

Short Term Outcomes of Gastric Cancer at University Teaching Hospital of Kigali (CHUK), Rwanda.

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Abstract

Background: Gastric cancer is the 4th most common cause of cancer death worldwide with an annual global incidence of 985,600; two thirds of them being in the developing countries. Gastric cancer is endemic in the so called stomach cancer region comprising Rwanda, Burundi, South Western Uganda and eastern Kivu province of Democratic Republic of Congo and its incidence in Rwanda is estimated around 13 to 15 per 100,000 population. To date, the outcomes of gastric cancer in the East African region are under investigated, and the survival rate in Rwanda is not known. The aim of this study was to describe the short term outcomes (in-hospital mortality rate, length of hospital stay, 3, 6, 12 and 24 months survival rates) in patients treated for gastric cancer at CHUK.

Methods: We retrospectively reviewed the data collected from records of patients who consulted CHUK over a period of 10 years from September 2007 to August 2016. Patients were followed in hospital and after discharge for survival length. Descriptive statistics were used for baseline demographic data, Kaplan-Meier model and univariate cox regression were used for survival analysis.

Results: Of the 199 patients enrolled in the study, 92 (46%) were males and 107 (54%) females. The mean age was 55.4 ranging between 24 and 93. The mean symptoms duration was 15 months. Most patients consulted with advanced disease, 62.3% with distant metastases. Treatment with curative intent was offered for only 19.9% of patients. The in-hospital mortality rate was 13.3%. The 3, 6, 12 and 24 months survival rate was 52%, 40.5%, 28% and 23.4% respectively. The Overall survival rate was 7 months.

Conclusion: Patients with gastric cancer have delayed consultations and advanced disease at the time of presentation. This cancer is associated with poor outcomes in terms of hospital mortality and post discharge survival rates.

Introduction

Gastric cancer is one of the most common malignant diseases with significant geographical, ethnic, and socioeconomic differences in distribution. It used to be the leading cause of cancer deaths in the world until the 1980s when it was overtaken by lung cancer [1], but until now, it has remained a major public health concern.

The three most common primary malignant gastric neoplasms are adenocarcinoma (95%), lymphoma (4%), and malignant GIST (1%) [2].

The annual global incidence of gastric cancer is approximately 985,600 with about two thirds of them being in the developing countries with 738,000 minimum expected deaths [3]. In the United States, approximately 22, 220 patients are diagnosed each year, of whom 10,990 are expected to die [1].

The incidence of gastric cancers is high in China, Japan, Korea, South America and Eastern Europe, but comparatively low in most of Europe, North America and Africa. The prevalence of gastric cancer is low in

sub-Saharan Africa with the lowest incidence rates in Western Africa [3].

Gastric cancer is endemic in the so called stomach cancer region comprising Rwanda, Burundi, South Western Uganda and eastern Kivu province of Democratic Republic of Congo [4]. The incidence in the great lakes region is reported to be 3.2/100,000 population. The reason for gastric cancer to be common in this region is unclear, but lack of trace minerals in its volcanic soil is among suspected causes.

The incidence of gastric cancer in Rwanda was estimated to be around 13 to 15 per 100,000 population which is high compared to the regional incidence (3.2 per 100,000 in Great Lakes region)[5].

Over the last decades, gastric cancer has been showing improved outcomes evidenced by low early postoperative mortality rates, shorter lengths of hospital stay and improved overall survival but treatment results remain poor with the prognosis depending mainly on the stage of the disease [6].

In low and middle income countries, patients delay to reach care and they get diagnosed when the cancer is advanced with lymph nodes and distant metastasis. Most of these patients get palliative surgery because the possibility of cancer resection is very low [7, 8, 9]. The outcomes are subsequently poor with high post-operative complications rate (up to 37.1%), increased post-operative mortality rate (13.8–18.1%) and shorter survival rates compared to high income countries [8, 10, 11, 12].

Late patient presentation, scarcity of diagnostic tools and staff, limited treatment modalities, shortness of surgeons and many other factors compromise the outcome of patient with gastric cancer in countries with limited resources.

This is the first study reporting outcomes of gastric cancer in terms of survival rates in Rwanda.

The aim of this study was to describe the short term outcomes (in-hospital mortality rate, length of hospital stay, 3 months, 6 months, 1 and 2 years survival rates) in patients with gastric cancer at University Teaching Hospital of Kigali (CHUK).

