

RESEARCH COMMUNICATION

"See and Treat" Approach is Appropriate in Women with High-grade Lesions on either Cervical Cytology or Colposcopy

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Abstract

This study was undertaken to evaluate the overtreatment rate of women with abnormal cervical cytology undergoing colposcopy followed by loop electrosurgical excision procedure (LEEP), the so-called "see and treat" approach. Overtreatment was defined as LEEP specimens containing cervical intraepithelial neoplasia (CIN) 1 or less. In this study, medical records of 192 women with abnormal Pap smears undergoing the "see and treat" approach in Chiang Mai University Hospital between October 2008 and October 2010 were reviewed. The preceding Pap smears were as follows: 124 (64.6%) with high-grade squamous intraepithelial lesion (HSIL); 35 (18.2%) with atypical squamous cells cannot exclude high-grade squamous intraepithelial lesion (ASC-H); 20 (10.4%) with low-grade squamous intraepithelial lesion (LSIL); 9 (4.7%) with squamous cell carcinoma (SCCA); and 4 (2.1%) with atypical squamous cells of undetermined significance (ASC-US). Histologic results obtained from loop electrosurgical excision procedure (LEEP) were as follows: CIN 2-3, 106 (55.2%); invasive cancer, 41 (21.4%); CIN 1, 15 (7.8%); adenocarcinoma in situ (AIS), 1 (0.5%); and no lesion, 29 (15.1%). Overall, 22.9% of LEEP specimens contained CIN 1 or less. Significant predictors for overtreatment were type of preceding smears and colposcopic impression. If the "see and treat" approach was strictly carried out in women who had either smears or colposcopic findings revealing high-grade disease, the overtreatment rate was only 7%. Hemorrhagic complication was 6.2% and all could be treated at an outpatient department. In conclusion, the overtreatment rate of the "see and treat" approach in women with various degree of abnormal Pap smears is 23% which would be diminished to the acceptable rate of lower than 10% if strictly performed in those with either smears or colposcopic impressions revealing high-grade abnormality. Peri-operative LEEP complications were mild and acceptable.

Keywords: Cervical lesions - see and treat - single visit - overtreatment - Thailand

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Introduction

Pap smear remains the principal methods for cervical cancer screening. The management of an abnormal Pap smear depends on various factors including the severity of abnormalities, types of Pap smear preparation, availability of human papillomavirus (HPV) testing, and patients' compliance and desire.

In previous studies from Chiang Mai University Hospital, an extraordinary high incidence of invasive lesion was observed across all grades of abnormal Pap smears even in women with minimal cytological abnormality. (Charoenkwan et al., 2006; Kantathavorn et al., 2008; Kiatiyosnusorn et al., 2010; Kietpeerakool et al., 2008; Sawangsang et al., 2010). Therefore, immediate colposcopy is the most preferred evaluation method in the authors' institute in order to detect and treat underlying high-grade cervical lesion in a timely fashion.

The "see and treat" approach is an alternative

management for women with abnormal Pap smears. In this approach, women are immediately treated after colposcopic examination. There is no requirement of histologic diagnoses prior to definite treatment. The most common treatment method used in the "see and treat" approach is loop electrosurgical excision procedure (LEEP).

The "see and treat" approach has become increasingly common in the Colposcopy Clinic of Chiang Mai University Hospital. The present study was undertaken to evaluate the outcomes of women with an abnormal Pap smear who had undergone the "see and treat" approach. The results of this study will provide important data for auditing performances of the "see and treat" approach.

Materials and Methods

In the authors' institute, the data of women undergoing LEEP including patients' characteristics, types of abnormal

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Pap smears, colposcopic findings, detailed histologic diagnoses, and perioperative LEEP complications, were routinely recorded. After approval from the Research Ethics Committee, the records of women with an abnormal Pap smear of any grade who had undergone the “see and treat” approach using LEEP during October 2008 to October 2010 at Chiang Mai University Hospital, were reviewed.

