Distinguished Expert Series

Colposcopy used in a primary setting (routine colposcopy): advantages and concerns

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Introduction

The colposcope is a binocular instrument used to study human tissue in vivo with magnification ranging from x5 to x25. It allows recognition of tissue changes not visible to the naked eye and can aid in the diagnosis of fine structural abnormalities that will have an important impact on patient management. It can be used in all parts of the body accessible for colposcopy in whatever way. However, it is mostly used to diagnose epithelial changes of the uterine cervix and, less frequently, lesions of the vulva and vagina. The colposcope was devised by Hinselmann in Germany as an instrument applicable for vaginal examination, hence the name (colpos - vagina).

In many parts of the world including Western Europe, the USA, Australia, etc., colposcopists see patients with an abnormal screening test, e.g. abnormal cytology, or who have a clinically suspicious cervix. This approach is called selective colposcopy, a practice with a plethora of literature.

Apart from the triage role, colposcopy has been used traditionally over generations as part of routine gynaecological examinations (routine colposcopy) in Central and Eastern European countries and in some other parts of the world, for example, over seven decades in Hungary as this country was the second to introduce colposcopy after Germany. This more general use of the colposcope has a number of advantages, but not without concern and has many opponents. The purpose of this editorial is to highlight the benefits of routine colposcopy and discuss the possible limitations apparently attached to it.

The role of colposcopy in cervical cancer screening

The role of colposcopy in managing women with abnormal cytology in the absence of a grossly visible lesion is relatively well defined, and colposcopy in this setting is rather and on aid to diagnosis and not a diagnostic test itself. "In this role it has become an integrated component of structured cervical screening programmes and an essential diagnostic step in those areas where, although not structured, cytology is used in a proportion of women" [1]. Cytology screening (Pap test) has been reported to carry the risk of false negativity in a varying magnitude of 20 to 50%, and several measures have been taken to overcome the high false-negative rates. These include the introduction of liquid-based cytology, automated cytology, HPV-testing in routine screening, etc. Surprisingly, screening colposcopy has not been recommended in reducing the drawbacks of cytology screening.

Colposcopy as a primary screening tool

The recognition that with the colposcope cervical intraepithelial carcinoma (CIN) can be identified, even in the absence of abnormal cytology, has lead to the "textbook's" recommendation that abnormal colposcopic findings constitute an indication for conisation. Such recommendation is still in place officially but conisation has been replaced by loop excision. Not surprisingly, the first systemic evaluation of this approach by the author, including approximately 1,500 patients who underwent conisation due to abnormal colposcopic and or cytologic findings, revealed a 20-30% unnecessary surgical rate, which is certainly unacceptable. On the other hand, in the presence of low-grade cervical intraepithelial neoplasia (CIN 1 and 2) only the colposcopic findings were abnormal in 66% of the cases, and abnormal Pap smears occurred only in 8%, whereas, in 26% both the colposcopy and cytology were abnormal. In the CIN 3 group, abnormal colposcopic findings alone occurred in 10%, abnormal cytology only in 20%, and in 70% of the cases both cytology and colposcopy indicated high-grade lesions. Several subsequent studies have confirmed these findings, suggesting that 1) approximately 30% of cytology-negative abnormal colposcopic findings does not represent CIN, and 2) as much as 50% of CIN, particularly but not invariably low-grade lesions, is missed with cytology screening. Thus, colposcopy is more sensitive but less specific than cytology in CIN screening and the probability that a person with positive cytology and abnormal colposcopy has CIN is high. Abnormal cytological findings, particularly low-grade squamous intraepithelial lesions (LSIL) and atypical squamous cells of undetermined significance (ASCUS), do occur in the absence of CIN in a substantial proporion, i.e. cytology is also associated with false-positive rates.

Based on the experience with screening colposcopy, gynaecologists face the following dilemma: 1) the high-false positive rates of colposcopy, i.e. its low specificity, 2) cytological screening is invariably associated with false-nega-

tive rates of variable degree, which may be quite high; the magnitude is significantly greater than the generally quoted 10-20%, 3) what the clinical implication is of cytology-negative CIN, and, 4) how to interpret abnormal colposcopic features when the cytology is negative and what the therapeutic recommendations are. Noone would argue that performing loop excision based on abnormal colposcopic features not due to CIN or an invasive lesion is an unnecessary overtreatment. Missing high-grade lesions or invasive carcinoma as a result of false-negative cytology, however, has more serious consequences.

