



Comparing the Effectiveness of Different Scoring System in “See and Treat Approach” for Cervical Precancerous Case Management

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Abstract

Indian healthcare is largely in the private domain which is not covered under any reimbursement program. Patients below the poverty line (BPL patients) show higher prevalence of sexually transmittable infections, of which HPV is one of the major contributor. “See and Treat” approach is largely favoured for treating the high grade cervical or lower genital abnormalities suspected to proceed to invasive disease in the foreseeable future. Colposcopy procedure is both diagnostic as well as curative for high grade cervical precancer and thus occupies an undisputed centre stage of cervical cancer prevention and control program in the clinical set up. A Reid Colposcopy Index (RCI) for grading the lesion severity determines colour change due to acetic acid, Margin Vascular pattern of the lesion along with change in colour with Lugol’s iodine and converts the subjective threshold for diagnosis and hence treatment intervention into a semiobjective one. The swede score has added the parameter of size of the lesion as well. The colposcopy grade scoring system therefore guides prediction of histologic diagnosis of the disease as well as determines which of these high grade lesions warrant immediate treatment by simple procedures like cryotherapy, thermocoagulation, leep therapy. “See and Treat” approach is particularly also beneficial in the rural population settings where a trained clinical or pathological expertise may not be immediately available and skilled health workers may be trained to detect and eliminate the precursor disease. In our study, out of 650 cases who underwent colposcopy for varied reasons, 84 cases were detected to have lesions (12.9%). These lesions were scored according to RCI and Swede scoring systems. The lesions were biopsied for prospective histopathological findings. The clinical sensitivity, specificity, PPV, NPV, concordance and discordance between the two scoring systems were determined with histopathological diagnoses of high grade disease. In Reid’s scoring system, RCI score of ≥ 4 is taken as qualifying for HSIL detection and thus warrants treatment. In Swede scoring, a score of ≥ 5 is considered positive, warranting treatment. As per standard guidelines and protocol, CIN 1 cases are usually kept under surveillance whereas CIN 2 and CIN 3 cases are taken up for treatment. In our practice, all case of CIN 1 were recalled for follow up, RCI scored well in terms of all the above parameters. RCI scored better as compared to Swede in terms of comparing overtreatment – RCI 24 % as compared to 42 % in swede. In our data of 84 samples the correlation between the scoring system of Swede and RCI was 0.65. However, the REID scoring had high concordance with histopathology compared to Swede system ($R = 0.71$ between REID and HP and $R = 0.65$ between Swede and HP). RCI is a better scoring system to avoid unnecessary over treatment as compared with Swede system in “See and treat” programs adopted in rural areas and camp set up. As per our study, our recommendation will be to safely use Swede score cut-off at ≥ 5 , in the case of Reid score a cut-off of at ≥ 4 in “See and Treat” program.

Keywords: High-Grade Squamous Intraepithelial Neoplasia (HSIL); Loop Electrosurgical Excision Procedure (LEEP); Cervical Intraepithelial Neoplasia (CIN).

Introduction

The cervix is the lower part of the uterus. Cervical cancer is caused by a virus called HPV. The virus spreads through sexual contact. Most women's bodies are able to fight HPV infection. But sometimes the virus leads to cancer. Epidemiological studies have established human papillomavirus (HPV) infection as the central cause of invasive cervical cancer (ICC) and its precursor lesions [1]. Identifying HPV types that preferentially progress from high-grade squamous intraepithelial lesions (HSIL) to (ICC) invasive cervical cancer has implications not only for follow-up protocols in ICC screening programmes, but also for prophylactic type-specific HPV vaccine trials [2]. According to the study by Smith JS., *et al.* ICC refers both to squamous cell carcinoma (SCC)/unspecified histology (85% of included cases) and adeno/adenosquamous carcinoma (ADC, 15%). HSIL refers both to cytologically-detected lesions as classified by the Bethesda system (44% of included cases), and those reported as histologically diagnosed cervical intraepithelial neoplasia (CIN)2 (17%), CIN3 (37%), or carcinoma in situ (2%) [3].

In developed countries, regular screening with a Pap smear has been shown to effectively lower the risk for developing invasive cervical cancer, by detecting precancerous changes. However, in developing countries, only approximately 5% of eligible women undergo cytology-based screening in a 5-year period [4]. If women ever do go to a clinic, which they do so when the disease has advanced to a stage that cannot be successfully treated with local resources. Efforts to improve awareness of the target population can result in early detection of precancerous lesions, leading to improved survival from cervical cancer in developing countries [5].

