</sup>

South Africa remains a country with great inequality and disparity.<sup>36,37</sup> The Eastern Cape is a poor province with a population of 6.5 million and an unemployment rate of 37%, the highest in South Africa.<sup>4</sup> The public health sector in the Eastern Cape province is indeed one of the areas hit hardest by lack of funds and infrastructure.<sup>38</sup> The aim of this study was to compare the management of patients with oesophageal cancer at two teaching hospitals, Frere Hospital in East London and Groote Schuur Hospital in Cape Town, with special reference to palliative treatment of dysphagia.

## Methods

Patients who were diagnosed with oesophageal cancer at the endoscopy units at Frere Hospital and GSH from January 2015 to December 2015 were included in the study. At GSH, patient details were retrieved from a prospectively maintained Research Electronic Data Capture (REDCap) based institutional database for patients with Upper Gastrointestinal Cancer, whereas at Frere Hospital patients were prospectively captured in an Excel spreadsheet. Demographic and clinical data captured are shown in Table 1. The criteria for diagnosing oesophageal cancer were similar for the two units: the diagnosis was based on the endoscopic picture of an obvious exophytic/ulcerative tumour in the oesophagus. The diagnosis was confirmed with biopsy unless the patient had a very obvious lesion and was deemed completely unfit for any oncological intervention. Endoscopic procedures were performed under conscious sedation at both facilities. Endoscopic interventions (dilatation with serial Savary-Gilliard dilators and SEMs placement) were performed using a Seldinger guidewire technique at both hospitals. At GSH the use of fluoroscopy for guidance of endoscopic intervention was standard, whereas at Frere Hospital interventions were performed without fluoroscopy.

There were, however, notable differences in the patient assessment and referral algorithms, the availability of treatment options and the institutional policies regarding treatment allocation. At GSH, all patients with an Eastern Cooperative Oncology Group (ECOG) performance status  $\leq 3$  were referred to a dedicated multidisciplinary team (MDT) conference for assessment and treatment planning.

All treatment modalities were available and patients were allocated to a treatment according to currently applied international guidelines. Specifically, in patients where palliative endoscopic intervention of dysphagia was recommended, SEMs placement was the preferred method, with dilatation only performed as a bridge to stenting or where there was a contraindication for SEMs. Adjunctive EBRT was offered to those patients who were already stented with an ECOG status of  $\leq 3$  and an expected survival of at least 3 months. Palliative care facilities for terminal care of patients were available.

At Frere, patients considered fit for surgery by the endoscopist were referred to the local surgical unit for staging, and then referred to the nearest thoracic surgery unit in Port Elizabeth (300 km away) if curative-intended intervention was considered possible. Patients considered fit for oncological treatment by the endoscopist were referred to the local oncology department. Patients considered not fit for oncological therapy were managed primarily through the endoscopy unit. With limited availability of SEMs, endoscopic treatment of palliation was monthly serial dilatation of the tumour with SEMs being reserved for patients with a tracheo-oesophageal fistula (TOF) or where a perforation occurred during dilatation. There were no palliative facilities available for patients for terminal care.

## Statistical analysis

Statistical analysis was performed with IBM SPSS Statistics version 25. Numerical variables were assessed for normality and subsequently analysed by appropriate parametric and nonparametric tests. Categorical variables were analyzed by the Chi-squared test. Unless otherwise indicated, a two-tail test hypothesis was used with 0.05 as discriminator for rejection of the null-hypothesis.

## Results

During 2015, 346 and 108 patients were diagnosed with oesophageal cancer at Frere Hospital and GSH respectively. The demographic and clinical parameters of patients presenting to the two units are shown in Table 1. Notable were the long intervals between symptom onset and diagnosis, median 3 (IQR 1-4) months for Frere Hospital patients and 4 (IQR 3-6) for GSH patients ( $p < 0.001$ ). At presentation, dysphagia was present in 86% and 82%, and loss of weight in 43% and 69% of patients presenting to Frere Hospital and GSH respectively.

The endoscopic tumour characteristics of the two populations were comparable. In 76% of cases diagnosed at Frere hospital, a biopsy was taken for histological confirmation, compared to 86% at GSH. There were significantly more patients with an adenocarcinoma at GSH, with 12% of biopsies confirming this result as compared to 3% of cases at Frere Hospital ( $p < 0.001$ ). Staging CT was performed in 11 patients (3%) at Frere Hospital compared to 27 patients (25%) at GSH ( $p < 0.001$ ).

