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DIEGO RODRIGUES MENDONÇA E SILVA

CÂNCER DE ESÔFAGO NO CENTRO-OESTE DO BRASIL:

INCIDÊNCIA, MORTALIDADE E TENDÊNCIAS

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Orientadora: Profa. Dra Maria Paula Curado
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Dedico este trabalho...

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SÍMBOLOS, SIGLAS E ABREVIATURAS

APC – Annual Percentage Change

ASRW - Age-Standardized Rates World

CEC – Carcinoma de Células Escamosas

CID-O – Classificação Internacional de Doenças Oncológicas

CS – Clinical Stage

EC – Estadiamento Clínico

EUA – Estados Unidos da América

HPV – Papilomavírus Humano

IARC – International Agency Research for Cancer

ICD-O – International Classification of Diseases for Oncology

IMC – Índice de Massa Corporal

INCA – Instituto Nacional de Câncer

IS – *in situ*

LC – Localizado

MT – Metastático

OR – Odds Ratio

PBCR – Population-Based Cancer Registry

RCBP – Registro de Câncer de Base Populacional

RE – Regional

SD – Sem Dados

SEER – Surveillance Epidemiology and End Results

SCC – Squamous Cell Carcinoma

SPSS – Statistical Package for the Social Sciences

TNM – Tumor, Linfonodos e Metástases

TNM – Tumor, Nodes, Metastasis

USA – United States of America

RESUMO

Introdução: O câncer de esôfago é uma neoplasia de alta mortalidade em todo mundo. Estudos de base populacional no Brasil sobre essa neoplasia são escassos. No centro-oeste do Brasil existem registros de câncer de base populacional que monitoram o impacto do câncer, entretanto, não existem estudos avaliando o perfil epidemiológico desse tumor na região. Outra razão para esse estudo é a migração interna em grande escala que houve na década de 70 da população do sul (Porto Alegre) para o centro-oeste. Tal migração pode ter influenciado nas taxas de incidência do câncer de esôfago na região.**Objetivo:** Avaliar o desempenho do Registro de Câncer de Base Populacional de Goiânia (RCBP de Goiânia) na coleta de variáveis básicas e uma variável recomendada (estadiamento clínico) nos casos incidentes de câncer de esôfago. Determinar a incidência, a mortalidade e as tendências do câncer de esôfago nas capitais do centro-oeste brasileiro (Goiânia, Brasília, Cuiabá e Campo Grande). **Metodologia:** Para o desempenho do RCBP de Goiânia no período de 1988-2008 avaliou-se os casos de câncer de esôfago quanto à exaustividade das variáveis referentes ao paciente, tumor e o estadiamento clínico. A análise do perfil epidemiológico de incidência e mortalidade abrangeu os seguintes períodos: Cuiabá (2000-2005), Brasília (1999-2002) e Goiânia (1995-2008). Dados da mortalidade foram obtidos do DATASUS (2010) no período 1980-2008. Na análise estatística utilizou-se o software SPSS versão 15.0 para Windows®, o teste X^2 e Odds Ratio foram calculados, com nível de $p<0,05$; utilizou-se o Joinpoint Regression Program para análise de tendência. **Resultados:** No período de 1988 a 2008 foram notificados 827 casos do câncer de esôfago em Goiânia na proporção de 3:1 (homem/mulher). A maioria dos casos foram diagnosticado em estádio avançado. Na análise do RCBP de Goiânia identificaram-se índices bons de exaustividade das variáveis básicas referentes ao paciente e tumor, para o estadiamento clínico o índice foi ruim (5%). Em relação ao impacto da incidência do câncer de esôfago no centro-oeste do Brasil foi maior em Cuiabá e menor em Goiânia, sendo que as taxas em mulheres foram semelhantes em Brasília e Cuiabá. A mortalidade apresentou padrões heterogêneos com tendência crescente entre os homens em Cuiabá e Campo Grande e entre mulheres em Goiânia. **Conclusões:** O RCPB de Goiânia apresentou bom desempenho na coleta das variáveis básicas do câncer de esôfago, e ruim para o estadiamento clínico. O perfil da incidência do câncer de esôfago no centro-oeste do Brasil mostrou taxas elevadas em Cuiabá e Brasília, sendo estas taxas de incidência em homens semelhantes às taxas de Porto Alegre em alguns períodos. A mortalidade aumentou em homens em Cuiabá e Campo Grande, e em mulheres em Goiânia. Estudos a longo prazo poderão confirmar a influência da migração nas taxas de incidência do câncer de esôfago nessa região.

Palavras-chave: Câncer de esôfago, Estadiamento Clínico, Registro de Câncer, Epidemiologia, Tendências.

ABSTRACT

Introduction: Esophageal cancer is a malignancy of high mortality worldwide. Studies on Population-based of this neoplasm in Brazil are scarce. In the central-western of Brazil there are population-based cancer registries to monitor the impact of cancer. However there are no studies describing the profile of this tumor in the central-western of Brasil. Another reason for this study is the large-scale of internal migration happened in the 70's from Porto Alegre to the central-western. Such migration may have influenced the incidence and mortality rates of esophageal cancer in the region. **Objective:** To evaluate the performance of the Population-Based Cancer Registry of Goiânia (PBCR of Goiânia) in the collecting of basic variables and recommended variable (clinical staging) of incident cases of esophageal cancer. To describe the epidemiological profile of the incidence, mortality and trends esophageal cancer in central-western Brazil. **Methods:** From the PBCR of Goiânia it was analyzed the completeness of variables related to the patient, tumor and clinical staging of esophageal cancer cases for incidence analysis the period were: Cuiabá (2000-2005), Brasília (1999-2002) and Goiânia (1995-2008). Mortality data were obtained from DATASUS (2010) for the period 1980-2008 for all capitals of central western region. For statistical analysis we used version 15.0 of SPSS for Windows ®, the X^2 test and odds ratios were calculated by applying significance at $p<0.05$ and Joinpoint Regression Program for trend analysis. **Results:** In the period from 1988 to 2008 were reported 827 cases of esophageal cancer in Goiania in a 3:1 ratio (men/women). Most cases were diagnosed in advanced stages. The analysis of variables collected by RCBP Goiânia identified indices of good completeness of the basic variables related to the patient and tumor, whereas for clinical staging was low (5%). The highest incidence of esophageal cancer in the center-western of Brazil was observed in Cuiabá and lowest in Goiania, while rates in women were similar in Brasilia and Cuiaba. The mortality rates have a heterogeneous increase trend among men in Cuiaba and Campo Grande and among women in Goiania. **Conclusions:** The RCPB Goiânia had a good performance in collecting of basic variables of esophageal cancer, and low for clinical staging. The profile of incidence of esophageal cancer in the central-western of Brazil was higher in Brasilia and Cuiaba, with incidence rates for men similar to those of Porto Alleger in some periods. There was an increased in mortality in men in Cuiaba and Campo Grande and among women in Goiania. Long-term studies may confirm the influence of migration on the incidence rates of esophageal cancer in this region.

Keywords: Esophageal cancer, Clinical staging, Cancer registry, Epidemiology, Trends.

1 INTRODUÇÃO

O câncer é uma doença definida como uma enfermidade multifatorial crônica caracterizada pelo crescimento desordenado das células. Sabe-se que apenas uma pequena parcela dos cânceres é herdada sendo uma doença de genes vulneráveis à mutação, resultado da interação entre fatores endógenos e ambientais (especialmente, devido à exposição a estes fatores ao longo da vida). Assim o risco de desenvolvimento de um câncer aumenta com a idade (WCRF, 2007; WHO, 2012).

As taxas de incidência de câncer no mundo apresentam variações geográficas quanto às topografias mais incidentes, porém para o sexo masculino os mais comuns são os cânceres de pulmão, próstata, colón e reto e estômago. Nas mulheres são mais comuns os cânceres de mama, colón e reto, colo do útero e pulmão (FERLAY et al., 2008). A seguir aborda-se a epidemiologia, incidência, mortalidade, estadiamento, fatores de risco e tipos histológicos do câncer de esôfago.

1.1. Epidemiologia

1.1.1. Incidência

O câncer de esôfago é a oitava neoplasia de maior incidência no mundo em ambos os sexos (FERLAY et al., 2008). Essa neoplasia apresenta distribuição heterogênea de incidência no mundo, com altas taxas em regiões do Irã, da China, da África do Sul, da América do Sul e do Sul do Brasil (GABBERT et al., 2000; LEHRBACH et al., 2003).

Os coeficientes de incidência podem ser distribuídos em grupos: baixa (<1/100.000: Noroeste da África); intermediária (5/100.000: Caribe e Sudeste da América Latina e Índia); alta (15/100.000: África do Sul) e muito alta (>50/100.000: Irã e Litoral Cassiano) (ALVES, 2002).

As maiores taxas de incidência para o câncer de esôfago no mundo são observadas em Linxian, China com taxas de incidência >100/100.000 pessoas na Província de Golestan, nordeste do Irã, onde até a década de 70 as taxas eram superiores a 100/100.000 pessoas, atualmente as taxas estão abaixo de 50/100.000 pessoas (KAMANGAR et al., 2007). Taxas intermediárias são observadas entre homens em Goiânia, Bahia Blanca e EUA variando 5,1/100.000 a 8,1/100.000 (Tabela 1).

Tabela 1. Taxas padronizadas de incidência do câncer de esôfago para ambos os gêneros no mundo. (CURADO et al., 2007)

	Taxas de incidência por 100.000 pessoas	
Regiões	Masculino	Feminino
Linxian, (China)	>100	>100
Província Golestan (Irã)	50	50
Zimbabwe (Africa)	15,1	5,3
Brasilia (Brasil)	13,1	3,9
Cuiaba (Brasil)	11,7	2,7
Inglaterra (Norte)	10	3,8
Hong Kong (China)	9,5	1,7
Valdivia (Chile)	9,2	4,9
Inglaterra (Sul e Oeste)	8,8	3,6
Goiania (Brasil)	8,1	2,6
Bahia Blanca (Argentina)	6,7	3,1
EUA (SEER - 14 registries)	5,1	1,3

A literatura demonstra variações também nas tendências para o câncer de esôfago por morfologias específicas, evidenciando aumento da incidência de adenocarcinoma de esôfago nas últimas décadas em diversos países, sendo que o carcinoma de células escamosas (CEC) continua o tumor maligno mais frequente (BOSETTI et al., 2008; SHIBATA et al., 2008; CHERIAN et al., 2007). Em muitos países do ocidente os casos de adenocarcinoma de esôfago já correspondem a aproximadamente metade dos casos de CEC (KAMANGAR et al., 2007).

As diferentes tendências para o CEC e adenocarcinoma de esôfago podem estar atribuídas à heterogeneidade dos fatores de risco por

sexo ou idade (ORENGO et al., 2006). No Brasil são escassos os estudos de tendências de incidência para o câncer de esôfago, por tipo histológico.

