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Sarina Pasricha
University of North Carolina at Chapel Hill

Nan Li
University of North Carolina at Chapel Hill

William J. Bulsiewicz
University of North Carolina at Chapel Hill

Richard I. Rothstein
Dartmouth University School of Medicine

Anthony Infantolino
Thomas Jefferson University, anthony.infantolino@jefferson.edu

See next page for additional authors

Authors
Sarina Pasricha, Nan Li, William J. Bulsiewicz, Richard I. Rothstein, Anthony Infantolino, Atilla Ertan, Daniel S. Camara, Evan S. Dellon, George Triadafilopoulos, Charles J. Lightdale, Ryan D. Madanick, William D. Lyday, Raman V. Muthusamy, Bergein F. Overholt, and Nicholas J. Shaheen

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Sex and race/ethnicity differences in patients undergoing radiofrequency ablation for Barrett's esophagus: Results from the U.S. RFA Registry

Sarina Pasricha, MD, MSCR[1,*], **Nan Li, MS**[1,*], **William J. Bulsiewicz, MD, MSC**[1], **Richard I. Rothstein, MD**[2], **Anthony Infantolino, MD**[3], **Atilla Ertan, MD**[4], **Daniel S. Camara, MD**[5], **Evan S. Dellon, MD, MPH**[1], **George Triadafilopoulos, MD**[6], **Charles J. Lightdale, MD**[7], **Ryan D. Madanick, MD, MSCR**[1], **William D. Lyday, MD**[8], **Raman V. Muthusamy, MD**[9], **Bergein F. Overholt, MD**[10], and **Nicholas J. Shaheen, MD, MPH**[1]

[1]University of North Carolina at Chapel Hill, Center for Esophageal Diseases and Swallowing, Division of Gastroenterology and Hepatology, Chapel Hill, NC

[2]Dartmouth University School of Medicine, Hanover, NH

[3]Thomas Jefferson University School of Medicine, Philadelphia, PA

[4]University of Texas School of Medicine, Houston, TX

[5]Digestive Health Physicians, Cheektowaga, NY

[6]Stanford University School of Medicine, Palo Alto, CA

Corresponding Author: Nicholas J. Shaheen, MD, MPH, Professor of Medicine and Epidemiology, Director, Center for Esophageal Diseases and Swallowing, University of North Carolina School of Medicine, CB#7080, Chapel Hill, NC 27599-7080, Phone: (919) 966-2513, Fax: (919) 843-2508.

*Co-first authors

Author Contributions: Sarina Pasricha: study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, statistical analysis; Nan Li: study concept and design, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content; William J. Bulsiewicz: study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, statistical analysis; Richard I. Rothstein: study concept, acquisition of data, interpretation of data, critical revision of the manuscript for important intellectual content; Anthony Infantolino: study concept, acquisition of data, interpretation of data, critical revision of the manuscript for important intellectual content; Atilla Ertan: study concept, acquisition of data, interpretation of data, critical revision of the manuscript for important intellectual content; Daniel S. Camara: study concept, acquisition of data, interpretation of data, critical revision of the manuscript for important intellectual content; Evan S. Dellon: study concept, acquisition of data, interpretation of data, critical revision of the manuscript for important intellectual content; George Triadafilopoulos: study concept, acquisition of data, interpretation of data, critical revision of the manuscript for important intellectual content; Charles J. Lightdale: study concept, acquisition of data, interpretation of data, critical revision of the manuscript for important intellectual content; Ryan D. Madanick: study concept, acquisition of data, interpretation of data, critical revision of the manuscript for important intellectual content; William D. Lyday: study concept, acquisition of data, interpretation of data, critical revision of the manuscript for important intellectual content; Raman V. Muthusamy: study concept, acquisition of data, interpretation of data, critical revision of the manuscript for important intellectual content; Bergein F. Overholt: study concept, acquisition of data, interpretation of data, critical revision of the manuscript for important intellectual content; Nicholas J. Shaheen: study concept and design, analysis and interpretation of data, critical revision of the manuscript for important intellectual content, study supervision.

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[7]Columbia University School of Medicine, New York, NY

[8]Atlanta Gastroenterology Associates, Atlanta, GA

[9]UCLA School of Medicine, Los Angeles, CA

[10]Gastrointestinal Associates, Knoxville, TN

Abstract

Background—Little is known about differences in Barrett's esophagus (BE) characteristics by sex, and race/ethnicity, or these differences in response to radiofrequency ablation (RFA).

