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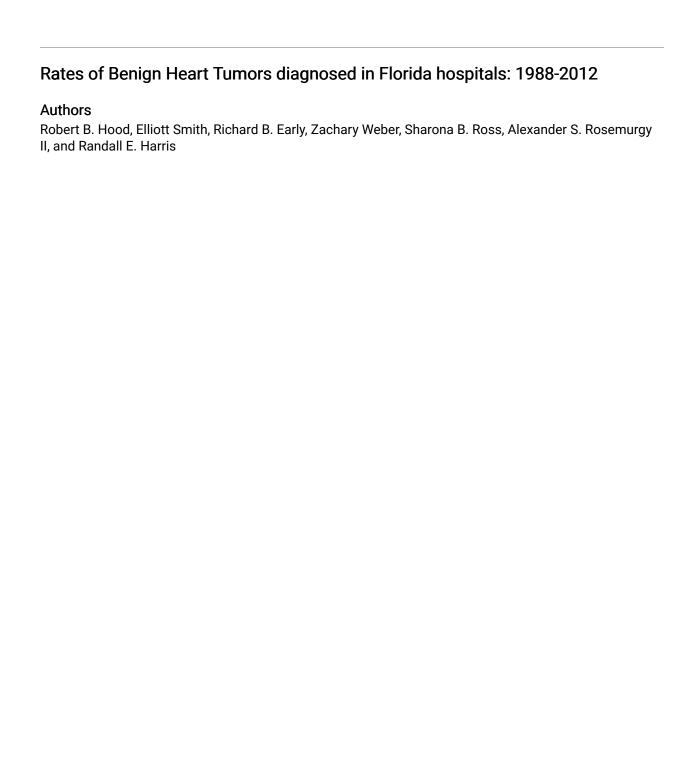
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RATES OF BENIGN HEART TUMORS DIAGNOSED IN FLORIDA HOSPITALS: 1988-2012

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INTRODUCTION

Heart tumors are rare primary tumors with benign heart tumors (BHTs) accounting for a majority of these tumors. BHTs have several subtypes and differ by age. Pediatric cases tend to be either rhabdomyomas or fibromas. In adults, the most common BHT is left atrial myxoma.

Symptoms of these tumors are dependent on the size and location of tumor.^{2,3} In approximately a third of cases, the tumor has non-specific cardiac symptoms include dyspnea, syncope and arrhythmias.^{1,5} Furthermore, BHTs have the potential to mimic other cardiac conditions by causing embolisms leading to cerebrovascular events or heart failure depending on tumor size and location. 1,2,5 The mimicry of these tumors and non-specific symptoms can cause diagnosis to be difficult. Once these tumors are diagnosed, treatment is straightforward. Most often the tumor is resected in adults, unless surgery is contraindicated by underlying health conditions.^{2,3} In pediatric cases, resection of the tumor is possible but it may not be necessary because rhabdomyomas tend to decrease in size over time.4 Even with all this clinical information, data on the incidence of BHTs is limited. Knowledge of the incidence of BHTs is necessary to understand a potential source of cardiac disease that may be underdiagnosed. Currently available estimates stem from autopsy or surgery studies or from a single hospital or registry. ⁶⁻¹⁰ Each of these presents a limited picture of the incidence. To alleviate this issue, we describe the incidence as well as demographic and clinical characteristics of all patients diagnosed with BHT's from 1988 to 2012 in Florida.

METHODS

Florida's Center for Health Information and Transparency (FCHIT) provided these data for the analysis. Briefly, FCHIT is a branch of Florida's Agency for Healthcare Administration that collects discharge data from all Floridian hospitals. We utilized discharge data for inpatient records collected from 1988 to 2012. In total, we reviewed over 55 million discharge records for inpatient hospitalization. We reviewed each record's principal ICD-9 diagnosis code. We looked for ICD-9 code 212.7 to indicate if a patient was diagnosed with a BHT. To be consistent with the literature, we used 212.7 as our main diagnostic code rather than searching for tumor specific codes since they were unavailable in these data. From these data, demographic and clinical data were obtained. Using only Florida residents, we estimated the yearly incidence of these BHTs. We used age adjustment to account for population differences using the 2000 United States Census population counts. We standardized to the 2000 Census to be consistent with the literature and to have a constant standard population. All other descriptive statistics of the cases include a mix of Floridian and non-Floridian residents.

