



Incidence patterns for myoepithelial carcinoma: a Surveillance, Epidemiology, and End Results (SEER) study

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Background: Myoepithelial carcinoma is a rare malignancy, and has been described only in case reports or small case series. Its patterns of incidence are largely unknown due to the rarity of the condition, thus hampering the effective development of its diagnosis and management. In addition, demographics and risk factors that affect myoepithelial carcinoma incidence reported from previous series conflict with each other. Here we aim to analyze a relatively extensive, population-based cancer registry to study the association between the incidence and patient age, gender, race, tumor location, and other factors to investigate incidence changes over the past decade.

Methods: Data were retrieved from the Surveillance, Epidemiology, and End Results (SEER) database from 1973 to 2012. Histological codes were used to determine myoepithelial carcinoma cases. Age-adjusted incidence-rates were compared by confidence intervals (CIs) in the SEER*Stat Version 8.2.1 program, while Joinpoint regression analysis was used to determine annual percentage changes and to locate substantial changes in incidence, respectively.

Results: Three hundred sixty-eight patients were identified from the SEER database. The observed incidence rate per 100,000 person-years was found to be significantly higher ($P < 0.05$) in oral cavity/pharynx compared other sites, but did not differ with respect to gender and race of patients (males 0.013 ± 0.002 , females 0.013 ± 0.002 ; white 0.011 ± 0.001 , black 0.020 ± 0.005 , or American Indian/AK Native/Asian/Pacific Islander 0.020 ± 0.005). There was a significant difference in the primary location of the disease between adult and pediatric patients and between female and male patients (both $P < 0.05$): children were more likely to harbor myoepithelial carcinoma in the soft tissues (including heart), whereas adults were more likely to develop the malignancy in the head and neck areas. Females were significantly more likely to develop myoepithelial carcinoma in the breast (26.8% *vs.* 0, Chi-square value =46.52, $P < 0.001$), whereas in males it more commonly presented in the skin, (7.4% *vs.* 0.6%, Chi-square value =10.83, $P = 0.001$) and oral cavity/pharynx (68.2% *vs.* 57.0%, Chi-square value =4.363, $P = 0.037$). Between 2000 and 2012, the incidence increased significantly among male patients, which was 0.009 in 2000 and 0.058 in 2012, with an annual percentage change of 10.8 ($P < 0.05$). However no increase was seen for females, with 0.007 in 2000 and 0.025 in 2012. After age adjustment, there were no rapid changes at any single year.

Conclusions: Both genders and different races have an equal overall incidence of myoepithelial carcinoma. Oral cavity/pharynx was the most common site. Children versus adult and female versus male comparisons display different site presentations. The incidence in males seems to have increased over the past decade; however, such phenomenon was not observed in females.

Keywords: Myoepithelial carcinoma; incidence; epidemiology

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Introduction

Myoepithelial carcinomas are rare malignant tumors arising from myoepithelial cells. It was first described in the salivary glands, and accounts for approximately 1% of all salivary gland tumors (1-5); however, it can also occur in the breast, upper aerodigestive tract, skin, and soft tissue (6-11). Due to its rarity, myoepithelial carcinoma is not well reported and understood, and is usually reported along with myoepithelioma, its more commonly diagnosed benign counterpart. To our knowledge, the largest series for myoepithelial carcinoma published in the English literature included only 40 cases (12), and most literature on myoepithelial carcinoma are individual case reports or small case series (13). There have been no reports with sufficient sample sizes that could enable the analysis of demographics and clinical risk factors which influence its incidence and pattern of occurrence. The lack of such knowledge certainly hampers the understanding of the disease as well as the development of proper diagnostic and treatment techniques. In the present study, therefore, we aimed to determine how age, gender, ethnicity, and the primary tumor location influence the incidence, by analyzing an extensive, population-based sample of both adult and pediatric myoepithelial carcinoma.

Methods

The SEER database was used to select all myoepithelial carcinoma cases from 18 regional cancer registries in the U.S. from 1973 through 2012. All cases of myoepithelial carcinoma diagnosis (ICD-O-3 histology codes 8982) were selected from the registry, and the primary tumor locations were determined by site codes ICD-O-3/WHO 2008.

Age-adjusted incidence rates were determined using the SEER*Stat 8.2.1 program. Differences in the incidence rates between the 2 genders, 3 races, and various tumor locations with the highest frequency (tumor location distinguished by site codes ICD-O-3/WHO 2008) were then compared using a 95% confidence interval (CI). A chi-square test was used to investigate the associations between

age, gender, and tumor location by SPSS Version 21.

