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Impact of Delayed Care on Surgical Management of Patients with Gastric Cancer in a Low-Resource Setting

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Abstract

Background: Gastric cancer is the fifth most common cancer in Eastern Africa. Diagnostic delays in low-resource countries result in advanced disease presentation. We describe perioperative management of gastric cancer in Rwanda.

Methods: Retrospective review of records at three hospitals was performed to identify gastric adenocarcinoma cases from January 2012 – June 2016. Multiple perioperative and tumor-related variables were collected. Descriptive and bi-variate analyses were performed.

Results: Final analysis included 229 patients with gastric cancer. Median age was 58 years (IQR 49–65) and 49.6% were female (n=114). Patients reported symptoms (i.e., weight loss, epigastric pain) for median time of 12 months (IQR 7.5–24). On presentation, 18.8% (n=43) had gastric outlet obstruction; 13.5% (n=31) had a palpable mass. Fifty-one percent (n=117) underwent an operation; of these, 74% (n=86) received gastrojejunostomy or were inoperable; 29% (n=34) underwent curative resection. Palliative care referrals were made for 9% (n=20). Pathology reports were available for 190 patients (83.0%). Only 11.3% (n=26) had *H. pylori* testing, and 65.4% tested positive (n=17).

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Study Sites:
Rwanda Military Hospital; Kigali, Rwanda
University Teaching Hospital of Butare; Butare, Rwanda
Butaro District Hospital/Butaro Cancer Center of Excellence; Butaro, Rwanda

Conclusions: A majority of patients presented with advanced disease. Very few patients had a curative resection. Significant advances in diagnosis and treatment are needed to improve care of gastric cancer in Rwanda.

Keywords

Africa; Rwanda; gastric cancer; low-resource; cancer surgery

Introduction

There remains a paucity of epidemiologic data related to non-communicable diseases (NCDs) in sub-Saharan Africa. Cancer has been identified as the second leading cause of NCD-related mortality, and nearly two-thirds of all cancer deaths come from low- and middle-income countries (LMICs).[1, 2] The Global Burden of Disease Study 2013 reiterated that while age-standardized cancer mortality rate is decreasing, the overall number of cancer-related deaths is increasing. This is multifactorial and can be attributed to environmental and behavioral risk factors, such as infections, like *H. pylori*, smoking and obesity, as well as to increasing average age of persons in LMICs.[3–5] Currently available statistics suggest that gastric cancer is the 12th most common cancer in Africa.[6] Rates are highest in East African countries, including Rwanda, which has an estimated incidence and mortality of 8.3 and 8 per 100,000, numbers which likely underestimate the actual problem.[6] A bias likely exists due to multiple factors, including differential availability of country-specific cancer registries, access to care, and diagnostic modalities, such as upper endoscopy and pathology services.[6, 7]

Rwanda is a small country in East Africa with a population of 11.9 million. As of 2016, there were forty-five hospitals in Rwanda, comprised of forty-two district hospitals, two provincial referral hospitals with university affiliations, and one tertiary care hospital in the capital, Kigali. There are profound deficiencies that exist in surgical and endoscopy infrastructure, personnel and training within Rwanda, with only 1.2 operating theaters per 100,000 persons and only 1.5 general surgeons per million persons, numbers well below the recommended international minimum of 20 surgical, anesthesia and obstetric providers per 100,000 persons as established by the Lancet Commission for Global Surgery.[8] There are currently a limited number of public facilities in Rwanda where gastric cancer operations are capable of being performed. Diagnostic delays result in advanced disease presentation for patients with gastric cancer in Africa.[6] Poor diagnostic capacity, limited screening, and low treatment rates for patients with *H. pylori* are among the potential causative factors that further accentuate high gastric cancer rates in East Africa.[9]

The current study represents the first attempt to characterize surgical management and outcomes for patients presenting with gastric cancer in Rwanda. The primary aim was to describe surgical management and characteristics of patients undergoing surgery for primary gastric adenocarcinoma.

Methods

Study design and variable definitions

This is a retrospective cohort study of all patients with pathologically- or surgically-confirmed gastric adenocarcinoma treated at three Rwandan hospitals between January 1, 2012 and June 30, 2016. Two hospitals—Rwanda Military Hospital (RMH) and University Teaching Hospital of Butare (CHUB)—are teaching/referral hospitals; the third is the Butaro District Hospital (BDH) where the Butaro Cancer Center of Excellence (BCCOE) was established through a partnership with the Dana-Farber/Brigham and Women's Cancer Center (DFBWCC) in Boston, Massachusetts and Partners In Health/Inshuti Mu Buzima in Rwanda in 2012. BDH/BCCOE is one of few public facilities in Rwanda where eligible patients may receive chemotherapy.