No Brasil, para o ano de 2012, são estimados 10.420 novos casos de câncer de esôfago, sendo 7.770 novos casos para o sexo masculino e 2.650 novos casos para o sexo feminino, com taxas de 8,10/100.00 em homens, e 2,67/100.000 em mulheres. As regiões brasileiras com maiores taxas de incidência são as regiões Sul e Sudeste com taxa de 9,23 a 18,01/100.000 em homens (INCA, 2011). Estimou-se para o ano de 2012, em Goiânia, taxas de incidência de 6,63/100.000 em homens e 2,35/100.000 em mulheres. Para Brasília são estimadas taxas de 4,39/100.000 em homens e 1,73/100.000 em mulheres, enquanto que para Cuiabá taxas esperadas são de 5,87/100.000 em homens (INCA, 2011).

No Brasil as maiores taxas de incidência do câncer de esôfago foram observadas no sul, em Porto Alegre, com taxas de 15,4/100.000 no sexo masculino e 4,5/100.000 no sexo feminino período de 1993-1997. No centro-oeste, o Distrito Federal apresentou taxas semelhantes 14,7/100.000 em homens e 4,5/100.000 em mulheres no período de 1996-1998 (GUERRA et al., 2005). Não há, entretanto estudos que demonstrem as possíveis razões para essa semelhança nas altas taxas de incidência entre Porto Alegre e Brasília.

Em Cuiabá, no período de 2001-2005, a incidência para câncer de esôfago foi de 10,30/100.000 em homens e 2,61/100.000 em mulheres. Em Goiânia, no mesmo período foram notificadas taxas de 10,41/100.000 e 2,72/100.000, para homens e mulheres, respectivamente (INCA, 2010).

1.1.2. Mortalidade

A mortalidade por câncer de esôfago corresponde à sexta causa de óbito entre todas as neoplasias no mundo (FERLAY et al., 2008). As taxas de mortalidade apresentam variações no mundo. Por exemplo, na Holanda, no período de 1989-2003, verificou-se declínio considerável de mortalidade por câncer de esôfago (SIESLING et al., 2007). Na União Européia, as taxas de mortalidade passaram de 6/100.000 (1980-1990) a 5,4/100.000 entre 1990-2000, com mudança percentual anual (APC) = -1,1% no sexo masculino. Enquanto para o sexo feminino manteve-se estável nas últimas duas décadas (BOSETTI et al., 2008).

Nos EUA, a base de dados da Vigilância em Epidemiologia e Resultados Finais (SEER - Surveillance Epidemiology and End Results) evidenciou que as taxas de mortalidade por câncer de esôfago eram quase duas vezes maiores para negros em relação aos brancos (7,79/100.000 vs. 3,96/100.000, no período 1991-2000) (BAQUET et al., 2005). Mas recentemente estudo do SEER no período de 2003-2007 observou redução na diferença das taxas de mortalidade entre negros e brancos, tanto em homens como em mulheres (ALTEKRUSE et al., 2010).

No Brasil a mortalidade para o câncer de esôfago no período de 1980 a 1995, demonstrou queda em ambos os sexos, influenciadas pelo declínio nas regiões Sul e Sudeste. Porém nas demais regiões a mortalidade por essa neoplasia está em ascensão. Na região Centro-Oeste a mortalidade por câncer de esôfago entre 1980-1995 aumentou 14,8% no sexo masculino e 100,0% para o sexo feminino (WUNSCH FILHO;

MONCAU, 2002). Estudo recente de mortalidade do câncer de esôfago no sexo feminino para as regiões Sul e Sudeste do Brasil de 1980-2005 descreve declínio nas taxas (BASILIO; MATTOS, 2008).

1.1.3. Estadiamento

O câncer de esôfago apresenta alta letalidade, característica relacionada principalmente ao diagnóstico tardio dessa neoplasia, o que ocorre na maioria dos casos, uma vez que esse tumor raramente manifesta sintomas em seu estágio inicial (DIETZ et al., 2000; THULER et al., 2006). Dentre os principais sintomas nos casos avançados estão descritos dor, salivação excessiva, associados à perda ponderal progressiva, sangramento, dor torácica e vômitos (MONTEIRO et al., 2009).

A esofagoscopia constitui-se o melhor método diagnóstico para o câncer de esôfago. A ressonância magnética e a tomografia computadorizada são fundamentais para o estadiamento clínico deste tumor, sendo o estadiamento clínico um importante fator prognóstico e essencial na escolha do tratamento do câncer (VIEIRA et al., 2002; GOSPODAROWICZ et al., 2004; STEIN et al., 2001; LAYKE; LOPEZ, 2006).

A extensão da doença é uma variável também reportada no momento de diagnóstico da doença, estabelecida de acordo com o exame histológico e/ou informe clínico por ocasião do estadiamento clínico, avaliando a localização anatômica do tumor, a invasão de linfonodos e a presença de metástases à distância.

O estadiamento clínico é atribuído de acordo com as normas do manual de Classificação de Tumores Malignos (TNM/UICC), sendo estabelecido com base em 3 parâmetros: T (invasão do tumor primário), N (linfonodos regionais) e M (Metástase a Distância). Os dados TNM podem ser agrupados, em estádios clínicos I, II, III ou IV (UICC, 2009), como descrito abaixo para o câncer de esôfago (Tabela 2).

Tabela 2. Grupos por Estádio para o câncer de esôfago, Classificação dos Tumores Malignos (TNM), 7ª edição (UICC, 2009).

Estádio 0	Tis	N0	M0
Estádio IA	T1	N0	M0
Estádio IB	T2	N0	M0
Estádio IIA	T3	N0	M0
Estádio IIB	T1, T2	N1	M0
Estádio IIIA	T4a	N1	M0
	T3	N0	M0
	T1, T2	N2	M0
Estádio IIIB	T3	N2	M0
Estádio IIIC	T4a	N1, N2	M0
	T4b	Qualquer N	M0
Estádio IV	Qualquer T	Qualquer N	M1

1.1.4. Fatores de risco

O câncer de esôfago acomete com maior freqüência pacientes do sexo masculino, acima de 50 anos (ZAN et al., 2005; QUEIROGA; PERNAMBUCO, 2006; HENRY, 2007).

A etiologia do câncer de esôfago envolve a interação de diversos fatores de risco, dentre: fatores ambientais e alimentares. O baixo nível socioeconômico aumenta o risco para o câncer de esôfago de 2 a 4 vezes (BARROS et al., 2000; TRAN et al., 2005; BROWN et al., 2001; WEI et al., 2005 KAMANGAR et al., 2009).

Entre os fatores de risco importantes do câncer de esôfago são descritos o tabagismo e o etilismo. Evidências demonstram que o fumo isoladamente aumenta o risco em 2 a 4 vezes. Já o consumo excessivo de bebidas alcoólicas aumenta o risco, além de agir como um solvente para outros carcinógenos e podem causar deficiência nutricional (QUEIROGA; PERNAMBUCO, 2006; KAMANGAR et al., 2007; BOFFETTA; HASHIBE, 2006).

A associação do fumo e consumo de bebidas alcoólicas potencializam o risco de se desenvolver câncer de esôfago (TANABE et al., 2001; GARÓFOLO et al., 2004; KAMANGAR et al., 2009), principalmente o CEC de esôfago (FREEDMAN et al., 2007).

Em algumas áreas da América do Sul como no sul do Brasil, noroeste da Argentina, Uruguai e Paraguai o hábito de consumir grandes volumes de chá mate e/ou chimarrão em altas temperaturas é muito frequente. Estudos realizados nessas regiões associam o consumo dessa erva principalmente consumida em água muito quente, com as altas taxas de incidência de câncer de esôfago (CASTELLSAGUÉ, et al., 1999; SEWRAM et al., 2003; KAMANGAR et al., 2009).

A deficiência vitamínica de riboflavina, vitaminas A, C e E, zinco e molibdênio (devido à baixa ingesta de frutas e legumes frescos), são

consideradas fatores de risco para o CEC de esôfago (HENRY et al., 2007; KAMANGAR et al., 2009). A ingestão de alimentos e bebidas quentes como fator de risco é bastante estudada, mas os resultados ainda são controversos (KAMANGAR et al., 2009).

Algumas afecções como o megaesôfago chagásico, esôfago de Barrett, refluxo gastro-esofágico, agentes infecciosos como o HPV e a acalasia são fatores de risco, sendo que pacientes com essa doença têm 10 vezes mais risco de desenvolver CEC e adenocarcinoma de esôfago do que a população geral (BARROS et al., 2000; QUEIROGA; PERNAMBUCO, 2006; ZENDEHDEL et al. 2007; HENRY et al., 2007; MONTEIRO et al., 2009).

Em relação aos fatores ocupacionais a exposição a longo prazo à poeira de sílica, hidrocarbonetos aromáticos, policíclicos e metais, também tem sido incluídos como fatores de risco para o câncer de esôfago (PAN et al., 1999; YU et al., 2005; MONTEIRO et al., 2009).

Considerando os tipos histológicos e sua etiologia, o CEC é 2 a 3 vezes mais comum em homens do que em mulheres, sendo que a displasia escamosa esofágica é uma lesão precursora para essa neoplasia (KORT et al., 2009; KAMANGAR et al., 2009).

Dentre os fatores de risco para o adenocarcinoma de esôfago estão descritos o refluxo gastroesofágico, esôfago de Barrett, o alto índice de massa corporal (IMC), (CHERIAN et al., 2007; DeMEESTER, 2009; KORT, 2009, QUEIROGA; PERNAMBUCO, 2006; KAMANGAR et al., 2009), associação do IMC elevado aumentou a incidência do adenocarcinoma de esôfago sendo a obesidade um fator de risco independente para o

adenocarcinoma de esôfago (CORLEY; BUFFLER, 2001; RYAN et al., 2006; WHITEMAN et al., 2008; KORT et al., 2009; KAMANGAR et al., 2009).

Estudos descrevem também aumento do risco de desenvolvimento de adenocarcinoma de esôfago para pacientes com hérnia hiatal, com risco relativo de 2 a 6 vezes (CHOW et al., 1995; FARROW et al., 2000; WU et al., 2003; GARCIA RODRIGUES et al., 2006).

1.1.5. Tipos histológicos

Os principais tipos histológicos para o câncer de esôfago são o CEC e adenocarcinoma.

O CEC é o tipo histológico mais freqüente no mundo inteiro (LEHRBAHC et al., 2003), acomete o epitélio estratificado não-queratinizado, característico da mucosa normal do esôfago, atingindo principalmente o seu terço médio e o inferior. O carcinoma invasor é caracterizado pela rotura da membrana basal e extensão à lâmina própria do epitélio ou às camadas mais profundas do tecido (GABBERT et al., 2000 QUEIROGA; PERNAMBUCO, 2006).

O adenocarcinoma se desenvolve na região distal do esôfago, no interior do epitélio colunar próximo à junção esôfago-gástrica (cárdia), sendo um tumor epitelial de esôfago com diferenciação glandular Este tumor pode infiltrar a cárdia e ser assim confundido com um tumor de cárdia. (GABBERT et al., 2000; QUEIROGA; PERNAMBUCO, 2006).

