Gynecologic Oncology xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Trends in cervical cancer incidence in younger US women from 2000 to 2013

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HIGHLIGHTS

- Pap testing before age 21 declined in recent years, suggesting guideline adoption.
- ICC incidence rates among 21–25 year olds in the US are very low.
- ICC incidence in young women has not increased even in recent birth cohorts.
- The delay in screening age hasn't resulted in population-level ICC rate increases.

ARTICLE INFO

Article history:
Received 9 September 2016
Received in revised form 16 November 2016
Accepted 20 November 2016
Available online xxxx

Keywords:
Cervical cancer
Screening
Pap test
SEER
Epidemiology

ABSTRACT

Objective. This study aimed to assess the temporal trends in invasive cervical cancer (ICC) incidence rates among 21–25 year-olds. US guidelines no longer recommend screening prior to age 21, and concerns have been raised that delayed screening initiation may increase ICC incidence among young women.

Methods. This study utilized ICC incidence data from 18 US population-based cancer registries in SEER from 2000 to 2013 and Pap test prevalence data from the Behavioral Risk Factor Surveillance System from 1996 to 2012. Trends were evaluated with annual percent changes (APCs) using Joinpoint regression.

Results. The prevalence of never having a Pap test before age 21 increased from 22.0% in 1996–2004 to 38.3% in 2006–2012 (APC = +5.48, 95%CI = +4.20, +7.50). Despite this decline in screening, ICC incidence among 21–23 year olds significantly declined between 2000 and 13 (APC = −5.36, 95%CI = −7.83,−2.82), particularly from 2006 to 2013 (APC = −9.70, 95%CI = −15.79, −3.17). ICC incidence remained constant among 24–25 year olds (APC = +0.45, 95%CI = −2.00, 2.97). Compared to women born in 1978–1985, women born in 1986–1991 had a higher prevalence of never receiving a Pap test prior to 21 (35.4% vs. 22.1%, $p < 0.001$), but a lower ICC incidence at 21–23 (0.98 vs. 1.55 per 100,000, $p < 0.001$).

Conclusion. While US females born in 1986–1991 were less likely to receive a Pap test before age 21, diagnoses of ICC in the early 20s were rare and lower than for those born in earlier years. This provides reassurance that the updated guidelines to delay screening until 21 has not resulted in a population-level increase in ICC rates among young women.

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1. Introduction

US cervical cancer screening guidelines have increasingly recommended against Pap testing among women younger than 21 years old. Prior to 2002, the guidelines were to begin screening at age 18 or with the onset of sexual intercourse [1]. In 2002–2003, the American Cancer Society, American Congress of Obstetricians and Gynecologists (ACOG), and US Preventive Services Task Force (USPSTF) recommended screening initiation at age 21 or three years after the onset of vaginal intercourse. In 2009, ACOG recommended screening at age 21 regardless of sexual history; other organizations had adopted this guideline by 2012 [1–5].

Reflecting these evolving guidelines, the percentage of 18–20 year old women who never had a Pap test has nearly doubled from 2000 to 2010 [6]. Cervical cancer is rarely diagnosed at younger ages, but concern has been raised that not screening and treating pre-cancerous lesions prior to age 21 could result in increased risk of invasive cervical cancer (ICC) among 21–25 year olds [7].

While previous studies report that ICC incidence rates in young women have declined over the past several decades [8], more recent

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http://dx.doi.org/10.1016/j.ygyno.2016.11.031
0090-8258/Published by Elsevier Inc.

trends have not been explored. Given the decline in screening uptake prior to age 21, it is important to examine recent ICC incidence rates in younger women. We utilized US population-based data to assess Pap test prevalence and ICC incidence rates over time among 21–35 year-old women.

2. Methods

2.1. Cancer/Pap testing data

The primary outcome of this study was incident invasive cervical cancer (ICC). ICC incidence data was evaluated during 2000–2013 from 18 population-based cancer registries from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program. SEER represents ~28% of the US population and has reliable and detailed ascertainment of cancer diagnoses [9]. ICCs were defined using ICD-0-3 codes C53.0–C53.9 and restricted to microscopically-confirmed, invasive cases [10]. Stage was categorized using SEER summary stage [11], and histology was defined with the IARC classification using ICD-0-3 histology codes as squamous cell carcinoma, adenocarcinoma or other [12]. The other category includes other specified carcinoma, unspecified carcinoma, sarcoma, other specified malignant neoplasm, and unspecified malignant neoplasms [12].

The Centers for Disease Control and Prevention's Behavioral Risk Factor Surveillance System (BRFSS) was used to estimate the US trends of Pap testing from 1996 to 2012. The BRFSS is a cross-sectional, phone-based survey that provides nationally-representative estimates of risk factors. Every other year from 1996 to 2012, the BRFSS asked >1500 20 and 23 year-old women: "A Pap test is a test for cancer of the cervix. Have you ever had a Pap test?" We utilized survey weights to account for the complex sampling design. From 1996 to 2010 the survey weights were developed through post stratification, while in 2012 the weights were developed through iterative proportional fitting which accounts for the supplemental cell phone use that was added in 2011 [13]. We evaluated the weighted percentage of women aged 20 and aged 23 who reported never having a Pap test (i.e., no pap test prior to age 21 and 24, respectively) [14,15]. States included in SEER were dichotomized as having Pap test uptake prevalence above or below the median at ages 20 and 23 in 2010.