The age-adjusted rates of disease incidence were determined and analyzed using 95% CIs for a combined incidence rate, which was an estimate for the entire population over the past decade, while Joinpoint analyses were performed using the Joinpoint Regression Program (Version 4.2.0.2, NCI, NIH, USA) to ascertain the annual percentage changes and substantial changes in incidence, respectively.

Results

Three hundred sixty-eight cases were identified from the SEER database by our search criteria. Patients' characteristics are detailed in *Tables 1* and *2*. 45.1% of the patients were male and 54.9% of the patients were female; 75% of patients were white and the rest were of other ethnic backgrounds. The median and the mean ages at diagnosis of all patients were 72 and 52.2 years, respectively. Three hundred fifty three (95.9%) patients were adults (>19 years) and 15 (4.1%) were children/adolescents (≤ 18).

Across all age groups, the oral cavity/pharynx were the most common sites of occurrence, followed by breast, soft tissue (including heart), respiratory system, and skin. Age-adjusted incidences (per 100,000 person-years) based on gender, ethnicity, five tumor locations with the highest frequency distinguished by site codes ICD-O-3/WHO 2008 are detailed in *Table 3*. The incidence was significantly higher ($P < 0.001$) in oral cavity/pharynx as compared to the other four sites, but did not differ significantly with respect to gender or ethnicity ($P = 0.302$ and $P = 0.119$, respectively).

Subsets of 15 children/adolescents and 327 adult myoepithelial carcinoma were classified by site code into oral cavity/pharynx, respiratory system, soft tissue (including heart), breast, and skin in *Table 4*. Chi-square analysis that compared age versus disease site showed a statistically significant difference in primary location between adult and pediatric/adolescent patients ($P < 0.0001$). Children/adolescents were significantly more likely to develop myoepithelial carcinoma in the soft tissues, including heart, whereas adult more commonly had oral cavity/pharynx.

Table 1 Locations of diagnosis of myoepithelial carcinoma (SEER data base between 1973–2012)

Location of occurrence	No. (%)
All sites	368 (100.0)
Oral cavity/pharynx*	203 (55.0)
Tongue	6 (1.6)
Salivary gland	163 (44.3)
Floor of mouth	2 (0.5)
Gum and other mouth	24 (6.5)
Nasopharynx	1 (0.3)
Tonsil	4 (1.1)
Oropharynx	2 (0.5)
Hypopharynx	1 (0.3)
Eye and orbit	1 (0.3)
Respiratory system*	23 (6.3)
Nose, nasal cavity and middle ear	17 (4.6)
Lung and bronchus	5 (1.4)
Trachea, mediastinum and other respiratory organs	1 (0.3)
Digestive system	2 (0.5)
Esophagus	1 (0.3)
Colon and rectum	1 (0.3)
Colon excluding rectum	1 (0.3)
Cecum	1 (0.3)
Breast*	60 (16.3)
Soft tissue including heart*	52 (14.1)
Skin excluding basal and squamous*	14 (3.8)
Other non-epithelial skin	14 (3.8)
Bones and joints	4 (1.1)
Female genital system	2 (0.5)
Vagina	1 (0.3)
Other female genital organs	1 (0.3)
Urinary system	1 (0.3)
Urinary bladder	1 (0.3)
Miscellaneous	6 (1.6)

*, 342 patients with myoepithelial carcinoma diagnosed in the 5 most commonly diagnosed locations were included in further analyses of this study.

Table 2 Characteristics of 368 patients with myoepithelial carcinoma from SEER data base between 1973–2012 other than sites

Characteristic	No. (%)
Total	368 (100.0)
Gender	
M	166 (45.1)
F	202 (54.9)
Age (years)	
≤18	15 (4.1)
>19	353 (95.9)
Race	
White	276 (75.0)
African American	54 (14.7)
American Indian/AK Native, Asian/Pacific islander	36 (20.9)
Unknown	2 (0.5)

Table 3 Age-adjusted incidence of myoepithelial carcinoma by gender, race and site (SEER data base between 1973–2012)

Factor	Incidence ± SE*	95% CI	P value**
Gender			0.302
Male	0.013±0.002	0.010–0.017	
Female	0.013±0.002	0.010–0.017	
Race			0.119
White	0.011±0.001	0.011–0.016	
African American	0.020±0.005	0.009–0.014	
American Indian/AK Native, Asian/Pacific islander	0.020±0.005	0.012–0.032	
Site			
Oral cavity and pharynx	0.0079±0.0009	0.0062–0.0099	0.000
Respiratory system	0.0006±0.0003	0.0002–0.0013	
Soft tissue (including heart)	0.0018±0.0004	0.0010–0.0028	
Skin excluding basal and squamous	0.0007±0.0003	0.0003–0.0015	
Breast	0.0015±0.0004	0.0008–0.0025	

*, rates are per 100,000 and age-adjusted to the 2000 US Standard Population (19 age groups—Census P25-1130) standard; **, Chi square is used to calculate P value.

