

## CHAPTER X

### DISCUSSION

Cervical neoplasia is a very important health problem. Early diagnosis is the clue to success in management of this disease. The diagnosis of cervical neoplasia has create a lot of difficulties to the physicians and the patients. Although the prevalence of cervical neoplasia is rather low in the total population, but it is still a major problem because of its burdens. The burdens of disease not only come from the disease itself but also come from the therapeutic procedures. The burdens include complications of the disease, complications of the therapeutic procedures and the payments. Complications of the disease are very serious. Some complications are life threatening. Bleeding from the tumour, lung metastasis and local invasion are serious causes of morbidity and mortality. Complications of the treatment are high as well. The mortality rate of Wirtheim's operation is up to 20 % ( Meigs,1951). Bleeding, post operative infection and urinary problems are the complications that cause morbidity to the patients. Cost of treatments are high especially in surgical therapy.

Because of its high burdens, many of health strategies have been used to solve problem. Early detection is accepted to be the most suitable method. The complications of the disease and the therapeutic procedures for the patient in the early stage are lower. By using Pap smear as a screening test, many cases are detected early. Lots of benefit come from early detection. The patients can receive the treatments in the early disease stage. The complications of the disease and the therapeutic procedures are reduced. Some patients can be cured from the disease. Although a lot of benefit comes from early detection, some patients still suffer from the screening test. Because Pap smear is a screening test. It must have high sensitivity in order to minimize the false negative cases. The false negative is very dangerous to the patients. Because the disease will progress and the patients will face with higher complications. Pap smear has high sensitivity then the false positive rate is high. False positive cases are the normal patients diagnosed as the disease patients. In this group, many of them will receive unnecessary diagnostic procedures. The complications in some procedures are very dangerous to them.

The diagnostic tests of the cervical neoplasia is final histopathology of the cervical tissue. The problem of the test is the methods of tissue sampling. Suspected cervical tissue must be taken from the patients' cervix to be examined by the pathologists. Cervical neoplasia is the dysplastic change of the cervix. By nature of disease, the changes are small and composed of many foci. Some foci are different from

others. This means that there can be various stages of changes in the same cervix. Diagnostic procedure includes taking the cervical tissue at the most serious change and accurately examined by the pathologists. Sometimes the dysplastic change can be detected easily. Sometimes the dysplastic changes looked similar to the other non dysplastic lesions. Condyloma accuminata the wart-like lesions caused by Human Papilloma Virus can make the physicians confuse with the cervical neoplasia (Coppleson, 1981). Sometimes many stages of changes occur in the same cervix. If the physicians take biopsy from the wrong lesions or from the lesions that are not the most severe changes, the wrong diagnoses occur. The wrong diagnoses are always less severe than the actual disease. The patients will receive the inadequate treatments and the disease will progress. The patients will suffer from invasive cancer many years later. The best method that proved to be highly accurate in diagnosis of cervical neoplasia is cervical conization. But its complications are too dangerous to perform in all suspected cases.

From the last paragraph, Pap smear is the screening test. The abnormal Pap smear consists of true positive cases and false positive cases. In false positive cases (non disease cases), conization in these patients is not appropriate; because it will increase unnecessary risk to the healthy patients. The patients will suffer from complication of the conization. In true positive cases (disease cases), conization is not appropriate in all cases; because in mild and moderate dysplasia cases, they have high chance to regress to normal

epithelium. The conization increases additional risk to them. The problem of the diagnostic test in cervical neoplasia is how can we detect the disease as much as possible by the method that has the lowest risk. In addition, we must decrease the need for conization as low as possible however must not miss the invasive cases.

The previous reports about colposcopy (Townsend, 1970; Stafl and Mattingly, 1973; Benedet and Boyes, 1976) focussed on the accuracy of colposcopy in diagnosis of cervical neoplasia compared with final histopathology. In their studies, conization was not performed in all cases. Only highly suspected cases were done. In some studies, the conization rate was only 5.8 % (Stafl and Mattingly, 1973). In their studies, the comparison between colposcopy and final histopathology comes only from the cases that had conization or hysterectomy. The majority of conization or hysterectomy cases were the cases that have colposcopy result indicating a staging more than moderate dysplasia. Conization was performed to rule out the invasive stage in these cases. In contrast, majority of their eligible patients who had only colposcopy result were not included in the comparison between colposcopy and final histopathology. This means that the high accuracy can be produced by selective biases. The patients who are highly suspected to have disease will receive the tests. And then, if the prevalence of the diseases increase, the accuracy of the test also increases. Further more, in the patients who were not suspected to have the diseases, how can we be sure that these were not false negative diagnosis. Benedet (1976)

used the follow up methods to confirm the disease stages in the patients who did not have performed conization. In these patients, the final diagnoses were the same as the first diagnosis made by colposcopy.

