

# Gastric Malignancy Survival in Zambia, Southern Africa: A Two Year Follow up Study

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## ABSTRACT

**Background:** Gastric cancer poses a significant global health burden. It is the second most common cause of cancer death worldwide and the ninth leading cause of cancer mortality in Zambia, at a rate of 3.8/100,000; comparable to USA (2/100,000) and UK (3.4/100,000). Survival data on gastric malignancy in Zambia is not known.

**Objectives:** To provide preliminary survival rates of patients with histologically proven gastric adenocarcinoma in Zambia.

**Study Design:** Using our prospective gastric cancer research database, we conducted a retrospective audit of patients diagnosed with gastric cancer at the University Teaching Hospital, Zambia, from June 2010 until January 2012. We contacted patients or their relatives using phone numbers provided at time of enrollment.

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**Main Outcomes:** We reviewed age, sex, demographic data (income, education), body mass index, symptoms, duration of symptoms, treatment (surgery, chemotherapy, radiotherapy or combination) and survival outcome. Analysis was performed using Kaplan-Meier models and log rank test.

**Results:** Fifty one patients were diagnosed with gastric adenocarcinoma during the study period, but follow-up data were available for 50. Median survival was 142 days. Age, sex, income, education, BMI, tumor location, and treatment modality were not significantly associated with overall survival. In Cox regression models, covariates associated with survival were a history of regular alcohol intake (HR 0.49, 95%CI 0.26,0.92;  $P=0.025$ ) and intestinal type cancer histology (HR 0.40, 95%CI 0.19,0.83;  $P=0.01$ ).

**Conclusion:** Prognosis of newly diagnosed gastric cancer in Zambia is poor with significant mortality within 1 year of diagnosis, particularly among patients with weight loss and dysphagia.

## INTRODUCTION

Gastric cancer is the fourth most common cancer and the second most common cause of cancer death worldwide.<sup>[1]</sup> The World Health Organization predicts an increase in cancer rates by over 50% over the next 20 years. According to GLOBOCAN 2008, the incidence and

mortality rate in Zambia, Southern Africa are 4/100,000 and 3.8/100,000 respectively.<sup>[1]</sup> The incidence in USA and UK is 4.1/100,000 and 5.5/100,000 respectively.<sup>[1]</sup> The mortality rate is higher in Zambia, 3.8/100,000, compared to USA and UK, 2/100,000 and 3.4/100,000 respectively. The 5-year survival of gastric cancer in USA is 17 %-25%,<sup>[2]</sup> similar to the UK at 17 %.<sup>[3]</sup> The incidence and mortality rates in Zambia are comparable to that of USA and UK yet there are no studies regarding outcomes and management. In a retrospective study, Kelly et al analyzed 2132 upper endoscopy and histopathology reports from 1999 to 2005, and reported the frequency of gastric cancer to be 5.3%, interestingly the incidence in individuals younger than 45 years was higher than in USA or UK.<sup>[4]</sup> Review of literature shows less than 5 published studies regarding gastric cancer in Zambia<sup>[5-7]</sup> and no studies about management survival outcomes.

Some factors that influence survival outcome include clinical presentation, patient demographics, cancer location, histopathology, stage at diagnosis and treatment.<sup>[8]</sup> A better understanding of these factors could impact management options, increase awareness amongst patients and ultimately impact survival outcome. The role of clinical presentation, duration of symptoms and treatment in gastric cancer outcome in the Zambian population has not been studied. Thus we evaluated risk factors associated with gastric cancer survival in Zambia. This data will help establish prognostic indicators and guide management.

## METHODS

We have previously reported a case-control study of gastric cancer from the Endoscopy Unit of the University Teaching Hospital, Lusaka, Zambia. Having subsequently been involved in their care and follow-up, we report survival data over a two year period. The University Teaching Hospital (UTH) is the largest tertiary hospital in Zambia, Southern Africa. Gastric cancer cases were defined as subjects with histopathologically proven gastric cancer.