1.2. Registros de Câncer de Base Populacional (RCBPs) na região Centro-oeste do Brasil

Os dados de incidência de câncer representam um ponto de partida para numerosos estudos epidemiológicos descritivos e analíticos, bem como são informações valiosas para o controle, o planejamento e a avaliação das ações das políticas nacionais de atenção oncológica (INCA, 2010).

No Brasil, o Instituto Nacional do Câncer (INCA) do Ministério da Saúde/MS, através da Coordenação de Prevenção e Vigilância (Conprev), é a instituição nacional responsável pelas ações orientadas a prevenção, vigilância e o controle do câncer, sendo os RCBPs fundamentais nesse trabalho. A incidência da doença no mundo é compilada a partir dos dados fornecidos pelos Registros de Câncer mundiais, através da Agência Internacional para Pesquisa em Câncer (IARC) (INCA, 2010).

O objetivo maior do RCBP é registrar de forma fidedigna e completa todos os casos novos de câncer incidentes em uma população em um período de tempo. Para alcançar esse objetivo os RCBPs realizam um processo contínuo e sistemático de coleta de casos novos de câncer da sua área de cobertura, fornecendo a estimativa de incidência (PARKIN et al., 2001; MOURA et al., 2006).

Nas capitais da região centro-oeste existe Registros de Câncer. O centro-oeste brasileiro é formado pelos estados de Goiás (Goiânia), Mato Grosso (Cuiabá), Mato Grosso do Sul (Campo Grande), e onde está localizado o Distrito Federal (Brasília), a seguir descreveremos os registros de câncer das capitais dessa região.

O Registro de Câncer de Base Populacional de Goiânia foi criado em 1986, para monitorar os casos incidentes de câncer na capital, atualmente possui uma base de dados de 21 anos (1988-2008) (INCA, 2012), esse registro é mantido pela Associação de Combate ao Câncer em Goiás, Hospital Araújo Jorge, desde 1994, atualmente conta com o apoio financeiro do convênio INCA/MS (Instuto Nacional do Câncer/Ministério da Saúde).

O RCBP de Brasília foi criado em novembro de 1997, sendo a coleta de dados iniciada no ano de 1996, os dados consolidados disponíveis são de 1999-2002 (INCA, 2012). O RCBP conta com apoio financeiro do convênio INCA/MS (Instuto Nacional do Câncer/Ministério da Saúde).

O RCBP de Campo Grande foi instituído em 2000, sendo a coleta de dados iniciada no ano de 2002. Este se localiza na Secretaria de Estado de Saúde, na Coordenadoria Estadual de Atenção Básica, os dados disponíveis perfazem o período de 2000 a 2003 (INCA, 2012).

O RCBP de Cuiabá foi criado em 1999, a cobertura desse registro inclui Cuiabá e Várzea Grande, iniciando a coleta de dados no ano de 2000, atualmente com dados disponíveis de 2000 a 2005 (INCA, 2012). Esse registro esta sob a coordenação do serviço de vigilância epidemiológica da Secretaria de Estado da Saúde de Mato Grosso (INCA, 2010).

Diante dos dados descritos obervamos que os registros do centro-oeste foram criados em diferentes períodos, entretanto os dados existentes nos permitem uma análise descritiva do perfil do câncer de esôfago nesta região.

2 JUSTIFICATIVA

Em 2008, o câncer foi responsável por 13% (7,6 milhões) de todas as mortes no mundo, destas mais de 70% ocorreram em países de média ou baixa renda (WHO, 2012). O câncer de esôfago, em 2009, no Brasil foi o sétimo de maior mortalidade devido principalmente ao diagnóstico tardio (DATASUS, 2011).

O câncer de esôfago aumentou nas últimas décadas devido às mudanças nos hábitos e ao aumento de expectativa de vida. (SIESLING et al., 2007; MONTEIRO et al., 2009). Diversos estudos epidemiológicos observacionais sobre o câncer de esôfago são descritos principalmente nas regiões Sul e Sudeste do país, em virtude de essas regiões apresentarem as maiores taxas de incidência do Brasil (WUNSCH FILHO; MONCAU, 2002; BASILIO; MATTOS, 2008; MONTEIRO et al., 2009).

Estudos no centro-oeste relatam taxas de incidência do câncer de esôfago em Brasília semelhantes às da região Sul (GUERRA et al., 2005), enquanto Cuiabá e Goiânia apresentam taxas intermediárias. No entanto, há pouca informação sobre o perfil epidemiológico do câncer de esôfago no centro-oeste do Brasil.

Os Registros de câncer de base populacional são sistemas de informação que produzem dados reais sobre a incidência de câncer em uma população de uma determinada área geográfica, é de suma importância que os dados produzidos pelos RCBPs, sejam confiáveis e de qualidade, para

isso existem procedimentos de rotina e indicadores de controle de qualidade que foram estabelecidos pela Agência Internacional em Pesquisa sobre o Câncer (IARC - International Agency for Research on Cancer) e a Associação Internacional de Registros de Câncer (IACR – International Association of Cancer Registries) e no Brasil o Instituto Nacional do Câncer (INCA).

Portanto, analisar o perfil epidemiológico do câncer de esôfago no centro-oeste do Brasil poderá trazer informações valiosas sobre o comportamento desta neoplasia, assim como a análise da qualidade dos dados desta neoplasia coletados pelo Registro de Câncer de Base População. Diante disto fez-se um estudo observacional retrospectivo, que descreve a exaustividade e a qualidade dos dados do RCBP de Goiânia, analisando as variáveis obrigatórias e recomendadas (CURADO et al., 2009) assim como o estadiamento clínico no câncer de esôfago. O segundo artigo faz uma análise da incidência, mortalidade e tendências do câncer de esôfago no centro-oeste do Brasil.

3 OBJETIVOS

3.1. OBJETIVO GERAL

1. Avaliar o perfil epidemiológico do câncer de esôfago na região centro-oeste do Brasil.

3.2. OBJETIVOS ESPECÍFICOS

1. Avaliar o desempenho do Registro de Câncer de Base Populacional de Goiânia na coleta de variáveis básicas e o estadiamento clínico no câncer de esôfago, no período de 1988 a 2008.
2. Determinar a incidência do câncer de esôfago em Goiânia, Brasília e Cuiabá no período 1995-2008, 1999-2002 e 2000-2005 respectivamente;
3. Determinar a mortalidade para o câncer de esôfago em Goiânia, Brasília, Cuiabá e Campo Grande no período 1980-2008.
4. Avaliar as tendências da mortalidade para o câncer de esôfago em Goiânia, Brasília, Cuiabá e Campo Grande no período 1980-2008.

4 PUBLICAÇÕES

Artigo 1 – PERFORMANCE OF A POPULATION-BASED CANCER REGISTRY IN ABSTRACTING CLINICAL STAGE OF ESOPHAGEAL CANCER

Autores: Diego Rodrigues Mendonça e Silva, Maria Paula Curado, José Carlos de Oliveira, Anderson Gomes de Oliveira.

(Submetido) ***Revista Panamericana de Salud Pública /Pan American Journal Public Health.*** Protocolo: RPSP 2012-00508

Artigo 2 – HIGH INCIDENCE OF ESOPHAGEAL CANCER IN CENTRAL-WESTERN BRAZIL: A MIGRANT EFFECT?

Autores: Diego Rodrigues Mendonça e Silva, Maria Paula Curado, José Carlos de Oliveira.

(Aceito para publicação) ***European Journal of Cancer Prevention.*** Protocolo: CEJ 200626

Artigo 1

Performance of a Population-Based Cancer Registry in abstracting Clinical Stage of Esophageal Cancer

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ABSTRACT

OBJECTIVE: To evaluate the performance of the Population-Based Cancer Registry (PBCR) of Goiania in collecting basic variables and clinical staging in esophageal cancer cases.

METHODS: We evaluated the completeness of basic variables: birth date, permanent address, topography, basis of diagnostic, extension of disease, morphology and clinical staging, all variables in both genders. We used version 15.0 of SPSS for Windows® for all statistical analyses. The χ^2 strength of the risk was calculated using the odds ratio with a significance level of 5% and confidence interval of 95%.

RESULTS: The PBCR of Goiania registered 827 cases of esophageal cancer from 1988 to 2008, 76.8% in men and 23.2% in women. The

completeness for basic variables related to patient and tumor was considered good. Regarding clinical stage 5.0% of the registered cases of esophagus cancer had staging information. Of all esophageal cancer cases with clinical stage, 64% were registered as advanced. Comparing extension of disease and clinical stage, the data were conflicting in 33.3% of early and 50.0% of the advanced cases.

CONCLUSION: Our results show a low rate of clinical staging records in the PBCR although clinical stage is an essential element for planning treatment. In addition the PBCR of Goiânia has a low ability to collect clinical stage data. Nevertheless the inclusion of qualitative variables such as clinical staging (TNM stage) provides valuable information for decision makers and improves information regarding the status at the diagnoses of the incident cancer cases.

Keywords: Neoplasm Staging, Esophageal, Cancer.

INTRODUCTION

Esophageal cancer has the eighth highest incidence and it is the sixth leading cause of death among all cancers worldwide (1). In Brazil, the estimates of cancer incidence for 2012 are 7.3/100,000 in men and 2.3/100,000 in women (2). The highest rates by region were observed in the south, in Porto Alegre, Brazil, age-standardized incidence rates of 18.2/100,000 and 4.3/100,000 in men and women, in 2000-2004, for the

period, 2001-2005, in Goiania, central-western Brazil, the age-standardized incidence rates were 10.4/100,000 in men and 2.7/100,000 in women (3).

Esophageal cancer is mostly diagnosed in the advanced stages because of a lack of symptoms in its early stages, thus decreasing the chances of curing the patient which contributes to the high mortality rates of this tumor (4-6). An important prognostic factor when establishing the diagnosis and essential for treatment planning is clinical staging (7-9). The clinical staging for esophageal cancer requires endoscopy, contrast radiology, and other tests such as computed tomography, PET-CT, magnetic resonance imaging of the abdomen to ensure the exact extension of the tumor (10).

Population-based cancer registries (PBCRs) routinely collect basic variables related to patients and tumors (11). One of the basic variables for tumors at the PBCRs is the variable extension of disease at diagnosis, which allows verifying the patient's clinical condition at diagnosis. Although clinical staging gives valuable information, it is a variable that gives more reliable information on patient condition at diagnosis. However, there are few PBCRs collecting routinely this variable. In the USA since 2004 clinical staging has become mandatory in all cancer registries (12-13).

The inclusion of the clinical stage as a basic variable in the database of a PBCRs enhances the quality of diagnosis and the possibility of planning for early diagnosis (12-13).

The PBCR of Goiania includes clinical staging as a recommended variable and the registrar must collect this variable if it is available. Given the importance of producing data with qualitative variables such as clinical stage,

we decided to analyze the completeness of the PBCR of Goiania in abstracting basic and qualitative variables evaluating clinical staging in esophagus cancer incident cases.

We selected esophageal cancer because it is a rare neoplasm for which to have information of stage at diagnosis is essential for treatment planning. Thus, we evaluated the performance of the PBCR of Goiania with respect to the collection of mandatory variables (patient and tumor) and TNM clinical staging over a period of 21 years.