In some situation, colposcopy can detect the abnormality more than conization or hysterectomy. Benedet (1976) found that 8% of their patients had colposcopy result more severe than conization. These were not the false positive because the diagnostic results of colposcopy were objective evidences. The slides of the tissues obtained from colposcopic directed biopsy have dysplastic cells with staging more severe than from conization. The reasons for this situation were discussed in the former chapter. Benedet stated that the final histopathology had to include the colposcopy results in combination with the results from conization or hysterectomy.

In this studies, the researchers perform the conization in nearly half of the eligible patients. The follow up method were strictly used only in the patients that were not suitable for conization. About the ethical concern, the researcher used many methods to prevent the patients from additional risks. Eventhough close follow up method can reduce the need for conization, the risk of missing invasive cases does not increase. Because the physicians are alert to perform conization if there have some suggestive evidences of disease progression.

The final histopathology is composed of histopathology of colposcopic directed biopsy, conization and hysterectomy. The final outcome will be the most severe disease stage from

three of the test results. To compare the colposcopy results with final histopathology result in the patients who did not perform conization, the final histopathology is the combination of colposcopy and follow up result. Although some comparisons looked like comparison within themselves, it is still logical, because the colposcopy was included in the final diagnosis. If the colposcopy has a major role in diagnosis of cervical neoplasia we can omit the unnecessary dangerous diagnostic procedures in some suitable conditions.

The overall accuracy of the colposcopic directed biopsy was 86 percent. It is in the range of standard compared to other studies (Stafl and Mattingly, 1973; Benedet and Boyes, 1976).

The under diagnosis group was the missed diagnosis group that colposcopy diagnosed the disease stage less severe than final histopathology. In this study, the under diagnostic rate 14.81 percent.

The previous studies used the accuracy as the percentage of correct diagnoses by colposcopy from total final diagnoses. The correct agreement include one stage more severe and one stage less severe than final diagnoses( Benedet and Boyes, 1976). If we use this definition the overall accuracy is 98.19 percent.

The overall accuracy is not useful in clinical situation. The term 'accuracy' can be describe as the probability to make the correct diagnoses from all diagnoses. It can simply explain that the physicians can be 95% sure that their diagnosis are correct if their colposcopy has 95 %

accuracy. How about the 5 % that are wrong ?. If the accuracy of one study exceed 99 % but the 1 % left are invasive cases, can colposcopy still be used in this setting?. Because the treatments of invasive stage are very different from the other stages. There is an agreement that the colposcopy must not miss the invasive cases (Benedet,1973). But if the missed diagnostic cases are severe dysplasia, can we still use it?. This is the controversy in the application of colposcopy in clinical practice.

For the other reasons, accuracy depended on prevalence of disease. If there are some changes in screening for cervical neoplasia, the accuracy will be changed. For example, if one hospital increases the sensitivity of Pap smear by improving the facilities to screen new cases, the incidence of abnormal Pap smear will be increased. That will change the prevalence of disease then the accuracy will change.

For these reasons, the researcher has used the sensitivity and predictive values to justify the benefits of colposcopy depending on clinical applications.

Table 5. shows the result of histopathology of the cervical tissue gained from colposcopic directed biopsy compared with final histopathology result from conization, hysterectomy and colposcopy plus follow up in 69 patients.

From table 5, overall sensitivity of colposcopy in diagnosis of Cervical Neoplasia in 69 abnormal Pap smear women is 94.3 %. Although colposcopy has high sensitivity, the clinical application is limited because 2 missed diagnosis cases were in serious stage. In this group, there is one

patient with invasive cancer that could not be detected by colposcopy. In reviewing the case, this patient came with abnormal uterine bleeding and found slight enlarged uterus by pelvic examination. In the line of management, the physician performed routine pap smear and found that the result was abnormal. Despite of no abnormal lesion seen on the cervix, the physicians proceeded according to the protocol. The colposcopy could not detect the abnormality. Then the conization was performed. The conization result was adenocarcinoma of the uterus invading cervix.

In this case the pitfall might come from the limitation of colposcopy that could not detect the disease up in the endocervical canal. In reviewing the history and physical examination, the possible disease of the patient could also be in the uterus. So the suggestion of the expertise of the team was that we should perform fractional curettage completely in the group of patients suspected to have abnormalities in the uterus in order not to miss the cases like this.

In the 49 patients who had final tissue diagnoses, the comparison of colposcopy results with final tissue results was shown in table 6.

From table 6., 10 patients were wrong diagnosed. One patients was invasive adenocarcinoma of uterus invading cervix. One invasive cervical cancer was missed diagnosed by colposcopy. Eight patients were severe dysplasia. The percentage of wrong diagnoses in this group was 16.3 % (10 from 49). Diagnostic performance of colposcopy in this



situation cannot be accepted.