Table 4 Comparison of the difference in locations of diagnosis between adults and children in 342 children and adults*

Age group (years)	Site	No.	%	Chi-square value	P
Age recode ≤18	Oral cavity and pharynx	2	13.3	27.017	0.000
	Respiratory system	1	6.7		
	Soft tissue (including heart)	10	66.7		
	Breast	0	0		
	Skin excluding basal and squamous	2	13.3		
Age recode >19	Oral cavity and pharynx	203	62.1		
	Respiratory system	21	6.4		
	Soft tissue (including heart)	43	13.1		
	Breast	48	14.7		
	Skin excluding basal and squamous	12	3.7		
Total	Total	342			

*, data on cases from 1973–2012. Only the most common sites of diagnosis were included. Chi-square test were used to search for an association between child/adult status and tumor location by SPSS Version 21. Chi-square analysis comparing age with tumor site demonstrated a significant difference in location between adults and children ($P<0.05$). Children were significantly more likely to harbor myoepithelial carcinoma at the Soft tissue (including heart) (13.3% vs. 62.1%, Chi-square value =14.19, $P=0.000$), whereas adult more commonly had oral cavity/pharynx (66.7% vs. 13.1%, Chi-square value =31.37, $P=0.000$).

As expected, females were significantly more likely to develop myoepithelial carcinoma in the breast (26.8% vs. 0, Chi-square value =46.52, $P<0.001$), whereas males more commonly presented in the skin, (7.4% vs. 0.6%, Chi-square value =10.83, $P=0.001$), oral cavity/pharynx (68.2% vs. 57.0%, Chi-square value =4.363, $P=0.037$) (Table 5).

Table 6 and Figure 1 demonstrate the correlations between the age range and the site of diagnosis. The age range of 60–69 has the highest frequency for myoepithelial carcinoma in the oral cavity/pharynx and skin; 70–79 has the highest frequency in breast; and 50–59 has the highest frequency in the respiratory system. The median ages of diagnosis of incidence of skin, oral cavity and pharynx, respiratory system, breast, and soft tissue/heart myoepithelial carcinoma were 55, 65, 55, 75, and 35, respectively.

Joinpoint analysis of the entire cohort of patients showed no significant changes in any single year (Figure 2), although we observed a trend of increasing in incidence in both genders. In female patients, the incidence per 100,000 person-years in 2000 and 2012 were 0.007 and 0.025, respectively, and there were no observed percentage changes of statistical significance in annual incidence. However, Joinpoint analysis of male patients showed significant changes in age-adjusted incidence over time. The incidence

per 100,000 person-years in 2000 and 2012 were 0.009 vs. 0.058, with an APC (annual percentage change) of 10.8 ($P<0.05$) in males.

Discussion

Myoepithelial carcinoma is a rare neoplasm composed entirely of myoepithelial cells that exhibit a dual epithelial and smooth muscle phenotype (14). Originally described by Stromeyer *et al.* in 1975 (15), and further expounded upon by Dardick, these initial reports were crucial in extending the understanding of myoepithelial tumors (8,16). Myoepithelial carcinoma was eventually added to the World Health Organization (WHO) classifications of malignant salivary gland tumors in 1991 (17).

Myoepithelial cells are typically located between the epithelial cells and the basal lamina of acini and ducts of salivary glands, sweat glands, and breasts. Thus myoepithelial neoplasms are more commonly arise in parotid gland (48–75%), followed by minor salivary glands (reported sites include the palate, cheek, gum, nasal cavity, maxillary sinus, nasopharynx, infratemporal fossa, oral cavity, base of tongue, supraglottic larynx), and the submandibular gland. It comprises approximately 1% of all salivary gland carcinomas (11). Occasionally,

Table 5 Comparison of the difference in location between male and female in 327 adult patients*