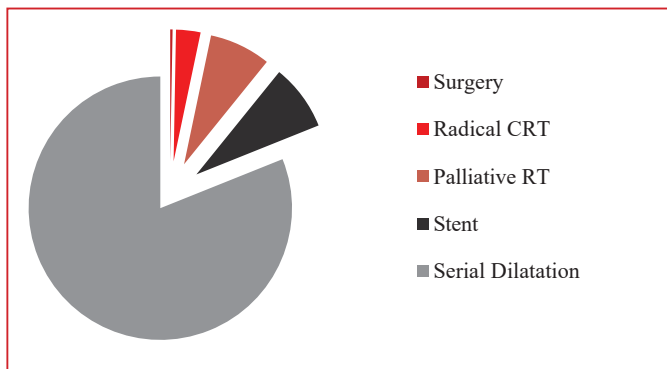


Figure 1a. Primary treatment modality at Frere Hospital

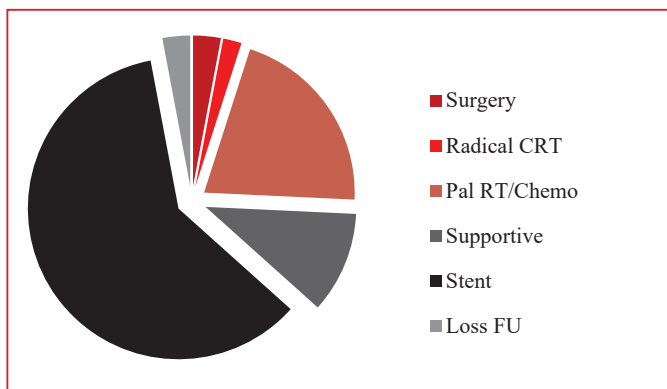


Figure 1b. Primary treatment modality at GSH

The management of patients is summarised in Table 2 and shown in Figure 1. At Frere Hospital, 15% of patients were referred to the Oncology unit for assessment, whereas at GSH 78% of patients were discussed in the MDT conference ( $p < 0.001$ ). At Frere Hospital, 3 patients were referred for resection of which 2 refused surgery and 1 underwent oesophagectomy. At GSH, 3 patients underwent oesophagectomy. Definitive chemoradiotherapy was given in 3% and 2% of patients, and 8% and 21% of patients underwent palliative oncological treatment at Frere Hospital and GSH respectively. In addition to palliative radiotherapy alone, 27%

of patients at GSH were given adjunctive radiotherapy after initial SEMS insertion.

At Frere Hospital, 281 patients (81%) were treated with intended serial dilatations, with the number of actual dilatations performed per person shown in Figure 2. Notably, more than 50% of patients selected for serial dilataion underwent two or more dilatations, with 47 patients returning 4 or more times, and one patient who had up to eleven dilatations. The median interval between dilatation sessions was 4 weeks (range 1-16 weeks). The failure rate for dilatation was 5%, while the perforation rate was 3%. At GSH, 9 patients received a single dilatation, but all of these were as a bridging intervention to palliative radiotherapy or stenting. No patients were allocated to serial dilatation.

At Frere, 28 patients (8%) were stented. The most common indication for stent placement was the presence of a TOF ( $n=15$ ), followed by iatrogenic perforation ( $n=7$ ) and luminal obstruction ( $n=5$ ). At GSH, 69 patients (64%) were stented, of whom 61 were for luminal obstruction only, four were for tracheo-oesophageal fistulae and in three patients it was as a bridge to surgery.

## Discussion

Most patients with oesophageal cancer treated at state health facilities in South Africa present with advanced disease with curative-intended intervention applicable in less than 20%.<sup>17,39,40</sup> The majority of patients require palliative measures aimed at the alleviation of symptoms, predominantly dysphagia and pain. This study shows significant differences in management of oesophageal cancer between the two study centres. Of concern are the discrepancies in the oncological and endoscopic palliation of patients available at the two centres.