There were 4 patients (8%) whose colposcopy were more severe than final histopathology from conization or hysterectomy. This result was compatible with Benedet et Al. (1976).

The overall agreement rate between colposcopy and final tissue diagnosis from conization and hysterectomy was low. Wrong diagnosis of Colposcopy was also serious because it could not detect the severe stage. Then colposcopy could not substitute the final tissue diagnosis from conization or hysterectomy.

The accuracy of colposcopy is higher in the satisfactory colposcopy (Benedet, 1976). From 69 patients, 54 patients were satisfactory colposcopy. The table 10 shows the result of histopathology of the cervical tissue from colposcopy directed biopsy compared with final histopathology in the satisfactory colposcopy group.

The accuracy of colposcopy is the percentage of CIN lesions (detected by colposcopic directed biopsy) that were within one degree of the final histopathological staging (same staging plus one higher and one lower staging) (Benedet, 1976).

The accuracy of colposcopic directed biopsy was 98.14 percent in the satisfactory group.

If the accuracy was defined as the exact agreement between colposcopy and final histopathology, the accuracy was 85.18 percent (bold letter in the table, 46 from 54).

From this table, 8 patients were wrong diagnosis. One patients was invasive adenocarcinoma of uterus invading cervix.

One patients was mild dysplasia. In mild dysplasia, the error was acceptable. Five patients were severe dysplasia. Although it was in the range of plus or minus 1 stage, this error could not be accepted; because missing potentially invasive disease was very dangerous to the patients. One invasive case was missed diagnosed by colposcopy. This was also dangerous to the patient. The percentage of wrong diagnoses in this group was 14.8 % (8 from 54).

Although accuracy of satisfactory colposcopy was higher than the overall group, diagnostic performance of colposcopy in this group could not be accepted; because the wrong diagnostic rate was still high and critically dangerous.

The sensitivity of satisfactory colposcopy in diagnosis of cervical neoplasia is 94.87% (37 from 39). The application of colposcopy must carefully avoid the wrong diagnosis of disease from upper genital tract such as uterine cancer.

In the satisfactory colposcopy group, 34 patients had further tissue diagnosis from conization or hysterectomy. Table 11. show the comparison between colposcopy results and final histopathology results from conization and hysterectomy.

The correct agreement rate was 67.64 % (23 from 34). The agreement in the acceptable range was 88.23 %. The satisfactory colposcopy although had high accuracy but the wrong diagnosis was serious, then colposcopy could not replace final tissue diagnosis from conization or subsequent hysterectomy.

## Suggestion

Colposcopy is one of the diagnostic test. It contains false negative or wrong diagnosis. The wrong diagnosis can be reduced by the increasing experience of colposcopists. The colposcopy cannot substitute the need for conization in low experience hand. The colposcopy cannot be the only diagnostic procedure of the cervical neoplasia. The colposcopy must be used in combination of other clinical procedures. Basic clinical methods such as History Taking, Physical Examination are still useful. The most important thing in the diagnosis of the disease is the clinical judgement of the physicians.

Limitation of this study is the time constraint for long term follow up. The researcher has a study time of only one year. This may not be enough for detection of silent neoplasia that are not diagnosed at the first time. The suggestion for the further study is that the researcher must have longer follow up time and strategies for keeping the patients on the follow up program. Another suggestion relates to the fact that the percentage of unsatisfactory group is higher than the other studies. This can result from the nature of disease in Thai women that differs from other countries. The factors contribute to this result should be studied in the future. Because colposcopy cannot be used accurately in these group of patients.

## CONCLUSION

Overall sensitivity of colposcopy in diagnosis of Cervical Neoplasia in 69 abnormal Pap smear women is 94.3 %.

The overall accuracy of colposcopy in 49 cases with final tissue diagnosis from Conization or Hysterectomy was 84 % in the range of standard compared to other studies. Colposcopy diagnosed the disease stage less severe than final histopathology in 16 % of the patients.

The sensitivity of colposcopy in diagnosis of cervical neoplasia in 54 satisfactory cases was 94.87%.

The accuracy of colposcopic directed biopsy compared with final tissue diagnoses in 34 satisfactory cases was 85.18 %.

Although colposcopy has high sensitivity and accuracy, the clinical application is limited because missed diagnosis cases were in serious stage. The application of colposcopy must carefully avoid the wrong diagnosis of disease from upper genital tract such as uterine cancer. Colposcopy could not replace conization in the diagnosis of cervical neoplasia. Diagnostic conization is still essential to rule out invasive disease in highly suspected patients. The physicians cannot rely on colposcopy when deciding to use conservative treatments. To use colposcopy in this setting, the colposcopists had to gain more experience than this situation.