Hospital logs including endoscopy logs, pathology records, surgical ward and case logs were reviewed to identify qualifying patients. Clinical and demographic factors collected and analyzed in this study included the following: primary site of tumor, hospital identification number, medical record number, phone number, date of first presentation to hospital, demographic factors (age, sex, insurance status, primary occupation, alcohol use, smoking history, marital status, surgical history, family history, past medical history, current medications, use of traditional medications), primary residence (province, district, sector, cell), primary treatment facility, blood type, presenting symptoms/physical exam findings (weight loss, gastric outlet obstruction, palpable mass, cachexia, lymphadenopathy), symptom duration, diagnostic imaging (endoscopy, computed tomography, ultrasound), laboratory values (hemoglobin, *H. pylori* testing), tumor location in stomach, pathology (grade, stage, histologic subtype), receipt of surgery, type of surgery (i.e., gastrojejunostomy, Roux-en-Y), intent of surgery (i.e., palliative versus curative), other treatment received (chemotherapy, radiation, palliative referral), length of stay, operative duration, treatment-related complications, most recent vital status, and date of death.

Data analysis

The distributions of demographic and clinical variables were analyzed and presented in a descriptive fashion. Characteristics for patients undergoing surgery versus no surgery were compared using bivariable analysis utilizing student's t-test and Pearson's chi square, as appropriate. Age was the only normally distributed, continuous variable and is reported as the mean with standard deviation. The distributional characteristics of other continuous variables were expressed using the median and interquartile range (IQR), and the statistical significance of differences in medians were assessed using the Mann-Whitney test. The threshold for statistical significance for each comparison was set at an alpha level of 0.05. Institutional Review Boards of the University of Virginia, RMH, and CHUB approved this study (IRB-HSR protocol #18494).

Results

Study demographics and epidemiology

A total of 229 patients from three hospitals (RMH, CHUB, BDH) were included in the study. The median age of the study population was 58 years (IQR 49–65). Half the patients were male (n=115, 50.2%) with a median symptomatic period of twelve months (IQR 7.5–24). The most common presenting symptoms were weight loss (n=53, 23%) and gastric outlet obstruction (GOO) (n=43, 18.8%); the most common physical exam finding was a palpable abdominal mass (n=31, 13.5%). Most patients were diagnosed with endoscopy and biopsy (n=164, 71.6%) and just over one-quarter of patients had a pre-treatment CT scan performed (n=63, 27.5%). Other demographic and perioperative variables are listed and summarized in Table 1.

Treatment and complications for patients with gastric tumors

Just over half of patients underwent any operative procedure (n=117, 51%, Table 2). Among those, 86 (74%) were only deemed to be eligible for palliative bypass given intraoperative findings of tumors invading adjacent structures or metastatic disease that precluded an attempt at curative resection. Among patients who were found to have distant disease at the time of operation, only 20 of 83 (8.7%) received palliative care or chemotherapy. Among the 117 patients who received surgery, 30 (25.6%) underwent surgery with a curative intent with either partial or sub-total gastrectomy and a Billroth I or II reconstruction (see Table 3). Among patients undergoing an operation, thirty-one (13.5%) patients experienced some type of complication.

Tumor pathology and H. Pylori testing

Pathology reports were available for 190 patients (83.0%). Among those reports, tumor grade was available in 18.4% (n=35); tumor stage was available in 13.2% (n=25) of cases. Slightly more than one-quarter (n=49, 25.8%) of reports had final tumor subtype consistent with diffuse or undifferentiated gastric tumors. Just under one-quarter (n=47, 24.7%) of all tumors were intestinal-type or well-differentiated gastric tumors. Only 11.3% (n=26) of all patients underwent *H. pylori* testing. Among those tested, 65.4% (n=17) had a positive result.

Discussion

In the present study, we have demonstrated that 86% of patients with gastric cancers presenting in Rwanda are late stage and, unfortunately, inoperable or only appropriate for palliative bypass. By comparison, in the US between 2004 and 2009, over 30% of all stomach cancers were diagnosed at an advanced stage [10] Patients elsewhere in sub-Saharan Africa, in similarly low-resourced settings, also suffer from delayed presentation and depend primarily on surgical management for the treatment of gastric cancer.[11–14]

