RESEARCH COMMUNICATION

How Can the Overtreatment Rate of "See and Treat" Approach be Reduced in Women with High-Grade Squamous Intraepithelial Lesion on Cervical Cytology?

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Abstract

The aim of this study was to determine the incidence and predictors of overtreatment in "see and treat" approach using loop electrosurgical excision procedure (LEEP) in women with high-grade squamous intraepithelial lesion (HSIL) on cervical cytology. The overtreatment was considered when LEEP specimens contained no cervical pathology. Between January 2001 and April 2006, 446 women with HSIL on Pap smear underwent colposcopy followed by LEEP at Chiang Mai University Hospital. Mean age of these patients was 45.6 years with a range of 25-78 years. One hundred and twenty-one (27.1%) women were menopausal. Unsatisfactory colposcopy was observed in 357 (80.0%) women. Of 446 women, histologically-confirmed HSIL, invasive cancer, low-grade squamous intraepithelial lesions, and adenocarcinoma in situ were detected in 330 (74.0%), 76 (17.0%), 9 (2.0%), and 5 (1.1%), respectively. The overtreatment rate on LEEP specimens was noted in 26 women or 5.8% (95% confidence interval [CI] = 3.8 to 8.4) of 446 women. By multivariate analysis, postmenopausal status was the only significant independent predictor of overtreatment with an adjusted odds ratio of 2.89 (95% CI = 1.30 to 6.43, P = 0.009). When postmenopausal women were excluded from analysis, the overtreatment rate was reduced to only 4.0%. In conclusion, "see and treat" approach appears to be an appropriate strategy in managing women with HSIL cytology. The overtreatment rate could be reduced when such policy is limited for premenopausal women.

Key Words: See and treat - loop electrosurgical excision procedure - overtreatment - predictors.

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Introduction

Cervical cancer is a major health burden. Annually, an estimated 470,000 new cases occur worldwide, of which nearly half die. Moreover, approximately 80% of these deaths occur in developing countries (Ferlay et al., 2000). To minimize this problem, early detection and proper treatment of cervical precancerous lesions are therefore inevitable. These two critical processes, however, are still problematic in developing countries because of the limitation of national screening and treatment program.

The "see and treat" or one-step management is an immediate treatment of cervical precancerous lesions by loop electrosurgical excision procedure (LEEP) without intervening colposcopically-directed biopsy. This strategy provides several advantages including a permission of simultaneous histological diagnosis and treatment of cervical precancerous lesions resulting in reduction of either patient visit or time interval from diagnosis to treatment, a more accurate histological diagnosis due to a larger specimens than those obtained by cervical biopsy, a decrease in cost and greater patient's convenience, thereby improving the compliance (Keijser et al., 1992; Ferris et al., 1996; Irvin et al., 2002; Dunn et al., 2003; Numnum et al., 2005). In Chiang Mai University Hospital, the "see and treat" approach has now almost entirely replaced the traditional two-step process which requires histological diagnosis before LEEP in women with Pap smear suggesting high-grade squamous intraepithelial lesions (HSIL). Although such approach seems to be clinically reasonable, there is a certain proportion of patient in whom cervical conization may be unnecessary treatment. This study was accordingly undertaken to evaluate the incidence and predictor of overtreatment in women with HSIL Pap smear who underwent "see and treat" LEEP at our institute.

Materials and Methods

After approval from the Research Ethics Committee, the medical records of women with HSIL Pap smear, who underwent colposcopy followed by immediate LEEP

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without a prior histological diagnosis of cervical neoplasia or suspicion of invasive cancer on colposcopy at the Department of Obstetrics and Gynecology, Chiang Mai University Hospital between January 2001 and April 2006, were reviewed. At our institute, human immunodeficiency virus (HIV) infection was routinely screened before colposcopy. Abstracted information included clinical characteristics, the status HIV infection, results of preceding Pap smears, colposcopic findings, and histology of LEEP specimens.

The overtreatment was considered when LEEP specimens contained no cervical lesions. Staging of invasive cervical cancer was clinically made according to the classification of the International Federation of Gynecology and Obstetrics (FIGO).

Frequency distributions were calculated for each variable. The chi-square or Fisher exact test were used to univariately identify factors related to the absence of significant lesions on LEEP specimens. For those factors with a P value of less than .10 in univariate analysis, a multivariate analysis using a logistic model was further used to find the independent factors. An odds ratio, with a 95% confidence interval that did not include unity, was considered statistically significant.

Results

During the study period, 446 women with HSIL Pap smear undergoing immediate LEEP after colposcopy were recruited for analysis. Mean age of these women was 45.6 years (median, 45.0, range 25 to 78 years). Twenty-five (5.6%) women were nulliparous. Mean parity among the remaining multiparous group was 1.9 (median, 2.0, range 1 to 14). One hundred and twenty-one (27.1%) women were menopausal and all did not receive hormonal replacement therapy within 6 months before colposcopy. HIV seropositive status was noted in 16 (3.6%) women. During colposcopy, unsatisfactory evaluation was observed in 357 (80.0%) women. Among 89 women with satisfactory colposcopic examination, 55 had lesion involving at least 3 quadrants of cervical transformation zone.

