RESEARCH ARTICLE

Is the Correlation between Papanicolaou Smear and Histopathology Results Affected by Time to Colposcopy?

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Abstract

Background: Time to colposcopy (TC) after abnormal Pap smears was evaluated for influence on cytohistologic correlation (CHC). Materials and Methods: This retrospective study assessed the correlation between TC and CHC of women who had abnormal Pap smears. Colposcopic chart review included participants from 2010-2013 who attended a colposcopic clinic, Thammasat University Hospital, Thailand. Results: Four hundred and sixty cases who had abnormal Pap smears were recruited. Pap reports were atypical smears with low grade squamous intraepithelial lesion (SIL), high grade SIL and cancer at 339, 114 and 7 cases, respectively. One hundred and twenty four patients underwent loop electrosurgical excision procedure (LEEP). A half of the cases were colposcopically examined within 1-2 months after abnormal Pap collection. CHC was 88 percent and not affected at all by TC. Subjects who attended cervical cancer screening from affiliated health providers had shorter TC than those screened in our tertiary hospital. Conclusions: Time to colposcopy with abnormal Pap smears conducted at Thammasat University Hospital had a highest frequency of 42 days, in line with the literature. Length of TC does not affect the correlation between Pap and histopathologic reports. A longer waiting period for colposcopy did not alter progression or regression of the disease.

Keywords: Pap smear - colposcopy - waiting time - histopathology - change

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Introduction

Cervical cancer is the second most cause of death in Thai women (Ferlay et al., 2010). Pap smear is the most popular cervical cancer screening used in Thailand and worldwide. The use of Pap smear for cytology-based screening has been a cost-effective tool for the prevention of cervical cancer in developing countries.

After the result of an abnormal Pap smear was revealed, colposcopy is the recommended procedure. Colposcopy is the gold standard of abnormal Pap smear investigation. A discordance between abnormal Pap smear and colposcopy means the result of abnormal Pap smear is more or less aggressive than the colposcopy biopsy. Loop electrosurgical excision procedure (LEEP) is the procedure recommended for later consideration.

Thammasat University Hospital is a tertiary health care provider located in the northern Bangkok area. The hospital received women with abnormal Pap smears from our cancer screening program and provided gynecological treatment to patients with abnormal Pap smear referred from our affiliated healthcare providers in central Thailand.

Time to colposcopy (TC) is varies in different practices. More aggressive Pap smear reports usually had shorter time for colposcopy (Kuo et al., 2010). Some low grade CIN can spontaneously regress and high grade CIN can progress during the colposcopy waiting period (Campion et al., 2010). The longer waiting TC resulted in more anxiety in women who had abnormal Pap smear.

This study investigated the correlation between colposcopic waiting time and cytohistologic result.

Materials and Methods

This was a retrospective study conducted between June 2010-May 2013 at gynaecologic clinic, Thammasat University Hospital, Thailand. Patients with abnormal Pap smear from Thammasat University Hospital and affiliated healthcare providers were recruited. This study was approved by Thammasat University Ethical Committee.

Four hundred and sixty women who had abnormal Pap smears were enrolled. Ninety one percent was conventional Pap smear. All cases of abnormal Pap smears were appointed for colposcopic examination per standard protocol. Colposcopic appointment for all cases

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with abnormal Pap smears from on-site gynaecologic unit and affiliated healthcare providers mainly hospitals and clinics in central Thailand were confirmed by a telephone call. The patients received colposcopic directed biopsy for histopathology study and LEEP as indicated for diagnosis and treatment. Demographic data, cytologic and histopathologic results were collected.

Time to colposcopy (TC) was the number of days from the date of Pap smear collection to colposcopic examination. Cytohistologic correlation (CHC) means the final histopathologic reports were corresponding to Pap smear reports. Inclusion criteria were the women that have abnormal Pap smear result with atypical Pap smear to cancer who visited Colposcopic unit at Thammasat University Hospital. Exclusion criteria were pregnant women, the women with previous abnormal Pap smear and the women previously diagnosed with cervical cancer.