Objective—We compared disease-specific characteristics, treatment efficacy, and safety outcomes by sex and race/ethnicity in patients treated with RFA for BE.

Design and Setting—The U.S. RFA Patient Registry is a multicenter collaboration reporting processes and outcomes of care for patients treated with RFA for BE.

Patients and Interventions—Patients with BE treated with RFA.

Main outcome measurements—We assessed safety (stricture, bleeding, perforation, hospitalization), efficacy (complete eradication of intestinal-metaplasia (CEIM)), complete eradication of dysplasia, and number of treatments to CEIM by sex and race/ethnicity.

Results—Among 5521 patients (4052 males; 5126 Caucasian, 137 Hispanic, 82 African-American, 40 Asian, 136 not identified), females were younger (60.0 vs. 62.1 yrs.), had shorter BE (3.2 vs. 4.4 cm), and less dysplasia (37% vs. 57%) than males. Females were almost twice as likely to stricture (OR 1.7; 95% CI, 1.2–2.3). Although Caucasians were predominantly male, about half of African-Americans and Asians with BE were females. African-Americans and Asians had less dysplasia than Caucasians. Asians and African-Americans had more strictures than Caucasians. There were no sex or race differences in efficacy.

Limitations—Observational study with non-mandated paradigms, no central lab for re-interpretation of pathology

Conclusions—In the U.S. RFA Registry, females had shorter BE and less aggressive histology. The usual male sex predilection for BE was absent in African-Americans and Asians. Post-treatment stricture was more common among females, and Asians. RFA efficacy did not differ by sex or race.

Keywords

Barrett's esophagus; radiofrequency ablation; sex; race

Introduction

Barrett's esophagus (BE) is a precancerous condition associated with a 10 to 30-fold increased risk of esophageal adenocarcinoma, a cancer with an approximately 6-fold increase in incidence over the past four decades (1–6). Radiofrequency ablation (RFA) is an effective and safe therapy for eradication of nondysplastic and dysplastic BE (7, 8). Past studies demonstrate a strong association of BE with male sex and Caucasian race (9–12).

However, little is known about sex and racial differences in the characteristics of BE among patients undergoing endoscopic therapy for BE. Similarly, the impact of sex and race on the response to RFA treatment is unknown.

Sex and race discrepancies in the incidence of esophageal adenocarcinoma are well established, with a male to female ratio of 3 to 8:1, and a Caucasian to African-American ratio of 5:1 (12–16). Sex and race differences have also been reported for Barrett's esophagus, which is 2 to 4 times as prevalent among males as females and five times as prevalent among Caucasians as African-Americans and Asians (10, 17–19). However, most of these studies are restricted by small numbers of minority patients and females, and are therefore limited in their ability to assess for sex and race differences in disease patterns. Previous studies of ablation therapy for BE also have had similar shortcomings with respect to numbers of females and minorities (7, 8, 20–22)

The aim of this study was to assess sex and race/ethnicity differences in the characteristics of BE in patients undergoing radiofrequency ablation for BE. Additionally, we investigated the impact of sex and race/ethnicity on RFA treatment efficacy and safety outcomes using a nationwide, multicenter registry of patients with BE.

Material and Methods

U.S. RFA Patient Registry

The U.S. RFA Patient Registry is a multicenter collaboration reporting processes and outcomes of care for patients treated with RFA for BE at 148 institutions in the United States (113 community-based, 35 academic-affiliated). The registry does not mandate protocols for care, but provides a suggested protocol for treatment and follow-up of patients with Barrett's esophagus. The registry was developed as a research tool to monitor clinical outcomes in patients undergoing treatment of BE with RFA using the HALO Ablation Systems (GI Solutions, Sunnyvale, Calif, a subsidiary of Covidien), and is funded by Covidien, Inc. All physicians participating in this registry either elected to use Western institutional review board (IRB) approval, or obtained IRB approval through their respective institutions.