Delay from the onset of symptoms to contact with an appropriate level health care facility is a major factor contributing to most patients presenting with advanced disease.<sup>39</sup> The lengthy time intervals between onset of symptoms and seeking medical attention observed in

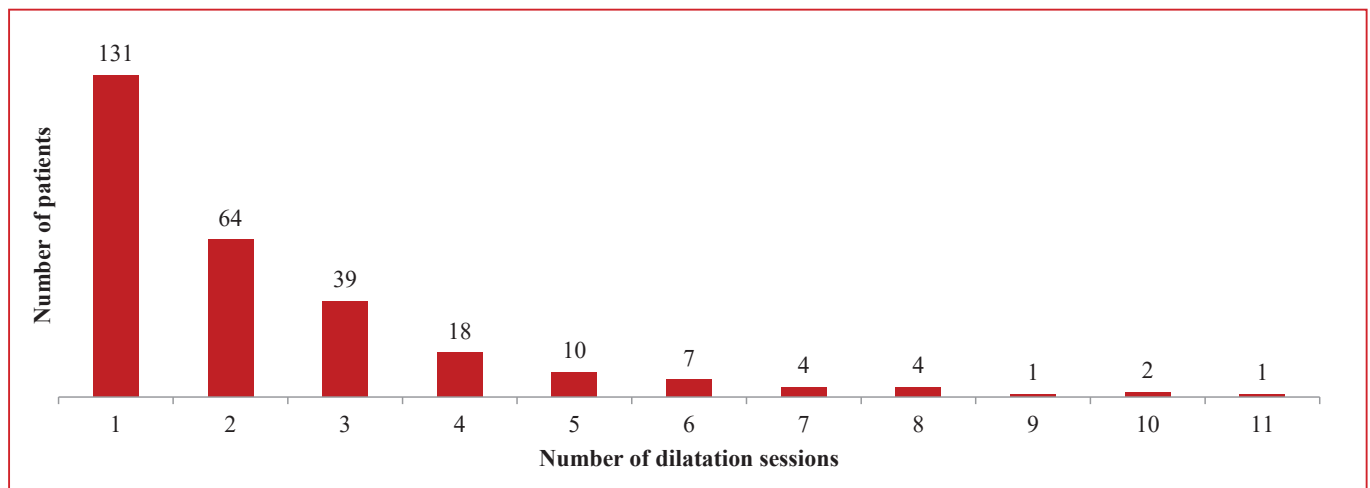


Figure 2. Number of dilatations per patient at Frere Hospital

<b>Table 1. Demographic, clinical and endoscopic parameters of patients</b>			
	<b>Groote Schuur Hospital</b>	<b>Frere Hospital</b>	
	n=108	n=346	p-value
<b>Demographic parameters</b>			
Age (median; range)	60 (34-82)	64 (35-95)	<b>0.01</b>
Male/female (%)	47/53	47/53	0.97
<b>Clinical parameters</b>			
Duration of symptoms in months (median; IQR)	4 (3-6)	3 (1-4)	<b>&lt;0.001</b>
Dysphagia (%)	82	86	0.17
History of weight loss (%)	69	43	<b>&lt;0.001</b>
<b>Endoscopic parameters</b>			
Tumour length (median; range)	6 (2-10)	6 (1-15)	0.52
Tumour position	85	340	
Cervical (%)	4	1	0.19
Upper thoracic (%)	12	14	0.67
Middle thoracic (%)	54	59	0.32
Lower thoracic (%)	30	26	0.87
Tracheo-oesophageal fistula (%)	6	5	0.40
<b>Pathological verification</b>			
n (%)	88 (81%)	245(71%)	<b>0.03</b>
Squamous carcinoma (%)	88	97	<b>&lt;0.001</b>
Adenocarcinoma (%)	12	3	<b>&lt;0.001</b>
<b>Staging workup</b>			
CT staging (n (%))	27 (25%)	11 (3%)	<b>&lt;0.001</b>

<b>Table 2. Treatment at the two hospitals</b>			
	<b>Groote Schuur Hospital</b>	<b>Frere Hospital</b>	
	n=108	n=346	p-value
MDT assessment (n (%))	84 (78%)	52 (15%)	<b>&lt;0.001</b>
<b>Curative-intended intervention (n (%))</b>			
Oesophagus resection (n (%))	3 (3%)	1 (0.3%)	0.09
Chemo-radiotherapy (n (%))	2 (2%)	10 (3%)	0.85
<b>Palliative oncologic treatment (n (%))</b>			
Chemotherapy (n (%))	2 (2%)	0	
EBRT(n (%))	21 (19%)	28 (8%)	<b>&lt;0.001</b>
EBRTadjunctive to SEMS	30 (27%)	0	
<b>Endoscopic treatment (n (%))</b>			
Serial dilatation (n (%))	0 (0%)	281(81%)	
SEMS (n (%))	69 (64%)	28 (8%)	<b>&lt;0.001</b>