The study was approved by the Ethics Committee of Thammasat University

Correlation between cytohistologic results and time from Pap smear to colposcopy was primarily looked at. CHC were defined as HSIL Pap smear but equal or more than CIN 2 or LSIL Pap smear but equal or more than CIN 1 histopathology from colposcopic directed biopsy and/or LEEP. A p-value of less than 0.05 was considered significant. SPSS 18.0 (SPSS Inc., Chicago, USA) was the analysis software used. Descriptive statistics were used for demographic data. Chi-square or Fisher's exact test, were used to compare the difference between groups when appropriated.

Results

Records of 460 woman aged between 17-80 years old who had abnormal Pap smear; result according to Bethesda method (atypical smear to cancer) were enrolled in the study. Overall mean time to colposcopy (TC) was 49.1 days, range from 7-188 days. Mean TC from affiliated gynaecologic units and our own institute were 47 and 51 days; respectively. The demographic data were composed of age groups, marital status (married and single), occupation (government officer, company officer, employee, self-employee and household), type of Pap smear, histopathology, LEEP and final diagnosis (Table 1). Mean age of on-site and referral groups were 41 and 39 years old, respectively. Normal histopathology, HSIL and cancer cases were found in 29.6, 20 and 1.5 percent, respectively. False positive rate of Pap smear in this study was 29.6 percent. Comparison of Pap smear and final histopathologic diagnosis was shown in Table 2.

The correlation between TC and demographic data were compared according to time period at 45 days as shown in Table 3. Time to colposcopy were separated in two groups, namely less than and more than 45 days. The participant who attended colposcopy within 45 days after date of Pap collection was defined as early colposcopy. Table 3 showed the comparison of early colposcopic group and demographic data. Early colposcopic groups were divided two groups. There was no difference among age of 40 and over, occupation and residency. The participants

Table 1. Demographic Data and Pap Source

Characteristics	On-site % (n=245)	Referral % (n=215)	Total % (n=460)	p-value
Age group (years)				
<30	17.96 (44)	24.19 (52)	20.87 (96)	0.22
31-40	28.16 (69)	31.16 (67)	29.57 (136)	
41-50	33.47 (82)	28.84 (62)	31.30 (144)	
> 51	20.41 (50)	15.81 (34)	18.26 (84)	
Marital status				
Marriage	53.06 (130)	51.63 (111)	52.39 (241)	0.76
Single	46.94 (115)	48.37 (104)	47.61 (219)	
Occupation				
Government officer	15.10 (37)	7.44 (16)	11.52 (53)	0.05*
Company officer	9.80 (24)	11.16 (24)	10.43 (48)	
Employee	39.18 (96)	47.91 (103)	43.26 (199)	
Self employee	3.27 (8)	5.12 (11)	4.13 (19)	
Household	32.65 (80)	28.37 (61)	30.65 (141)	
Pap abnormality				
Atypical	60.00 (147)	44.19 (95)	52.61 (242)	<0.01*
LSIL	22.86 (56)	27.91 (60)	25.22 (116)	
HSIL	15.92 (39)	25.58 (55)	20.43 (94)	
Cancer	1.22 (3)	2.33 (5)	1.74 (8)	
Histopathology				
CIN 1 or lesser	84.08 (206)	68.37 (147)	76.74 (353)	<0.01*
CIN 2/3	15.51 (38)	29.30 (63)	21.96 (101)	
Cancer	0.41 (1)	2.33 (5)	1.30 (6)	
LEEP**				
CIN 1 or lesser	34.55 (19)	21.74 (15)	27.42 (34)	0.12
CIN 2/3	65.45 (36)	75.36 (52)	70.97 (88)	
Cancer	0.00 (0)	2.90 (2)	1.61 (2)	
Final diagnosis				
CIN 1 or lesser	80.41 (197)	66.05 (142)	73.70 (339)	<0.01*
CIN 2/3	19.18 (47)	31.16 (67)	24.78 (114)	
Cancer	0.41 (1)	2.79 (6)	1.52 (7)	

*statistical significant, Atypical : atypical squamous cell and atypical glandular cell, LSIL: low grade squamous intraepithelial lesion, HSIL: high grade squamous intraepithelial lesion, CIN: cervical intraepithelial neoplasia, ** n=124

Table 2. Final Diagnosis with Abnormal Pap Smear

Abnormal Pap smear	CIN 1 or Lesser	CIN 2/3	Cancer	Total
Atypical smear	219	22	1	242
LSIL	102	14	0	116
HSIL	17	72	5	94
Cancer	1	6	1	8
Total	339	114	7	460