Patient Eligibility

Patients were enrolled from July 2007 to July 2011. Patients were eligible for inclusion in the registry if: (1) they had endoscopic evidence of columnar metaplasia in the tubular esophagus with accompanying biopsies demonstrating intestinal metaplasia, and (2) they received RFA for BE. Subjects were classified using standardized histological grading, including non-dysplastic BE (NDBE), indefinite for dysplasia (IND), low-grade dysplasia (LGD), high-grade dysplasia (HGD), intramucosal carcinoma (IMC), and invasive adenocarcinoma (EAC)(23). Those patients who had previously received one or more RFA treatments before enrollment had collection of retrospective data, with subsequent prospective collection of data for ensuing visits. Patients who had not yet undergone treatment were prospectively enrolled in the study.

Data Collection and Database Collation

Information collected in the registry includes demographic data, histology before treatment, endoscopic findings, number of treatment sessions, ablation outcomes, and adverse events. Race/ethnicity were classified using race/ethnic categorizations as suggested by the National Institutes of Health (ethnicity of Hispanic/non-Hispanic and race of Caucasian, African-American, American Indian or Alaska Native, Asian, Native Hawaiian or Other Pacific Islander). In this analysis, American Indian, Alaska Native, Hawaiian/Pacific Islander, and Asian were collapsed into a single categorization, due to small count data in those cells. Subjects who self-classified into more than one group were included in the non-Caucasian group to which they identified. All data were recorded on standardized case report forms (CRFs), and were entered online through an internet-based secured data entry and processing system. All CRFs are coded with a site code and patient code; no information identifying patients was contained on Registry documents. Data were collated into a central electronic database, with real-time monitoring for logic checks and consistency. Data were analyzed by investigators in the clinical epidemiology program at the UNC Center for Gastrointestinal Biology and Disease (T32 DK07634), who had complete access to the data.

Treatment Protocol

Data from previous clinical trials were given to all physicians as a guideline for treatment and follow-up protocols. However, because this is a registry study, institutions and individual physicians could deviate from the treatment protocols suggested, depending on individual patient requirements and physician preferences. The suggested treatment protocol provided to physician investigators has been previously described (23).

At enrollment, each patient was interviewed and a Baseline Encounter Form, which collected medical history information and demographics, was completed. The standardized protocol suggested medical therapy with twice-daily PPIs to minimize any baseline inflammatory changes of the esophageal mucosa and decrease acid reflux before and throughout RFA treatment, unless the patient had a documented history of antireflux surgery.

At the initial visit, patients were treated with one of two ablation devices: the HALO^{360} Circumferential Ablation System or the HALO^{90} Focal Ablation System. The decision as to initial treatment modality was based on the burden of disease (Barrett's segments of >3 cm are generally best treated with the circumferential catheter), as well as operator preference. Recommended treatment protocols were based on previously published data (24).

Follow-Up Protocol

Recommendations for the first follow-up visit, which was 2–3 months after treatment initiation, included additional circumferential or focal RFA treatment for any visible residual BE, depending on the extent of the disease. If no visible BE was observed, four-quadrant biopsies every cm were recommended throughout the length of the pre-treatment BE. If these biopsies were clear of BE on pathologic review, the patients entered the surveillance phase of follow-up. Initial surveillance was recommended at 3 months for those patients with HGD or 6 months for those patients with NDBE, IND, or LGD. If follow-up biopsies

revealed IM or dysplasia, recurrent treatment with RFA was recommended at the next endoscopy session.

Adverse events were reported using standardized forms and terminology. Each site also complied with reporting guidelines for their institution regarding reporting adverse events to their IRB and FDA under the MDR reporting regulation in 21 C.F.R. Part 803.

Outcomes

Safety outcomes included esophageal perforation, stricture formation, gastrointestinal (GI) bleeding, and hospitalization. A stricture was defined as any narrowing of the esophageal lumen requiring dilation. GI bleeding was considered clinically significant if hospitalization and/or blood transfusion was required. All patients treated with RFA were included in the safety analysis. Adverse event rates were reported per patient by sex and race group.

The rates of complete eradication of intestinal metaplasia (CEIM), rates of complete eradication of dysplasia (CED), and the number of RFA sessions were determined to assess the efficacy of treatment. CEIM was defined as an esophageal biopsy session in which no biopsy demonstrated IM, occurring at least 12 months after initial treatment. CED was defined as the absence of dysplasia (including indefinite dysplasia, LGD, HGD or worse) from biopsy specimens. All review was performed by local pathologists; results were reported on a standardized pathology form that specifically queried for the presence of intestinal metaplasia and dysplasia.