Methods

This was a retrospective study on the short term outcome of patients with gastric cancer who were treated at CHUK over a period of 10 years from September 2007 to August 2016.

Demographic data, clinical data, operative details, and post-operative follow up data were recorded from patients' record files. Post discharge data were obtained from data from Outpatient Department for those who came back for follow up, or via phone calls for those who did not. SPSS version 21 was used for data analysis. Descriptive statistics were used to describe demographic and other baseline characteristics of patients. Kaplan-Meier model and univariate cox regression were used to describe survival rate and find related prognostic factors respectively.

The primary outcomes were 3 months, 6 months, 12 months and 24 months survival rates. The secondary outcome was length of hospital stay.

Results

A total of 158 patients were enrolled in the study, 73 (46%) were males and 85 (54%) were females. The mean age was 55.4 (24–93) years, and the mean duration of symptoms was 15 months. Patients consulted from all 5 provinces of Rwanda, the Northern Province having the highest number of patients with gastric cancer as shown in Table 1:

Table 1
Patients demographics

Variables		Count	Percentage
Age	< 30	8	5.06
	30–39	19	12.02
	40–49	40	25.31
	50–59	23	14.55
	> 60	68	43.03
Sex	F	85	53.79
	M	73	46.20
Province of origin	Kigali	17	10.75
	East	29	18.35
	West	38	24.05
	South	23	14.55
	North	52	32.91
Symptoms duration (months)	Not Specified	35	22.15
	< 3 Months	14	8.86
	3–6 Months	28	17.72
	7–12 Months	41	25.94
	13–24 Months	19	12.02
	> 24 Months	21	13.29

The above table shows basic demographic data of patients with gastric cancer at University Teaching Hospital of Kigali (CHUK) from September 2007 to August 2016. A big number of patients 68(43.03) were

aged 60 years or above whereas only 8(5.06%) were aged 30 years or younger. The Northern Province was the most represented with 52(32.91%) patients and 41(25.94%) patients consulted after 7 to 12 months of onset of symptoms.

According to the Lauren classification, the most common histology type was adenocarcinoma, intestinal type 77(48.7%) patients, followed by diffuse type with 69(43.7%). According to the World Health Organization (WHO) classification, the signet ring cell carcinoma was the most common histologic type with 79(50%) patients.

Most of the patients presented with advanced disease (stage III & IV) representing 74% of enrolled patients including 62.3% with metastatic disease (Table 2).

Table 2
Histology types and stages at presentation

Classification		Count	Percentage
WHO histology type	Tubular	28	17.7
	Papillary	13.1	8.22
	Mucinous	28	17.7
	Signet ring	79	50
	Others	10	6.3
Lauren histology type	Diffuse	69	43.7
	Intestinal	77	48.7
	Mixed/Indeterminate	12	7.6
Stage at presentation	Stage I	28	17.6
	Stage II	13	8.2
	Stage III	19	11.7
	Stage IV	98	62.3

Surgical management was offered to 71 (45%) patients including 31 (19.8%) patients operated for curative intent and 40 (25.2%) patients operated for palliation. The curative surgical procedures included total gastrectomy in 2(1.3%) patients and partial gastrectomy in 29(18.5%) patients; whereas palliative surgical procedures included 32 (20.2%) gastric bypass procedures and 8 (5%) exploratory laparotomies without further action. The remaining 87 (55%) patients who did not undergo surgery were treated with non-operative palliative treatment including intravenous fluids, analgesics and palliative chemotherapy.

Table 3
Treatment offered and intention

Intention	Treatment	Count	Percentage
Curative	Partial gastrectomy	29	18.5
	Total gastrectomy	2	1.3
	Total	31	19.8
Palliative	Gastric bypass	32	20.2
	Explorative laparotomy	8	5.0
	Non-surgical palliation	87	55.0
	Total	127	80.2

The mean Length of Hospital Stay (LoHS) was 13.2 days with 69(43.7%) patients spending less than a week in the hospital and 23(14.5%) patients spent 3 weeks or more in the hospital (See table 4 for outcomes related data).

The overall hospital mortality rate for patients diagnosed with gastric cancer was 13.3%.