Colposcopy was carried out following the application of 3-5% acetic acid solution on the upper vagina and cervix. The colposcopic diagnoses were made based on the visualization of cervical transformation zone, density of acetowhite lesion, sharpness of the lesion margins, and patterns of underlying vessels. LEEP was performed under local anesthesia at an outpatient department. The electrical power was set in blend mode. Antibiotic prophylaxis was not routinely prescribed. Patients were advised to avoid sexual intercourse and vaginal douching for at least four weeks after LEEP. Women with invasive lesions were clinically staged according to the International Federation of Gynecology and Obstetrics (FIGO) staging system. Overtreatment was defined as the LEEP specimens contained cervical intraepithelial neoplasia (CIN) 1 or less.

Intraoperative hemorrhage was defined as a complication when it required cervical suturing and/or vaginal packing for adequate hemostasis after LEEP. Early and delayed postoperative hemorrhage were defined as bleeding occurring within 24 hours, and bleeding occurring later than 24 hours after LEEP, which required some hemostatic interventions i.e. an application of Monsel’s solution, suturing or vaginal packing. Postoperative infection was defined as purulent vaginal discharge, cervicitis, endometritis, and pelvic inflammatory disease.

The statistical analysis was carried out using SPSS computer software version 17 (SPSS, Chicago, IL, USA). Descriptive statistics were used for demographic baseline characteristics. Chi-square was used as a univariate analysis to determine the association between the factors. Logistic regression was used as a multivariate analysis to find an independent factor. An odds ratio with a 95% confidence interval, which did not include unity and a P-value of <0.05, were considered statistically significant.

Results

During the study period, 192 women with an abnormal Pap smear who had undergone the “see and treat” approach were reviewed. Mean age ± standard deviation was 47.3 ± 9.7 years (range 25-82 years). Sixty-six (34.4%) women were postmenopausal. Twenty-three (12.0%) were nulliparous. Human immunodeficiency virus (HIV) infection was noted in 30 (15.6%) women. Approximately two-third (67.7%) of the women had had a Pap smear taken from other hospitals.

The preceding Pap smears of the 192 women were as follow: 124 (64.6%) with high-grade squamous intraepithelial lesion (HSIL); 35 (18.2%) with atypical squamous cells cannot exclude high-grade squamous intraepithelial lesion (ASC-H); 20 (10.4%) with low-grade squamous intraepithelial lesion (LSIL); 9 (4.7%) with squamous cell carcinoma (SCCA); and 4 (2.1%) with atypical squamous cells of undetermined significance (ASC-US). All cervical smears were conventional Pap.

One hundred and fifty-nine (82.8%) women had unsatisfactory colposcopic evaluation. The colposcopic diagnoses of the 192 women were as follows: 147 (76.6%) with CIN 2-3; 3 (1.6%) with suspected invasive lesions; 17 (8.9%) with CIN 1; and 25 (13.0%) without lesions.

Table 1. LEEP Histopathology Stratified by Types of Preceding Pap Smears

Pap types	Number of women	LEEP histology results					
		No lesion	CIN 1	CIN 2-3	AIS	Cancer	High-grade lesion†
ASC-US	4	0 (0.0)	0 (0.0)	4 (100)	0 (0.0)	0 (0.0)	4 (100)
ASC-H	35	18 (51.4)	0 (0.0)	14 (40.0)	0 (0.0)	3 (8.6)	17 (48.6)
LSIL	20	2 (10.0)	10 (50.0)	7 (35.0)	0 (0.0)	1 (5.0)	8 (40.0)
HSIL	124	9 (7.2)	5 (4.0)	77 (62.1)	1 (0.8)	32 (25.8)	110 (88.7)
SCCA	9	0 (0)	0 (0.0)	4 (44.4)	0 (0.0)	5 (55.6)	9 (100)