Of the 446 women, 330 (74.0%) had HSIL, 76 (17.04%) had invasive lesion, 9 (2.0%) had LSIL, 5 (1.1%) had adenocarcinoma in situ (AIS), and 26 (5.8%) had no lesion on LEEP specimens. Based on these findings, the incidence of significant lesions, i.e. HSIL and invasive cancer was 92.2% (95% confidence interval [CI] = 89.3 to 94.5) and the overtreatment rate was 5.8% (95% CI= 3.8 to 8.4).

In Table 1, the univariate analysis revealed that advanced age (≥ 60 years) and postmenopausal status were significant predictors for overtreatment of the "see and treat" approach. Multivariate analysis using a forward logistic regression model which included these two significant covariates was performed. Only postmenopausal status remained statistically significant predictor with an adjusted odds ratio of 2.89 (95%CI= 1.30-6.43, P = 0.009). If postmenopausal women in this study were excluded, the overtreatment rate would be reduced from 5.8 % to only 4.0%.

Table 1. Univariate Analyses for Prediction of Overtreatment After "See and Treat" Approach in Women with HSIL Cytology

Variables	Number (%)	P-value
Age (years)		
≥ 60	5/27 (18.5)	< 0.01
< 60	21/419 (5.0)	
Menopausal status		
Postmenopausal	13/121 (10.7)	< 0.01
Premenopausal	13/325 (4.0)	
Parity		
Nulliparous	2/25 (8.0)	0.65
Multiparous	24/421 (5.7)	
HIV infection		
Positive	0/16 (0)	0.61
Negative	26/430 (6.1)	
Colposcopic findings		
Unsatisfactory	20/357 (5.6)	0.62
Satisfactory	6/89 (6.7)	

HSIL, high-grade squamous intraepithelial lesion; HIV, human immunodeficiency virus

Discussion

Tradditionally, the management algorithm of cervical precancerous lesions has involved multiple steps including initial colposcopy, appropriated colposcopically-directed biopsy, selection of subsequent treatment, and post-treatment surveillance. Meanwhile, the multiple visits are required and sometimes have plagued treatment efficacy due to poor compliance. To improve patient compliance, an alternative strategy using LEEP for cervical conization method without prior histogic diagnosis at the time of initial colposcopy, the so-called "see and treat" is proposed because it could reduce the number of visits compared with that of the traditional management. Due to its several advantages, LEEP has become the preferred conization methods among gynecological practice particularly for "see and treat" approach.

The chance of having no cervical lesions on LEEP specimens, the so-called overtreatment mainly depends on the severity of epithelial lesion suggested by preceding cervical smear. For mild or borderline cytological abnormalities, the overtreatment rate is highly expected (Lopes et al., 1989). For example, in a study of Keijser et al (1992), 25 % of women with mild dysplasia on cervical smear who underwent the "see and treat" had no significant cervical histology on LEEP specimens compared to that of only 6 % in women with higher grade of dysplasia. Additionally, Ferris et al (1996) noted that approximately 41% of women with low-grade lesion on their referral Pap smear had normal histological finding after "see and treat" LEEP compared to that observed incidence of only 7 % in women with HSIL smears. These data strongly suggested that "see and treat" policy was inappropriate strategy for women with low-grade cytological abnormality because of the high incidence of the overtreatment. In this study, overtreatment was noted in 5.8% of women which was comparable to those previous reported incidence that ranged form 0 % to 8 % when "see and treat" LEEP were strictly implemented in women with HSIL on preceding

abnormal Pap smears (Irvin et al., 2002; Dunn et al., 2003; Charoenkwan et al., 2004; Numnum et al., 2005).

In this study, we systematically evaluated demographic and colposcopic variables for determination of their relation to overtreatment after "see and treat" approach in women with HSIL cytology. A multivariate analysis revealed that only postmenopausal status was a significant independent predictor (P=0.009) with an approximately 3 times increase in probability of receiving overtreatment after such management. The incidence of overtreatment in this series would be reduced from 5.8% to 4.0% when "see and treat" approach was solely implemented in premenopausal group. The higher rate of overtreatment in postmenopausal women may theoretically be explained by the higher false positive rate of HSIL Pap smear. The difficult in distinguishing atrophy-related epithelial changes from high-grade abnormality has been well described. Exfoliated atrophic epithelial cells commonly show markedly reduced maturation and may show nuclear abnormalities such as nuclear enlargement, atypical chromatin pattern, or hyperchromasia (Bulten et al., 2000; Qiao et al., 2005; Saad et al., 2006). It is important to note that there was no postmenopausal women in the present study using hormonal replacement therapy, therefore, the predictive significance of postmenopausal status for overtreatment might alter in series that includes women receiving hormonal replacement therapy.

We did not attempt to determine the correlation of colposcopic impression and final LEEP histology because the high proportion of women (80.0%) in this study had unsatisfactory colposcopy resulting in that the most severe cervical lesion could not be accurately identified.

In conclusion, the "see and treat" policy using LEEP is an appropriate management in women with HSIL on Pap smear with an overtreatment rate of 5.8%. The incidence of overtreatment could be further reduced to 4.0% when such policy was strictly carried out in only premenopausal women.

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