METHODS

We analyzed all incident cases of esophageal cancer identified in the database of the PBCR of Goiania from 1988-2008 regarding completeness of the information available (completeness is a measure of data quality in a PBCR it measure the ability of the PBCR to abstract and included all basic variables necessary to produce incidence data in a defined population in a period of time).

We evaluated its completeness of the basic variables as for patient: birth date, address and sex. For tumor variables were analyzed: topography, basis of diagnostic, extension of disease, morphological classification, and clinical staging (TNM) by sex. Basis of diagnostic relating to the tumor were classified as: clinical, histology of the primary, and death certificate; extension of disease in: *in situ*, localized, regional, metastatic, missing data; the morphological classification was grouped as: squamous cell carcinoma (SCC), adenocarcinoma, malignant neoplasm and others morphologies. All cases of esophageal cancer regarding stage it was classified as not staged

or staged. The quality of the data was classified according to its completeness in excellent (100-90%), good (89-70%), fair (69-50%), and low (<49%).

For patient information, variables were considered complete if the birth date had 1 or 2 pieces of information (i.e., birth date and age); if the address included the street name, block, lot and/or number; in relation to the tumor if the cases has the description of the sub site such as, C15.0, C15.3, C15.4, or C15.6) according to International Classification of Diseases for Oncology (ICD-O3) (14).

Variables were classified as incomplete for the following reasons: lack of data on birth date, or missing information on age; incomplete address, no description of the street, block, lot, and/or number; incomplete topography was considered when there is not classification by sub site according to the International Classification of Diseases for Oncology, 3rd Edition (ICD-O3) (14).

Clinical stage was compared to extension of disease to evaluate the disparities. Extension of disease is a variable that describes the situation of the tumor in the moment of the diagnosis; it is based on anatomical location of the neoplasm, positive or negative regional lymph node involvement, and distant metastatic disease (15). The clinical stage similarly attempts to evaluate the cancer at diagnosis based on 3 parameters T (Tumor); N (Nodes) and M (Metastasis) grouped in clinical stage according to the pre treatment tumor evaluation (16). Both systems use the same parameters although, for extension of the disease, it is summarized in four groups as in situ, localized, regional and metastatic.

All variables were analyzed by sex from 1988-2008. Cases were grouped into four 5-year periods by sex: 1988-1992, 1993-1997, 1998-2002 and 2003-2007; the data from 2008 were not included in the analysis for the 5-year periods to evaluate the changes occurred.

We compared the two initial 5-year periods, 1988-1992 and 1993-1997, and the last two 5-year periods, 1998-2002 and 2003-2007, to evaluate the changes in the completeness of basic variables regarding patients, tumors, and clinical stage, we did this to evaluate two five years period and finally verify the difference occurred in the 20 years period.

All cases were registered for clinical stage were assigned according to the Classification of Malignant Tumors (TNM) data were grouped as clinical stage I, II, III, or IV (16). Clinical stage was analyzed in 2 groupings: Stage I/II as early and Stage III/IV as advanced. We analyzed the cases staged according to sex and, age below and above 55 years, and compare with extension of disease classification.

We used SPSS version 15.0 for Windows® for all statistical analyses. The χ^2 strength of the risk was calculated using the odds ratio with a significance level of 5% and confidence interval of 95%.

RESULTS

In Goiania 827 cases of esophageal cancer were incident from 1988-2008; of these, 635 (76.8%) were men and 192 (23.2%) women, the ratio men women was approximate 3:1. The data base shown that 53.0% of cases of esophageal cancer come from a single source of data (Cancer Hospital of

Goiania, Goias, Brazil). It was found that only 5.0% (42/827) of cases had clinical staged noted.

The completeness of the basic variables related to the patient, such as birth date, address, as well as topography, staging, basis of diagnostic, extension of disease and morphological classification of the tumor was not significantly different between men and women over the 20-year period (Table 1). The completeness was considered excellent for basic variables related to patient information the average percentage were 95% in the 21 years period.

The completeness for basic variables such as data for birth date it has been rated as excellent, reaching 100,0% and did not change significantly in the periods (Table 2).

There was a significant improvement in completeness of the variable address in the last 2 periods (1998-2002 to 2003-2007) for men (p = 0.010) with an excellent rate (97% to 100%) of complete information in the last 5 years (2003-2007). For women, the variable address was rated as good in the first two periods (1988-1992 and 1993-1997, p = 0.029), changing to excellent in the most recent (80.0% to 97.1%).

TABLE 1. Completeness of basic variables and clinical stage of esophageal cancer in the Population-Based Cancer Registry of Goiania, Brazil, 1988-2008.

	Men n (%)	Women n (%)	All	*P*
Birth date				
Complete	618 (97.3)	187 (97.4)	805 (97.3)	0.956
Incomplete	17 (2.7)	5 (2.6)	22 (2.7)	
Address				
Complete	610 (96.1)	183 (95.3)	793 (95.9)	0.646
Incomplete	25 (3.9)	9 (4.7)	34 (4.1)	
Topography				
Complete	90 (14.2)	19 (9.9)	109 (13.2)	0.125
Incomplete	545 (85.8)	173 (90.1)	718 (86.8)	
Stage				
Staged	32 (5.0)	10 (5.2)	42 (5.1)	0.926
Not staged	603 (95)	182 (94.8)	785 (94.9)	
Basis of diagnostic				
Clinical	8 (1.3)	7 (3.6)	15 (1.8)	
Histology	569 (89.6)	168 (87.5)	737 (89.1)	0.095
Death certificate	58 (9.1)	17 (8.9)	75 (9.1)	
Extent of disease				
In situ	2 (0.3)	1 (0.5)	3 (0.4)	
Localized	281 (44.3)	91 (47.4)	372 (45.0)	
Regional	40 (6.3)	11 (5.7)	51 (6.2)	0.708
Metastatic	86 (13.5)	19 (9.9)	105 (12.7)	
Missing data	226 (35.6)	70 (36.5)	296 (35.8)	
Morphological classification				
Squamous cell carcinoma	502 (79.1)	149 (77.6)	651 (78.7)	
Adenocarcinoma	33 (5.2)	10 (5.2)	43 (5.2)	0.762
Malignant neoplasm	67 (10.6)	25 (13)	41 (5.0)	
Others morphology	33 (5.2)	8 (4.2)	92 (11.1)	

Information about the sub site classification of the tumors in relation to their anatomical origin didn't change in the analysis over time and by gender with completeness ranging between 7.0-21.0% and 5.0-12.0% in men and women respectively, which is considered low according our parameters.

Regarding clinical staging, there was no change in over 20 years in either sex: 8.5% in men and 7.7% and in women (both low).

Information regarding basis of diagnostic improved significantly for both sexes (p = 0.006 for men and p = 0.047 for women) during the first decade of data but remained unchanged in the last decade being excellent for men (92%) and good for women (87.0%).

Data on extension of disease improved only for men in the first 5-year period, in the last 5 years this information improved for both sexes. We observed that for women, localized and metastatic disease increased in the last 5 years (2003-2007) while in men, there was a decrease in regional disease and an increase in metastasis. The level of incompleteness of the basic variables for extension of disease was 51.0% in 1988, decreasing to 31.0% in 2007 for men; for women, this reduction was even greater: 64.0% in 1988 to 24.0% in 2007.

The information regarding the morphological classification of the tumor in both sexes improved, with an increase in squamous cell carcinoma for men (28.0%) and women (17.5%); meanwhile, adenocarcinoma (5%) remained stable in both sex during the period.

TABLE 2. Evaluation of the completeness of basic variables and staging of esophageal cancer by 5-year periods and sex. Goiania, Brazil, 1988-2007.

	Men						Women					
	1988-1992	1993-1997	*p*	1998-2002	2003-2007	*p*	Total	1988-1992	1993-1997	*p*	1998-2002	2003-2007	*p*	Total
	n (%)	n (%)		n (%)	n (%)			n (%)	n (%)		n (%)	n (%)		
Birth date														
Complete	94 (94.9)	110 (95.7)	0.808	161 (97.6)	212 (99.1)	0.249	557	23 (92.0)	32 (91.4)	0.937	54 (100.0)	65 (100.0)		174
Incomplete	5 (5.1)	5 (4.3)		4 (2.4)	2 (0.9)		16	2 (8.0)	3 (8.6)		– (0.0)	– (0.0)		5
Address														
Complete	88 (88.9)	106 (92.2)	0.41	160 (97.0)	214 (100.0)	0.010	568	20 (80.0)	34 (97.1)	0.029	52 (96.3)	65 (100.0)	0.118	171
Incomplete	11 (11.1)	9 (7.8)		5 (3.0)	(0.0)		25	5 (50.0)	1 (2.9)		2 (3.7)	– (0.0)		8
Topography														
Complete	11 (11.1)	8 (7.0)	0.287	35 (21.2)	29 (13.6)	0.048	83	3 (12.0)	2 (5.7)	0.385	6 (11.1)	6 (9.2)	0.735	17
Incomplete	88 (88.9)	107 (93)		130 (78.8)	185 (86.4)		510	22 (88.0)	33 (94.3)		48 (88.9)	59 (90.8)		162
Stage														
Staged	– (0.0)	2 (1.7)	0.187	14 (8.5)	14 (6.5)	0.473	30	0 (0.0)	1 (2.9)	0.394	4 (7.4)	5 (7.7)	0.953	10
Not staged	99 (100.0)	113 (98.3)		151 (91.5)	200 (93.5)		563	25 (100.0)	34 (97.1)		50 (92.6)	60 (92.3)		169
Basis of diagnostic														
Clinical	4 (4.0)	1 (0.9)		1 (0.6)	2 (0.9)		8	1 (4.0)	1 (2.9)		1 (1.9)	4 (6.2)		7
Histology	76 (76.8)	106 (92.2)	0.006	152 (92.1)	198 (92.5)	0.904	532	20 (80.0)	34 (97.1)	0.047	45 (83.3)	57 (87.7)	0.169	156
Death certificate	19 (19.2)	8 (7.0)		12 (7.3)	14 (6.5)		53	4 (16.0)	0 (0.0)		8 (14.8)	4 (6.2)		7
Extent of disease														
In situ	– (0.0)	– (0.0)		2 (1.2)	– (0.0)		2	– (0.0)	– (0.0)		– (0.0)	1 (1.5)		1
Localized	25 (25.3)	59 (51.3)		89 (53.9)	95 (44.4)		268	7 (28.0)	17 (48.6)		24 (44.4)	36 (55.4)		84
Regional	0 (0.0)	6 (5.2)	<0.001	16 (9.7)	14 (6.5)	0.009	36	– (0.0)	1 (2.9)	0.201	9 (16.7)	1 (1.5)	0.035	11
Metastatic	23 (23.2)	6 (5.2)		12 (7.3)	38 (17.8)		79	1 (4.0)	– (0.0)		6 (11.1)	11 (16.9)		18
Missing data	51 (51.5)	44 (38.3)		46 (27.9)	67 (31.3)		208	17 (68.0)	17 (48.6)		15 (27.8)	16 (24.6)		65
Morphological classification														
Squamous cell carcinoma	58 (58.6)	86 (74.8)		137 (83.0)	186 (86.9)		467	16 (64.0)	32 (91.4)		38 (70.4)	53 (81.5)		139
Adenocarcinoma	5 (5.1)	10 (8.7)	0.001	10 (6.1)	6 (2.8)	0.437	31	2 (8.0)	2 (5.7)	0.015	3 (5.6)	1 (1.5)	0.191	8
Malignant neoplasm	29 (29.3)	10 (8.7)		11 (6.7)	12 (5.6)		62	7 (28.0)	1 (2.9)		7 (13.0)	9 (13.8)		24
Other morphology	7 (7.1)	9 (7.8)		7 (4.2)	10 (4.7)		33	– (0.0)	– (0.0)		6 (11.1)	2 (3.1)		8

The variable clinical staging was complete in 5.0% of the 857 cases analysed (32 men and 10 women) this is low according to the criteria adopted. Advanced clinical stage (CS III/IV) prevailed with 68.7% (22 cases) in men and 50% (5 cases) in women (Table 3); there was no significant difference in staging distribution by age group.

