RESEARCH ARTICLE

Incidences of Cervical Intraepithelial Neoplasia 2-3 or Cancer Pathologic Diagnoses in Patients with a High Grade Squamous Intraepithelial Lesion Pap Smear Attending a Colposcopy Clinic at Srinagarind Hospital

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Abstract

The aim of this study was to evaluate the outcomes of women with high-grade squamous intraepithelial lesion (HSIL) smears who had undergone the "see and treat" approach compared to those who underwent a conventional approach. The records of women with HSIL smears undergoing colposcopy at Srinagarind Hospital were reviewed. In those undergoing the conventional approach, the final histological diagnosis was made on the most severe histological results obtained after initial colposcopy. In the "see and treat" group, the final histological diagnosis was made on the examination of LEEP specimens obtained after initial colposcopy. Overtreatment in the see and treat group was defined as the LEEP specimens containing cervical intraepithelial neoplasia (CIN) 1 or less. During the study period, 302 women with HSIL underwent colposcopy. Twenty (6.6%) were nulliparous. One hundred and ninety-four (64.2%) underwent conventional management while the remaining 108 (35.8%) received the see and treat management. The prevalence of underlying high-grade lesions in women undergoing the conventional approach was significantly higher than that observed among women undergoing the see and treat approach (89.2% and 47.2%, respectively, P<0.001). The overtreatment rate in the see and treat group was 52.8%. Multivariate analysis revealed that only parity status was a statistically significant factor for predicting the overtreatment after undergoing the see and treat approach. In conclusion, the overtreatment rate among women undergoing see and treat in this study is notably high and therefore this approach should not be routinely practiced.

Keywords: Cervical lesion - see and treat - overtreatment - cervical cytology

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Introduction

High-grade squamous intraepithelial lesion (HSIL) smear is one of the categories of squamous cell abnormality in the 2001 Bethesda System. HSIL denotes cases who have abnormal squamous cells with an increased nuclear/cytoplasmic ratio, marked atypical nucleus, and irregular nuclear border (Wright et al., 2011). At the present, HSIL is acknowledged as a high-grade cervical smear abnormality. Accordingly, comprehensive management among women with HSIL smears is mandatory.

Generally, conventional approach of abnormal cervical smears has involved multiple steps including colposcopy, biopsy, and discussion of histological findings and treatment options. Therefore, multiple hospital visits are needed, resulting in high treatment cost. To avoid this circumstance, immediate treatment using loop electrosurgical excision procedure (LEEP) without intervening colposcopically-directed biopsy (CDB) at the time of colposcopy, or the so-called "see and treat" approach, is proposed. The "see and treat" approach provides several advantages, including the enablement of obtaining histological diagnosis and treatment in a first visit, resulting in reducing number of hospital visits and treatment time required (Kietpeerakool and Srisomboon, 2010). This approach also provides more accurate histological diagnosis of underlying high-grade disease and decreases in treatment cost and the patient'anxiety (Holschneider et al., 1999; Balasubramani et al., 2007; Kietpeerakool et al., 2009).

Nowadays, the "see and treat" approach has become increasingly common in the Colposcopy Clinic of

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Srinagarind Hospital, Khon Kaen University. The aim of this study was to evaluate the outcomes of women with HSIL smears who had undergone the "see and treat" approach compared to those who had undergone conventional approach.

Materials and Methods

After approval from the Research Ethics Committee, the records of women with HSIL smears undergoing colposcopy at Srinagarind Hospital between January 2007 and December 2010 were reviewed. Abstracted data included patient baseline characteristics, colposcopic findings, histopathology of CDB and LEEP.

Colposcopic examination was performed following the application of 3-5% acetic acid solution on the upper vagina and cervix. The severity of colposcopic findings was graded based on the severity of acetowhite lesions, sharpness of the lesion margins, and vascular patterns within the acetowhite lesions.

In the women undergoing conventional approach, the final histological diagnosis was made on the most severe histological results obtained after initial colposcopy.