82 (52%) and 64(40.5%) were respectively still alive 3 and 6 months after discharge from the hospital.

The one year survival rate was 27.8% whereas the 2 years survival rate was 23.4%.

The overall median survival for patients diagnosed with gastric cancer was 7months. The median survival rate for patients operated for gastric cancer was 10.4 months while it was only 1.6 months for patients who did not undergo surgery.

Considering the survival rate with respect to the treatment offered, 75% of patients operated with curative intent survived beyond 2 years while only 11.1% of those who underwent palliative procedures were still alive after 2 years of follow up. None of the patients who were not operated on survived for 2 years.

The prognostic factors were age of the patient, the degree of differentiation of the tumor and the intention of surgery.

Patients aged from 30 to 40 years were 2 times more likely to die of gastric cancer compared to patients aged 60 years and above (Hazard Ratio (HR): 2.082, 95% CI: 1.217–3.562, p-value: 0.007). Patients younger than 30 years and those aged from 40 years to 59 did not show any survival benefit compared to those aged 60 years and above.

Patients with poorly differentiated gastric cancer were 2.6 times more likely to die of gastric cancer compared to those with well differentiated tumors (HR: 2.594, 95% CI: 1.235–5.444, p-value: 0.012).

Patients operated with palliative intent were 3 times likely to die compared to those operated with curative intent (HR: 3.101, 95% CI: 1.766–5.445, p-value: 0.001) (See table 5 for prognostic factors of gastric cancer).

Discussion

This study aimed at evaluating the short-term outcomes of patients diagnosed with gastric cancer in terms of hospital mortality and survival rates. It represents the first study of such kind ever done in the country, and is among few available in the sub-Saharan Africa.

In addition to outcomes, the present study established baseline demographic data of patients diagnosed with gastric cancer and identified some of the factors associated with mortality.

The mean age of patients with gastric cancer in this study was 55.4 years and this corroborates the findings from other sub-Saharan countries where the mean age is usually between 50 and 55 years [7, 8, 12]. Our patients developed gastric cancer at a younger age compared to patients from developed countries where a mean age above 60 years is usually reported [14, 15, 16].

The patients in this study had a delayed presentation with a mean duration of symptoms of 15 months from the onset of the first symptom to the time of the diagnosis. The delay in consultation and diagnosis is explained by the asymptomatic nature of the disease at its early stages. Several patients (74%) presented with advanced gastric cancer (Stage III and IV) at the time of the diagnosis. Delayed presentation was reported in other sub-Saharan countries with 92.1% patients presenting with advanced gastric cancer [8]. The fact that patients presented with advanced disease has negatively affected their management, limiting the treatment options to palliative surgery in 25.3% or to non-surgical palliative treatment, like intravenous fluid therapy, analgesics, nutrition and oxygen supplementation for 55% of patients. In our study, only 45% of total patients underwent surgery and among them, only 19.8% were operated for curative intent while the remaining 25.2% underwent palliative procedures. Palliative surgical procedures mainly consisted of gastrojejunostomy (with or without jejunostomy) and feeding jejunostomy. Similar findings were reported in Togo where the surgical management was possible in 46% of patients with gastric cancer including 15% palliative surgeries [7]. Though the proportion of patients who undergo palliative surgeries is still high in Rwanda, it has markedly decreased compared to the findings of previous study done in 2007 where 97.1% of operated patients underwent palliative procedures [9].

The in-hospital mortality rate in our study was 13.3% which is consistent with the mortality rate reported in other sub-Saharan countries varying between 13.8% and 18.1% [7, 8, 12].

Gastric cancer was associated with poor outcomes, with an overall median survival of 7 months which is almost half of the median survival of 13.6 months found in Nigeria [12] and 1.09 years found in China [13]. The 1 year survival rate of 28% found in this study was low compared to 51% and 52% reported in China for males and females respectively [13]. The median survival rate was better in patients who

underwent surgery with a post-operative median survival rate of 10.4 months compared to 1.6 months survival rate in patients who did not get surgery. This was expected because patients who were not operated on were judged to be in poor clinical status either due to the disease itself or due to the presence of other poor prognostic factors like severe malnutrition, comorbidities, or advanced malignancy. Those patients were managed with non-operative palliative measures such as intravenous fluids, pain killers, oxygen therapy and nutrition support where applicable.