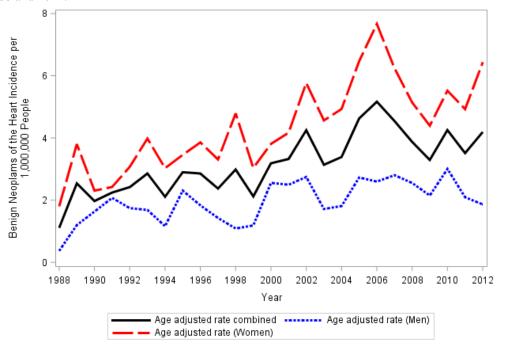
Basic demographic characteristics included: age at diagnosis, sex, and race. We collapsed race into three categories, white, black, and other minority races. Clinical characteristic included: admitting diagnosis (patients after 2005 only), admission type, length of stay, and status at discharge. We categorized admitting diagnosis based on the major organ systems of the body and using the ICD-9 broad diagnosis categories. We created five categories for status at

discharge including died in hospital, home or homecare, short and intermediate inpatient care, long-term inpatient care, and other. Other included other institutions such as hospice and psychiatric care etc. We performed all statistical analyses in SAS version 9.4 (SAS Institute, Cary N.C.).

RESULTS

Overall, 1656 BHTs were diagnosed in Florida from 1988 to 2012. The incidence of these tumors increased (Figure 1

Figure 1. Age-adjusted incidence rates of Benign Heart Tumors among hospital discharge data from Florida between 1988 and 2012.^a



^a Incidence rates are age-adjusted to the 2000 U.S. Census.

The average yearly age-adjusted incidence of these tumors among Florida residents was 3.17 per one million (standard deviation (SD): 0.97). Women had twice as many of these tumors than men (Table 1). The average age-adjusted yearly incidence was 1.95 per one million in men (SD: 0.66) while women had an average age-adjusted yearly incidence of 4.35 per one million people (SD: 1.45). Our sample was predominately white (84.8%) and female (69.2%). While the median age of onset was 63 years (Range: 0 - 96). Age of onset does appear to be bimodal with

a peak occurring in children less than 10 years old and in adults in their sixties and seventies. Patients generally had a brief length of stay (<10 days) with 46.9% of patients being discharged to home or selfcare. Approximately 2.5% of patients diagnosed with a BHT died in hospital. Of the patients whose admitting diagnosis were reported, a majority (55.9%) of them were admitted for either a benign or malignant tumor with another 16.6% were admitted for a disease of the circulatory system (Data not shown).

Table 1. Basic demographic and clinical characteristics of patients with a primary diagnosis of Benign Heart Tumors in Florida hospitals from 1988 to 2012.

	Characteristic	n	%
Sex	Female	1146	69.2%
	Male	510	30.8%
Age (in years)	<10	53	3.2%
	10-19	21	1.3%
	20-29	31	1.9%
	30-39	90	5.4%
	40-49	197	11.9%
	50-59	284	17.1%
	60-69	433	26.1%
	70-79	382	23.1%
	80+	165	10.0%
Race ^a	White	1279	85.2%
	Black	159	10.6%
	Other	64	4.3%
	Missing	154	
Ethnicity	Hispanic	158	10.6%
	Non-Hispanic	1338	89.4%
	Missing	160	
Resident status ^b	Florida	1572	95.8%
	Other	69	4.2%
	Missing	15	
Admission type ^c	Emergency	438	26.4%
	Urgent	497	30.0%
	Elective	711	42.9%
	Newborn/Other	10	0.6%
Discharge status ^d	Died	41	2.5%
	Home or Homecare	1282	77.4%
	Short & Intermediate Inpatient	158	9.5%
	Long-term care	124	7.5%
	Other	51	3.1%
Length of stay (in days)		Median	Range
		7	0 - 201

^a Other category of race includes Asian, American Indian or Alaskan Native, and anyone reporting their race as other.

DISCUSSION & CONCLUSION

In our study, the incidence of BHTs increased over time and women consistently had higher incidences of these tumors than men. The apparent rise in incidence may be attributed to better

diagnostic tools as well as the increased awareness of these tumors. However, it is unclear if the rise in incidence is due to etiological factors or simply better diagnostic tools. Our incidence of BHTs differs from

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^b Other resident status includes anyone who stated their home state was not Florida.