In the "see and treat" group, the final histological diagnosis was made on the examination of LEEP specimens obtained after initial colposcopy. Additionally, overtreatment in the see and treat group was defined as the LEEP specimens contained cervical intraepithelial neoplasia (CIN) 1 or less as per the National Health Services of Cervical Screening Programme (NHSCSP) 2010 Guidelines (Luesley and Leeson, 2010).

High-grade lesion was defined as CIN 2-3, adenocarcinoma in situ (AIS) and invasive cancer. Invasive cervical cancer was clinically staged according to the International Federation of Gynecology and Obstetrics (FIGO).

Descriptive statistics were used for demographic data. A logistic regression analysis was used to find the independent factor. An odds ratio with a 95% confidence interval (CI), which did not include unity, was considered statistically significant.

Results

During the study period, the medical records of 302 women with HSIL were reviewed. Mean age was 41.5 years. Twenty women (6.6%) were nulliparous. Thirty-one women (10.3%) were postmenopausal Almost all of the women (98.0%) had abnormal colposcopic findings. One hundred and ninety-four (64.2%) women underwent the conventional management while the remaining 108 (35.8%) underwent the see and treat management.

Mean age of women undergoing the conventional approach and of those who underwent the see and treat approach was 41.9 years and 41.3 years, respectively. The proportion of postmenopausal women in the conventional group and in the see and treat group was comparable (10.8% vs. 9.3%, respectively, P=0.84). Nine (8.3%) of women in the see and treat group were nulliparous which was slightly higher than that observed among women undergoing conventional approach (5.6%, P=0.47).

The final pathological results of 302 women were as follows: CIN 2-3, 195 (64.6%); invasive cancer, 28 (9.3%); AIS, 1(0.3%); CIN 1, 69 (22.8%); and no lesion, 9 (4.6%). Overall, the prevalence of high-grade lesions was 74.2% of women in this study (95%CI, 68.8%-79.0%). The FIGO clinical staging of 28 women who had underlying invasive cervical cancer included stage IA1 (8), stage IA2 (1), stage IB1 (15), and not recorded (4)

Table 1 displays the pathology results of CDB cross-tabulated with the results those obtained from LEEP specimens. Among 34 women who had CIN 1 or less on CDB, 13 were subsequently found to have high-grade lesions on LEEP specimens. Of 144 women having CIN 2-3 on CBD, nine were noted to have invasive cancer on LEEP specimens.

Table 2 shows the comparisons of the final pathology results of women with HSIL stratified by types of management. The prevalence of underlying high-grade lesions in women undergoing the conventional approach was significantly higher than that observed among women undergoing the see and treat approach (89.2% and 47.2%, respectively, P<0.001).

Based on the LEEP histology findings in the see and treat group, the overtreatment rate, which was considered when the LEEP specimen contained CIN 1 or less, was 52.8% (Table 2). Multivariate analysis using a logistic regression model, which included patients' age, menopausal status and parity, was performed. Only parity status was observed to be a statistically significant factor for predicting the overtreatment after undergoing the see and treat approach. Nulliparous women who had undergone the see and treat approach had 9.8 times the risk

Table 1. Pathologies of CDB Cross-tabulated with those Obtained from LEEP in 194 Women Undergoing Conventional Approach

CDB results	LEEP pathology results				
	No lesion	CIN 1	CIN 2-3	AIS	Cancer
No lesion	4	3	3	0	0
CIN 1	1	13	10	0	0
CIN 2-3	6	25	103	1	9
Cancer	0	0	7	0	9
Total	11	41	123	1	18

*CDB, colposcopically-directed biopsy; LEEP, loop electrosurgical excision procedure; CIN, cervical intraepithelial neoplasia; AIS, adenocarcinoma in situ

Table 2. Comparisons of Final Pathology Results According to Management Types

Final Pathology	Management types	
	Conventional approach (N=194)	See and treat approach (N=108)
No lesion	4 (2.1)	5 (4.6)
CIN 1	17 (8.8)	52 (48.1)
CIN 2-3	147 (75.8)	48 (44.4)
AIS	1 (0.5)	0 (0)
Cancer	25 (12.9)	3 (2.8)

*Data are present as number (percentage), CIN: cervical intraepithelial neoplasia; AIS, adenocarcinoma in situ

of receiving overtreatment (95%CI of 1.1-85.7) compared to multiparous women.