The present study identified that age group in the thirties, presence of a poorly differentiated tumor, and the surgical procedure with palliative intent were associated with poor prognosis.

With regard to the age, most of the existing literature agrees that it does not affect the outcomes [17, 18, 19, 20] or that advanced age negatively impacts outcomes in patients with gastric cancer [15, 16, 21, 22]. However, some studies reported high prevalence of aggressive forms of cancer such as poorly differentiated tumors, diffuse type and signet ring cell carcinoma and other poor prognostic factors such as upper location of the tumor advanced stage at presentation in the young population [14, 23, 24]. The fact that the younger patients had better survival rates compared to old patients despite the presence of these factors suggests that age is not an independent predictor of mortality in patients with gastric cancer.

A poor prognosis in patients younger than 35 years was reported in some countries [25, 26] and there is some evidence that gastric cancer could be associated with poor outcomes in extremes of age (in younger population and in elderly) because of high prevalence of poor prognostic factors in the former group and the presence of comorbidities and cellular senescence in the latter, suggesting that, as far as age is concerned, a better prognosis is expected in the middle aged population [14]. There is no conventional age cutoff to define elderly patients but the age of 65, 70 or 75 are commonly considered in the literature [27, 28, 29, 30, 31]

We did not find any factor that could explain high mortality in patients aged between 30 and 39 since none of poor prognostic factors reported in the literature was most prevalent in this specific age group and a large study with multivariate analysis is required to establish the role of the age on the survival of patients with gastric cancer in Rwanda.

Regarding the grade of the tumor, this study found that poorly differentiated tumors were negative predictors of survival ($p: 0.012$) and this corroborates the existing evidence of gradual decrease of survival with respect to the differentiation status [32].

The association between palliative surgery and mortality was expected since palliative procedures were performed on patients with advanced disease.

The effect of neoadjuvant and adjuvant therapies on patients' outcomes was not assessed in this study because of insufficient data on patients who underwent chemotherapy. There was no radiation therapy available in the country before and during the study period.

Strengths And Limitations

This is the first study assessing the outcomes of gastric cancer in Rwanda, and was conducted in the largest public hospital of the country. It covered an extended period of time (10 years) and included patients from all the provinces of the country.

The limitations of this study are that it is a single center study based on retrospectively collected data. There were missing data especially about classification and follow up, which decreased considerably the number of study participants. The future studies should focus on a long term follow up project conducted on a larger population in order to provide much more information on outcomes of patients with gastric cancer and to help to evaluate the impact of treatment modalities other than surgery alone on the outcomes.

Conclusion

Gastric cancer is associated with delayed presentation and advanced disease at the time of the diagnosis, with the treatment options limited to palliative care in many patients. Gastric cancer has poor outcomes as evidenced by high mortality and short survival. This knowledge will improve gastric cancer awareness among the general population and will help clinicians to communicate with patients diagnosed with gastric cancer about the expected treatment outcomes.

Abbreviations

CHUK: Centre Hospitalier Universitaire de Kigali (University Teaching Hospital of Kigali)

WHO: World Health Organization

SPSS: Statistical Package for Social Sciences

LOHS: Length of Hospital Stay

HR: Hazard Ratio

CI: Confidence Interval

AJCC: American Joint Committee on Cancer

Declarations

Ethics approval and consent to participate: This study was approved by the Institutional Review Board of the College of Medicine and Health Sciences, University of Rwanda (IRB/CMHS/UR) and the Research and Ethical Committee of the University Teaching Hospital of Kigali (CHUK). Participants were enrolled after an informed consent.

Competing interests: The authors declare that they have no competing interests.

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Availability of data and materials: The datasets used and analyzed in the current study are available from the corresponding author upon reasonable request.

Authors contributions: IN and EA: Protocol conception; IN, JCU and AN: Design of the work; VM, JMVK and KID: acquisition and analysis of the data; IN, IS and EA: Interpretation of the data, drafting of the work and its revision.