Efficacy analysis was restricted to patients who have been in the registry for at least 12 months beyond treatment initiation and who had a biopsy performed 12 months or more after initial treatment.

Statistical Analysis

Statistical analysis was performed using Stata software (version 12.0; StataCorp LP, College Station, TX). Means and standard deviations were reported for continuous variables, and percentages were reported for continuous variables. Efficacy and safety outcomes were reported for patients in different sex and racial groups. Comparative analyses were performed with the Student t test or the Wilcoxon rank sum test for continuous variables, and Pearson χ^2 test or the Fisher exact test for categorical variables. P values less than 0.05 were considered statistically significant. We performed multivariable logistic regression to compare stricture rates and efficacy outcomes between males and females, using predictor variables suggested by the bivariate analysis ($p<0.2$). These models were reduced using the likelihood ratio test to assess for independent associations between sex/race and stricture or CEIM. Due to the small numbers in some ethnic groups, logistical regression could not be performed by race.

Results

A total of 5521 patients with BE were enrolled in the U.S. RFA Patient Registry between July 2007 and July 2011 from 148 institutions. Of these patients, 4052 (73.4%) were males and 5126 (92.8%) were Caucasian. Pre-treatment histology included: 2674 (48.3%) NDBE,

406 (7.4%) IND, 1113 (20.2%) LGD, 1054 (19.1%) HGD, 209 (3.8%) IMC, and 65 (1.2%) EAC (Table 1). The mean length of BE segment was 4.1 ± 3.3 cm with an average of 2.8 ± 1.8 RFA treatment sessions were performed. 1541 (27.9%) patients were treated at an academic center. 320 (20.8%) of patients treated at an academic center had NDBE at baseline compared to 2354 (59.1%) of patients treated at a community practice.

BE characteristics and outcomes by sex

Of the 5521 patients who underwent RFA, 1469 (26.6%) were females. Females were somewhat younger in age (60.0 years vs. 62.1 years, $p<0.001$) and had shorter length of BE than males (3.2 cm vs. 4.4 cm, $p<0.001$) (Table 2). A higher proportion of females with BE were non-Caucasian than males (9.5% vs. 6.3%, $p<0.001$). Additionally, females were markedly less likely to have dysplastic BE than males (36.8% vs. 56.9%, $p<0.001$). In the safety analysis, we found that females were less likely to be hospitalized than males (0.3% vs. 1.0%; $p = 0.013$). Among the 5 female patients who were hospitalized, 1 was admitted with abdominal pain, 2 with chest pain, 1 with mucosal tear, and 1 with heart block. Among the 42 male patients who were hospitalized, 20 (48%) were admitted with upper GI bleeding, 5 (12%) with abdominal pain, 3 (7%) with chest pain, and 14 (33%) for other unknown reasons. There were no statistically significant differences in GI bleeding or perforation rates between females and males in our bivariate analysis. However, females were almost twice as likely as males to develop stricture (OR 1.7; 95% CI, 1.2 – 2.3) in multivariate logistic regression analysis, after adjusting for baseline level of dysplasia (IND or worse), race, length of BE segment, EMR treatment before RFA, pre-treatment fundoplication, treatment at academic center, age, PPI compliance, and the number of total RFA treatment sessions (Table 3).

Of the 5521 patients, 4118 (1067 females and 3051 males) had a biopsy session performed 12 months or more after initial treatment and thus were included in our gender efficacy analysis. The comparisons of BE characteristics between females and males in the efficacy cohort were similar to that in safety cohort. Slightly fewer RFA sessions were required for females to achieve CEIM (2.8 vs. 3.2, $p< 0.001$) (Table 2), although this association dissolved in multivariable regression analysis. In bivariate analysis, females had a higher CEIM rate compared to males (89% vs. 84%, $P<0.001$), however, after controlling for age, length of BE segment, and the number of total RFA treatment sessions, and treatment settings, there were no sex differences in CED or CEIM rates in multivariable logistic regression analysis (Table 3).