Sex	Site	No.	%	Chi-square value	P
Male	Oral cavity and pharynx	101	68.2	54.903	0.000
	Respiratory system	12	8.1		
	Soft tissue including heart	24	16.2		
	Skin excluding basal and squamous	11	7.4		
	Breast	0	0.0		
Female	Oral cavity and pharynx	102	57.0		
	Respiratory system	9	5.0		
	Soft tissue including heart	19	10.6		
	Skin excluding basal and squamous	1	0.6		
	Breast	48	26.8		
Total	Total	327			

*, data on cases from 1973–2012. Only the most common sites of diagnosis were included. Chi-square tests were used to search for an association between sex status and tumor location by SPSS Version 21. Result: Chi-square analysis comparing age with tumor site demonstrated a significant difference in location between male and female ($P < 0.05$). Female were significantly more likely to harbor myoepithelial carcinoma at Breast (26.8% vs. 0%, Chi-square value =46.52, $P = 0.000$), whereas male more commonly at skin excluding basal and squamous (7.4% vs. 0.6%, Chi-square value =10.83, $P = 0.001$) and oral cavity and pharynx (68.2% vs. 57.0%, Chi-square value =4.363, $P = 0.037$).

Table 6 Comparison of the difference in location between age groups

Age (years)	Oral cavity and pharynx		Respiratory system		Soft tissue including heart		Skin excluding basal and squamous		Breast		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
1–9	0	0	0	0	2	100	0	0	0	0	2	100
10–19	2	16.7	1	8.3	8	66.7	1	8.3	0	0	12	100
20–29	6	37.5	1	6.3	8	50.0	1	6.3	0	0	16	100
30–39	11	47.8	1	4.3	9	39.1	2	8.7	0	0	23	100
40–49	29	61.7	6	12.8	4	8.5	2	4.3	6	12.8	47	100
50–59	35	58.3	8	13.3	7	11.7	2	3.3	8	13.3	60	100
60–69	51	78.5	3	4.6	4	6.2	3	4.6	4	6.2	65	100
70–79	44	60.3	1	1.4	4	5.5	2	2.7	22	30.1	73	100
80+	27	61.4	2	4.5	7	15.9	0	0	8	18.2	44	100
Total	205		23		53		13		48		342	

Result: analysis of chi-square test using SPSS Version 21 showed Pearson chi-square =112.901, $P = 0.000$. Chi-square analysis comparing age groups with tumor site demonstrated a significant difference in location ($P < 0.05$).

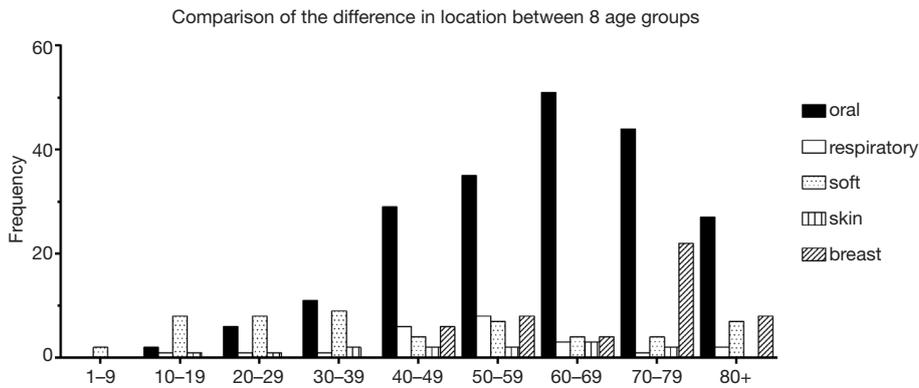


Figure 1 Age range of 60–69 has the highest frequency for myoepithelial carcinoma in oral cavity and pharynx, skin excluding basal and squamous. Age range of 70–79 has the highest frequency for myoepithelial carcinoma in breast. Age range of 50–59 has the highest frequency for myoepithelial carcinoma in respiratory system.