TABLE 3. Staging of esophageal cancer by sex and age. Goiania, Brazil, 1988-2008.

	All	CS[a] I/II	CS III/IV	*P*	OR[b] (CI[c] 95%)
	N	n (%)	n (%)		
Women	10	5 (33.3)	5 (18.5)	0,28	1
Men	32	10 (66.7)	22 (81.5)		2.2 (0.5-9.4)
≤55	19	6 (40.0)	13 (48.1)	0,61	1
≥55	23	9 (60.0)	14 (51.9)		0.7 (0.2-2.6)

[a] Clinical Stage
[b] Odds Ratio
[c] Confidence Interval

Comparing the clinical staging classification with extension of disease it has been observed that 22 cases in both genders had localized disease; among these, it has 11 cases were included which had been coded as stage III/IV - equivalent to regional or metastatic disease, thus extension of disease was underreport in advanced cases of esophagus cancer (Table 4).

Cases classified as initial stage (CS I/II), 1 of 15 cases, was classified as metastatic disease. The extension of disease misclassified in comparison with clinical stage; it was underreported in 40% (11/27) of the clinical stage III/IV cases (advanced).

TABLE 4. Comparison between extension of disease and clinical stage of esophageal cancer by sex. Goiania, Brazil, 1988-2008.

		LC[a]	RE[b]	MT[c]	MD[d]	*p*	
	CS[e]	n (%)	n (%)	n (%)	n (%)		Total
Women	I/II	5 (71.4)	– (0.0)	– (0.0)	– (0.0)	0.38	5
	III/IV	2 (28.6)	3 (100.0)	– (0.0)	– (0.0)		5
Men	I/II	6 (40.0)	2 (18.2)	1 (33.3)	1 (33.3)	0.7	10
	III/IV	9 (60.0)	9 (81.8)	2 (66.7)	2 (66.7)		22
	All	22	14	3	3		42

[a] Localized
[b] Regional
[c] Metastatic
[d] Missing data
[e] Clinical Stage

DISCUSSION

The main aim of PBCRs is to monitor cancer incidence in a given population of region or country by making reliable available data for cancer control (13, 17). Data produced by PBCRs should be of high quality to ensure adequate monitoring of cancer incidence according to the international standards of the International Agency for Research on Cancer (IARC) and of the National Cancer Institute (INCA) in Brazil (17-18).

Quality control of data is crucial for the identification of major problems in the region covered by the cancer registry. Thus enabling an accurate interpretation of the data and the need for changes in procedures in acquiring reliable information (18). Among the routine procedures for the quality control of data in PBCRs is the validation of incident cases, which is performed by checking inconsistencies in the database such as topography and

morphological classification and code which can be performed by the PBCR using free softwares such as IARC tools (19).

In addition to checking the consistency of the information, another way to assess the completeness of a PBCR is by analyzing basic and recommended variables which been collected. Here, recommended variables refer to qualitative ones. In this case, clinical staging is considered a qualitative variable (5).

The completeness of basic variables in the incident cases of esophageal cancer in the PBCR of Goiania, showed an excellent completeness for the period from 1988-2008, demonstrating a good performance in the registry. Although the qualitative variable clinical stage has a low performance over the period.

The treatment planning for a malignancy depends on the patient's clinical condition and the clinical staging of the tumor at the time of diagnosis. Therefore, clinical staging is important information regarding patient conditions at the moment of diagnosis and to plan treatment. However this is data for esophageal cancer is lacking in the PBCR of Goiania in the last 20 years

Over 20 years, the PBCR of Goiania recorded 827 cases of esophageal cancer in both sex. It was found that only 5.0% (42/827) of the cases had clinical stage, which is considered low rated for the completeness standards. More as clinical stage is essential in both prognosis and treatment planning and is an indicator of the quality of health care of a health system (12).

In this study, the clinical staging information on esophageal cancer for men improved in the last decade compared to the first decade, which only

had 2 staged cases (2/30). However, when we compare the consistency between extension of disease and clinical staging, it was observed among esophageal cancer classified as an extension localized in both sex, in reality, they were stage III/IV according to TNM classification, consistent with advanced disease. In this case, the TNM clinical stage was more accurate than the diagnosis of tumors based on extension of disease extent generally recorded by the PBCRs.

According to the literature, the majorities of cases esophageal cancer are diagnosed in the advanced stage or are regional (5-6), which is concordant with our present data (64.0% in advanced clinical stages). The use of the classification by extension of disease underestimated the situation of the case at the moment of the diagnosis in relation to the TNM clinical stage. Therefore, information between extension of disease and clinical stage was conflicting in 33.0% of the incident cases of esophageal cancer misclassifying the cases as regional and metastatic while they were in fact it was initial esophageal cancers (CS I/II). More than 50.0% of esophageal cases classified as localized by the extension of disease were, in fact, advanced cases (CS III/IV) according to clinical stage.

Lack of information on clinical stage (TNM) in PBCR of Goiania may be due to several factors which include: a lack of ability of the registrar to collect information, difficulty in accessing medical records, and an absence of physician-declared staging at the medical records. As clinical stage is not a mandatory variable, it results as in minor effort to collect this qualitative variable by the PBCR.

The inclusion of clinical TNM staging as a mandatory variable may expand the role of PBCRs in the analysis situation at diagnosis when the case has access to treatment. This is important to all cancers but mainly for patients with highly mortality cancers such as esophageal cancer, since early detection can significantly reduce the mortality associated with treatment and improve overall long-term survival (20).

In conclusion, PBCRs have the ability to collect basic data on patient and tumor characteristics to estimate incidence; nevertheless, if it includes qualitative variables clinical stage (TNM staging), such information will be valuable for health policies to monitor the burden of neoplasms at the health care system.

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Artigo 2

HIGH INCIDENCE OF ESOPHAGEAL CANCER IN CENTRAL-WESTERN BRAZIL: A MIGRANT EFFECT?

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Running title: Esophageal cancer in central-western Brazil

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ABSTRACT

Objective: To determine the incidence and mortality rates of esophageal cancer in central-western Brazil: Goiânia, Brasília, Cuiabá and Campo Grande. **Methods:** Incidence data of Cuiabá (2000–2005) and Brasília (1999–2002) were obtained from the National Cancer Institute [1], and data from Goiânia (1995–2008) from Population-Based Cancer Registry of Goiânia. Mortality data for the cities of central-western Brazil were obtained for the period 1980–2008 from Ministry of Health [2]. Age-standardized incidence and mortality rates were calculated using the world population of Segi. Mortality trends were assessed with the Joinpoint Regression Program and *P* value less than 0.05 was defined as significant. **Results:** The highest incidence of esophageal cancer among men was in Cuiabá (16.0/100,000); the lowest was in Goiânia (6.5/100,000). Among women, the incidence rates were similar in Brasília and Cuiabá, but in Goiânia the incidence declined. There was a significant increase in mortality among men in Cuiabá (2.4%, *P*=0.03) and Campo Grande (1.2%, *P*=0.05), and in women (1.6%, *P*=0.04) in Goiânia. Mortality by age group increased significantly in Campo Grande by 1.9% for men aged at least 50 years and in Goiânia by 2.7% among women aged at least 50 years; the mortality decreased in Goiânia by 2.2% for women aged less than 50 years. **Conclusion:** The incidence of esophageal cancer in Brasília and Cuiabá was similar to that of southern Brazil in some periods. There was an increase in mortality trends for men in Cuiabá and Campo Grande, and for women in Goiânia.

Keywords: Brazil, epidemiology, esophageal cancer, trends.

Introduction

The incidence of esophageal cancer varies worldwide, esophageal cancer is more frequently observed in Iran, China, South Africa, and South America [3-4]. Esophageal cancer has the eighth highest incidence worldwide, and it is the sixth leading cause of death among all cancers [5]. Incidence rates approach mortality rates because of the poor prognosis of this neoplasm [6].

The highest incidence rates for esophageal cancer worldwide were described in Golestan province in northeast Iran; in 1970, the incidence in this region was 100/100,000, and currently, it is 50/100,000 [7]. In Zimbabwe, Africa, the incidence of esophageal cancer was 15.1/100,000 men and 5.3/100,000 women from 1998 to 2002. In the USA (SEER), the incidence of esophageal cancer is low: 5.1/100,000 for men and 1.3/100,000 for women.

The highest esophageal cancer incidence rates in Brazil were observed in the south; in Porto Alegre in 2000–2004, the incidence was 18.2/100,000 men and 4.3/100,000 women [9]. Similar rates were found for the Federal District in 1996–1998: 14.7/100,000 men and 4.5/100,000 women [10]. In central region of Brazil, the cities of Goiânia, Brasília and Cuiabá have intermediate incidence rates of esophageal cancer (8.1/100,000 to 13.1/100,000 men; Fig. 1) [8].

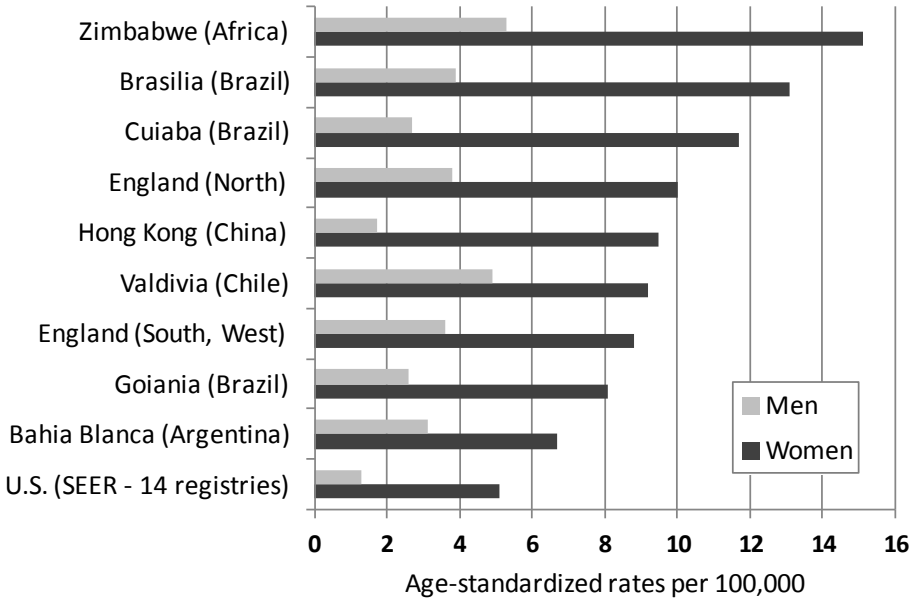

Figure 1. Age-standardized incidence rates esophageal cancer for both sexes in some regions of the world [8].

