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Current Practices and Opportunities to Optimize Esophageal Cancer Care in Tanzania: A Retrospective Cross-Sectional Study

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Abstract

Background
Esophageal cancer is a serious malignancy with regards to its associated morbidity of inability to swallow and the grave prognosis. Coordinated care, including multidisciplinary approach has the potential to impact outlook for these patients. This requires adequate staging, addressing nutritional and performance status, and treatment stratification in a more objective manner. Marked with low resection rates, the management practices at our hospital have not been highlighted. This would identify snags and allow addressing improvements and overall patient's outcome.

Aim
To determine if EC patients are adequately investigated, staged and optimized prior to any form of cancer targeted treatment and discuss opportunities to optimize care.

Methodology
A retrospective, descriptive hospital based study that included all histologically conformed cases of esophageal cancer diagnosed between 2017 and 2018 at Muhimbili National Hospital. We identified medical records for 251 patients. Using data abstraction forms, patient's demography, diagnostic and staging investigations, and the planned or offered optimization and cancer related treatment identified. Additional tumor characteristics like location, and grade was collected. Descriptive statistics were summarized into tables and figures using SPSS version 26 and MS Excel for windows for figures.

Results
Almost all patients with esophageal cancer had an endoscopy and biopsy done. Few patients had esophagograms and adequate staging investigations done as was in 20% and 23.5% respectively. None of the patients had nutritional assessment or performance status documented. Majority of the patients (72.4%) were planned for palliative therapy with radiation therapy. Only about 10% of the patients had esophagectomy done with low adjuvant therapy rates.

Conclusion and recommendation
We found lack of coordinated approach towards patients presenting with esophageal cancer. Improved staging investigations and functional status assessment would allow patients optimization and appropriate treatment stratification. The hospital needs to explore all its locally available resources towards improving the treatment landscape of patients with esophageal cancer.

Keywords: *Optimal Esophageal Cancer Treatment, Evidence Based Challenges to Care Pathways, Treatment Outcomes, Optimal Work Up, and Appropriateness of Investigations Done.*

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Introduction

According to the GLOBOCAN report of 2020, it was estimated that esophageal cancer (EC) has 604,100 incident cases and 544,076 deaths making it the seventh and sixth in cancer incidence and mortality respectively globally (1). This highlights an increase in incidence in the last decade and is expected to continue rising (2). EC is characterized by rapid progression and low survival rates (3). Its 5-year survival is just below 20% despite the advances in the field of oncology (4). In sub-Saharan Africa, EC is one of the leading causes of cancer morbidity and mortality especially on the eastern coast of Africa (5). In Tanzania, it has a high incidence affecting 9.2 per 100,000 individuals of both sexes (6). With limited treatment facilities and resources, coupled with advanced dysphagia affecting nutritional status at presentation, the disease has a high case fatality rate (7).

Addressing treatment for patients with EC in Tanzania is particularly important, more so to Muhimbili National Hospital (MNH) as it is the leading cause of admission to its surgical wards. In spite of this, there is no standard guideline addressing the management of these patients including what set of investigations to be done. This leaves optimal management strategies for EC in Tanzania to be unclear and there are limited studies concerning this subject in similar settings in the sab Saharan Africa (8). It is for this lack of uniformity that we set to document the landscape of EC workup and treatment stratification at MNH. This study provides an understanding of the local practices for EC patient's workup, staging, and treatment. The findings from this study will be key to clarifying the challenges on EC management and thus provide the cornerstone of improving EC patient's care and outcomes research. Furthermore, it will provide a basis for suggesting and piloting EC patients' treatment pathways with aim of increasing curative treatment strategies including resections, improved approach to patient’s optimization, and utilization of neoadjuvant therapies.