Data are number (percentage); CIN, cervical intraepithelial neoplasia; AIS, adenocarcinoma in situ; ASC-US, atypical squamous cells of undetermined significance; ASC-H, atypical squamous cells cannot exclude high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; SCCA, squamous cell carcinoma † Including CIN 2-3, AIS, and cancer

Table 2. LEEP Histopathology Results Stratified by Types of Pap Smears and Colposcopic Impressions

Pap types	Colposcopic impression	Number	LEEP histology results			Adjusted odds ratio* (95% CI)
			CIN 1 or less	CIN 2-3/ AIS	Cancer	
HSIL/SCCA	High-grade	110	8 (7.2)	67 (60.9)	35 (31.8)	Reference
HSIL/SCCA	Low-grade	23	6 (26.1)	15 (65.2)	2 (8.7)	4.09 (1.23-13.61)
ASC/LSIL†	High-grade	40	17 (42.5)	19 (47.5)	4 (10.0)	8.83 (3.36-23.21)
ASC/LSIL†	Low-grade	19	13 (68.4)	6 (31.6)	0 (0.0)	26.3 (7.73-89.28)

Data are number (percentage); CIN, cervical intraepithelial neoplasia; AIS, adenocarcinoma in situ; CI, confidence interval; HSIL, high-grade squamous intraepithelial lesion; SCCA, squamous cell carcinoma† Including atypical squamous cells of undetermined significance (ASC-US), atypical squamous cells cannot exclude high-grade squamous intraepithelial lesion (ASC-H), low-grade squamous intraepithelial lesion (LSIL) cytology *Odds ratio for having CIN 1 or lesser on LEEP histology-known as overtreatment, and adjusted by age, parity, menopausal status, and site of Pap smear taken

Of the 192 women, the "see and treat" LEEP histological results were as follows: cervical intraepithelial neoplasia (CIN) 2-3, 106 (55.2%); invasive cervical cancer, 41 (21.4%); CIN 1, 15 (7.8%); adenocarcinoma in situ (AIS), 1 (0.5%); and no lesion, 29 (15.1%). Table 1 displays LEEP histologic results stratified by severity of preceding Pap smears. Therefore, the Overtreatment rate was 22.9%.

Among 41 women who had invasive cervical cancer, 37 had squamous cell carcinoma histology. The remaining four women had adenocarcinoma (3) and adenosquamous carcinoma histology (1), respectively. FIGO staging included IA1 (27), IA2 (6), and IB1 (8).

By univariate analysis, the risk of having CIN 1 or less on the "see and treat" LEEP histology was significantly associated with types of the preceding abnormal Pap smears ($P < 0.001$) and colposcopic diagnoses ($P < 0.001$). Age, parity, and menopausal status did not show significant impact on the severity of LEEP histology.

Table 2 demonstrates the "see and treat" LEEP histology stratified by types of abnormal Pap smears and colposcopic findings. The risk of having CIN 1 or lesser on LEEP specimens substantially increased among women whose preceding cervical cytology and/or colposcopic findings suggested a low-grade abnormality.

LEEP-related complications were observed in 18 (9.4%) women including two (1.0%) with intraoperative hemorrhage; one (0.5%) with early postoperative hemorrhage; nine (4.7%) with delayed postoperative hemorrhage; and six (3.1%) with postoperative cervicitis. All cases could be successfully treated at an outpatient department.

Discussion

Generally, women with abnormal Pap smears require several visits for definite diagnosis including making an appointment for colposcopy, undergoing colposcopic examination, discussing histologic results and treatment planning, and making an appointment for definite treatment if indicated. Therefore, time-consuming and costly care is anticipated. As mentioned earlier, the "see and treat" approach using LEEP enables histologic assessment and therapeutic excision carried out in the same visit. Therefore, it is worthy of consideration particularly in areas with low resource and poor patients' compliance.