BE characteristics and outcomes by race/ethnic group

Among the 5521 patients who underwent RFA for treatment of BE, 5126 were Caucasians, 82 were African American, 40 were Asian/Pacific Islander and 137 were of Hispanic ethnicity. 136 patients were of unknown race/ethnicity and thus were excluded from the safety analysis. There were marked baseline differences between the groups in sex distribution, age, BE length, and severity of pretreatment histology (Table 4). Although Caucasians demonstrated the expected strong predilection toward male sex (74%), there was a near even distribution between the sexes in African Americans (male sex, 50%) and Asians (male sex, 53%) ($p < 0.001$). Caucasians had longer pre-treatment BE length

compared to all the other racial groups (4.1 cm Caucasians, 3.8 cm Hispanics, 3.1 cm African Americans, 2.2 cm Asians; $p < 0.001$) and were markedly more likely to have baseline dysplasia compared to other races (52% Caucasians, 36% Hispanics, 33% African Americans, 35% Asians; $p < 0.001$). Hispanics and African Americans were diagnosed and treated for BE at a younger mean age (Hispanics 58.2 years, African Americans 58.6 years, Caucasians 61.7 years, Asians 63.6 years; $p < 0.001$). There were no significant difference in the rates of GI bleeding, perforation, or hospitalization among different racial groups, but Asians had a significantly higher stricture rate compared to Caucasians (10.0% vs. 4.1%; $p = 0.02$) (Table 4). Among females, stricture rate is 4.8% (26 out of 541) among patients with dysplastic BE, and 4.8% (45 out of 928) among patients with non-dysplastic BE. Among males, stricture rate is 5.6% (130 out of 2306) among patients with dysplastic BE, and 1.8% (32 out of 1746) among patients with non-dysplastic BE. Among the 43 Caucasians who were hospitalized, 17 (40%) were admitted with upper GI bleeding, 5 (12%) were with chest pain. Among the 2 Hispanics who were hospitalized, one was admitted with abdominal pain, and the other was admitted with upper GI bleeding.

Of the 5521 patients, 4004 patients (3825 Caucasians, 93 Hispanics, 54 African Americans, and 32 Asians) had a biopsy session performed 12 months or more after initial treatment and were included in the racial efficacy analysis. An additional 114 patients had a biopsy session performed 12 months or more after initial treatment but were with unreported race/ethnicity, and therefore they were excluded. The comparisons of BE characteristics among different racial groups in the efficacy cohort were similar to that in safety cohort. There were no significant differences in the rate of CEIM or number of RFA sessions to achieve CEIM in bivariate or multivariable analysis (Table 4).

Discussion

In the largest reported cohort of patients treated with RFA for BE, there were marked differences in BE disease patterns noted between different sex and race/ethnicity groups. In this registry, females and non-Caucasians had shorter length of BE and less aggressive baseline histology compared to males and Caucasians, respectively. Additionally, there was a complete lack of male sex predilection for BE in African Americans and Asians. In multivariate logistic regression analysis, strictures were almost twice as frequent among females as males. CEIM and CED efficacy outcomes were comparable across sex and race.

Previous studies have reported the male-to-female sex ratio of Barrett's esophagus to be approximately 2 to 4:1; however, this ratio is very likely to be driven by the sex ratio of the dominant Caucasian group in these studies (10, 17–19). In the present study, male-to-female ratio was assessed by race. The male-to-female sex ratio among Caucasians was approximately 3:1, which is consistent with previous findings (10, 17, 18). Khoury et al. examined BE dysplasia prevalence among various ethnic groups (25). Although they found that most patients were male in all racial groups, there was a higher percent of females in the African American and other category (females: 31% non-Hispanic whites, 44% African Americans, 50% other). Similarly, our study found that sex ratios were more evenly distributed among African Americans and Asians (male-to-female ratio, 1:1). The reason for the different sex ratios in the races is not known. Perhaps the differential effects of obesity,

differences in diet, cultural differences in healthcare utilization by sex, or referral bias by physicians may play a role in detection and severity of BE. Similarly, the reason for the increased stricture rate among females, African-Americans and Asians is unclear. Whether this represents differences in the healing process by sex/race, differences in the depth of injury or other factors is unclear.

The impact of gender on CEIM remains unclear. In this registry, there were no sex differences in CED or CEIM rates in multivariable analysis. Haidry et al. and Gupta et al. have also shown no gender effect on CEIM rates. In contrast, however, a study by Qumseya et al. found that females take a longer time to achieve CEIM and have a 55% decreased rate in CEIM compared to males (22, 26, 27). This study was limited in that it was a single-center, retrospective study with small numbers of females.

