



The incidence of oesophageal cancer in Eastern Africa: Identification of a new geographic hot spot? [☆]



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ABSTRACT

The incidence of oesophageal cancer (OC) varies geographically, with more than 80% of cases and deaths worldwide occurring in developing countries. The aim of this study is to characterize the disease burden of OC in four urban populations in Eastern Africa, which may represent a previously undescribed high-incidence area. Data on all cases of OC diagnosed between 2004 and 2008 were obtained from four population-based cancer registries in: Blantyre, Malawi; Harare, Zimbabwe; Kampala, Uganda; and Nairobi, Kenya. Age-standardized incidence rates (ASRs) were calculated for each population, and descriptive statistics for incident cases were determined. In Blantyre, 351 male (59%) and 239 (41%) female cases were reported, with ASRs of 47.2 and 30.3. In Harare, 213 male (61%) and 134 (39%) female cases were reported, with ASRs of 33.4 and 25.3, respectively. In Kampala, 196 male (59%) and 137 female (41%) cases were reported, with ASRs of 36.7 and 24.8. In Nairobi, 323 male (57%) and 239 female (43%) cases were reported, with ASRs of 22.6 and 21.6. Median age at diagnosis was significantly different among the four populations, ranging from 50 years in Blantyre to 65 years in Harare ($p < 0.0001$). Except in Nairobi, incidence among males was significantly higher than among females ($p < 0.01$). Squamous cell OC was the predominant histologic subtype at all sites. ASRs at all four sites were remarkably higher than the mean worldwide ASR. Investigation to evaluate potential etiologic effects of dietary, lifestyle, environmental, and other factors impacting the incidence in this region is needed.

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1. Introduction

The mean worldwide age-standardized incidence rates (ASRs) for oesophageal cancer (OC) were estimated in 2012 to be 9.0 in males and 3.1 per 100,000 in females [1]. However, this statistic does not reflect remarkable geographic variations in incidence rates. Currently, more than 80% of cases and deaths from OC occur

within developing countries [1]. One of the most striking features of OC is the presence of high-incidence geographic regions, which have been previously identified in locales including northern China, Northeastern Iran, Eastern South America, and South Africa [2,3]. Even within Africa, incidence rates for OC may vary widely; GLOBOCAN 2012 reported an ASR of 9.7 in Eastern Africa, compared to ASRs of 0.6 and 2.2 in Western and Northern Africa [1].

Both scattered historic reports and emerging descriptive data suggest that high-incidence geographic areas may be present in Eastern Africa. Western Kenya was reported as a high-incidence region for OC as early as the 1960s [4], and more recent data published by the Nairobi Cancer Registry reported OC to be the most common site of cancer among men from 2000 to 2002, accounting for 10% of all pathologically confirmed malignancies [5]. The Zimbabwe National Cancer Registry reported ASRs for OC

[☆] This work was previously presented in an oral presentation by Dr. Van Loon at the 2013 AORTIC Meeting, Durban, South Africa and by Dr. Cheng at the 2014 NCI/CUGH Symposium on Global Cancer Research, Washington, DC, United States (Abstract 8).

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in the black males and females of Harare ranging from 18.9 to 24.6 between 1991 and 2010 [6]. The cancer registry of Kyadondo County, Uganda reported OC to be the second most common cancer amongst men between 1981 and 1991, second only to Kaposi's sarcoma [7]. At a tertiary care center in Bomet, Kenya, a hospital-based retrospective review of all pathologically confirmed malignancies between 1999 and 2007 reported that OC accounted for 34.6% of all newly diagnosed cancers, with increasing trends over time and disproportionate numbers in very young patients [8].

OC has potential to represent a tremendous burden to healthcare systems throughout Eastern Africa. However, due to the inadequacies and outdated nature of existing data, current ASRs for this region of the world are largely unknown. Data regarding the current disease burden, time trends, and risk factors are required to direct investigations of etiology and to begin building capacity to provide effective oncologic care for this disease. Characterization of the magnitude of this problem will be a first step toward systematically defining the nature of the disease burden from OC. In an effort to further define the incidence of OC in Eastern Africa, we report data on OC from population-based cancer registries representing four urban areas in Eastern Africa.