Methodology

Study design and setting

This was a hospital-based retrospective chart review carried out at Muhimbili National Hospital (MNH). The study involved patients who were histologically diagnosed and treated for esophageal cancer in 2018. The hospital is located in the coastal city of Dar es Salaam, in Tanzania. It is believed that the hospital receives the vast majority of patients with dysphagia from all over the country due to its proximity to the only public cancer treatment center. The hospital has an endoscopy suite that is well equipped to offer diagnostic and

stenting services, 2 CT scan and MRI suites for advanced imaging for staging purposes, fluoroscopy machine for esophagograms, chest x-ray, and ultrasound machines. The hospital also enjoys the histopathology services within the house and ready access to operating suites for the two surgical units on daily basis including an emergency operating room.

Furthermore, the hospital enjoys improved surgical services with trained gastroenterology surgeons and well equipped surgical intensive care unit. Since 2015, the hospital had started performing esophagectomy on regular basis. At the same time, there have been improvements in EC services with the introduction of stenting through the African Esophageal Cancer Consortium (AfrECC) initiative, improved radiation delivery by the introduction of 3D delivery systems, and improved availability of chemotherapy. In its 120 surgical beds, 25 – 30 are occupied by EC patients at any point in time in a month. EC patients with histological confirmation who will not undergo surgery as the surgical team has decided are then sent to the cancer hospital for palliative chemotherapy or radiation or both: this referral does not go through the usual multidisciplinary tumor board conducted on weekly basis.

Study population and sample size

The recruited patients of any age and sex with a histological confirmation of EC treated at MNH. No patient with a histological confirmation was to be entirely excluded except for the missing variables at analysis. Being a descriptive study, we included all the patients of any age and sex that had information relevant for this audit of practice.

Variables collected

Study variables collected included sociodemography (sex, age in years, occupational activity, and level of education), investigations done for diagnosis and staging purposes, tumor characteristics (location from upper incisor in centimeters, histologic subtypes, tumor grade, and clinical stage), and the planned/offered treatments.

Retrieval and data collection

We identified patients admitted in the surgical wards with a diagnosis of dysphagia and or presumptive diagnosis of EC in 2018. We further searched the operating theatre logs for any patient treated with esophageal resection. The registration numbers of these patients were searched in the hospital histopathology registry maintained at the central pathology

laboratory for a diagnosis of EC of any histological subtype. Case notes of those with histological confirmation of EC were pulled for data abstraction. Using a specially designed data capture spreadsheet, study variables were abstracted by two research assistants generating two sets of data. The two lists were reconciled for agreement and missing information corrected.

Data analysis plan

All variables were handled as categorical and summarized descriptively into the frequency with proportions. Sociodemographic characteristics of the patients, tumor characteristics, and disease stage were summarized as the frequency with percentages. The proportion of all the patients completing a diagnostic and staging investigation, and various treatment modalities offered to these patients was determined and presented as columns. Subgroup analysis of patients who had thoracic CT scan was done to describe the treatment modalities offered/planned.

Ethical consideration

This study was approved by MUHAS Institutional review board and separate permission from MNH research and training Unit to use its patient records was obtained. The study received waiver from obtaining direct patients' consent to utilize the medical records. Confidentiality was maintained by de-identifying the patient's records at the end of data collection before transfer into SPSS for analysis. The study did not judge negatively the treatment offered to patients with EC.

Results

We identified 251 case notes of patients who had a histological diagnosis of EC and were treated at MNH in 2018. From Table 1 below, it can be seen that male patients were the majority comprising 180(69%) of the cohort making a male to female ratio of 2:1. Most of the patients were in the age group between 41 – 60 years in 116(44.4%) followed by those between 61 – 80 years in 81(31%) and those that were ≤ 40 years in 56(21.5%). The majority of our patients had either a primary level of education or less at 190(72.8%). On occupation, most of the participants were peasants as was in 117(44.8%) followed by those with formal employment in 72(27.6%) and merchants in 51(19.5%). Note that the retired and those with formal employment status were categorized as patients with stable income.

