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Invasive Cervical Cancer and Screening: What are the Rates of Unscreened and Underscreened Women in the Modern Era?

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Abstract

Objective—It has been reported that approximately 50% of invasive cervical malignancies are diagnosed in patients that have never been screened and 10% of the remaining cervical cancer patients have not had a Pap smear in the five years prior to diagnosis. We sought to determine if this holds true amongst a university based gynecologic oncology patient population.

Methods—Following IRB approval, a retrospective chart review of women in a university based gynecologic oncology group with cervical cancer from 2002-2007 was conducted. Patient demographics, referral Pap smear, method of diagnosis, histology, clinical stage, treatment, and time since last Pap smear were collected. Descriptive statistics were used during data analysis.

Results—419 women with cervical cancer were identified. 67% of patients were Caucasian, 18% Hispanic and 6% African-American. The most common referral Pap smear to our institution was HSIL (21%). Diagnosis was primarily made by cervical punch biopsy (47%). The most common histologic type was squamous cell carcinoma (70%). Clinical stage I disease was diagnosed in 80% of patients., Stage II cervical cancer 9%, and Stage III and IV were uncommon. The most common therapy was radical hysterectomy with lymph node dissection performed in 250 patients (60%). The length of time from last reported Pap smear to diagnosis of invasive cervical cancer ranged from 1-65 years with a median of 3 years. Stage IA1 patients ranged from 1- 12 years from last reported Pap with a median of 1 year (SD = 3.38); while Stage III/IV patients ranged from 1-20 years since last screening, with a median of 4 years (SD = 6.39). Regarding length of time since last reported Pap smear, 235 patients (56%) were unable to report the length of time since their last Pap smear. Of those who reported their last Pap smear, 4 patients (1%) reported never having a Pap smear, 39 patients (9%) reported last Pap smear greater than 10 years ago, and 10 patients (2%) reported a Pap smear greater than 20 years ago. 85 patients (20%) reported a Pap smear within 2 years. Of these 85 patients, 71 patients (84%) were diagnosed at Stage I, while more advanced stages were uncommon.

Conclusions—Traditionally, patients diagnosed with an invasive cervical malignancy are either unscreened or underscreened with cervical cytology. Our patient population was noncompliant with screening measures. A fraction of our patients were compliant with screening within the last 2 years, yet still developed a cervical malignancy – albeit early stage disease. As such, our data

suggests that compliance continues to be an issue. However, even with adherence to screening guidelines, cervical cancer continues to develop.

Keywords

cervical cancer; screening; compliance

Introduction

The Pap smear, developed by George Papanicolaou in the 1920s, is one of the most effective cancer screening tests used to detect premalignant cervical disease. The widespread use of cytologic screening derives from its ease, cost-effectiveness, and ability to identify premalignant disease.

A 1996 NIH cervical cancer consensus reported that 50% of invasive cervical malignancies are diagnosed in patients that have never been screened and 10% of the remaining cervical cancer patients have not had a Pap smear in the five years prior to diagnosis [1]. In fact, past studies have shown the greater time between Pap smears the greater the risk of developing invasive cervical cancer. Shy et al in 1989 reported a 12 fold greater risk of invasive cervical cancer in patients screened at 10 year intervals versus annually [2], while Andrae et al in 2008 reported 2.5 times greater odds of developing cancer in patients without routine screening [3]. Overall, it has been demonstrated by Sawaya et al that a disproportionate burden of cancer occurs in patients lacking screening for more than 3 years [4].

In the last ten years, there has been a renewed focus on cervical cancer screening. Reasons include the description of the natural history of cervical cancer and dysplasia as stemming from the oncogenic human papilloma virus (HPV), the development and application of HPV testing, to routine screening and finally the introduction of HPV vaccination. However, despite these advances, over 10000 cases of invasive cervical cancer are reported yearly [5]. As such, in this study, we seek to evaluate if invasive cervical cancer is associated with non-adherence to cervical screening guidelines in patients referred to university based gynecologic oncology clinic.