Mortality rates also vary worldwide, with reports of a decline in The Netherlands (1989–2003) [11], the European Union (1990–2000), France and Italy (men only) [12], and China [13]. In Brazil, mortality rates from esophageal cancer declined from 1980–1995 [14].

The etiology of esophageal cancer involves interactions among several risk factors as important environmental and food-related risk factors such as smoking, alcohol intake, mate consumption, and low consumption of fruits and vegetables [6, 15-17].

The central-western region of Brazil has several opportunities for work and, in the 1970s there was a huge internal migration, mainly from south part of the country to this part of Brazil [24].

However, esophageal cancer is poorly studied in central-western Brazil, and trends associated with its incidence and mortality are not well described. There are population-based cancer registries in central-western

Brazil since 1988 and information on mortality is also available for long-term period (>15 years). In this study, we aimed to determine the incidence, mortality, and trends of esophageal cancer in central-western Brazil.

Methods

Data on the incidence of esophageal cancer were obtained from a population-based cancer registry (PBCR) in central-western Brazil.

The states that comprise this region are Goiás (Goiânia), Distrito Federal (Brasília), Mato Grosso (Cuiabá), and Mato Grosso do Sul (Campo Grande) (Fig. 2), however for incidence we were able to have data from 3 cities (Goiânia, Brasília and Cuiabá), while for mortality we obtained data from all cities in this region.

Figure 2. Map of Brazil by regions

The incident data analyzed were based on the availability of incident data in each registry; they ranged from 2000 to 2005 for Cuiabá (including Várzea Grande); from 1999 to 2002 for Brasília [1], from 1995 to 2008 for Goiânia (data from the PBCR of Goiânia, 2011). However annual data from Campo Grande were not available for this analysis.

The incident cases of esophageal cancer were classified according to the International Classification of Diseases-Oncology, 3rd ed. (C15.0, C15.3, C15.4, C15.6, C15.9) [18].

To calculate the mortality rates, data were acquired from Mortality Information System of the Ministry of Health for all cities and Brasilia for the period 1980–2008. Mortality data were stratified by gender and age. All cases were classified according to ICD-10 BR for esophageal cancer [2].

Incidence and mortality rates were calculated using census data provided by the Brazilian Institute of Geography and Statistics [19]. The rates were stratified by age/year for all cities for the period 1980–2008.

The crude incidence and mortality rates were defined as ratios of the number of new cases occurring during the period specified by the population at risk, multiplied by 100,000 people. After calculation of the crude incidence and mortality rates for esophageal cancer, we calculated age-standardized rates using the world population of Segi (1960) [20]. These rates were also stratified by sex and age; two age groups were included: patients aged less than 50 years and patients aged at least 50 years to evaluate mortality trends.

To organize the database, we used SPSS version 15.0 for Windows®, and Microsoft Office Excel® 2007 to calculate the incidence and mortality rates and to produce the figures and tables.

Time trends mortality were analysed using Joinpoint [21] regression program version 3.5.1 (July 2011; Statistical Methodology and Applications Branch and Data Modelling Branch, Surveillance Research Program National Cancer Institute). The dependent variable was the age-

standardized mortality rates and the independent variable was the year. The *p* value of $p < 0.05$ was defined as significant, with confidence interval 95%.

The Joinpoint regression analysis was used to identify point at which statistically significant changes in temporal trend occurred. The annual percentage change (APC) in each joinpoint segment is the rate of change in cancer rates per year in a given time frame. Changes in rates included a shift in the magnitude or a change in the direction of the rate. A negative APC indicates a decreasing trend, whereas a positive APC indicates an increasing trend [21].

Results

The incidence rates for esophageal cancer in central-western Brazil were heterogeneous by gender, while there was a variation in mortality rates among the studied cities.

The highest age-standardized incidence rates of esophageal cancer were observed for men in Cuiabá (16.0/100,000 in 2001) and in Brasília (15.6/100,000 in 1999). Among women, they were observed in Brasília (4.3/100.000 in 2000) and in Cuiabá (3.6/100,000 in 2002) (Table 1).

Table 1. Age-standardized incidence rates for esophageal cancer in central-western Brazil by sex

	ASRW[a]/(Number of cases)					
	Men			Women		
Year/city	Goiânia	Brasília	Cuiabá	Goiânia	Brasília	Cuiabá
1995	6.6 (20)			2.9 (10)		
1996	7.4 (25)			2.8 (11)		
1997	8.3 (30)			1.3 (5)		
1998	10.6 (38)			1.5 (7)		
1999	6.8 (24)	15.6 (71)		2.8 (12)	3.8 (24)	
2000	7.7 (34)	12.9 (66)	9.9 (22)	2.1 (11)	4.3 (27)	2.1 (5)
2001	6.6 (32)	7.6 (44)	16.0 (31)	2.0 (11)	2.6 (17)	2.0 (5)
2002	7.8 (36)	13.0 (69)	8.4 (17)	2.5 (13)	2.3 (16)	3.6 (8)
2003	9.6 (44)		7.8 (16)	1.8 (10)		1.8 (5)
2004	8.3 (39)		11.4 (23)	2.8 (16)		2.8 (6)
2005	9.1 (46)		8.3 (18)	2.1 (12)		2.8 (6)
2006	8.1 (40)			2.3 (13)		
2007	7.6 (45)			1.7 (14)		
2008	6.5 (42)			1.7 (13)		

[a] Age-incidence rate standardized by world population

In Goiânia, the incidence of esophageal cancer in women declined from 2.9/100,000 in 1995 to 1.7/100,000 in 2008, representing a 41% reduction, however the incidence rates in men in the same period remained stable (Fig. 3).

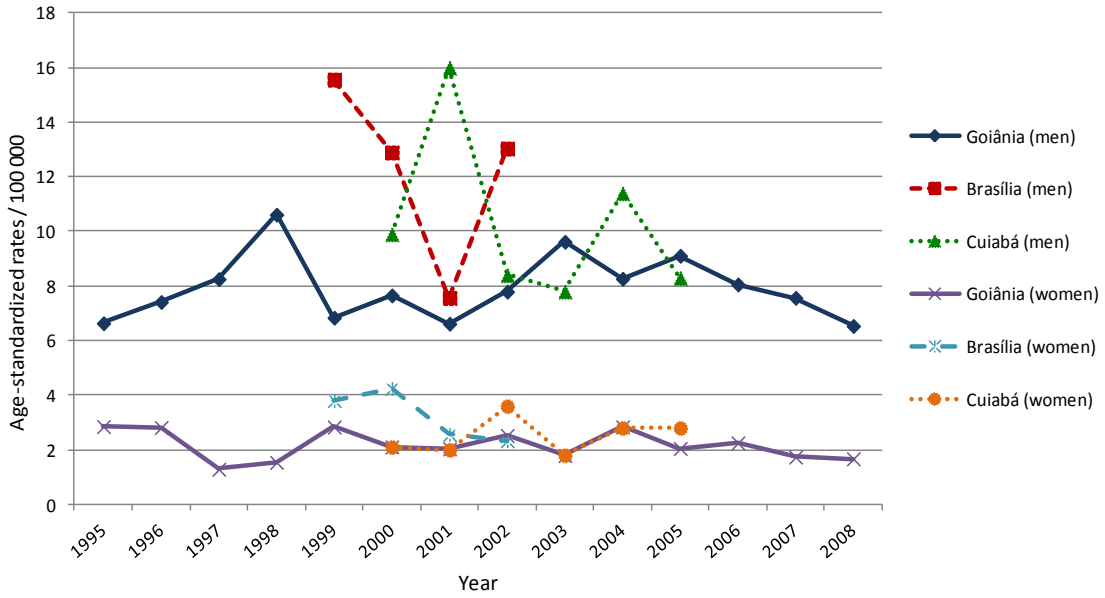

Figure 3. Age-standardized incidence rates by world population of esophageal cancer for both sexes in Goiânia (1995–2008), Brasília (1999–2002), and Cuiabá (2000–2005).

Mortality from esophageal cancer in central-western Brazil remained stable among men, ranging from 5.9/100,000 (1980–1984) to 6.1/100,000 (2005–2008) in Goiânia, the mortality rates increased in Cuiabá 4.7/100,000 to 6.2/100,000 and in Campo Grande from 6.9/100,000 to 8.9/100.000, in Brasília the mortality rates decreased from 7.8/100,000 (1980–1984) to 6.1/100,000 (2005–2008) (Table 2). Among women the mortality remained stable in central-western Brazil below 3.0/100,000 in the period 1980-2008 (Fig. 4).

Table 2. Age-standardized world mortality rate for esophageal cancer, by sex, in central-western Brazil, 1980-2008

	ASRW[a]/(Number of cases)															
	Men								Women							
Year/City	Goiânia		Brasília		Cuiabá		Campo Grande		Goiânia		Brasília		Cuiabá		Campo Grande	
1980–1984	5.9	(57)	7.8	(73)	4.7	(16)	6.9	(29)	1.1	(12)	1.7	(21)	0.6	(2)	1.8	(9)
1985–1989	5.4	(66)	5.8	(76)	5.3	(28)	6.2	(46)	1.5	(20)	1.5	(27)	0.3	(3)	2.6	(16)
1990–1994	5.2	(74)	5.9	(102)	3.5	(25)	7.8	(59)	1.0	(17)	1.8	(36)	1.2	(8)	1.2	(9)
1995–1999	6.9	(115)	6.8	(152)	6.3	(55)	8.3	(75)	1.5	(30)	2.7	(64)	1.8	(16)	2.9	(29)
2000–2004	7.6	(171)	7.4	(204)	7.7	(76)	9.1	(108)	1.7	(45)	1.5	(53)	1.1	(13)	1.9	(27)
2005–2008	6.1	(136)	6.1	(164)	6.2	(65)	8.9	(103)	1.7	(45)	1.8	(61)	1.4	(16)	2.2	(28)