### *Data collection*

Informed consent was obtained from all patients at time of study enrollment. A questionnaire was used to collect

demographic data (age, gender, occupation, socio-economic status and education level); a medical history was obtained including symptoms, duration, treatment modality (surgery, chemotherapy, radiotherapy or combination) family and social history (alcohol consumption and smoking). A physical examination was performed on all subjects at initial enrollment and body mass index (BMI) calculated. Management was at the discretion of the surgical or oncology team. Chart review and discussion with patient was used to determine treatment plan. *Treatment included surgery, chemotherapy, radiation therapy or a combination.* Information about cancer stage was unavailable for most patients because patient financial limitations precluded testing for staging or because patients died before oncology referral.

### *Statistical analysis*

Stata version 13 (Stata Corp, College Station, TX) was used for statistical analysis. Descriptive analysis was used to calculate the mean  $\pm$  standard deviation. Overall survival was calculated as the number of days between diagnostic endoscopy and death or censored at last follow-up. Cox proportional hazard regression models were constructed to describe univariate associations between potential determinants of survival and factors with  $P < 1.0$  or of a *priori* interest were included in multiple regressions models. The association between histological type and survival was tested using the log-rank test and displayed as a Kaplan-Meier plot.

## RESULTS

Fifty one patients were diagnosed with gastric adenocarcinoma during the study period. Their mean age was 61.7 years  $\pm$  15.5 (62% male). One patient was excluded because time to death was unknown, leaving 50 patients to be analyzed. Their demographic characteristics and the features of their presenting illness are shown in Table 1. Three patients (6%) were HIV positive, but one result was missing. All HIV positive patients had a CD4 count below 350 cells/ $\mu$ L. The majority of gastric cancers were located in the antrum, and most were intestinal adenocarcinoma. Due to resource limitations, the majority of patients did not receive treatment considered optimal by international

standards. However, prompt treatment with chemo-radiotherapy was available and is shown in Table 1.

Survival is shown in Figure 1. Univariate and multivariate analysis is shown in Table 2. A history of regular alcohol intake was associated with better survival, as was intestinal histology and education. (Table 2, Figure 2).

**Table 1** Demographic data and Clinical Features

	Male	Female	P
Age			
<45 years	8	3	0.78
46 – 60 years	5	4	
>60 years	19	12	
HIV status			
Seropositive	2	1	1.00
Seronegative	29	18	
Education			
None	0	9	0.001
Primary	11	7	
Secondary	18	1	
College/University	3	1	
Monthly Income			
<250,000K	3	4	0.36
251,000 – 500,000	6	1	
501,000 – 1,000,000	3	4	
1,000,000 – 5,000,000	4	0	
>5,000,000	2	1	
Irregular income	1	1	
Unsure	12	8	
Body mass index (kg/m <sup>2</sup> )	20.8 (SD 4.2)	19.3 (SD 4.0)	0.22
Histological type			
Intestinal	25	15	1.00
Diffuse	3	4	
Mixed	2	0	
Not classified	2	0	
Smoking			
Ever	11	3	0.20
Never	21	16	
Regular alcohol consumption			
Ever	17	4	0.04
Never	15	15	
Symptoms present			
Dysphagia	3	2	1.00
Vomiting	9	7	0.55
Abdominal pain	24	13	0.75
Treatment delivered			
Surgery (palliative)	9	3	0.50
Chemotherapy	4	2	1.00
Radiotherapy	4	2	1.00

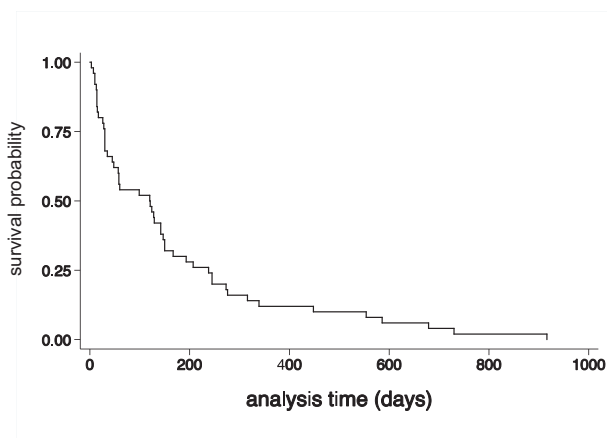
Conversion \$1USD = approximately K5,000