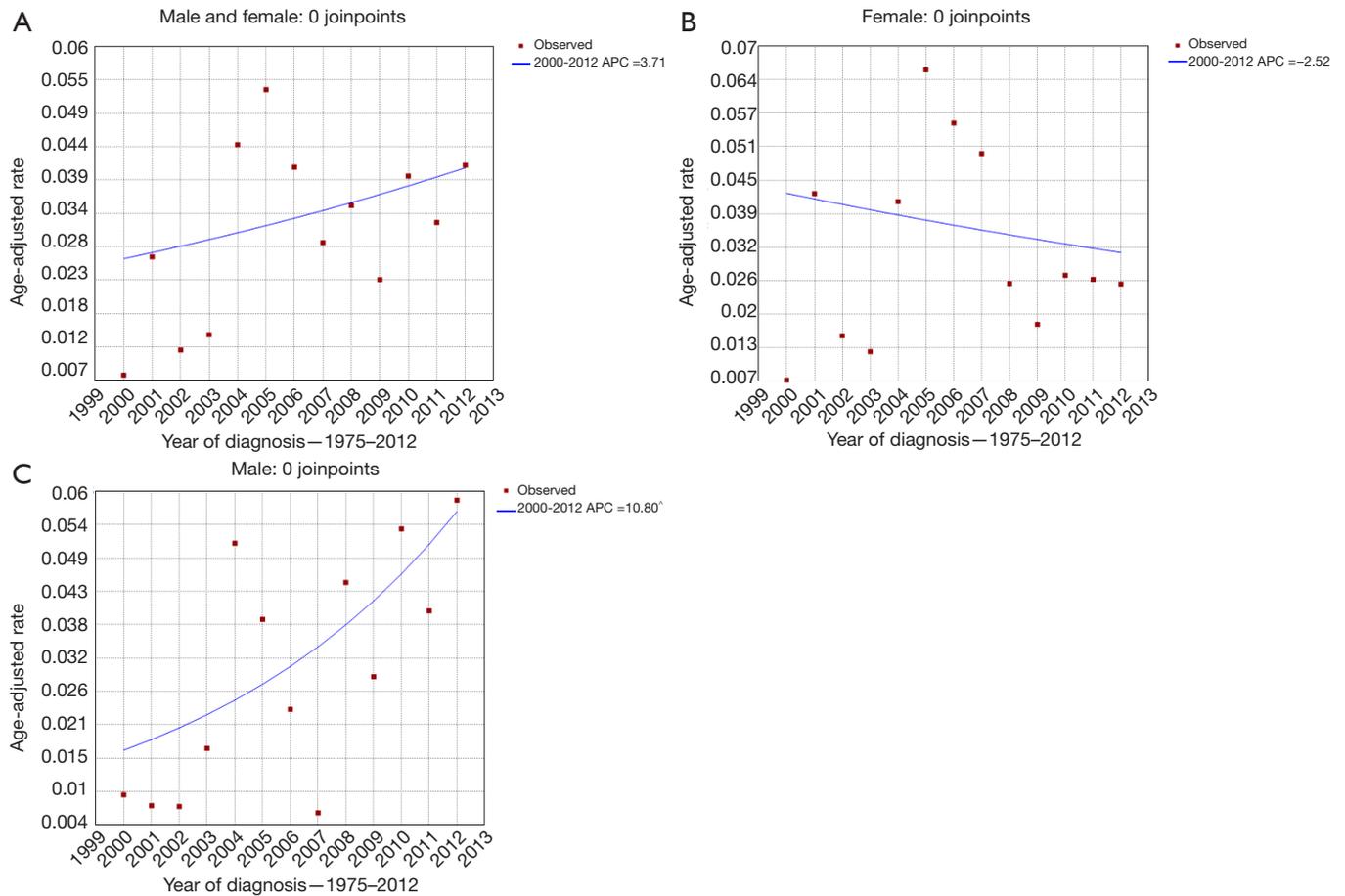


Figure 2 Scatterplots showing age-adjusted incidence trends from 2000 to 2012. There are no significant changes in incidence over time and no sharp changes at any single year among all patients (A) or female(C), but the incidence rises significantly among male (B). APC, annual percentage change.

cases have been reported in the sublingual gland (18-29). Myoepithelial carcinomas diagnosed in other parts of the body are exceedingly rare.

Due to the rarity of myoepithelial carcinoma, its growth patterns, biological behavior, survival data and prognostic factors are largely unknown. The lack of knowledge on the incidence and biological properties of the condition certainly hamper further investigation for the more optimal management of the disease. Therefore, we conducted this study with an aim to describe the basic clinical patterns of the disease occurrence including the most common pathogenic locations, age, differences between adult versus children and male versus female using the SEER.

In our study, 368 patients were collected from the SEER database in 22 different sites over 40 years (*Table 1*). This is the largest population-based myoepithelial carcinoma distribution study with largest numbers of tumor sites, validating and improving the information described in previous small series or case reports of myoepithelial carcinoma. Across all age groups, oral cavity/pharynx were the most common locations of origin, followed by breast, soft tissue (including heart), respiratory system, and skin where myoepithelial cells are typically located.