Unnecessary treatment or the so-called "overtreatment" is the major concern of the "see and treat" approach. At present, both the American Society for Colposcopy and Cervical Pathology (ASCCP) and the National Health Service (NHS) of the United Kingdom in collaboration with the British Society for Colposcopy and Cervical Pathology (BSCCP) recommend that the overtreatment rate is defined as the proportion of women whose excised specimens contained CIN 1 or less (Luesley and Leeson, 2010; US National Cancer Institute, 2004). Additionally, the NHS Cervical Screening Programme (NHSCSP) 2010 guidelines also state that the overtreatment rate should be periodically audited and an overtreatment rate of less than 10% should be set as a standard requirement which is consistent with the recommendation of the Cochrane

Colposcopy and Cervical Cytopathology Collaborative (Kyrgiou et al., 2006; Luesley and Leeson, 2010).

In this study, 22.9% of LEEP specimens contained CIN 1 or less which was well above the NHSCSP standard (<10%) (Luesley and Leeson, 2010). The degree of preceding cytologic abnormality and colposcopic findings was associated with the risk of overtreatment (Table 2). When cross tabulated between type of Pap smear and colposcopic diagnosis, the overtreatment rate was only approximately 7% in women who had either Pap smears or colposcopic diagnoses suggesting a high-grade abnormality. On the other hand, the rate of overtreatment was extremely high (68%) in women with ASC/LSIL smears who had only low-grade lesions on colposcopy. These findings suggested some important practical considerations in that the overtreatment rate of the "see and treat" approach in the authors' institute was an achievable standard if it was solely performed in women who had either cervical smears or colposcopy revealing high-grade lesions.

Despite a high overtreatment rate, the significance of the incidence of occult invasive lesions (9-10%) found among women who had one of Pap smears or colposcopic impressions suggesting high-grade disease however could not be overlooked. In women who are at a risk of being nonattendance, the "see and treat" LEEP might be appropriate in order to minimize the possibility of occult invasive lesion going unrecognized. However, information regarding the chance of overtreatment and the benefit of immediate LEEP should be discussed during patient's counseling.

The most common complication following LEEP is perioperative hemorrhage (Kietpeerakool et al., 2006). The NHSCSP 2010 guidelines state that incidence of hemorrhage complication following treatment of CIN should be less than 5% and the admission rate owing to treatment complication should be less than 2% (Luesley and Leeson, 2010). In this study, hemorrhagic complication following the "see and treat" LEEP was 6.2%. However, all patients could be treated at an outpatient department. Although the rate of hemorrhagic complication in this study was slightly higher than that recommended by the NHSCSP guidelines (Luesley and Leeson, 2010), all were only minimal hemorrhage and did not pose any serious adverse event.

A previous study reported an increased risk of adverse pregnancy outcomes including preterm delivery, premature rupture of membrane, and low-birth weight in pregnant women who had undergone LEEP (Crane 2003; Kyrgiou et al., 2006; Sadler et al., 2004; Sjoborg et al., 2007). Therefore, the "see and treat" approach should be meticulously viewed in reproductive women aiming to avoid these possible complications.

An extraordinarily high incidence of underlying invasive cervical cancer among women with abnormal Pap smear was noted in this study (21.4%) which confirmed our previous findings (Charoenkwan et al., 2006; Kantathavorn et al., 2008; Kietpeerakool et al., 2008; Kiatiyosnusorn et al., 2010; Sawangsang et al., 2010) and highlighted the necessity of aggressive evaluation in order to exclude occult invasive lesion.

In conclusion, the overtreatment rate in this study was approximately 23%. The overtreatment rate could be diminished to be lower than 10% as recommended by the NHSCSP 2010 guidelines if the “see and treat” approach was strictly carried out in women whose either preceding cervical smears or colposcopic impressions revealed high-grade abnormality. Peri-operative LEEP complications in this study were mostly mild and at an acceptable rate.

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