MDT multidisciplinary team; SEMS self-expanding metal stent; EBRT external beam radiotherapy

this study is in keeping with results of Govender et al. where combinations of delay in seeking medical attention, inaccessibility of health care and delays in assessment and treatment resulted in average times of symptom-onset to treatment of 7 months. Even though the proportion of patients that eventually underwent curative-intended intervention was similarly low between the two centres, it is nonetheless of concern that only 3% of patients at Frere Hospital were even investigated for this possibility by having a staging CT performed. This rate is significantly lower when compared to the GSH cohort and indeed any described in the literature, including studies from similarly resourced settings in South Africa and other African countries.<sup>11-15,17</sup> Furthermore as opposed to GSH where, in line with international consensus guidelines 76% of patients were assessed in a MDT setting, there was no formal MDT at Frere Hospital and only 15% of patients were referred at the discretion of the endoscopist.<sup>17,18,35</sup> The decision to do a staging CT and refer to the oncology unit is based on a subjective assessment of patient fitness by the diagnosing endoscopist, and thus the lack of a standardised and objective assessment protocol may have contributed to fewer patients being offered and receiving oncological therapy.

Of the palliative strategies available, SEMS is the most commonly used as it offers rapid, safe and effective relief of dysphagia.<sup>19-24</sup> Despite enough skill and eagerness to use SEMS by the endoscopy staff at Frere Hospital, the limited availability of SEMS has forced clinicians to apply a very selective stenting policy, resorting to serial dilatation as the primary dysphagia directed modality. Besides being associated with rapid recurrence of symptoms, this strategy is not ideal for several additional reasons, particularly so in the Frere Hospital context.<sup>30-33</sup> First, the significant burden serial dilatations place on the unit means longer endoscopy waiting lists. Second, many patients from rural areas are extremely poor and the long distance to travel to hospital for monthly dilatation is a significant challenge and financial burden. Third, although inexpensive for a single session, repeated dilatation sessions become increasingly expensive to the health system as well as to the patient. Although the once off cost of a SEMS compared to single dilatation is greater, this perceived cost advantage will be eroded by the cumulative costs involved in repeated dilatation sessions. The fact that more than 50% of patients underwent multiple dilatations, with 47 receiving 4 or more dilatations and some patients undergoing up to 11 dilatations, underscores the ineffectiveness of the serial dilatation strategy in this setting.

As a retrospective comparative study, the study has several weaknesses. Patients were not staged according to the TNM staging system as the majority of patients did not undergo a staging CT. The perceived superior outcome of SEMS as opposed to serial dilatations, although published earlier, was not investigated with follow-up and, more specifically, quality of life (QOL) assessment in the patient cohorts. Furthermore, a health-economic assessment and comparison of the cost of SEMS and serial dilatation, including the potential financial implications for patients, is needed.

Despite the weaknesses, the paper addresses an important aspect, namely ongoing inequalities in the delivery of healthcare in the state service in South Africa. It is particularly disturbing that this inequality is present and needs to be highlighted in patients with advanced presentation of a disease with a dismal prognosis and debilitating symptoms. The results of this article can be used as benchmark to assess the effect and success of any remedial measures to rectify this significant disparity in healthcare provision to patients with oesophageal cancer in South Africa.

## Conclusion

This study highlights that in a hospital with a high prevalence of oesophageal cancer, facilities for the appropriate management of patients are totally inadequate when compared to another referral hospital in a different province. Access to the most effective form of palliation (SEMS) needs to be addressed as a matter of urgency. Using modern technology to establish an MDT, where patients can be assessed for appropriate therapy in a standardised manner, should be the foundation step for research to determine the optimal palliative treatment and integration of care pathways.

## Ethics approval

The registry from which patients were included from GSH as well as the specific research reported on was approved by the Human Research Ethics Committee (HREC) of the University of Cape Town. The study was also approved by the Ethics Review Board of Frere Hospital.

The authors have no conflicting interests to declare.

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