One approach of reducing unnecessary surgical excisions (conisation, loop-excision) associated with colposcopic screening may be the use of the colposcopy grading system in treatment planning; performing excisional biopsy in cytology-negative cases only when the score is high. Women with low scores may be colposcopically and cytologically folllowed-up at regular intervals, with directed-punch biopsy if the lesion persists. Although there are some valuable colposcopic grading systems [2], separation of abnormal colposcopic findings into minor and major changes based on the latest Federation for Colposcopy and Cervical Pathology (IFCPC) terminology recommendations is a simple and practical approach. Indeed, in the presence of major abnormal colposcopic findings the incidence of non-CIN lesions is very low (approximately 5%, unpublished data). Whether the price for improving the specificity of colposcopy as a screening tool by indicating surgical interventions only in the presence of major colposcopic abnormalities when cytology is negative, is reducing its sensitivity remains to be elucidated. HPV typing has been suggested as an alternative; excising the lesions only when an oncogenic HPV type is identified. However, the implication of HPV testing is far from conclusive, and this approach is controversial at best. The role of molecular markers in this setting has yet to be determined and further research is warranted.

The concept of cytology-negative CIN

As discussed, studies on screening colposcopy have invariably demonstrated that a substantial number of CIN is not detected with cytology, and this has led to the concept of "cytology-negative CIN", a possible clinical entity that has not been recognised and studied adequately. Approximately 90% of cytology-negative CIN is low grade and not more than 10% is CIN 3 or CIS. CIN develops as a continuum from the basal layers up to the superficial layers of the squamous epithelium, replacing the lower part at the beginning with continuous growth ending up with full replacement of the epithelium as carcinoma in situ. One explanation of cytology-negative CIN may be that in the presence of low-grade CIN the exfoliated cells come from the normal superficial layers and the transformed dysplastic cells remain hidden. This theory is in line with the findings that the vast majority of cytology-negative CIN is low-grade; CIN 1 and 2. We do not know the natural history of low-grade cytology-negative CIN. It is likely that many of such lesions (perhaps more than 90%) regress spontaneously and therefore require no treatment. This further increases the rate of unnecessary biopsies in the cohort of women selected by abnormal colposcopy not associated with cytological abnormalities. It may also be possible that progressing low-grade lesions may be identified by subsequent cytology before invasive cancer develops, depending on the time interval elapsing between the two Pap smear screenings. Whether or not this is the case has yet to be determined and therefore cytology-negative CIN remains of concern. This is particularly true when high-grade CIN is not detected by cytology. The latter may well be due to false-negative cytology rather than the inherent ability of cytology to identify such lesions.

What makes matters more confusing includes the findings that CIN is commonly multifocal with low- and high-grade CIN frequently occurring in the same patient. In young women, HPV infection is not uncommon, mostly transient and re-infection or exacerbation of the primary HPV infection is also frequent. Similarly, multiple HPV types, including oncogenic and non-oncogenic types, can be identified in the same lesions. CIN also frequently occurs in teenagers and in women in their twenties, and as pointed out previously, most of them regress spontaneously, a few, however, can progress to high-grade CIN within a short period of time. Consequently, such women require continuous surveillance. All of these demonstrate the difficulties in explaining the relation between colposcopic and cytological findings and clearly show that further studies are needed regarding the clinical implications and the oncogenic risk of cytology-negative CIN before drawing final conclusions.

Additional thoughts for and against primary screening colposcopy

1. The prevalence of a disease in a target population has influence on the positive and negative predictive values (PPV, NPV) of a test, in this case colposcopy. Due to the significantly lower incidence of CIN in the general population as compared to that among women with abnormal cytology, the majority of primary colposcopic examinations will be normal and identification of CIN is a relatively rare event. This is reflected in the difference between the predictive values of the two approaches (66% in the abnormal cytology group versus 5% in the population) [1].

2. One might consider performing colposcopy in a low-yield population "waste of time and money", which does not appear to be the case. In addition to reassuring women with negative cytology that CIN is indeed not present, provided the colposcopy is satisfactory, affords the opportunity to see a great deal of normal colposcopic findings and benign lesions when colposcopy is used in the primary setting. Such experience is bound to increase the ability to identify

abnormalities and suspicious lesions. Additionally, long-term colposcopic evaluation of benign diseases helps towards a better understanding of the natural history of the diseases. When colposcopy is used as part of the triage in evaluating cytological abnormalities, the learning curve of normal colposcopy may be quite long and in some respects inadequate. The contrary is also true; not seeing enough abnormal colposcopic findings may render the colposcopist inexperienced in diagnosing delicate details of abnormal findings, which can have clinical significance.