^c Other admission type are those admission not covered by the other four categories.

^d Other status at discharge would include institutions not covered by the other four categories, including Hospice, psychiatric institutions, and Medicare institutions.

previously reported incidences of these tumors. Cresti et al (2016) found incidence around 1.38 per 100,000 people while Sigurjonsson et al (2011) found an incidence of 0.11 per 100,000 people.^{6,9} Both of these studies examined different rates in different populations, specifically primary benign and malignant tumors in a European community from 1998 to 2010 and only cardiac myxomas in Europe, respectively. ^{6,9} Additionally, the timing of the Cresti et al, (2016) does not match our study as we include a longer time period.^{6,9} It is possible that during these additional years these tumors were underdiagnosed.. The timing of between Sigurjonsson et al, (2011) and our study does match more closely but the standard population for age-adjusted are vastly different (world standard population versus the U.S. population). However, these differences likely do not account for the entire disparity between the incidence rates. Another U.S. based study provides a closer estimate of 0.63 per million but this study only evaluate primary malignant tumors. Primary malignant tumors only account for a small percentage of tumors so our estimated incidence is closer to what we would expect based on malignant tumor data. Even so this does account for the apparent disparity in cardiac tumors between U.S. and European populations.

Based on our analysis these tumors are ill defined. While a majority were patients admitting diagnoses were benign or malignant tumors, we believe this may represent an error in large number of cases. BHTs are not apparent unless the patient has previously undergone a diagnostic procedure and the tumor had previously been discovered. Based on this it is possible that the admitting diagnosis was not defined, and the healthcare provider simply imputed the final diagnosis. However, over one sixth of the patients were admitted for a cardiac condition and almost a quarter were admitted for an ill-defined symptom.

The apparent 2 to 1 ratio of BHTs in women to men is interesting but not usual and is consistent with previous findings.³ It is currently unclear why a sex difference exists for BHTs. The primary population affected by BHTs in our study were over the age of 40, white and non-Hispanic. Additionally, while a quarter of patients with BHTs were emergency admissions and less than one third were urgent admissions, most patients survived with limited hospital stays.

While we have discharge records from inpatient hospitalizations, these do not describe the entire clinical picture. We do not have pathological reports which would confirm these diagnoses. However, these tumors are extremely rare, and it is unlikely that

they would misdiagnosed or miscoded. Future studies should include pathological reports to describe the incidence of BHTs by type. Another potential bias is the recurrence of these tumors. Recurrence has been reported in less than 5% of patients.² With this recurrence rate it is unlikely that it would have a meaningful impact on the incidence of these tumors. Furthermore, both limitations would cause the incidence to appear higher than it is which would widen the disparity between our report and the European reports if these cases were identified. Additionally, we are confident in our results as they are similar in magnitude to reported malignant heart tumors in the US. Another potential limitation is the possibility of multiple visits per patient. However, because once these tumors are found they are readily removed it is unlikely that individuals would have more than one visit. Furthermore, if patients had more than one visit this would bolster our estimated incidence and removal of these cases would further separate our results from studies in Europe. Therefore, it is unlikely that there were multiple repeated visits for each patient.

Benign heart tumors are rare tumors that can mimic cardiac conditions and can lead to disability and death. We described the increasing incidence of these tumors utilizing hospital discharge records which may reflect increased awareness and better diagnostic tools. The incidence described here is similar in magnitude to other US reports but differs from European reports. We believe this is due to inherent differences in study design and diagnostic procedures. Regardless, even with the incidence of these tumors in question, the tumor etiology is unknown and requires case-control studies to examine etiological factors.

AUTHOR CONTRIBUTIONS

RBH contributed to the design of the study, analysis, data interpretation, and writing the manuscript. ES contributed to the design of the study, data interpretation, and revising the manuscript. RBE, SBR, and ASR contributed to the design of the study, data collection, and revising the manuscript. ZW contributed to the analysis, data interpretation, and revising the manuscript. REH contributed to the design of the study, data interpretation, and revising the manuscript. All authors approved the final manuscript and agreed to be accountable for all aspects of the work.

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