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Cervical excisional treatment of young women: A population-based study☆☆

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HIGHLIGHTS

- Biopsies of <CIN2 with HSIL cytology carried as much risk for CIN3+ on LEEP as did CIN2 with HSIL cytology.
- CIN2 and cytology <HSIL preceded more LEEPs than any other combination in every age group studied.
- The opportunity to reduce excisional harm will be lost if CIN3 and CIN2 are merged into a single histologic category.

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ABSTRACT

Objective. Assessment of cytology and biopsy results preceding cervical excisional treatment and their association with excisional histology, to evaluate compliance with treatment recommendations and the potential effect of revisions in cervical histology terminology and usage.

Method. Data from a unique statewide population-based screening registry was used to describe the use and histologic outcomes of cervical excisional procedures in the year following an abnormal cervical screening cytology.

Results. From 2007 to 2011, LEEP rates decreased 87%, 45%, and 16% for women aged 15–20, 21–24, and 25–29 years, respectively. Reductions were attributable to an overall decline in cervical screening and colposcopy, and a decrease in LEEP following a diagnosis of less than cervical intraepithelial neoplasia grade 2 (<CIN2) or CIN2 histology preceded by any abnormal cytology other than high-grade squamous intraepithelial lesion (<HSIL). LEEP rates did not change significantly ($p > 0.7$) for women aged 30–39 years. Irrespective of age, CIN2 was the most common histologic antecedent of excisional treatment (42%), with most (80%) preceded by <HSIL cytology.

Conclusion. Cervical excisions are an unavoidable consequence of cervical screening. Adherence to treatment guidelines stipulating conservative follow-up of young women with biopsies ≤CIN2 could significantly decrease the number of excisional procedures and associated harms. This opportunity will be lost if cervical intraepithelial neoplasia grade 3 (CIN3) and some or all of CIN2 are merged into a single histologic category, as has been recently recommended in the United States.

Introduction

In March 2012, the United States Preventive Services Task Force (USPSTF), the American Cancer Society (ACS), the American Society for Colposcopy and Clinical Pathology (ASCCP), and the American Society for Clinical Pathology (ASCP) released new guidelines recommending cervical screening at three-year intervals starting at age 21, with the option to substitute cytology plus human papillomavirus (HPV) DNA testing ("cotesting") at five-year intervals starting at the age of 30. The cotesting regimen was preferred for women aged 30 years and above by all groups except the USPSTF [1, 2].

☆☆ **Condensation**: Adherence to treatment guidelines stipulating conservative follow-up of young women with biopsies ≤CIN2 could significantly decrease the number of excisional procedures.

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These recommendations, and the trend towards less screening over a woman's lifetime that has been the focus of guideline changes over the past decade, are driven by the recognition that screening is not without harms and that many if not most of the lesions treated as a consequence of screening would not have progressed to cancer [3, 4]. Sasieni et al. showed that screening women 20–24 years old has no effect on cervical cancer incidence up to age 30 [6]. For women aged 13–25 years in Kaiser Northern California, 68% of cervical intraepithelial neoplasia grade 2 (CIN2) resolves spontaneously within 3 years, supporting the recommendation that observation is preferred over treatment in young women [7, 8].

Concerns have been raised about risks of preterm birth, premature rupture of membranes, low birth-weight, and cesarean section following cervical excisional treatment [9–11]. In addition, the discomfort, anxiety, and negative impact on sexual function that have been associated with excisional treatment are of concern in circumstances where treatment may not contribute to cancer prevention. The risk/benefit calculation for treatment is least favorable in young women, prompting the June, 2009, Practice Improvement in Cervical Screening and Management (PICSM) symposium and, subsequently, the American College of Obstetrics and Gynecology (ACOG) to recommend discontinuing cervical screening in women younger than age 21 [5]. Despite the low risk for cervical precancer (cervical intraepithelial neoplasia grade 3; CIN3) and cervical cancer in young women and the potential harms of excisional procedures, studies involving provider responses to hypothetical clinical scenarios suggest major deviations in cervical screening practice from clinical practice recommendations, with reflex HPV testing done for high-grade cytology, testing for low-risk HPV, and screening annually with all tests regardless of the clinical situation as the most common preference of survey respondents [12–15].

Prior to this assessment, the association of cervical screening and excisional treatment has never been investigated in actual practice in the United States (US), and modeling studies are hampered by the assumption that clinical practice guidelines are followed, which the investigations of screening practices cited above suggest may be significantly inaccurate. It is also recognized that self-selection by respondents to studies of clinical vignettes may not produce a representative sample of care providers, and thereby reflect an imperfect view of provider compliance with guideline recommendations. Using data from a population-based statewide surveillance program, we sought to quantify the utilization of excisional treatment associated with cervical screening by age, to infer the actual indications for excisional treatment from the antecedent cytology and biopsy diagnoses, and to examine the diagnostic yield of CIN3+ associated with different combinations of antecedent test results.