2. Methods

2.1. Study population

Four population-based cancer registries within Eastern Africa, as demarcated by the geographical definition of the United Nations, were identified as having registry data available beginning in 2004 or earlier. The Kampala Cancer Registry was established in 1954 as a population-based cancer registry at the Department of Pathology, Makerere University College of Health Sciences, and collects data on the population of the surrounding area in Kyadondo County, Uganda. The Zimbabwe Cancer Registry was established in 1985 and is housed in the Parirenyatwa Group of Hospitals in Harare, which provides most of the specialized cancer care for northern Zimbabwe and is one of two teaching hospitals of the University of Zimbabwe's College of Health Sciences. The Nairobi Cancer Registry was established in 2001 and is situated at the Centre for Clinical Research (CCR), Kenya Medical Research Institute (KEMRI) headquarters, Nairobi. The Malawi National Cancer Registry was established in 1989 and expanded in 1993 to incorporate a population-based registry for the Blantyre District.

As member organizations of the African Cancer Registry Network (AFCRN), each met membership criteria by achieving $\geq 70\%$ coverage of its target population and agreed to participate in a retrospective review of all cases of OC reported between 2004 and 2008. Participating registries provided data from four major urban areas in Eastern Africa: Blantyre, Malawi; Harare, Zimbabwe; Kampala, Uganda; and Nairobi, Kenya. All are capital cities with the exception of Blantyre, which is the largest city and center of commerce and finance in Malawi. This project was sanctioned and approved by the Research Committee of AFCRN. It was also approved by the Committee on Human Research at the University of California, San Francisco (IRB #13-11275).

Government-sanctioned population censuses were performed in Blantyre in 1998 and 2008 [9]; Harare in 1992, 2002, and 2012 [10]; Kampala in 1991 and 2002 [11]; and in Nairobi in 1999 and 2009 [12]. For these years, data regarding the four populations are available according to sex and five-year age group. Annual intercensal estimates were prepared. We assumed the following: (1) a constant rate of growth within age groups, for both males and females, between census counts; and (2) that the age distribution following the most recent census remains the same in subsequent years.

2.2. Data collection

All registries employ a combination of active and passive case finding, with staff that travel to institutions within the healthcare delivery system of their respective catchment areas. Each registry also relies on voluntary notifications from participating institutions, because cancer is not mandated by the respective governments as a reportable disease. Data regarding cancer cases are abstracted from a variety of sources, including, but not limited to, pathology reports, inpatient and outpatient medical records, and death registries. Cancer notification forms were completed for each identified case and populated with information that included patient demographic data (names, date of birth or age, gender, race, and permanent residential address). Basic data on initial treatment and follow-up data were also collected, when available. The abstracted forms were coded and entered into the CanReg4[®] or CanReg5[®] cancer registration software (International Agency for Research on Cancer, Lyon, France). Tumor site and morphology were coded according to the third edition of the International Classification of Diseases (ICD) for Oncology [13].

2.3. Statistical methods

Frequency distributions and medians were used to describe subject demographics and baseline characteristics for categorical and continuous variables, respectively. Univariate analyses among variables were assessed using the two-sample *t*-test, Wilcoxon-rank-sum test, Chi-square test, as appropriate. Statistical significance was declared based on alpha level of 0.05. All statistical analyses were performed by using R statistical software (<http://www.r-project.org>) [14].

For the purpose of comparing several populations that differ with respect to age structure and accounting for the powerful influence of age on cancer, ASRs were calculated by applying the observed age-specific rates in a reference population, the world standard population [15]. Adjusted age-standardized rates (AASRs) were calculated to account for missing data on age in three of the four registries [16]. Age data were missing for 17.6% of cases from Blantyre; 1.2% of cases from Harare; 4.5% of cases from Kampala; and 0% of cases from Nairobi.

The standard error of the ASR was calculated. Using the estimates of ASRs and their standard errors, we compared two age-standardized rates, ASR_1 and ASR_2 , for males and females, respectively. A standardized rate ratio (SRR) was calculated as the ratio of ASR_1 to ASR_2 for each population. If the SRR did not include 1, the standardized rates ASR_1 and ASR_2 were considered significantly different at the significance level of alpha (0.05). For detailed information regarding the statistical methods applied, please refer to Supplement A.

3. Results

3.1. Patient characteristics

A total of 1832 cases of OC were reported by the four participating cancer registries during the years 2004–2008. The baseline characteristics of OC cases reported by each of the four cancer registries are summarized in Table 1. The median age at diagnosis was significantly different among the four populations, ranging from 50 years in Blantyre, Malawi to 65 years in Harare, Zimbabwe ($p < 0.0001$). The age distributions of cases for each population are shown in Fig. 1. Overall, 59% of all OC cases were male, with similar male predominance seen in each of the individual populations (range 57–61%).

Only 42% of all cases classified as OC by the registries were pathologically confirmed, and the remainder of cases was

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