**Table 2:** Univariate and multivariate analysis of covariates of survival using Cox regression analysis

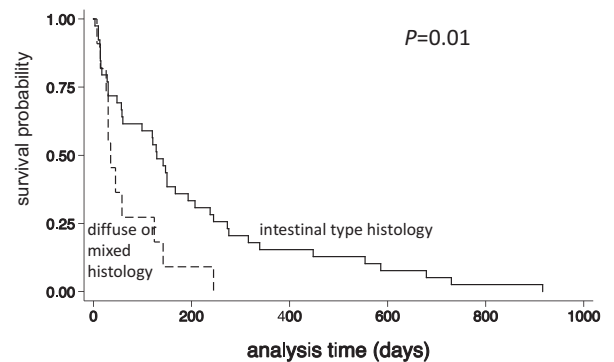
Variable	Univariate		Multivariate	
	HR	P	HR (95%CI)	P
Female sex	0.71	0.24	-	
Age under 45 years	0.56	0.12	-	
No education	0.58	0.14	-	
BMI <18.5 kg/m <sup>2</sup>	0.68	0.24	-	
Gastric atrophy	1.08	0.79	-	
Regular alcohol intake	0.52	0.04	0.49 (0.26,0.92)	0.025
Dysphagia	2.47	0.07	-	
Vomiting	0.96	0.89	-	
Abdominal pain	0.84	0.59	-	
Intestinal type histology	0.44	0.02	0.40 (0.19,0.83)	0.01
Surgery	1.33	0.42	-	
Chemotherapy	0.38	0.07	-	
Radiotherapy	1.49	0.37	-	

HR: hazard ratio. Gastric atrophy was defined as low pepsinogen 1:2 ratio (<4.0). Variables associated (P<0.1) in univariate analysis were tested in multivariate analysis.

**Figure 1:** Overall survival of Zambian patients with gastric cancer. Kaplan-Meier plot of survivorship against time in the whole group (n=50)



**Figure 2:** Survivorship (Kaplan-Meier plot) of gastric cancer patients according to histological type (Lauren classification): intestinal type (n=39) against all other types (n=11). P=0.01 by the log rank test.



## DISCUSSIONS

There are few data on cancer survivorship in Africa. This study is limited in size, and data were collected in a secondary/tertiary hospital. However, we believe that useful conclusions can be drawn. It is clear that there were very few patients who might have had resectable tumours, and in no case was curative resection attempted. Several factors may account for this: late presentation, delays in referral within the health service, inexperience and reluctance to perform curative surgery, or resource constraints. The first line of treatment for gastric malignancy is surgery when it is possible, so clearly this is a major contributor to poor survival. It is unfortunate that the great majority of our patients were unable to afford staging investigations, the most important of which would be CT scanning or intra-operative evaluation.

In multivariate analysis we found that clinical features did not predict survival, and nor did the presence of gastric atrophy. Surprisingly, we found no evidence of an effect of malnutrition on survival. Only two factors were associated with improved survival: a history of alcohol intake, and histology (Lauren classification). The adverse prognosis of diffuse type cancer and mixed histology is not unexpected. However, the observation about alcohol is harder to explain.

The findings in our study suggest a poor prognosis of gastric cancer with late survival within one year of diagnosis (30%). In United Kingdom the one year survival is 42.2% in men and 41.7 % in females.<sup>[9]</sup> Other African countries seem to have a poor overall one year survival outcome, Senegal 39.1%<sup>[10]</sup>, Mali 15.5%<sup>[11]</sup>, Tunisia 7%.<sup>[12]</sup> According to the World Health Organization, non-communicable diseases are the leading cause of global mortality affecting low and middle income countries, and projected to surpass communicable disease by the year 2030.<sup>[13]</sup> Overall global cancer rates are expected to increase by 50% over the next 20 years.<sup>[14]</sup> Therefore, it is imperative for further research to increase understanding and improve patient outcomes. Information regarding gastric cancer within most countries in Africa is lacking, primarily due to under-reporting because of lack of diagnostic resources and limited manpower.

## CONFLICT OF INTEREST AND DISCLOSURE

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