Methods

Following Institutional Review Board (IRB) approval, a computerized database identified patients diagnosed with invasive cervical cancer referred to or treated by the Division of Gynecologic Oncology at the University of Alabama at Birmingham (UAB) from 2002-2007. All patients diagnosed with an invasive cervical malignancy were included.

A retrospective chart review was conducted to collect patient demographics, referral Pap smear, method of diagnosis, histology, clinical stage, treatment, and time since last Pap smear. Method of diagnosis included biopsy, excisional procedure, or incidental discovery. Data was analyzed and reported using descriptive statistics.

Results

Through retrospective chart review 419 women with cervical cancer were identified. The majority of patients were Caucasian and the average age was 43 years (Table 1). Referral Pap smears encompassed a wide range of cytology results. The most common referral Pap smear to our institution for patients with cervical cancer was high-grade squamous intraepithelial lesion (HSIL) in 87/419 patients (21%). The second most common referral Pap smear was atypical glandular cells (AGC-NOS) in 46 (11%). Atypical squamous cells of undetermined significance (ASCUS) and low-grade squamous intraepithelial lesion (LSIL) combined were identified in 23 patients, composing 5% of all Pap smears referred to our institution (Table 1). Method of diagnosis (Table 1) was primarily by cervical punch biopsy in 197 cases (47%). Other common methods of diagnosis included cold-knife conization in 105 patients (25%), LOOP procedure in 63 cases (15%), and incidental diagnosis via hysterectomy for nonmalignant reasons such as menorrhagia or leiomyomata in 43 patients (10%).

In our patient population, the most common histologic type was squamous cell carcinoma observed in 293 of 419 cases of invasive cervical carcinoma (70%). 97 of our patients (23%) presented with adenocarcinoma of the cervix; while the remainder 7% (29 patients) including neuroendocrine and clear cell, were categorized as other (Table 2). The majority of patients were diagnosed with early stage disease. Stage I disease was diagnosed in 334 (80%), Stage II in 38 (9%), Stage III in 21 (5%) and Stage IV disease in 6 (1%).

A variety of treatment modalities were employed in the treatment of our patient population including cold-knife conization, simple hysterectomy, radical hysterectomy with or without lymph node dissection, and chemoradiation therapy when appropriate (Table 3). The most common therapy was radical hysterectomy with lymph node dissection performed in 250 patients (60%). Chemoradiation therapy was primarily used in 98 patients (23%). All other modalities were used in less than 10% of our patient population.

The length of time from last reported Pap smear to diagnosis of invasive cervical cancer ranged from 1-65 years with a median of 3 years (Table 4). Patients with microinvasive Stage IA1 disease reported the time since last Pap smear from 1-12 years with a median of 1 year (SD 3.38), while patients with Stage IA2-IB2 disease had Pap smears reported from 1-37 years ago with a median of 3 year in the past (SD 6.33). Patients with Stage II disease reported time since last Pap smear of 1-65 years with a median of 1 year (SD 17.1). Finally, patients in our referral population presenting with advanced disease – Stage III and IV – reported receiving their last Pap smears from 1-20 years in the past with a median of 4 years ago (SD 6.39).

Regarding length of time since last reported Pap smear (Table 5), 235 patients (56%) were unable to report the length of time since their last Pap smear. Of those who reported their last Pap smear, 4 patients (1%) reported never having a Pap smear, 64 patients (15%) reported their last Pap smear greater than 5 years, 39 patients (9%) reported their last Pap smear greater than 10 years ago, and 10 patients (2%) reported a Pap smear greater than 20

years ago. 71 patients (17%) reported a Pap smear within the year and 85 patients (20%) reported a Pap smear within 2 years.

Of these 85 patients reporting a Pap smear within 2 years, the majority was diagnosed at an earlier stage (Table 6). 71 patients (84%) were diagnosed at Stage I, while 8 patients (9%) with Stage II disease. A total of 5 patients (6%) were diagnosed with advanced Stage III and Stage IV disease.

Discussion

Cervical cancer is a major cause of gynecologic morbidity and mortality worldwide with more than 80% of new cases arising in developing countries [6]. In developed nations, mortality from invasive cervical cancer has dramatically decreased primarily due to the introduction of cervical cytology screening. In the United States in 2009, there were an estimated 11270 newly diagnosed cases of invasive cervical cancer and 4070 estimated mortalities [7]. The ability to screen and detect early premalignant changes facilitates early treatment and ultimately prevention of progression to invasive cancer.