Age-standardized rates of stomach cancer in Eastern Africa have been estimated at 5.2 and 3.9 per 100,000 for men and women, respectively.[15] There are very few prior studies evaluating gastric cancer epidemiology or management in Rwanda.[16] Recognizing the vast

differences in access to care for rural versus urban-dwelling Rwandans, the BDH/BCCOE was established as a new center for quality cancer care within the country. In the facility's first two years, over 2000 patients were treated for various cancers; among this population, gastric cancer was identified as the sixth most common solid, non-skin cancer tumor.[17] In 2014, a one-year observational study at two Rwandan referral hospitals demonstrated that out of 82 total patients with GOO, over two-thirds were diagnosed with gastric cancer.[18] Ntakiyiruta described a retrospective case series of 35 patients with gastric cancer collected over a period of one year at Kibogora hospital in Rwanda. More than three-quarters of tumors were considered T3, and pathology results, available in only 57% of cases, revealed intestinal type gastric adenocarcinoma in all specimens. There was no evaluation of *H. Pylori* infection, nor of alcohol and tobacco consumption.[19]

Earlier detection of gastric malignancies may be achieved through increasing awareness among practitioners of prevalence of the disease and how it presents—primarily with dysphagia and weight loss; increasing capacity for upper endoscopy and *H. Pylori* testing and eradication; and training surgeons to perform resection rather than bypass, if feasible. Elsewhere in East Africa, Ugandan researchers have indicated that the addition of alarm symptoms or new dyspepsia symptoms after age 35–40 should be an absolute indication for evaluation and management of symptoms.[20] Lessons from settings with high rates of gastric malignancy might potentially be applied in a setting such as Rwanda. Shen and colleagues published resource-stratified guidelines for targeting gastric cancer management in Asia. In their paper, the authors stressed awareness of the cost-effectiveness of cancer interventions and recommended evaluation only for patients with a combination of risk factors, including male sex, age, and long-standing *H. pylori*.[21]

The median time between symptom onset and diagnosis was 12 months in our study. In the case of symptomatic patients or those strongly suspected of having a malignancy, earlier referral is often inhibited by a lack of providers and lack of financial coverage for cancer treatments, an issue not specific to Rwanda.[22, 23] If a symptomatic patient is not referred to a facility with diagnostic capabilities after presenting to a more remote facility, the patient is unlikely to receive timely medical care. Delays in referrals result in more advanced disease presentation that can necessitate palliative, rather than curative surgery. In Nigeria, patients with gastric malignancies commonly presented with advanced tumors, limiting use of partial gastrectomy and jejunostomy.[24] Only 37% of patients in our study underwent distal gastrectomy. Surgeons should perform curative resection whenever possible and should be trained to recognize and perform curative resections in situations where distal gastrectomy and reconstruction are possible, rather than dependence on palliative bypass.

It remains unclear what the capacity is for evaluating patients presenting with early symptoms of gastric cancer, such as dyspepsia, in Rwanda. Nearly 75% of patients in our study underwent at least one endoscopy; however, only 11% of study participants had *H. pylori* testing, which highlights a potential area for improvement for patients with symptomatic dyspepsia and, potentially, gastric cancer. A recently completed study at the CHUB reported that over 1000 upper endoscopies were performed in a 12-month period during 2011–2012. Among this study population, there was a 4.5% rate of malignancy diagnosis.[25] The main indication for gastroscopy was dyspepsia (84% of cases; 812/961).

Few patients (10%; 97/961), who had received ‘triple therapy’ (H. pylori eradication therapy usually consisting of amoxicillin, metronidazole and omeprazole in Rwanda) prior to their gastroscopy, were on current anti-secretory therapy at the time of gastroscopy (7.8%; 75/961) or had undergone prior gastroscopy (5.2%; 50/961). This finding demonstrates a disproportionally large percentage of malignancy among Rwandans; not only does it demonstrate a potential opportunity to expand on this study, but also to prospectively collect data on patients undergoing upper endoscopy.[25]

The present study has several important limitations. Not all facilities that treat cancer patients are included in the present analysis. Rwanda is a small country with only four public teaching and referral hospitals, however the majority of cancer care is delivered at the three included facilities. Patients presenting for surgical management exclusively at the teaching hospital in Kigali or a private hospital may be missing from the current analysis. The lack of a tumor registry means that comprehensive outcomes data related to cancer surgery is not currently available in Rwanda. This results in an inability to evaluate those who underwent curative intent surgery and a lack data on mortality.