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Table 1: Socio-demographic attributes of patients with EC at MNH. n = 251

Variable	Frequency (%)
Sex category	
Female	81 (31)
Male	180 (69)
Age group	
≤ 40	56 (21.5)
41 to 60	116 (44.4)
61 to 80	81 (31)
> 80	8 (3.1)
Education level [a]	
Primary and below	190 (72.8)
Secondary and above	52 (19.9)
Not documented	19 (7.3)
Occupation category [b]	
Retired	14 (5.4)
Petty traders	51 (19.5)
Formally Employed	72 (27.6)
Peasant	117 (44.8)

[a] *Education in Tanzania is divided into primary for the first seven years of schooling, secondary for the next 6 years before college education. Hence, we grouped the last two together since they were few.*

[b] *This category considered retired as citizens on monthly pension and insurance cover, formally employed as those on monthly payment and insurance cover, petty traders as those claiming to be running small business but were unable to meet medical bills and thus treated on exemption and the peasants were patients who came from up country surviving on subsistence farming.*

In Figure 1 below, we present list of investigations that were done for diagnosis and staging purposes among the 251 patients with EC. Majority of the patients, 98.8%, had an endoscopic evaluation for obtaining biopsy for histological diagnosis. About 19.9% of the patients had an esophagogram, mostly barium swallow, done. . Another 21.5% and 23.1% had a chest x-ray and abdominal ultrasonography for metastatic assessment. CT scan was done in 23.5% of the patients.

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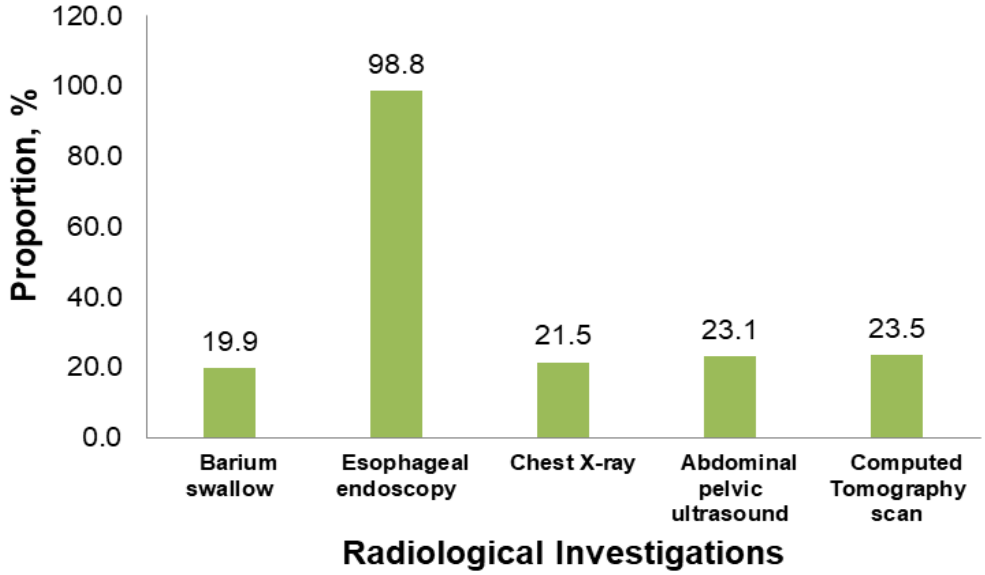

Figure 1. Columns showing various investigations done to esophageal cancer patients at managed at MNH in 2018

From Table 2 below, we present EC endoscopic location, histologic type, tumor grade, and stage as were documented on the treatment chart. EC occurring in the lower and middle of the esophagus were the most predominant as was seen in 104(39.8%) and 92(35.2%) respectively. Squamous cell carcinoma is the predominant histologic type seen in 239(91.6%) of the patients. Tumor grade reported as the degree of differentiation was not reported in 129(49.4%) of the patients: most common tumor grades were 1 and 2 in 62(50.8%) and 51(41.8%) respectively. Most patients did not have cancer stage documented as was in 155(61.8%): in those that had the stage of their cancer, all were in stage 3 or 4 at 84(87.5%) and 12(12.5%) respectively.