Results from previously published series suggested that median age of diagnosis of myoepithelial carcinoma was 60 years (30,31). We had found, similarly, that the median age at diagnosis of all patients was 72 in our series, and the mean age was 52. The age range of 60–69 had the highest frequency for myoepithelial carcinoma in oral cavity and pharynx.

Myoepithelial carcinoma is commonly reported with its benign counterpart, myoepithelioma, in pediatric series; however, it is usually not well represented in most publications. Several authors concluded that they are more aggressive in the pediatric population than in adult patients as half of the cases developed distant metastasis and 43% succumbed from disease progression (8). Because of this apparent difference in biology, patients were stratified by age at the time of their initial diagnosis into children/adolescents (≤ 18 years) and adults (>19 years) in our study. Only 15 children/adolescents were identified in the database between 1973–2012. Further, we found that adults, particularly males, more commonly had oral cavity/pharynx, which may be induced by more frequent consumption of tobacco and alcohol in adults compared to children, whereas children were more likely to harbor disease arising in soft tissues (including heart), which was highly consistent with the previous reports for myoepithelial carcinoma in

children (32,33).

Different single-institution series of myoepithelial carcinoma have showed variability in sex distribution, from equal sex distribution (1:1) to female predominance (4:1) (18,20,22). Our results indicated that the incidence did not differ significantly with respect to sex. Approximately 45% of the patients were male, and 55% were female. The fact that female patients were more likely to harbor myoepithelial carcinoma in the breast as compared to male is not difficult to understand. On the other hand, why the condition occurred more commonly in the skin and oral cavity/pharynx in male patients is perplexing. We speculate that the more frequent use of tobacco and alcohol in males than in females could be the cause of such difference. However, the interesting finding, that the incidence of myoepithelial carcinoma remained stable for females, but demonstrated a trend of increase in male in our series was also puzzling, as the use of tobacco in males has been on a decreasing trend in the U.S. in the past several decades. The underlying mechanism for the increasing trend of myoepithelial carcinoma in males remains unknown. Among all the ethnic groups in the U.S., the predominant race was White as compared to other races including African American, American Indian/Alaskan Native, and Asian as expected because of the overall racial compositions of U.S., no difference in incidence were demonstrated by race of the patients.

The SEER data is inherently limited due to the voluntary nature of data collection, and represents only 28% of the U.S. cancer patient population. The two previous reports on pediatric myoepithelial carcinoma had 36 patients combined (32,33). And the fact that only 15 patients in our SEER analysis were younger than 19 clearly illustrated the incompleteness of the data on pediatric patients. Nevertheless, the majority of the patients in the two reports on pediatric myoepithelial carcinoma had soft tissue myoepithelial carcinoma. Such findings were highly consistent with our results.

Ideally, the analysis of a rare event, such as myoepithelial carcinoma, should be analyzed from a more complete dataset that is gathered over an effective period of time and is further subjected to variability from different suppliers of data. However, changes in the diagnostic criteria in the past few decades can also result in the under-reporting of myoepithelial carcinoma cases in the SEER registry. The diagnostic process is typically done locally and information including immunohistochemistry or electron microscopic confirmation of the diagnosis is not always available. Even

with complete information, definite pathological criteria of myoepithelial carcinoma are not always well delineated. Although we tried to analyze the data collected between 1973–2012, the missing details, especially those in the earlier years, make it difficult to accurately analyze the trend of the disease over a longer period of time. As a result, we could only get the trend of incidence patterns over the last decade. Despite all of the aforementioned limitations, this series is the largest study to analyze the incidence patterns of patients with myoepithelial carcinoma and may prove useful in providing insight and directing future investigations on patient outcomes.

Conclusions

This SEER analysis is the largest observational study that examines the associations of age at diagnosis, gender, ethnicity, and primary tumor location and correlates with the incidence of myoepithelial carcinoma. The incidence was higher in oral cavity/pharynx than other sites, but did not differ in overall incidence with respect to gender or ethnicity. The median age of diagnosis was 70 years. In addition, our study demonstrated that the overall incidence of myoepithelial carcinoma seems to have increased over the last decade. Such an observation is largely driven by the male patient population. Understanding these incidence patterns with respect to the location of the disease and age may facilitate in the advancement our understanding of the biology of myoepithelial carcinoma and its management.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/tcr.2017.04.15>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This article does not contain any studies with human participants performed by any of the authors.

Institutional ethical approval and informed consent were waived.

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