The Shifting Trends of Esophageal Cancer in U.S., 1975-2008

[1,2]M. J. TenNapel MS, MBA., [1]Charles Lynch, M.D., M.S., Ph.D.

[1]The Department of Epidemiology, the College of Public Health, and the [2]Department of Radiation Oncology The University of Iowa

Introduction

Esophageal cancer is an aggressive disease with a dismal outcome. Over the past 30 years there has been a dramatic shift in histological and racial trends of esophageal cancer. Identification of these trends through descriptive epidemiology can generate hypotheses to better understand this disease and decrease mortality.

Methods

SEER*stat version 7.0.4 was accessed to identify trends in esophageal cancer from 1975-2008.1 For incidence and mortality statistics the following 9 SEER registries were used: San Francisco-Oakland, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah and Atlanta. This represents approximately 10% of the US population. Rates and figures 1-5 are age-adjusted to the 2000 U.S. population.

Histology definitions - ICD-O-3 histology codes:

- Squamous cell carcinoma = 8050 - 8089
- Adenocarcinoma = 8140 - 8389

Subsite definitions

- Upper Esophagus C15.0 (cervical esophagus)
  C15.3 (upper third of esophagus)
- Middle Esophagus C15.1 (thoracic esophagus)
  C15.4 (middle third of esophagus
- Lower Espophagus C15.2 (abdominal esophagus)
  C15.5 (lower third of esophagus)

Chi-square tests were performed on rate ratios for blacks and whites in 11-year increments. The 'other race' category was excluded from analysis since there was a small number of these cases in this population from 1975-2008.

Figure 1.

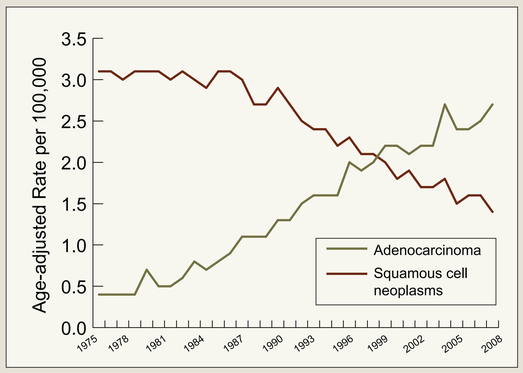


Figure 2.

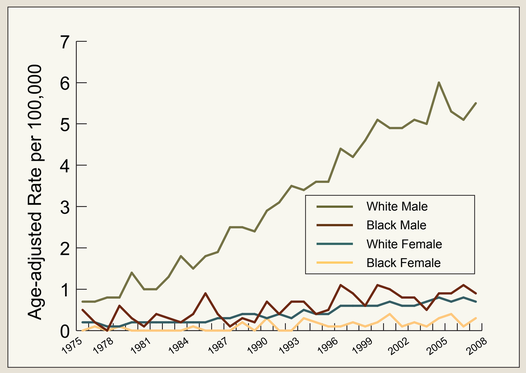


Figure 3.

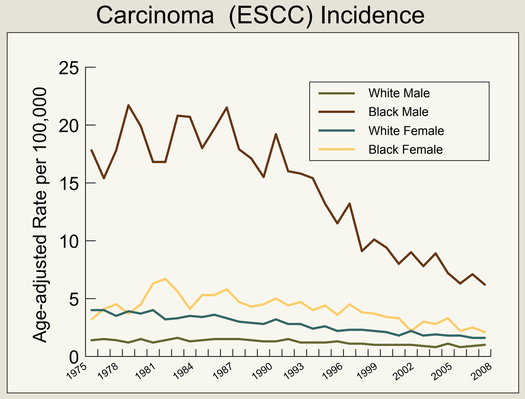


Figure 4.

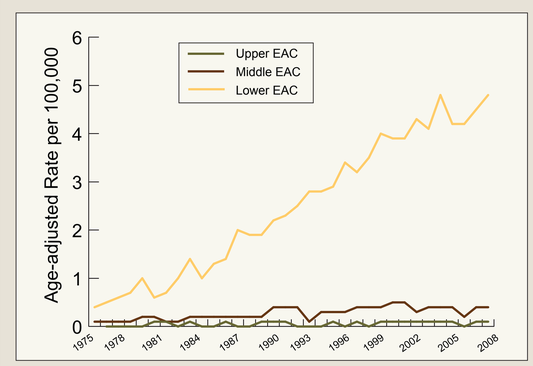


Figure 5a.

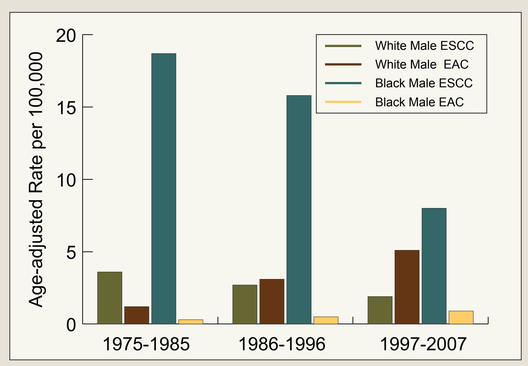
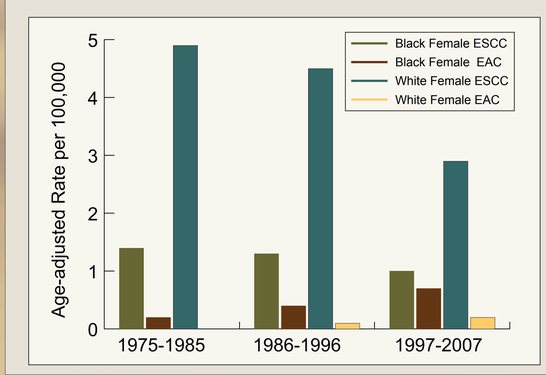


Figure 5b.