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Figures

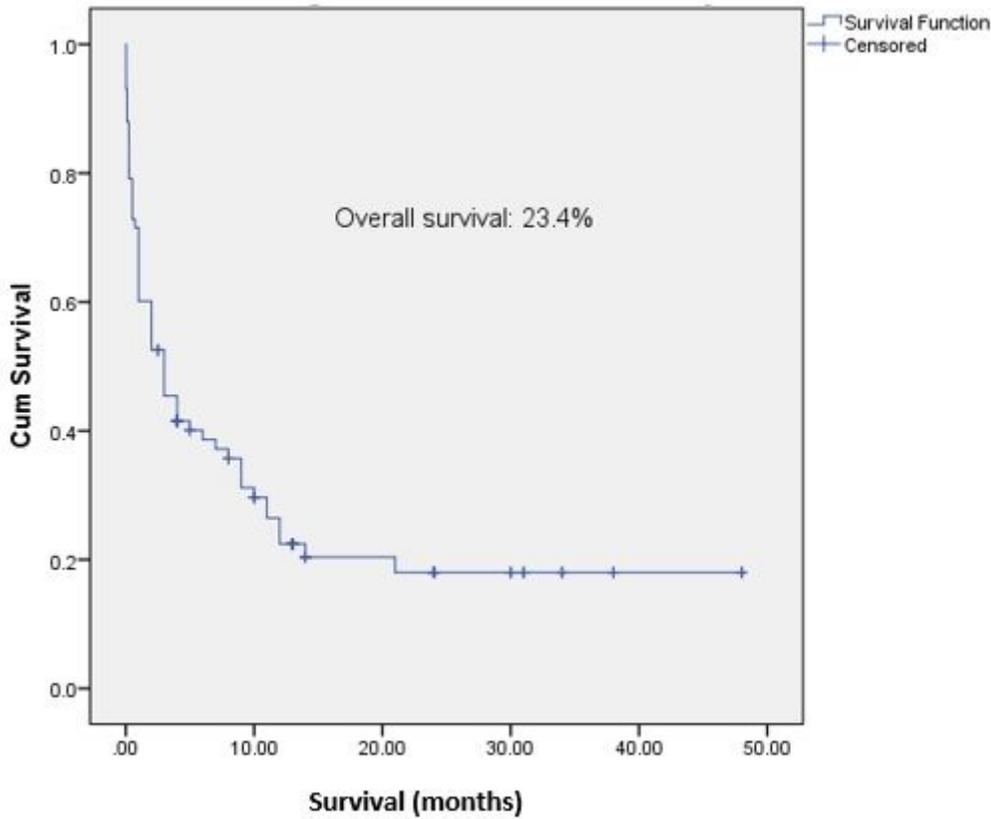


Figure 1

Overall 2 years survival for patients with gastric cancer

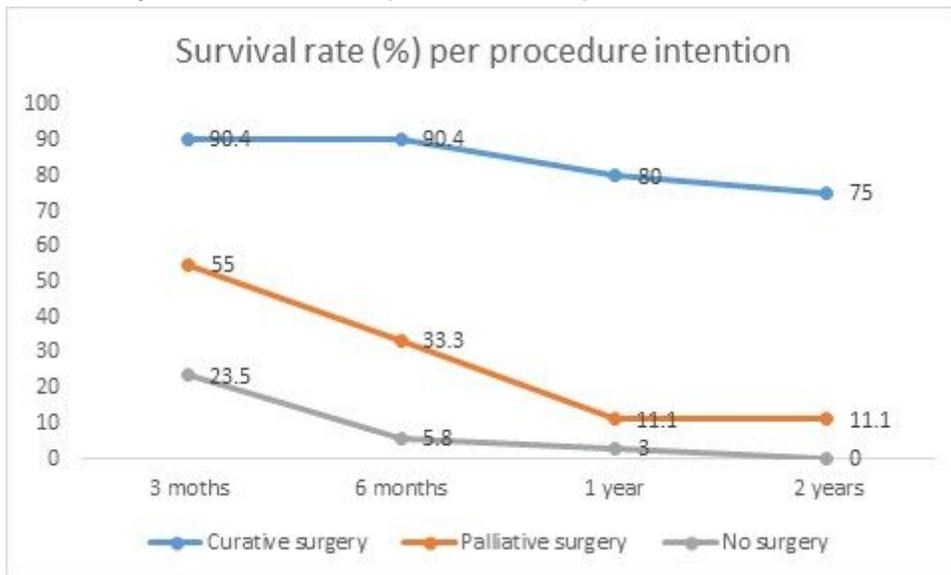


Figure 2

Survival rates per procedure intention