It follows that patients diagnosed with invasive cervical cancer are traditionally either unscreened or underscreened in accordance with cervical cytology guidelines. In fact, a 1996 NIH consensus statement reported that 50% of invasive cervical malignancies are diagnosed in patients that have never been screened and 10% of the remaining cervical cancer patients have not had a Pap smear in the five years prior to diagnosis [1].

Shy et al in 1989 in their study of 92 patients reported an increased risk of squamous cell cervical cancer with increased time between Pap smears. Patients with Pap smears at 3-year intervals had 3.9 times the risk and patients with Pap smears at 10-year intervals had 12.3 times the risk of annually screened patients [2].

Similar results were suggested by Andrae et al in 2008. In their study of 1230 patients with invasive cervical cancer between 1999-2001 in the Swedish Cancer Registry, they reported an increased odd of 2.52 for invasive cervical cancer in patients not undergoing appropriate screening as compared to individuals with adherence to recommended guidelines [3]. These results were further supported by Sawaya et al, who detailed a disproportionate burden of invasive cervical cancer patients lacking screening for more than 3 years [4].

Our patient cohort supports these previous studies. Compliance with current screening guidelines continues to be an issue in our studied population at the University of Alabama. Not only were the majority of our patients unable to recall their screening history, but those with reported cervical screening reported a median of 3 years since their last Pap smear. Despite relative non-adherence, the majority of our patients were diagnosed with early stage disease – as those diagnosed with IAI cervical cancer had a reported Pap smear within the last year. Meanwhile patients with advanced disease had a greater time since last Pap smear at 4 years.

However, in our proportion of patients who were compliant with current screening guidelines, invasive cervical cancer was still noted. 20% of our patients reported a Pap

smear within the last 2 years, yet still were diagnosed with invasive disease. Yet, these patients were overwhelmingly diagnosed with Stage I disease.

As such, our patient population suggests that compliance with screening guidelines continues to be an issue. However, even despite adherence to screening guidelines, cervical cancer continues to develop. But, those compliant tend to be diagnosed with earlier stage disease. Given the continued presence of cervical cancer, further focus and initiatives should be targeted on continued education, compliance with screening guidelines, and future vaccination.

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Table 1
Patient Demographics, Referral Pap smear and method of diagnosis

Race	
Caucasian	67%
African-American	6%
Hispanic	18%
Other	9%
Average age	43 years (Range 17-80)
Referral Pap Smear	
ASCUS	2%
LSIL	3%
HSIL	21%
ASC-H	4%
AGUS	11%
Unknown	59%
Method of diagnosis	
Punch Biopsy	47%
LOOP	15%
CKC	25%
Incidental	10%
Unknown	3%

Table 2**Histology and stage of cancer**

Histology	
SCC	70%
Adenocarcinoma	23%
Other	7%
Stage	
I	80%
II	9%
III	5%
IV	1%
Unknown	5%

Table 3
Treatment of cancer in our patient population

CKC	1%
Simple hysterectomy	5%
Radical hysterectomy	2%
Radical hysterectomy ± LND	60%
Radiation therapy	23%
Other (parametrectomy, trachelectomy)	9%

Table 4
Time period (yrs) since last reported Pap smear

Overall years since last pap	1-65 (Median 3)	
Stage IA1	1-12 (1)	Standard Deviation 3.38
Stage IA2-IB2	1-37 (3)	6.33
Stage II	1-65 (1)	17.1
Stage III and Stage IV	1-20 (4)	6.39

Table 5
Reported interval since last Pap smear

Not identifiable	56%
Never	1%
Greater than or equal to 5 years	15%
Greater than 10 years	9%
Greater than 20 years	2%
Within 2 years	20%
Within 1 year	17%

Table 6
Cervical Cancer Stage for Patients with reported Pap smears within 2 years

Stage I	84%
Stage II	9%
Stage III	2%
Stage IV	4%
Unknown	1%

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