Results

From 1975 to 2008 there has been a reversal in frequency of esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC) when considering all races (Figure 1). The increase of EAC has increased nearly 6-fold during this time, a rate greater than that of any other cancer in the United States.[2] This increase is seen almost exclusively in the white male population (Figure 2). In 1975, ESCC was dominant in the black male population. The marked increase in adenocarcinoma in white males makes these incidence rates nearly the same (Figure 2 and 3). The increase in EAC in white males is almost exclusively located within the lower esophagus (igure 4).

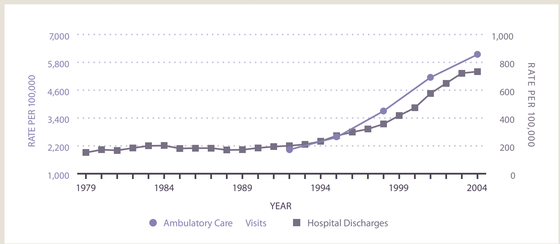
Comparing the periods 1975-1985 to 1986-1996 and 1986-1996 to 1997-2007 there was an increase in the incidence of EAC in white males ($p<0.001$ for both) and in white females ($p<0.001$ for both). Incidence of EAC in black males and black females did not see an increase when comparing 75-85 to 86-96 ($p=0.15$ and $p=0.058$ respectively) but did see an increase when comparing 86-96 to 97-07 ($p=0.0009$ and $p=0.022$ respectively). Figure 5a and 5b demonstrate the rate changes over these time periods.

Considering the same time periods for ESCC, there was a decrease in incidence in white males ($p<0.001$ for both) and black males ($p<0.001$ for both). There was a no decrease in white or black women comparing 75-85 to 86-96 ($p=0.64$ and $p=0.21$ respectfully) but there was a decrease in white and black women from 86-96 to 97-07 ($p<0.001$ for both). Figure 5a and 5b demonstrate the rate changes over these time periods.

Obesity has also been associated with an increased risk of EAC. It is thought that central obesity may increase intragastric esophageal pressure gradient, thereby facilitating gastrointestinal esophageal reflux disease (GERD).[2] The increase in incidence of lower EAC for white males and females corresponds to increased ambulatory care visits and hospital discharge rates for GERD (Figure 6). Normally the esophagus is lined with stratified epithelium. GERD causes stomach acid to back up into the lower esophagus, causing chronic irritation. GERD is a major predisposing factor for Barrett's esophagus. Barrett's esophagus is characterized by metaplasia of the distal esophagus resulting in columnar epithelium.[3] EAC subsequently develops in the columnar epithelium. The overall prevalence of Barrett's is low in the general population making it unfavorable for routine screening.3 Interestingly, studies have shown there is no difference in frequency of GERD symptoms between white and black populations[4] (Table 1). However, there is a striking difference in rates of Barrett's esophagus and EAC.[4,5]

Figure 6.

Gastroesophageal Reflux Disease: Age-Adjusted Rates of Ambulatory Care Visits and Hospitals Discharges With All-Listed Diagnoses in the United States, 1979-2004



SOURCE: National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS) (averages 1992–1993, 1994–1996, 1997–1999, 2000–2002, 2003–2005), and National Hospital Discharge Survey (NHDS)

Table 1.

Gastroesophageal Reflux Desease: Number and Age-Adjusted Rates of Ambulatory Care Visits and Hospital Discharges With First-Listed and All-Listed Diagonises by Age, Race and Sex in the United States, 2004

Demographic Characteristics		AMBULATORY CARE VISITS		HOSPITALS DISCHARGES	
		First-listed diagnoses	All-listed diagnoses	First-listed diagnoses	All-listed diagnoses
		Rate per 100,000	Rate per 100,000	Rate per 100,000	Rate per 100,000
RACE	White	2,267	6,002	49	987
	Black	2,872	8,075	65	1,107
SEX	Female	2,209	6,733	54	1,183
	Male	2,462	5,506	51	937
Total		2,332	6,246	54	1,086

SOURCE: National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS) (3-year average, 2003-2005), and Healthcare Cost and Utilization Project Nationwide Inpatient Sample (HCUP NIS).

Conclusions

Over the past 30 years, rates of EA in white males are increasing faster than any other cancer. Rates of GERD are similar between white males and black males; however rates of Barrett's esophagus and EA are markedly different, indicating an environmental or genetic difference exists. Further investigation and clinical studies of these differences will help to better understand esophageal cancer, identify its risk factors, and decrease mortality

References

1. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 9 Regs Research Data, Nov 2010 Sub (1973-2008) <Katrina/Rita Population Adjustment> - Linked To County Attributes - Total U.S., 1969-2009 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2011, based on the November 2010 submission
2. Falk, G. W. Risk factors for esophageal cancer development. Surge Oncol Clin N Am 18, 469-485. (2009).
3. Wood, R.K. & Yang, Y. X. Barrett's esophagus in 2008: an update. Keio J Med 57, 132-138 (2008).
4. Sharma, P., Wani, S., Romero, Y., Johnson, D. & Hamilton, R. Racial and geographic issues in gastroesophageal reflux disease. Am J Gastroenterol 103, 2669-2680 (2008).
5. Abrams, J.A., Fields, S., Lightdale, C.J. & Neugut, A.I. Racial and ethnic disparities in the prevalance of Barrett's esophagus among patients who undergo upper endoscopy. Clin Gastroenterol Hepatol 6, 30-34, (2008).