Importantly, this study demonstrates variability in quality of medical records and of pathology reports. Less than a quarter of study patients had tumor stage available. Despite this, available records showed a trend towards most tumors being poorly differentiated and advanced stage. This is representative of a significant challenge to rolling out cancer services in low-resource settings that has been recognized in other similar settings.[26, 27] Researchers at the BDH/BCCOE sought to tackle this challenge in a way that is potentially replicable in similarly-resourced settings through careful procurement of equipment for processing of specimens and specialized training for histopathologists and technicians [7] Furthermore, biopsies may be difficult to transport centrally if performed at facility without a pathologist or they may sit in a long queue and go unprocessed for long periods of time. Improving pathology services is essential to providing accurate diagnoses for patients evaluated both endoscopically and operatively for suspected gastric cancer in Rwanda. Further research into *H. pylori* epidemiology and other potential risk factors for gastric cancer unique to East Africa is required. Given limited diagnostic and treatment modalities, increased awareness and education of providers may improve diagnostic delays without significantly impacting outcomes. However, implementation of these educational programs and their impact on time to curative surgery will require further investigation as this is one potential avenue to improving outcomes for patients with gastric cancer in Rwanda.

Conclusions

Patients in Rwanda with gastric malignancies are diagnosed at late stages. Earlier diagnosis of gastric cancers may enhance the ability of surgeons to provide a curative option for this disease in Rwanda and likely elsewhere in similarly-resourced settings. Substantial challenges in quality and validity of pathologic analysis and multimodality therapies remain in this setting.

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Synopsis

Patients diagnosed with gastric cancer in Rwanda are often late stage and only eligible for palliative surgery or, in selected cases, chemotherapy. We describe the current landscape for gastric cancer management in a low-resource setting.

Table 1:

Study demographics (N=229)

Age (in years), median (IQR)	**58 (49-65)**
Female sex, n (%)	114 (49.6)
Self-reported weight loss, n (%)	53 (23.0)
Palpable abdominal mass, n (%)	31 (13.5)
Gastric outlet obstruction, n (%)	43 (18.7)
Cachexia, n (%)	24 (10.4)
Symptom duration (in months), median (IQR)	12 (7.5-24)
Overall stage, n (%)[a] Stage 1 Stage 2 Stage 3 Stage 4	 5 (2.2) 7 (3.0) 11 (4.8) 25 (10.9)
Tumor grade, n (%)[b] Poorly differentiated Moderately differentiated Well differentiated	 35 (15.2) 15 (6.5 12 (5.2)
Tumor subtype, n (%) Diffuse Intestinal	 49 (21.3) 47 (20.4)
Chemotherapy received, n (%) Neoadjuvant chemotherapy, n (%)	28 (12.2) 15 (6.5)[c]
CT Abdomen performed, n (%)	63 (27.4)
Endoscopy performed, n (%)	164 (71.3)
Surgery performed, n (%)	117 (51.1)

IQR: interquartile range

[a]Data needed to determine overall stage was incomplete or missing for 182 (79.1%) of patients.

[b]Grade was missing for 168 (73.04%) of patients.

[c]These 15 are a subset of those receiving chemotherapy. The percent is related to the overall study population N of 229.

Table 2:

Characteristics of patients undergoing surgery versus no surgery (N=229)

	Surgery (n = 117)	No Surgery (n = 112)	p-value[a]
Age (in years), median (IQR)	58 (50-64)	59 (48-67)	0.457
Female sex, n (%)	58 (50)	56 (50)	0.948
Self-reported weight loss, n (%)	37 (36)	16 (20)	0.018
Palpable abdominal mass, n (%)	13 (11)	18 (16)	0.285
Gastric outlet obstruction, n (%)	39 (33)	4 (3.5)	<0.001
Symptom duration (in months), median (IQR)	18 (8-36)	12 (6-12)	0.015
Overall stage, n (%)			
Stage 1	5 (17.9)	0 (0)	
Stage 2	7 (25.0)	0 (0)	
Stage 3	6 (21.4)	5 (25.0)	
Stage 4	10 (35.7)	15 (75.0)	0.004
Tumor grade, n (%)			
Poorly differentiated	19 (55.9)	16 (57.1)	
Moderately differentiated	6 (17.7)	9 (32.1)	
Well differentiated	9 (26.5)	3 (10.7)	0.200
Tumor subtype, n (%)			
Diffuse	25 (50.0)	24 (52.2)	
Intestinal	25 (50.0)	22 (47.8)	0.831
Chemotherapy received, n (%)	25 (21.4)	3 (2.7)	<0.001
Neoadjuvant/palliative chemotherapy, n (%)	12 (54.6)	3 (100.0)	0.250

IQR: interquartile range

[a] p-value less than 0.05 considered significant

Table 3:

Type of surgery received (n = 117)

Curative surgery, n (%)	30 (25.6)
Distal gastrectomy, n (%)	11 (36.7)
Other gastrectomy, n (%)	19 (63.3)
Palliative surgery, n (%)	86 (73.5)
Gastrojejunostomy, n %)	71 (82.6)
Exploratory laparotomy/primary repair of perforation, n (%)	15 (17.4)
Unknown intent of surgery, n (%)	1 (0.85)