2.2. Statistical analysis

ICC incidence rates per 100,000 woman-years were age-standardized using the 2000 US standard population. ICC incidence was stratified by age group (21–25, 26–30, and 31–35 year-olds), while women aged 21–25 years were further stratified into 21–23 and 24–25 year-olds. Rates were also stratified by cancer stage, histology, and race. Annual percent changes (APCs) in age-standardized ICC incidence and Pap testing prevalence were evaluated over calendar year and year of birth with were estimated with Joinpoint regression [16]. To assess whether trends in ICC rates among 21–23 year-olds were influenced by contemporaneous declines in Pap testing prevalence in this age group, we carried out a sensitivity analysis. We assumed that all ICC cases were diagnosed among women screened with Pap testing and adjusted the rate denominator for each year to represent the estimated screened population (i.e., adjusted denominator = Pap testing prevalence at age 23* general population in SEER areas).

3. Results

3.1. US ICC incidence trends from 2000 to 2013

During 2000–2013, 766 cases of ICC occurred in women aged 21–25 years (IR = 1.87 per 100,000 person-years, 95%CI = 1.74, 2.01 per 100,000 person-years). The majority of cases were squamous cell carcinoma (68.8%) and local stage at diagnosis (68.4%) (Table 1). The age-standardized ICC incidence among 21–25 year old women significantly declined (APC = −1.94%/year, 95%CI = −3.42, −0.44) during 2000–2013; from 2.02 per 100,000 in 2000–2004 to 1.71 per 100,000 in 2009–2013 (Fig. 1). Similarly, ICC incidence significantly declined in 26–30 year-olds (APC = −3.40%/year, 95%CI = −4.55, −2.23) and 31–35 year-olds (APC = −1.75%/year, 95%CI = −2.54, −0.95) during 2000–2013 (Fig. 1).

The decline in ICC incidence among 21–25 year-old women was driven by a steeper decline among 21–23 year-olds (eFigure 1; APC = −5.36%/year, 95%CI = −7.83, −2.82), while remaining constant among 24–25 year-olds (APC = +0.45%/year, 95%CI = −2.00, +2.97). The decline in ICC incidence among 21–23 year-olds primarily occurred in 2006–2013 (APC = −9.70%/year, 95%CI = −15.79, −3.17). The APC was not significant when restricted to 2000–2006 (APC = +0.32%/year, 95%CI = −8.16, +9.57; Joinpoint p-value = 0.09). The trends in ICC incidence were similar by histology, stage, and race in both 21–23 and 24–25 year-olds (Table 1).

3.2. Pap testing trends in the US

The prevalence of never having a Pap test prior to age 21 significantly increased during 1996–2012 (APC = +5.84%/year, 95%CI = +4.25, +7.47; eTable 1 in the Supplement) from 22.0% in 1996–2004 to 38.3% in 2006–2012 ($p < 0.01$). In addition, the prevalence of never having a Pap test prior to age 24 significantly increased between 1996 and 2012 (APC = +4.47%/year, 95%CI = +2.33, +6.65) from 9.6% in 1996–2004 to 13.8% in 2006–2012 (eTable 1 in the Supplement).

3.3. ICC incidence and Pap test trends by birth cohort

Fig. 2 presents ICC incidence rates and prevalence of never having a Pap test within age groups across birth cohorts. Compared to women born in 1978–1985, women born in 1986–1991 were more likely to not receive a Pap test prior to age 21 (35.4% vs. 22.1%; $p < 0.001$), but were less likely to be diagnosed with ICC at ages 21–23 (0.98 vs. 1.55 per 100,000; $p < 0.001$; Fig. 2).

The decline in ICC incidence in 21–23 year-old women was similar in states with lower and higher reported Pap uptake prior to age 21 (Table 1). In a sensitivity analysis, the ICC incidence decline in 21–23 year olds was similar when restricting the denominator of the incidence rate to the estimated screened population with rates declining from 1.66 to 1.13 per 100,000 in 2000–2008 to 2009–2013.

4. Discussion

Similar to other guidelines [1–3,17], the USPSTF suggests that there is moderate certainty that the harms of Pap testing prior to age 21 outweigh the benefits [4]. These recently updated guidelines likely have led to the decline in Pap testing before age 21 in young women born in the late 1980s and early 1990s as observed in this study and others [6,18,19]. This study provides reassurance that population-level increases in ICC incidence have not occurred among young women despite an increasing fraction of women delaying Pap testing until age 21 years or older.

There are several potential explanations for declining ICC rates among 21–23 year-old women. These declines could be due in part to lack of detection of asymptomatic local stage ICCs among the growing unscreened population, as a large fraction of these ICCs are likely detected through Pap testing. However, most women born in the late 1980s and early 1990s were still screened in their early 20s, and our analyses restricting to the estimated population of women who were screened suggested similar trends. Nonetheless, future studies are needed to confirm that the declining cancer incidence is not attributable to reduced screening at ages 21–23 and to confirm that future ICC incidence at older ages (i.e. 26–35) is not subsequently elevated in those born in the late 1980s and early 1990s.

Please cite this article as: D.C. Beachler, et al., Trends in cervical cancer incidence in younger US women from 2000 to 2013, Gynecol Oncol (2016), http://dx.doi.org/10.1016/j.ygyno.2016.11.031