Figure 2 shows the treatment modalities offered to patients with EC at MNH: a patient had a possibility of receiving multiple options. We considered each option against all the 251 patients as presented in the columns. Neoadjuvant therapy was considered in 19(7.6%) of the patients while 24(9.6%) had an esophagectomy offered of which 10(41.7%) proceeded to adjuvant therapy. The remaining patients were treated by a palliative intent with the majority of patients either being on radiation therapy alone or a gastrostomy feeding tube in 75.3% and 67.3% respectively. Self-expanding metallic stents (SEMS) were deployed in 29.1% of the patients.

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Table 2: Showing tumor endoscopic location, histological features and the stage of EC patients attended at MNH

Variable	Frequency (%)
Tumor location [a]	
Lower	104 (39.8)
Middle	92 (35.2)
Upper	49 (18.8)
Undocumented	16 (6.1)
Histologic type[b]	
ADC	22 (8.4)
SCC	239 (91.6)
Differentiation (n=132)[b]	
Grade 1	62 (47.0)
Grade 2	51 (38.6))
Grade 3	15 (11.4)
Grade 4	4 (3.0)
Cancer stage (n=96)[c]	
Stage 3	12 (12.5)
Stage 4	84 (87.5)

[a] *Tumor location was as measured routinely from upper incisor teeth where by lower is up to 23cm; middle is between 23cm and 31cm; and upper is beyond 31cm.*

[b] *Histology and grade were both obtained from a copy of histology report maintained with the case notes*

[c] *Is as documented in the patients' case notes at the time of their treatment. Hence was subjective according to the treating physician.*

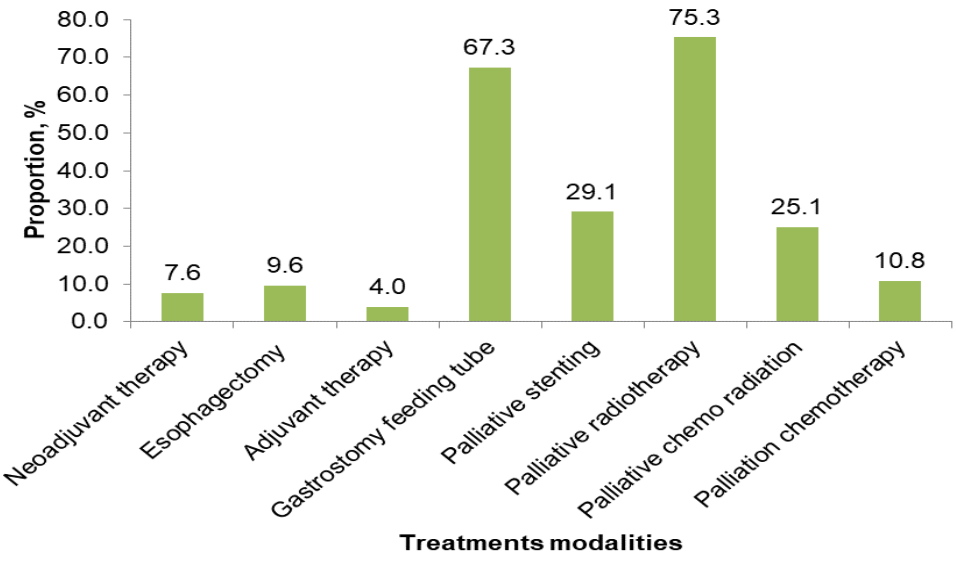

Figure 2. Columns showing treatments offered to the 251 patients with esophageal cancer at MNH in 2018

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Figure 3 displays the treatment decisions that were made for the 59 patients that had a thoracic CT scan evaluation for resectability. In 40.7% of the 59, an esophagectomy was done and the rest were either considered inoperable or had metastatic disease. These that were not offered esophagectomy were subjected to various palliative modalities SEMS (28.8%), radiation therapy (15.5%), and GFT (15.3%).