*Atypical smear: atypical squamous cell and atypical glandular cell; LSIL: low grade squamous intraepithelial lesion; HSIL: high grade squamous intraepithelial lesion; CIN: cervical intraepithelial neoplasia

Table 3. Time to Colposcopy with in 45 Days and Demographic Data

			Less than 45 days		
			On-site % (n=101)	Referral % (n=117)	p value
Age (years)	<40		50.50 (51)	52.99 (62)	0.71
	>40		49.50 (50)	47.01 (55)	
Occupation	Government officer		14.85 (15)	10.26 (12)	0.35
	Company officer		5.94 (6)	11.11 (13)	
	Employee		40.59 (41)	45.30 (53)	
	Self employee		2.97 (3)	5.13 (6)	
	Household		35.64 (36)	28.21 (33)	
Residency	Bangkok metropolitan		93.07 (94)	88.89 (104)	0.29
	Others		6.93 (7)	11.11 (13)	
Pap abnormality		Major[a]	16.83 (17)	29.06 (34)	0.03[c]
		Minor[b]	83.17 (84)	70.94 (83)	
Final histopathology		Major[d]	16.83 (17)	35.04 (41)	<0.01[c]
		Minor[e]	83.17 (84)	64.96 (76)	

[a]High grade squamous intraepithelial lesion (SIL) and higher; [b]Low grade SIL and atypical smear, [c]statistical significant; [d]Cervical intraepithelial neoplasia (CIN) 2/3 and higher, [e]CIN 1 and lesser

Table 4. Characteristics and Cytohistologic Reports Compared with Pap source

	Pap source		
	On-site % (n=245)	Referral % (n=215)	p-value
Age groups (years)			
<40	46.12 (113)	55.35 (119)	0.05*
> 40	53.88 (132)	44.65 (96)	
Pap abnormality			
Major*	17.14 (42)	27.91 (60)	< 0.01*
Minor**	82.86 (203)	72.09 (155)	
Final histopathology			
Major£	19.59 (48)	34.42 (74)	< 0.01*
Minor££	80.41 (197)	65.58 (141)	
LEEP***			
Performed	20.82 (51)	32.56 (70)	< 0.01*
Non applicable	79.18 (194)	67.44 (145)	
CHC			
Correlation	88.16 (216)	82.33 (177)	0.08
Discrepancy	11.84 (29)	17.67 (38)	

*High grade squamous intraepithelial lesion (SIL) and higher, **low grade SIL and atypical smear, * statistical significant, £Cervical intraepithelial neoplasia (CIN) 2/3 and higher, ££CIN 1 and lesser, ***Loop electrosurgical excision procedure, CHC: cytohistologic correlation

who had Pap smear from affiliated gynaecologic units had higher severity of Pap abnormality and major final histopathology in a significant manner.

Table 4 showed characteristics of cytohistologic reports compared with Pap smear reports sources. The participants who had Pap smear from affiliated gynaecologic units were younger, had more severity of Pap abnormality, major final histopathology and performed LEEP than on-site gynaecologic units, respectively. There was no difference of CHC between on-site and referral Pap smear source groups.

Discussion

Thammasat University Hospital is a tertiary healthcare centre and received referral cases from nearby healthcare provider units and central Thailand. Occupations of participants were government officers, industrial workers, farmers as well as entry level foreign workers from Myanmar. Participant's average age was forty years old. The cases from affiliated healthcare providers had wide range of socioeconomic status. Our affiliated healthcare providers are small to medium government hospital, private hospitals and clinics. Nearby area has the largest wholesale market (Talad Thai). Myanmar workers in all cases came from this marketplace.

Women with abnormal Pap smears referred to colposcopy by our affiliated healthcare providers had a significantly shorter time to undergo colposcopic investigation compared to participants from on-site gynaecology clinic. Time to colposcopy was measured from the date of Pap smear specimen collection to the date of colposcopic directed biopsy. Most affiliated healthcare providers were private units. The process from reading cervical samples for Pap smears and get Pap result back to participants was faster than the government unit could provide. Pap smear reports in private sectors took one week to come back to physicians while on site government hospital took two weeks due to high workload. Colposcopy referral protocol at Thammasat University Hospital was a stream line process. Affiliated healthcare providers could call Thammasat Hospital on the same days the Pap result was picked up to reserve colposcopy date at Thammasat University.