Few studies have examined differences in race/ethnicity among patients with BE. Fan and Snyder investigated race, age and sex differences between patients with and without gastroesophageal reflux disease (GERD) symptoms (28). Among 5019 patients who underwent endoscopy, 77 patients had confirmed histologic BE. There was no statistically significant association between prevalence of BE and racial/ethnic group (categorized as Caucasian, Hispanic, African American, and “other”), after adjusting for GERD symptoms. Using the Clinical Outcomes Research Initiative database, Wang et al. evaluated ethnic trends in patients with complicated reflux disease and suspected BE (29). The authors found increased esophageal strictures in white-non-Hispanic patients. However, this study was limited in that patients were included with “suspected” BE based on endoscopy findings, not histologically proven BE. Additionally, racial groups were based on provider assignment instead of patient designation, which increases susceptibility to bias. Khoury et al. found that among 115 patients with histologically confirmed BE, although non-statistically significant, non-Hispanic whites had increased dysplasia (7% non-Hispanic whites vs. 0% African Americans and Others; $p = 0.763$) (25). These studies are limited by small overall patient sizes and therefore few people in each ethnic group.

Importantly, our study focuses specifically on subjects enrolled in the United States. RFA registry undergoing RFA for BE, not a general and universal BE population. Our observations should not be generalized to all patients with BE, or even all patients who have undergone ablative therapy. Although our results are internally consistent, and represent differences between races and sexes in patients being referred for RFA at this large group of centers, the differences we see may be due to a number of factors. The differences in disease characteristics and outcomes may represent true biological differences between the groups. Alternatively, they may represent differences introduced by referral bias. For instance, if the finding of BE in a Hispanic patient or an African-American patient elicits more concern in a practitioner due to its relatively rare nature, that might in turn induce a referral for ablation. This bias might cause the proportion of subjects in these minority groups who have non-dysplastic BE in our study to be higher. Because we have no data on subjects with BE who were seen at these centers but not referred for RFA, we cannot address the relative effects of biology versus referral bias on these data. Because our data represent a broad cross-section of RFA performed in private practices and academic centers, their real value is in their utility to inform similar patients as to their likely outcomes. In terms of generalizability to

the BE population, it is notable that many of the previously reported findings for Caucasian populations with respect to male predominance of dysplasia, as well as BE length differences are replicated in our study (30, 31). Even if any un-measurable bias is operative with respect to the subjects enrolled in the study, the safety and efficacy treatment data should accurately reflect the outcomes in this patient cohort by sex and race.

There are several strengths to our study. Our study assesses the sex and race differences in safety and efficacy outcomes of patients treated with RFA for BE, and our cohort was large enough to provide adequate numbers of patients for analysis in multiple race/ethnicity categories. Our study offers prognostic information to patients who are not in the white male category, the demographic forming the majority of previous studies. In addition, as our study is a nationwide multicenter registry study that includes both academic-affiliated and community-based institutions from 148 institutions, our results are more representative of real-life practices than tertiary care center reports. This improves the external validity of our results and increases the generalizability. Furthermore, study definitions were *a priori*, and data were collected in a standardized fashion.

Our study has several limitations that must be considered. Because we used the nationwide RFA registry for our analysis, our study was strictly observational and we could not mandate care paradigms. Patients with NDBE who were treated with RFA were included in this registry, although some experts do not recommend treating these patients with RFA (32). Additionally, as there were a broad range of providers in this registry, it is conceivable that perhaps there were mistakes in disease definitions, such as patients with irregular Z lines were mis-diagnosed with Barrett's esophagus. However, we do not believe that these potential errors would preferentially occur in one racial group or gender. Given the size and nature of our study, and in line with other registry studies, there was no central lab for re-interpretation of pathological specimens, thus, as in all studies such as this, interobserver variation in the interpretation of biopsy specimens likely introduces error into our study (26, 33, 34). As this was a registry study with study outcomes defined *a priori*, we were often unable to collect specific details for each individual subject such as the reason for hospitalization or whether patients were symptomatic from strictures, etc.

Our research has several important implications for clnical practice. First, perhaps the utility of gender as a risk factor for the presence of BE may be lower in minority populations than in Caucasians given the lack of gender difference for BE in African Americans and Asians,. Second, given that females and Asians had increased stricture rates, we should be cautious about over-treatment in this patient population, and re-consideration of dosimetry in these patients may be necessary. This is especially true given the reduced length of BE and generally lower degree of dysplasia we found in women compared with men. Third, should females and Asians present with dysphagia symptoms after RFA, this population is more likely to reveal a stricture that may be amenable to endoscopic intervention, compared to Caucasian populations.