3. Cytologists find it tremendously helpful to be aware of the colposcopic findings prior to evaluating the cervical smears. Thus, screening colposcopy is also beneficial for cytopathologists.

4. As for cost-effectiveness, when colposcopy is part of the routine gynaecological examination, there is no extra charge. The expense of a colposcope itself is covered not only by indirect ways including reassurance, reduction of missing high-grade CIN on cytology, minimising anxiety and fear as compared to that associated with referring patients to a colposcopic clinic, etc., but by avoiding the enormous cost of the referral colposcopy.

5. Concerns of low-quality colposcopic practice in countries where all gynaecologists use the colposcope as a primary screening tool have been raised. Some of the reasons include a lack of studied CIN cases and a lack of specialised structured training in colposcopy. Colposcopy training is part of the specialty training in obstetrics and gynaecology and there are difficulties in quality control and audit due to the high number of colposcopists. However, these are not the inherent limitations of the general use of colposcopy; rather it is a matter of national health policy and organisation.

6. Unlike selective colposcopy, primary or routine colposcopy allows immediate treatment planning once the Pap smear result is available.

Colposcopic terminology in light of routine colposcopy

In the latest edition of the International Terminology of Colposcopy published by IFCPC, the term "unsatisfactory colposcopy" is used and defined as: "An unsatisfactory colposcopy examination occurs when the squamocolumnar junction cannot be visualised. It may also occur if associated trauma, inflammation, or atrophy preclude a full colposcopic assessment, or when the cervix is not visible" [3].

One may wonder what the term "unsatisfactory colposcopy" means. Does it mean that when the squamocolumnar junction cannot be visualised the colposcopy examination sheds no information? It is not the case. Using colposcopy and cytology for screening the possible findings when the squamocolumnar junction cannot be visualised, and their clinical implications are summarised in Table 1.

Table 1. — The value of colposcopy when the squamocolumnar junction cannot be visualised.

The squamocolumnar junction cannot be visualised		Clinical implications
Colposcopy of the exocervix	Cytology	
Abnormal	negative	CIN may be present, the cytology appears false negative
Abnormal	positive	The lesion is most likely located on the exocervix
Normal	negative	It is very unlikely that the patient has CIN or cancer; the false negative rate is next to zero
Normal	positive	The lesion is in the endocervical canal

With this in mind, the term "unsatisfactory colposcopy" may be restricted when "associated trauma, inflammation, or atrophy preclude a full colposcopic assessment, or when the cervix is not visible".

If the cervix but not the whole transformation zone can be colposcopically assessed, i.e. the squamocolumnar junction cannot be visualised, the following terms may be more appropriate:

- the squamocolumnar junction not visible, colposcopically normal ectocervix;
- the squamocolumnar junction not visible, colposcopically abnormal ectocervix.

Other advantages of routine colposcopy

1. Vulva and vaginal diseases

Subclinical diseases of the vulva and vagina that are not possible to identify with the naked eye, can only be picked up with the aid of screening colposcopy as these areas are not targets of cytology screeening. This has particular clinical implications in women with endometrial or vaginal carcinoma because the vagina is by far the most frequent site of recurrence (see follow-up).

In diagnosing visible lesions of the lower genital tract irrespective of whether they are benign, malignant or just a normal variant, colposcopy is very helpful, avoiding thereby false diagnoses and occasionally inappropriate treatment. Such approach may not be utilised when colposcopy is not at hand because these patients are rarely referred to colposcopy clinics.

Colposcopically aided treatment of vulva/vaginal diseases, particularly micro-lesions, has several advantages including precise application of topical treatment by delineating the margins clearly, and thereby decreasing complications

and avoiding insufficient therapy. In spite of this, most lesions of the vulva, vagina, perineum and perianal region are treated by general gynaecologists without colposcopy, i.e. outside the colposcopy clinics in those countries where colposcopy is not used in primary settings.