Discussion

We found that HSIL cytology is a high-risk indicator for underlying high-grade cervical lesions. It was particularly noteworthy in this study that among women with HSIL smears, there was approximately 9% risk of underlying invasive cervical cancer which was extraordinarily higher than that have been observed in well-screened population. Since the see and treat provides simultaneous diagnosis and treatment of cervical lesion in a timely fashion, this approach seems to be an appealing management option in regions where resources are scarce and poor patient's compliance is anticipated. To date, the 'see and treat' approach was accepted as an alternative management in women with HSIL smears by the American Society for Colposcopy and Cervical Pathology (ASCCP) 2006 consensus guidelines (Wright et al., 2007).

Although there are several advantages of the see and treat approach as mentioned earlier, the significant higher prevalence of underlying high-grade lesions in women undergoing the conventional approach compared to those women undergoing the see and treat approach (89.2% and 47.2%, respectively, P<0.001) raises the concerning of its appropriate in our routine practice. The major disadvantage when applying the see and treat approach in clinical practice is the risk of receiving overtreatment. Nowadays, the current definition of overtreatment recommended by NHSCSP 2010 guidelines which is considered when LEEP specimen contained CIN 1 or less is similar to that stated by the Cochrane Colposcopy and Cervical Pathology Collaborative (Kyrgiou et al., 2006). For maintaining the quality of clinical care, the NHSCSP and the Cochrane Colposcopy and Cervical Pathology Collaborative also stated that the rate of overtreatment should be less that 10% and routine audit of the overtreatment rate when applying the see and treat approach should be carried out periodically (Kyrgiou et al., 2006; Luesley and Leeson, 2010). Based on the 10% threshold for overtreatment rate given by these standard guidelines, the overtreatment rate of approximately 51% in the see and treat approach in this study was therefore unacceptably high.

Rather than the magnitude of overtreatment rate, clinicians should try to discern any patterns or characteristics of patients that might be addressed in order to reduce the risk of encountering overtreatment. Several studies have consistently shown that the risk of overtreatment is associated with the severity of preceding cervical cytology and patterns of colposcopic findings (Charoenkwan et al., 2004; Numnum et al., 2005; Errington et al., 2006; Kietpeerakool et al., 2007). The overtreatment rate appears to be lowest when the see and treat approach is solely carried out in women with high-grade lesion on either cervical cytology or coloposcopy (Aue-Aungkul et al., 2011).

We were able to note that parity status has a significant impact on the risk of receiving overtreatment among women in the see and treat group. Nulliparous women who had undergone the see and treat approach had 9.8 times the risk of receiving overtreatment (95%CI of 1.1-85.7) compared to multiparous women (adjusted by age and menopausal status). This finding is in line with that reported previously by Numnum et al. (2005) who also found that nulliparous women who had HSIL smears carried a higher risk of receiving overtreatment if the see and treat was performed. Thus nulliparous women with HSIL smears are not candidate for the see and treat approach if the rate of overtreatment is to be minimized.

This study was hampered by several limitations. Firstly, there was no central slide review, the accuracy of smear interpretation thus could not be determined. Secondly, retrospective design meant that it was not possible to determine patient and physician preferences that might affect the selection of management. Finally, relevant data including contraception practice, HIV status, LEEP margin status, detailed colposcopic findings, and perioperative LEEP complications were unavailable.

In conclusion, high prevalence of underlying cervical cancer found in this study (9.3%) confirms the high-risk by nature of HSIL smears requiring a comprehensive management. However, the overtreatment rate among women in the see and treat group (50.9%) in this study is notably high and therefore should not be routinely practiced. The significant factor for predicting overtreatment among women undergoing the see and treat approach is parity status.

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