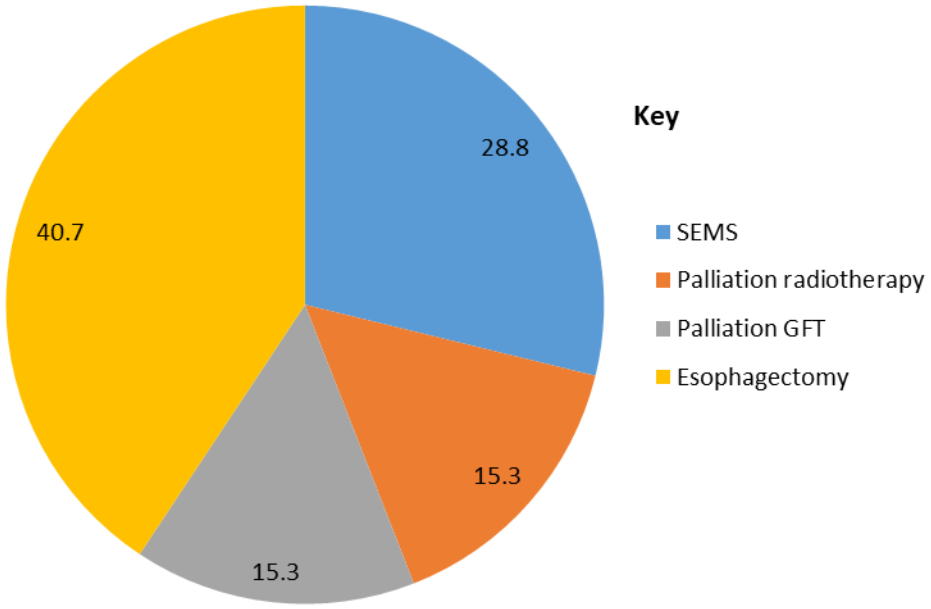

Figure 3. Shows 40.7% esophagectomy rate among patients who had thoracic CT scan at MNH in 2018

Discussion

Most patients with EC in our setting presented with dysphagia, typically a feature of advanced disease. Evaluating dysphagia is better accomplished first with a double-contrast barium swallow which has been found to have a positive predictive value of 42% (9). Barium study has the potential to differentiate benign from a malignant stricture (10). An esophagography can predict a malignancy based on tumor morphology as polypoid, infiltrative, varied, or ulcerative (11). In our setup, this modality is readily available even in lower facilities and should be the first investigation of choice when a patient presents with dysphagia. Despite its availability, only 1 in 5 of the patients had an esophagography reported to have been done.

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Once esophagography has demonstrated a surgical lesion in the esophagus and complete dysphagia, there are three controversial issues in our context: to proceed with visualization of the tumor through upper gastrointestinal endoscopy; perform thoracoabdominal CT scan to assess for resectability first; or urgently address nutritional issues by any means available. A choice of approach here has serious financial and decision consequences to the patient and caregivers. If resectability and extent of disease are known before visualization, the decision as to whether the patient will benefit from a nutritional rehabilitation, through self-expanding metallic stents (SEMS) deployment or Gastrostomy Feeding Tube (GFT) is an important aspect to consider. SEMS can be safely deployed during the first endoscopy suite visit regardless of the histological outcome if the patients can afford to pay directly or have an insurance cover. Patients who cannot afford to pay get a waiver for a rigid scope and GFT. Most of our patients fall in this last group based on low socio-economic status shown in the results.