In this study, half of cases had abnormal Pap smear report in atypical smear category. After colposcopic investigation, the final diagnosis of CIN 1 or lesser, CIN2/3 and cancer were 73.70, 24.78 and 1.52 percent, respectively. This finding indicated that approximately 90.5 percent of atypical smear had silent CIN 1 and 9.5 percent had silent CIN 2/3 and cancer. The result showed slightly decreased rate (9.5% *vs* 11.8%) compared to earlier work (Panyanupap et al., 2011).

The percentage of LEEP cases undergone by diagnostic reason was 64.5. A quarter of LEEP cases showed CIN 1 or lesser. This finding indicated that the unnecessary rate of LEEP was 27.42 percent. Around 70.97 and 1.61 percent of LEEP cases had CIN 2/3 and cancer, respectively. In this study around one point six percent of LEEP cases had silent cancer.

Cytohistologic correlation (CHC) of on-site and referral groups in this study were 88.16 and 82.33 percent, respectively. The result showed similar discrepancy rate (11.84 and 17.67 percent) compared to earlier work (Poomtavorn et al., 2013).

From this study, CHC was not altered from time to colposcopy or time from colposcopy to LEEP. A precancerous would lesion need a long time to progress the awaiting time for colposcopy. Time to colposcopy in this study was rather short compared to previous literature (Kuo et al., 2010; Baranoski and Stier, 2012; Tahseen and Reid, 2008).

A quarter of referral Pap smear showed major abnormalities and one-third of them showed major histopathology. LEEP intervention was found to be more frequent in cases from affiliated units. These cases from affiliated healthcare providers were younger patients than our on-site patients. Pap smears result and cervical histopathology from affiliated units showed more severe overall results than those of on-site units.

TC of the patients from affiliated health units was short compared to those of office workers and government workers who used their healthcare quota at Thammasat University. The appropriate time to colposcopy had no definite cut point. Baranoski et al stated that all colposcopy appointments should aim for providing the procedure within 2 weeks of Pap smear procedure for a HSIL Pap result, and within 4-6 weeks for a LSIL Pap result (Baranoski and Stier, 2012). The study from the United Kingdom (UK) indicated the TC was 28 and 56 days in HSIL and LSIL, respectively (Tahseen and Reid, 2008). Study from the United States (US) in year 2010 found that women with LSIL and HSIL received a colposcopy in 3-4 months (Kuo et al., 2010). Our mode data showed TC of 42 days within the average limit of Baranoski's and Tahseen's studies.

Previous study from Carns showed 95.2 percent correlation between cytohistologic correlations in

detecting high-graded cervical lesion (Carns and Fadare, 2008). While CHC from study of Poomtavorn et al 2013 was 75.8 percent (Poomtavorn et al., 2013). The present study conducted CHC of all grade cervical lesions. CHC of on-site and referral groups in this study were 88.16 and 82.33 percent.

Saayman et al 2013 from South Africa reported that there was no difference in the up- or downgrading of cervical dysplasia between early (<6 months) and late (>6 months) colposcopic referral groups (Saayman et al., 2013). This report explained why our TC showed no fluctuation in the correlation between Pap smears and cervical histopathology. Even some low grade CIN can spontaneously regress but it would take longer time than waiting time to colposcopy in this study.

Patients with TC in this study showed no cases with more progression of precancerous lesion. In this study, the period of 6 weeks do not show the any discordance in CHC. Colposcopy within 6 weeks was the recommendation from this study. It was known that individuals awaiting colposcopy had anxiety and depression (Tahseen and Reid, 2008). Patients should receive basic information about cervical cancer prevention, screening and other cancer related procedures during the waiting period to lesser the anxiety from healthcare providers or government unit. A hotline or web board services are also recommended.

In conclusion, time from abnormal Pap smears to colposcopy in abnormal Pap smear done at Thammasat University Hospital had the highest frequency of 42 days. Length of TC does not affect the correlation between Pap and histopathologic reports. The longer waiting period for colposcopy did not alter the progression or regression of the disease. Waiting time for colposcopy in this study was in line with other literatures. The shorter time from Pap smear to colposcopy would reduce patient anxiety.

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