Materials and methods

The New Mexico HPV Pap Registry (NMHPVPR) is located at the University of New Mexico and acts as a designee of the New Mexico Department of Health (NMDOH). The NMHPVPR operates under New Mexico Administrative Code (NMAC) 7.4.3, which specifies the list of Notifiable Diseases and Conditions for the state of New Mexico. In 2006, with the intention of monitoring cervical screening practices and outcomes and the impact of HPV vaccination, NMAC 7.4.3 specified that laboratories must report to the NMHPVPR all cervical or vaginal cytology, cervical pathology, and HPV tests performed on women residing in New Mexico. NMAC 7.4.3 was updated in 2009 to include vulvar and vaginal pathology (http://nmhealth.org/ERD/healthdata/documents/NotifiableDiseasesConditions022912final.pdf). Ongoing evaluations of cervical screening, diagnosis and treatment by the NMHPVPR have been reviewed and approved under exempt status by the University of New Mexico Human Research Review Committee.

In this analysis we used the NMHPVPR database to investigate the use of cervical excisional treatment over the period of 2007 through 2011 in New Mexico among women aged 15–39 years. The majority (80%) of cervical excisional procedures in which the method of excision was described were identified as loop electrosurgical excision procedure (LEEP). When not identified as LEEP, excisional procedures were generally identified only as cone biopsy (without specifying the excisional method), or infrequently as cold knife conization. Therefore, we elected not to attempt to stratify cervical excisional procedures by method of excision. Hysterectomy and the rarely used trachelectomy were not included as excisional treatment for the purposes of this analysis.

We evaluated the use of cervical excisional treatment by considering the likelihood that a woman would undergo excision within 1 year of an abnormal screening cervical cytology test with a result of atypical cells of unknown significance (ASC-US) or worse. We defined a screening cervical cytology test as one without any prior cervical cytology within 10 months (300 days) based on our earlier published findings [16]. We further restricted this analysis to those screening cytology tests without any preceding abnormal cervical cytology or histology within 15 months, and without any prior excisional procedure in the database. If a woman had more than one such cervical cytology test during the period of 2007–2010 we chose the earliest and refer to this as the "index" screening cytology exam. A total of 39,804 abnormal index screening cytology exams were identified, as were 2236 excisional procedures in the year following these index screens.

We calculated the proportion of women undergoing excisional treatment within 1 year of the abnormal index screening cytology within strata defined by the cytologic result of the index screen and the histologic result of the follow-up cervical biopsy or endocervical curettage (ECC). Abnormal cytologic results were classified as ASC-US [negative for high-risk HPV or HPV status unknown], ASC-US+ [positive for high-risk HPV; high risk HPV types are based on Hybrid Capture 2 (Germantown, MD, USA) clinical HPV assay results which detect HPV types, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68], low-grade intraepithelial lesion (LSIL), atypical squamous cells-cannot rule out high-grade (ASC-H), atypical glandular cells (AGC), and high-grade intraepithelial lesion (HSIL) and less than HSIL (<HSIL) which included ASC-US, ASC-US+, LSIL, ASC-H, and AGC. Cytologic results of carcinoma were classified as HSIL. The HPV status of ASC-US results was determined by linking the index cytology with a separate database of HPV tests.

Cervical biopsy results were classified as negative, cervical intraepithelial neoplasia grades 1, 2 and 3 (CIN1, CIN2, CIN3), carcinoma in situ (CIS), adenocarcinoma in situ (AIS), and cancer. The histologic interpretation CIN1–2 is included with CIN2, and CIN2–3 is included with CIN3. This is believed to represent current clinical practice, provides the most charitable view of the indications for excisional treatment, and recognizes the reported irreproducibility of these histologic designations, though it is understood that there is, at present, no published data about subsequent cancer risk to validate these choices.

We also computed population rates of cervical excision for the period 2007–2011. These rates were computed as the number of women treated in a given calendar year per 10,000 women in the population and also per 10,000 women receiving a screening cervical cytology test. New Mexico population counts are US Census estimates (www.census.gov). Using the 2007–2010 Centers for Disease Control bridged-race population files, 42.2% of NM women were non-Hispanic white, 42.2% were Hispanic white, 3.0% were African American, 10.5% were American Indian, and 1.9% were Asian.

Data analysis was conducted using SAS version 9.3. Confidence intervals for population excisional treatment rates are based on normal approximation and all confidence intervals for proportions are exact. Significance testing with the Cochran–Armitage test of linear trend was employed to discern changes over time.

Results

The rate of excisional treatment for cervical abnormalities decreased in New Mexico over the period 2007–2011 for women <30 years of age (Table 1). The decrease was greatest for women aged 15–20 years,