Dysphagia, malnutrition, and poor performance status are common presentations among patients with EC globally. Palliation of dysphagia and hence nutritional rehabilitation becomes an important component in therapy (12). Currently, esophageal SEMS are considered to be more cost-effective and an effective means of palliating dysphagia and addressing nutrition among patients with esophageal cancer (13). The deployment of SEMS is limited in our local context by availability and high cost to the patients, despite international attempts to improve its availability (14, 15). The first visit to endoscopy in our setup is only meant for biopsy and localization of tumor within the esophagus. This would be followed by a second visit, two weeks later for the histology report to be out, for SEMS deployment. This practice is known to increase the cost to the patients and delaying relief of dysphagia with ongoing nutritional deterioration. This paucity of SEMS has created space for GFT with controversy since it is not meant to relieve dysphagia (16).

While GFT was previously thought to be an unsafe procedure in patients who were to require esophagectomy, several studies have proved the opposite (17). A GFT has now been suggested to be a safe modality of addressing pre-operative nutritional support among patients with esophageal cancer with low complications rate (18). Most reports on the safety of GFT before Esophagectomy are coming from retrospective reports. There is a need to validate these in a prospectively designed study and MNH would be suited to do that given limited access to SEMS and the popularity of GFT among our patients. While centers that offer GFT nutritional support do so percutaneously, our practice is to perform an open

procedure that will be interesting to study among our patients. We are now witnessing patients who are "comfortable" with GFT without any additional treatment for their palliation.

Since EC is known to have both haematogenous and lymphatic metastasis, with lungs and liver being the common sites, precise localization of this extent is important in all patients diagnosed with the disease. (19). In our current context, a CT scan is the most reliable means of diagnosing the primary tumor status and extent of spread hence it is expected that all patients should have a thoracoabdominal CT to the minimum (20). Only one-quarter of the patients treated with EC at MNH had this investigation done. Failure to do cross-sectional imaging denies patients a chance to curative treatment options by not being properly staged. At the very minimum, abdominal ultrasonography can be of use in detecting liver and nodal (celiac and left gastric) involvement (21). It is also known that USS can help with FNAC in celiac nodes and hence diagnose lymphatic metastasis. Abdominal USS was only done to the same number as those with CT, 23%.

The bias in investigating EC patients is reflected in the treatment practices among patients with EC at MNH with most patients being condemned to palliation. Both the nutritional status and performance status of the patients was not documented in their case notes. Nutritional rehabilitation might be important in some of the patients who have loco-regional cancer. A study by Huddy et al demonstrated that it allows patients to maintain good nutritional status during Neoadjuvant therapy (22). However, the use of SEMS for this purpose was associated with increased postoperative complications but not in the oncological and mortality outcomes. In our setup, addressing nutrition would thus allow patients to complete planned chemo radiation plans, be it palliative or neoadjuvant as was shown in a previous retrospective study (23).

Conclusion

We conclude that there is under workup of patients with EC at MNH despite the ability of the center to do so. This has led to improper assignment of disease extent and few curative attempts including a low resection rates. This practice could be attributed to the current practice status where there is a lack of protocol for such patients locally. We propose to investigate and propose a workflow process for patients with dysphagia at MNH, first addressing nutritional rehabilitation before embarking on definitive diagnosis. We believe strategies to rapidly relieve dysphagia and/or offer nutritional rehabilitation should be urgently undertaken. Furthermore, good oncological practice demands that all patients get a stage of their disease for personalized care and prognosis.

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Abbreviations

AfrECC	Africa Esophageal Cancer Consortium
CT	Computed Tomography
EC	Esophageal Cancer
FNAC	Fine Needle Aspiration Cytology
GFT	Gastrostomy Feeding Tube
MNH	Muhimbili National Hospital
MRI	Magnetic Resonance Imaging
MUHAS	Muhimbili University of Health and Allied Sciences
SEMS	Self-Expanding Metallic Stents
USS	Ultrasound

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Author contributions

LOA conceived and designed the study, and reviewed the manuscript. RM designed, collected and analyzed data. DMA wrote the first draft manuscript. NEK wrote the first draft manuscript. KK reviewed the manuscript. JN reviewed the manuscript. All authors read and approved the study for publication.

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