[a]Age- incidence rate standardized by world population

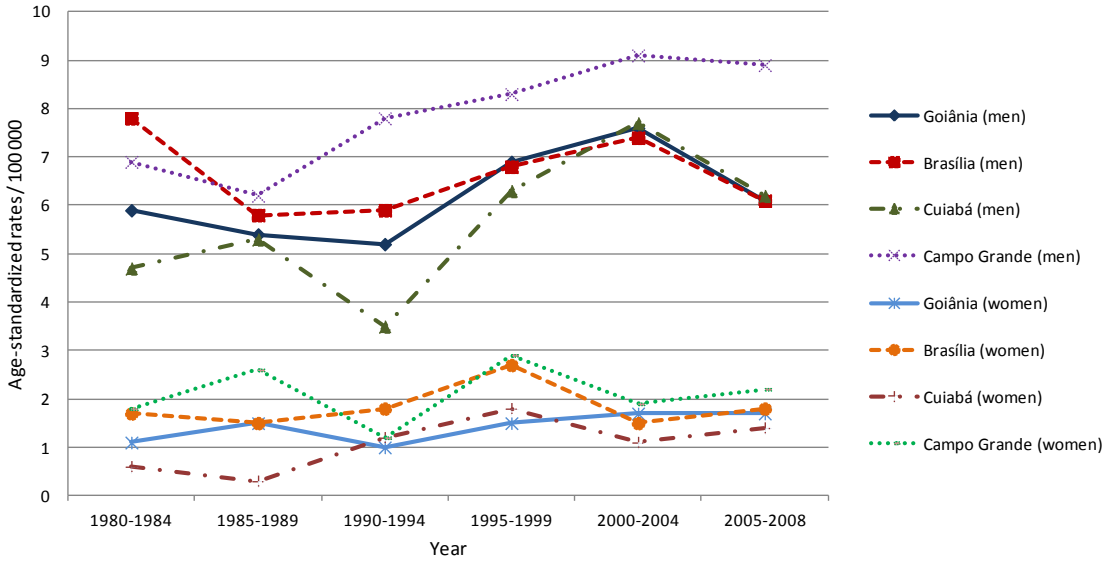

Figure 4. Age-standardized mortality rates by world population for esophageal cancer for both sexes in Goiânia, Brasília, Cuiabá and Campo Grande, from 1980 to 2008.

The mortality trends for esophageal cancer in central-western Brazil showed significant increase for men in Cuiabá (2.4%, *P*=0.027) (Fig. 5a) and in Campo Grande (1.2%, *P*=0.049) (Fig. 5b) (Table 3). Among women, there was a trend toward a significant increase of 1.6% in mortality in Goiânia (*P*<0.045) (Fig. 5c).

Analyses of trends in esophageal cancer mortality by age group indicated an increase of 1.9% in Campo Grande for men aged at least 50 years (Fig. 5d). For women, the mortality because of esophageal cancer decreased by 2.2% in Goiânia (Fig. 5e) for those aged less than 50 years, but increased by 2.7% for those aged at least 50 years (Fig. 5f) (Table 4).

Table 3. Mortality trends for esophageal cancer in central-wester Brazil by sex

	Men		**Women**	
City	APC (95% CI)	*P*	APC (95% CI)	*P*
Goiânia	1.0 (–0.4; 2.5)	0.162	1.6* (0.0; 3.1)	0.045
Brasília	0.1 (–1.3; 1.5)	0.079	1.0 (–1.4; 3.5)	0.381
Cuiabá	2.4* (0.3; 4.5)	0.027	–2.5 (–5.9; 1.0)	0.146
Campo Grande	1.2* (0.0; 2.5)	0.049	–1.0 (–4.0; 2.2)	0.537

APC, annual percentage change; CI, confidence interval.

*Significant, *P*<0.05

Table 4. Mortality trends for esophageal cancer, by age group and sex, in central-western Brazil.

Age	Men				Women			
	<50 years		≥50 years		<50 years		≥50 years	
City	APC (95% CI)	*P*	APC (95% CI)	*P*	APC (95% CI)	*P*	APC (95% CI)	*P*
Goiânia	0.0 (–2.7; 2.8)	0.984	1.2 (–0.5; 2.9)	0.157	–2.2* (–4.3; 0.0)	0.048	2.7* (0.9; 4.5)	0.004
Brasília	0.5 (–1.8; 2.9)	0.639	0.9 (–0.5; 2.3)	0.194	–2.6 (–5.3; 0.1)	0.060	0.7 (–1.7; 3.1)	0.575
Cuiabá	0.3 (–2.7; 3.5)	0.784	2.1 (–0.1; 4.5)	0.064	[a]	-	–2.8 (–6.5; 1.1)	0.144
Campo Grande	–2.2 (–4.8; 0.4)	0.088	1.9* (0.7; 3.1)	0.003	–3.8 (–8.1; 0.8)	0.087	–0.2 (–3.1; 2.8)	0.887

APC, annual percentage change; CI, confidence interval.

[a] Insufficient data for this analysis.

*Significant, *P*<0.05.

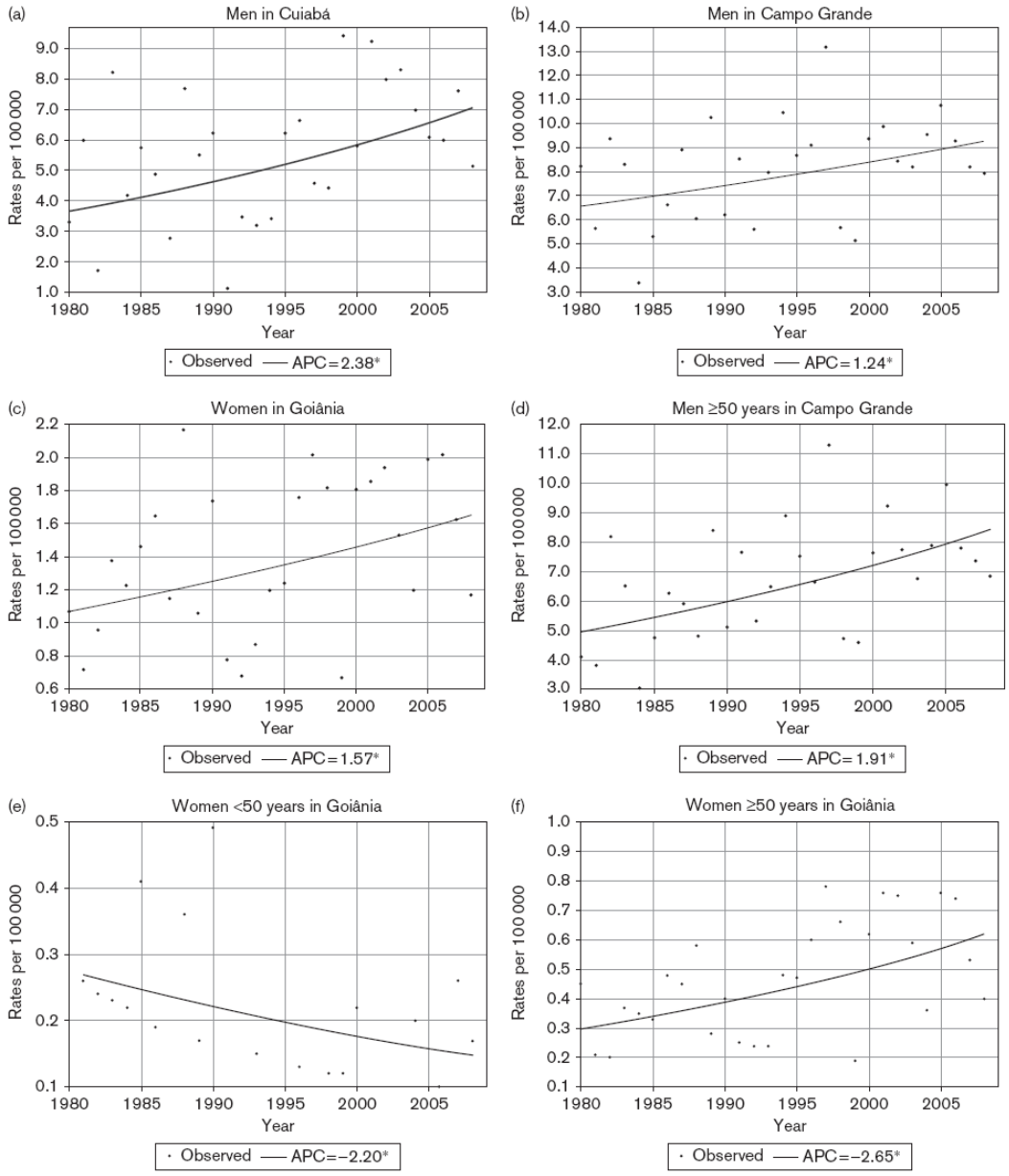

Figure 5. Mortality trends of esophageal cancer for both sexes from 1980 to 2008, in central-western Brazil. Mortality trends (a) for men in Cuiabá; (b) for men in Campo Grande; (c) for women in Goiânia; (d) for men ≥50 years in Campo Grande; (e) for women <50 anos years in Goiânia; and (f) for women ≥50 years in Goiânia. APC, annual percentage change.

Discussion

This study evaluated the incidence and mortality trends of esophageal cancer in central-western Brazil over the past 20 years. The population in central-western of Brazil represents 6.4% of the Brazilian population. We found that the incidence of esophageal cancer in central-western Brazil differed between the neighboring cities analyzed; for men, the incidence rates were intermediate in Goiânia, whereas in Cuiabá and Brasília, the incidence of esophageal cancer was similar to that in the south of the country, for Campo Grande (2000-2002) data published from INCA (2010) show age-standardized incidence rates of 12.3/100,000 in men and 3.0/100,000 in women, similar to south as well [9].

In the south of Brazil in Porto Alegre, the incidence of esophageal cancer was 18.2/100,000 in men and 4.3/100,000 in women from 2000 to 2004 [9]; this region had the highest incidence rates of the country [3-4]. High rates of esophageal cancer incidence are related to lifestyle, including the habit of consuming large volumes of mate, in hot water. This is a characteristic of south of Brazil, Uruguay, and northeastern Argentina, being the incidence rates of esophageal cancer high in these regions [17, 22, 23]. Moreover, smoking and alcohol consumption are also risk factors for this cancer [6, 15, 17].

The region of the Federal District had a population growth influenced by the construction of the federal capital which began in the 1960s; during the same period there was the expansion of agricultural frontiers in the central-western Brazil, contributing to the large-scale migration from southern to central-western Brazil between the 1970s and

1980s, particularly to Cuiaba and Campo Grande. Immigration rates in this period in the central-western part were heterogeneous, showing increases in Distrito Federal and Mato Grosso in the 60s and 70s with growth rates higher than 6%/year, while in Goiás and Mato Grosso do Sul growth rates were below 4%/year. In the 1980s, most states had decreases, but Mato Grosso remained with growth rates above 5%/ year [24, 25].

One characteristic of migrant groups is that they tend to maintain the typical eating habits and customs of their region of origin, and these eating habits persist for long periods [26]. Thus, the population of immigrants from southern Brazil likely retained typical habits such as the consumption of mate, alcoholic beverages and smoking tobacco [6, 15, 17]; to preserve these habits could have contributed to the high incidence of esophageal cancer identified in this study, particularly in Cuiabá and Brasilia.