In conclusion, in this large U.S. registry of RFA treatment for BE, marked differences in disease patterns were noted between different races or sex. Most notable, a lack of the usual male sex predilection for BE in African-Americans and Asians was noted. Strictures were

more frequent after RFA among females and Asians. Importantly, efficacy outcomes did not differ by gender or race.

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Acronyms

BE	barrett's esophagus
RFA	radiofrequency ablation
NDBE	non-dysplastic barrett's esophagus
IND	indefinite for dysplasia
LGD	low-grade dysplasia
HGD	high-grade dysplasia
IMC	intramucosal carcinoma
EAC	invasive adenocarcinoma
CEIM	complete eradication of intestinal metaplasia
CED	complete eradication of dysplasia
GERD	gastroesophageal reflux disease

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Table 1

Baseline Characteristics of all patients enrolled in the U.S. RFA Registry

	All Patients Treated with RFA for BE (n= 5521)
Age (mean ± SD, years)	61.6 ± 11.4
Race/Ethnicity, n (%)	
Caucasian	5126 (92.8)
African-American	82 (1.5)
Hispanic	137 (2.5)
Asian/Pacific Islander	40 (0.7)
Unreported	136 (2.5)
Male gender, n (%)	4052 (73.4)
Length of BE segment (mean ± SD, cm)	4.1 ± 3.3
Pre-treatment fundoplication, n (%)	295 (5.3)
Pre-treatment histology, n (%)	
Nondysplastic	2674 (48.3)
Indefinite dysplasia	406 (7.4)
Low-grade dysplasia	1113 (20.2)
High-grade dysplasia	1054 (19.1)
Intramucosal carcinoma	209 (3.8)
Invasive adenocarcinoma	65 (1.2)
Taking twice daily PPI, n (%)	4359 (79.0)
Total RFA treatments, (mean± SD)	2.8 ± 1.8
Circumferential treatments	0.7 ± 1.0
Focal treatments	2.1 ± 1.5
Total biopsies performed, (mean± SD)	2.8 ± 2.1
EMR treatment before RFA, n (%)	495 (9.0)
Treatment at an academic medical center, n (%)	1541 (27.9)
Total number of physicians, n	247

Table 2

Baseline characteristics and safety and efficacy outcomes by sex

	Females	Males	P-value
Safety cohort			
Baseline Characteristics			
N	1469	4052	
Age (mean ± SD, years)	60.0 ± 11.4	62.1 ± 11.4	<0.001
Race/Ethnicity, n (%)			
Caucasian	1330 (90.5)	3796 (93.7)	<0.001
Black	41 (2.8)	41 (1.0)	
Hispanic	44 (3.0)	93 (2.3)	
Asian/Pacific Islander	19 (1.3)	21 (0.5)	
Unreported	35 (2.4)	101 (2.5)	
Length of BE (mean ± SD, cm)	3.2 ± 2.8	4.4 ± 3.4	<0.001
Dysplastic at baseline (IND or worse), n (%)	541 (36.8)	2306 (56.9)	<0.001
Outcomes, n (%)			
Stricture	71 (4.8)	162 (4.0)	0.17
GI bleed	3 (0.2)	25 (0.6)	0.06
Perforation	0	2 (0.05)	0.39
Hospitalization	5 (0.3)	42 (1.0)	0.013
Efficacy cohort			
Baseline Characteristics			
N	1067	3051	
Age (mean ± SD, years)	60.5 ± 11.4	62.3 ± 11.0	<0.001
Race/Ethnicity, n (%)			
Caucasian	962 (90.2)	2863 (93.8)	<0.001
Black	28 (2.6)	26 (0.9)	
Hispanic	32 (3.0)	61 (2.0)	
Asian/Pacific Islander	16 (1.5)	16 (0.5)	
Unreported	29 (2.7)	85 (2.8)	
Length of BE (mean ± SD, cm)	3.2 ± 2.8	4.5 ± 3.4	<0.001
Dysplastic at baseline (IND or worse), n (%)	413 (39)	1811 (59)	<0.001
Outcomes			
CE-D, n/N (%)	386/413 (93)	1695/1811 (94)	0.99
CE-IM, %	954 (89)	2569 (84)	<0.001
Total RFA treatment sessions, (mean ± SD)	2.8 ± 1.9	3.2 ± 1.9	<0.001