2. Physiologic burden of referral to colposcopy examination

In studying the psychological aspect of colposcopy, *Freeman-Wang and Walker* [4] pointed out some aspects of anxiety attached to referral to a colposcopy clinic. Some may argue that this could be due to the knowledge of having an abnormal smear. The authors, however, highlight the importance of fear and anxiety from the colposcopy examination itself, as patients are not well informed what a colposcopy examination is about. They know they are facing an investigation for which they are scheduled and referred to. In contrast, experience with routine colposcopy practiced as part of gynaecological examination does not show significant, if any, anxiety associated with colposcopy.

3. Follow-up

Long-term, regular follow-up is commonly required for patients who have undergone treatment (punch or cone biopsy, hysterectomy, etc.) of CIN, for those with low-grade smears (ASCUS, LSIL) who were not treated, and even for women with benign lesions of the uterine cervix, e.g. congenital transformation zone. Similarly, continuous surveillance is needed in women with vulva/vaginal diseases as well as following treatment of invasive genital tract carcinomas. Although well conducted studies are lacking, many believe that colposcopy is an integral component of follow-up. In these cases, if the colposcopy is carried out in a colposcopy clinic and not by the patient's primary gynaecologist who is responsible for and does the regular check-up, two appointments are required. Alternatively, a woman may be followed-up by a colposcopist only and not by her primary physician who may have treated the patient. However, if the patient is also seen by her referral physician and not only in the colposcopy clinic, again the patient is examined twice apart in time. Concerns, including financial, psychological and other implications attached to this practice are obvious, and this is again an argument in favour of more general use of colposcopy.

What appeared particularly useful in following-up women with invasive cancer includes routine colposcopy of the vagina especially of the vaginal vault. Suspected lesions can readily be identified using acetic acid colposcopy. Vaginal walls stained positive when the iodine test is applied do not harbour lesions. Dark brown staining is easily recognised clinically, while the assessment of light brown Schiller staining is not always easy without colposcopy. In this setting, colposcopy is so reliable that cytology is necessary only when colposcopy is unsatisfactory, mostly due to dog ears of the vault. Advantages of replacing follow-up cytology with follow-up colposcopy are several: a) reassuring patients immediately when the follow-up examination is negative, thus avoiding anxiety attached to waiting for cytology, b) reassurance for the physician because the whole vagina can be examined colposcopically but not cytologically, and c) preventing early lesions from escaping early detection.

Is the practiced method of colposcopy different when used in primary setting?

The colposcopic appearance of cervical lesions including CIN and microinvasion may vary according to the technique used, and therefore it is important to set up guidelines on how to perform colposcopy. Such guidelines have been well established [5]. In brief, the cervix is exposed in the usual way and examined with the naked eye. This is followed by an acetic acid application and a colposcopy examination. Some colposcopists prefer examining the cervix with the colposcope at low magnification with or without applying a saline soaked cotton wool prior to the application of acetic acid. Lastly, Schiller's iodine test is performed, which, however, can be omitted in the majority of cases, as it does not add much to a proper colposcopy assessment. There are cases, however, when the iodine test is useful and should be applied, for example, it is particularly important in examining the vagina.

Colposcopic assessment is not much different when performed in a primary setting as compared to colposcopy in a selected setting. Saline application is uncommon, and, when cytological screening is performed, the Pap smear is taken just after the cervix is exposed prior to colposcopy. Primary colposcopic assessment does not take more than two to three extra minutes unless abnormal findings are present requiring detailed examination; similarly to that of performing colposcopy as part of a triage in women with abnormal cytology.

Conclusions

Whether colposcopy is used to evaluate abnormal cytology, i.e. selectively within cervical cancer screening programmes, or as part of a routine pelvic examination, is a matter of national health policy and tradition. Physician preference also plays a role. The author uses the colposcope in his everyday practice and for him routine colposcopy is an invaluable tool. It has a number of advantages as outlined above. The major concern in this setting is the low specificity of screening colposcopy, which, however, can be overcome with experience and proper judgement, e.g. by grading colposcopic abnormalities. In light of the benefits of routine colposcopy one may wonder why it is not used

more widely. If the reason is financial, it is perhaps unethical. The need for using the colposcope more liberally is also reflected in the increasing tendency of making referral criteria for colposcopy less stringent.

The purpose of this editorial is not to dictate but to pave the way by highlighting the major points and controversies of routine colposcopy for practicing clinicians in order to help them make their own decision in terms of routine or selective colposcopy practice. Whatever the approach, training, skills and evidenced-base practice with an outcome-based audit is a prerequisite for colposcopy.

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