However in the state of Goiás where there is not migration, the incidence of esophageal cancer in Goiânia was similar to that in developed regions such as Europe [8, 27] and North America [8, 28].

The estimated incidence and mortality rates for esophageal cancer are higher in less developed regions such as South Africa, East Asia, and Africa, and the lowest rates are found in more developed regions such as southern Europe and Southeast Asia (Fig. 6) [5]. Therefore in central-western Brazil there is a combination of both, which may be related to the lifestyle of the migrants in the area.

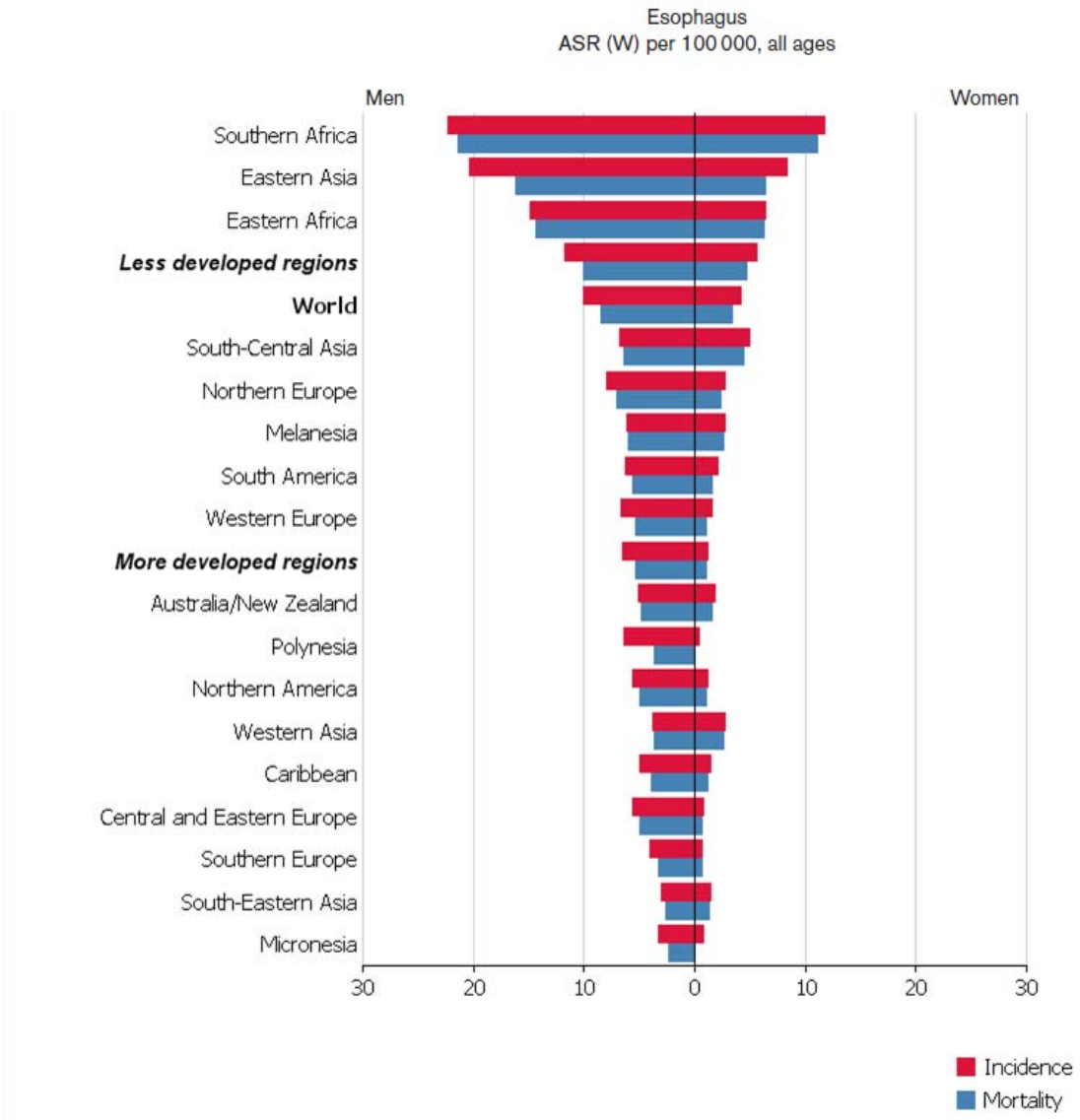

Figure 6. Worldwide estimated age-standardized incidence and mortality rates for esophageal cancer by sex [5]. ASR (W), age-incidence rate standardized by world population

Studies have reported that the risk for esophageal cancer increases by two- to four-fold in regions with low socioeconomic status compared with regions with high socioeconomic status [29-32]. In Brazil, the south and southeast regions have higher socioeconomic status, central-western Brazil has average socioeconomic status, and the northern and northeastern regions of Brazil have the lowest socioeconomic status [33]. The incidence of

esophageal cancer in Brazil must be related to the dietary habits and lifestyles of the population, since the highest rates of esophageal cancer are observed in the south and high and intermediate rates are observed in central-western Brazil.

The changes in living standards resulting from the urbanization process, along with the higher intake of processed products, reduced consumption of fruit and vegetables, increased consumption of alcoholic beverages, and smoking have also contributed significantly to the increased incidence of esophageal cancer [6, 15, 17].

Mortality rates from esophageal cancer are similar to incidence rates, because most cases have been diagnosed at an advanced stage of disease resulting in high lethality [5, 34-37] (Fig. 6).

In this study, mortality among men in central-western Brazil was found to be increased for Cuiabá and Campo Grande, whereas the literature has reported a decline in mortality rates in different countries [38], such as China [13], the Netherlands [11], France (APC = -3.4%), Italy (APC = -3.0%), and the European Union (APC = -1.1%) [12].

In Brazil, Wunsch Filho and Moncau (2002)[14] reported a 14.8% and 100% increase in mortality rates from esophageal cancer among men and women in the central-western during the period 1980–1995. In the current study (1980–2008), the mortality rates of esophageal cancer among men were found stable in Goiânia, decreased in Brasília and increased in Cuiabá and Campo Grande. Among men the mortality rates increased in Goiânia and were stable in Brasília, Cuiabá and Campo Grande, revealing a change in the pattern of mortality over the past 10 years by gender and city.

Study of the mortality rates for esophageal cancer among elderly women (aged ≥60 years) in the southern and southeastern regions of Brazil during the period 1980–2005 disclosed a continuing decline of this neoplasm [38]. In central-western Brazil, analysis by age group revealed a decrease in mortality among women aged less than 50 years in Goiânia, whereas mortality increased among women aged at least 50 years in Goiânia. These differences among women may be related to access and quality of care, as well as to changes in the lifestyle habits of these populations.

Conclusions

The different incidence and mortality rates of esophageal cancer observed in central-western Brazil may be related to differences in lifestyle, internal migration from south, high exposure to known risk factors for esophageal cancer, as well as differences in the access to diagnosis treatment and qualified care.

Furthermore, the incidence of esophageal cancer remained stable among men in central-western Brazil, but it is decreasing among women only in Goiânia. Mortality rates among men increased in Cuiabá and Campo Grande, and increased among women in Goiânia. Campo Grande was the only city with an increase in mortality among men aged at least 50 years and Goiânia among women aged at least 50 years.

This study, despite being limited by the relatively sparse incidence data for Brasília, Cuiabá and Campo Grande, revealed a high incidence of esophageal cancer in these cities in central-western Brazil. The higher

incidence of esophageal cancer in Brasília and Cuiabá may be due to migration of individuals from southern Brazil and maintenance of habits native to the south of the country in the central-western region.

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5 CONCLUSÕES

Esta dissertação possibilitou uma maior compreensão do perfil epidemiológico do câncer de esôfago no centro-oeste, bem como evidenciou a importância da qualidade dos dados fornecidos pelos Registros de Câncer de Base Populacional na produção do conhecimento epidemiológico.

O Registro de Câncer de Base Populacional de Goiânia apresentou bom desempenho na coleta das variáveis básicas do câncer de esôfago, entretanto, a variável estadiamento clínico mostrou uma exaustividade ruim no período analisado.

A incidência do câncer de esôfago na região centro-oeste (Goiânia, Brasília e Cuiabá) mostrou-se heterogênea, embora haja maior incidência entre homens em Brasília e Cuiabá, em Goiânia as taxas foram intermediárias. As taxas de incidência em mulheres na região centro-oeste foram baixas.

As taxas de mortalidade do câncer de esôfago em homens no centro-oeste foram maiores em Campo Grande, sendo semelhantes nas demais capitais. Para as mulheres a mortalidade foi mais alta em Campo Grande.

Há uma tendência de aumento da mortalidade do câncer de esôfago em Cuiabá e Campo Grande, sendo estável em homens em Goiânia e Brasília. Para as mulheres há uma tendência de aumento em Goiânia e estabilidade nas demais capitais.

Houve uma tendência de queda da mortalidade do câncer de esôfago em mulheres abaixo dos 50 anos em Goiânia. Observou-se uma tendência de aumento da mortalidade em mulheres acima dos 50 anos em Goiânia e em homens acima dos 50 anos em Campo Grande.

6 CONSIDERAÇÕES FINAIS

Conhecer o impacto de uma neoplasia maligna como o câncer de esôfago em uma população é de suma importância uma vez que sua incidência está aumentando em todo o mundo, e a morbidade e mortalidade são muito altas.

Para que haja qualidade na informação em câncer disponibilizada pelos Registros de Câncer, estes devem estar de acordo com os padrões nacionais e internacionais, agregando assim informações importantes para o controle do câncer, possibilitando avaliar a qualidade da assistência prestada no diagnóstico, como por exemplo, a informação do estadiamento clínico. O estadiamento clínico é fundamental para a escolha terapêutica adequada, principalmente para tumores altamente letais, como o câncer de esôfago. Sugere-se, portanto, que esta informação seja agregada à notificação do caso incidente de câncer.

Apesar da limitação da disponibilidade de dados de incidência para Brasília, Cuiabá e Campo Grande, a heterogeneidade observada nas taxas de incidência e mortalidade, e principalmente as altas taxas de incidência para o câncer de esôfago nestas cidades podem estar relacionados aos diferentes estilos de vida das populações regionais, as altas taxas de migrações internas da região sul, com a permanência do estilo

de vida da população migrante, as exposições aos fatores de risco conhecidos para o câncer de esôfago, como também as diferenças no acesso ao diagnóstico e tratamento da doença.

Portanto, por se tratar de uma doença de índice letalidade alta, com incidência crescente e por ser uma região que carece de estudos analíticos sobre os fatores epidemiológicos para esta neoplasia maligna, sugerimos, como método de prevenção à população da região centro-oeste a adoção de hábitos alimentares e estilo de vida mais saudáveis, e aos gestores de saúde pública o incentivo às campanhas contínuas para estes métodos de prevenção e diagnóstico precoce propiciando uma melhor qualidade de vida.

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ANEXOS

Anexo 1 – Parecer do Comitê de Ética

Anexo 2 – Submissão Artigo 1

Anexo 3 – Aceite para publicação Artigo 2