Table 3

Multivariate analysis for sex differences in safety and efficacy outcome

Odds ratio (95%CI)	Base model	Reduced model
Safety outcome (stricture rate)		
Female	1.67 (1.24 – 2.26)	1.36 (1.21 – 2.20)
Non-Caucasian	1.55 (0.99 – 2.42)	1.58 (1.02 – 2.47)
BE length, per cm	1.10 (1.06 – 1.15)	1.10 (1.07 – 1.15)
Pre-treatment dysplasia	1.39 (1.00 – 1.92)	1.54 (1.14 – 2.09)
Number of total RFA sessions	1.13 (1.06 – 1.19)	1.12 (1.06 – 1.19)
EMR treatment before RFA	1.51 (1.02 – 2.25)	1.64 (1.112.43)
Pre-treatment fundoplication	0.74 (0.39 – 1.42)	--
Treatment at academic center	1.20 (0.89 – 1.62)	--
Age, per year	1.01 (0.99 – 1.02)	--
PPI compliant	0.58 (0.30—1.13)	--
Efficacy outcome (CEIM rate)		
Female	1.21 (0.96 – 1.52)	1.24 (0.99 – 1.55)
Age, per year	0.98 (0.97 – 0.99)	0.98 (0.97 – 0.99)
BE length, per cm	0.85 (0.83 – 0.88)	0.85 (0.83 – 0.87)
Treatment at academic center	1.29 (1.04 – 1.59)	1.26 (1.03 – 1.54)
Number of total RFA sessions	0.92 (0.88 – 0.96)	0.92 (0.88 – 0.96)
Pre-treatment dysplasia	0.85 (0.69 – 1.05)	--
Non-Caucasian	0.91 (0.64 – 1.29)	--
Pre-treatment fundoplication	0.96 (0.66 – 1.41)	--
EMR treatment before RFA	0.87 (0.65 – 1.18)	--
PPI compliant	1.56 (0.97–2.48)	--

Base model: adjusting for all the variables listed in the table.

Reduced model: only adjusting for variables with an odds ratio provided.

Table 4

Baseline characteristics and safety and efficacy outcomes by race/ethnicity

	Caucasian	Hispanic	African American	Asian	p-value
Safety cohort					
Baseline characteristics					
N					
Male, n (%)	5126	137	82	40	
Age (mean ± SD, years)	3796 (74)	93 (68)	41 (50)	21 (53)	<0.001
Length of BE (mean ± SD, cm)	61.7 ± 11.4	58.2 ± 11.7	58.6 ± 12.9	63.6 ± 9.8	<0.001
Dysplastic at baseline (IND or worse), n (%)	4.1 ± 3.3	3.8 ± 3.3	3.1 ± 3.3	2.2 ± 1.8	<0.001
	2675 (52)	49 (36)	27 (33)	14 (35)	<0.001
Outcomes, n (%)					
Stricture	209 (4.1)	8 (5.8)	6 (7.3)	4 (10.0)	0.09
GI bleed	23 (0.4)	1 (0.7)	0	1 (2.5)	0.24
Perforation	2 (0.04)	0	0	0	0.99
Hospitalization	43 (0.8)	2 (1.5)	0	0	0.64
Efficacy cohort					
Baseline characteristics					
N	3825	93	54	32	
Male, n (%)	2863 (75)	61 (66)	26 (48)	16 (50)	<0.001
Age (mean ± SD, years)	61.9 ± 11.1	58.2 ± 12.0	59.7 ± 12.0	64.3 ± 10.1	0.003
Length of BE (mean ± SD, cm)	4.2 ± 3.3	4.0 ± 3.6	3.1 ± 3.0	2.2 ± 1.7	<0.001
Dysplastic at baseline, n (%)	2084 (54)	38 (41)	17 (31)	13 (41)	<0.001
Outcomes					
CEIM, n (%)	3274 (86)	80(86)	51 (94)	28 (88)	0.32
CED, n/N (%)	1946/2084 (93)	36/38 (95)	17/17 (100)	13/13 (100)	0.92
Total RFA treatment sessions, (mean ± SD)	3.1 ± 1.9	2.8 ± 1.5	3.0 ± 1.9	2.8 ± 1.3	0.51