Cervical intraepithelial neoplasia (CIN) is a premalignant lesion that may exist at any one of three stages: CIN1, CIN2, or CIN3. If left untreated, CIN2 or CIN3 (collectively referred to as CIN2+) can progress to cervical cancer. It is estimated that approximately 1–2% of women have CIN2+ each year. This rate is reported to be higher in women of HIV-positive status, at 10% (1–5). The standard practice is to screen women using cytology (Pap test), and when cytology results are positive the diagnosis of CIN is based on subsequent colposcopy, biopsy of suspicious lesions, and then treatment only when CIN2+ has been histologically confirmed. Available screening tests include a human papillomavirus (HPV) test, visual inspection with acetic acid (VIA), and cytology (Pap test). Available treatments include cryotherapy, large loop excision of the transformation zone (LEEP/LLETZ), and cold knife conization (CK).

‘See-and-treat’ electrosurgical loop excision of the cervical transformation zone is an excisional surgical procedure that enables simultaneous histologic diagnosis and treatment of cervical precancerous lesions, thus eliminating the need for a cervical punch biopsy and an additional visit [7]. In developed countries, selective use of ‘see-and-treat’ LEEP is practiced by experienced colposcopists who are able to reliably differentiate low-grade from high-grade disease by means of colposcopy; it is resorted to mostly if cytologic and colposcopy findings unequivocally indicate high-grade cervical intraepithelial neoplasia. On the other hand, the Indian studies [8,9] involved screen-positive women with all grades of precancerous lesions suspected at colposcopy. Thus, it is not surprising to see a high level of overtreatment reported in the Indian studies as compared to studies in developed countries.

Method and Materials

Tools used

- Digital colposcope
- 5% Acetic Acid
- Lugol's Iodine
- Histopathology

Histopathology	Number
CIN1	46
CIN 2	21
CIN 3	6
SCC	4
Chronic cervicitis	5
Normal	2
Total	84

Table 1: Histopathological findings of lesion biopsy.

Total 650 cases of Colposcopy were analysed during the time period from Jan 2015 to December 2016 at our referral colposcopy centre at Thane, Mumbai. Out of 650 cases 84 cases were detected to have lesions (12.9%). These lesions were scored according to RCI and Swede scoring systems. The lesions were biopsied for prospective histopathological findings. The clinical sensitivity, specificity, PPV, NPV, concordance and discordance between the two scoring systems were determined with histopathological diagnoses of high grade disease. Literature shows the histopathology including *in situ* hybridization (ISH) is less sensitive than the

HPV testing and hence it is best to use it as a confirmatory test on equivocal biopsies to resolve LSIL. It is also well known that nearly 30% CIN2s and 10% of CIN3s may be negative by histopathology including ISH. Therefore, a high precision colposcopic scoring pattern is very essential to arrive at a decision to treat to avoid under- or over-diagnoses.

Observation

In Reid’s scoring system, RCI score of ≥4 is taken as qualifying for HSIL detection and thus warrants treatment. In Swede scoring, a score of ≥ 5 is considered positive, warranting treatment. So, these are the criteria for accurate detection through different scoring systems as per the study done. Table 1 shows the histopathological findings of the lesion biopsy distinguished and categorised separately.

As per standard guidelines and protocol, CIN 1 cases are usually kept under surveillance whereas CIN 2 and CIN 3 cases are taken up for treatment. In our study we found good concordance with HP in cases of CIN 1 by both the scoring systems. CIN 1 cases were asked to come for follow up after a year.

Method	CIN 1		CIN 2		CIN3	
	SWEDE (n-20)	RCI (n-34)	SWEDE (n-43)	RCI (n-40)	SWEDE (n-21)	RCI (n-10)
CONCORDANCE	75% (n-15)	85% (n-29)	25% (n-11)	42% (n-17)	47% (n-10)	70% (n-7)
DISCORDANCE	25% (n-5)	14% (n-5)	74% (n-32)	57% (n-23)	52% (n-11)	30% (n-3)

Table 2: Comparative observation of concordance and discordance with HP by both the scoring systems.

We further carried on the analysis of discordance in cases of CIN 2 and CIN 3 with respect to HP using both the systems.

	SWEDE	RCI
CIN 2	32	20
CIN 3	3	0
Total	35	20
Percentage overtreatment	42%	24%

Table 3: Observation on Discordance of CIN 2 and CIN 3 reported by Swede and RCI with HP findings.

As per the guidance, all high grade lesions i.e. CIN 2 and 3 are treated in the See and treat program.

HP	CIN 2		CIN 3	
	SWEDE N = 32	RCI N = 23	SWEDE N = 11	RCI N = 3
Normal	1	1		
Chronic cervicitis	1	1	1	
CIN 1	30	18	2	
CIN 2			8	3
CIN3		3		
OVERTREATMENT	32	20	3	0

Table 4: Observative comparison on overtreatment using both the scores.

Comparison of the sensitivity, specificity, NPV, PPV values for both the scoring system Reid yielded a better rate of detection of CIN 1, CIN 2, and CIN3 confirmed by histopathology exam.

	CIN 1		CIN 2		CIN 3	
	Swede	RCI	Swede	RCI	Swede	RCI
Sensitivity	36%	63%	55%	81%	100%	70%
Specificity	55%	81%	50%	63%	85%	96%
NPV	59%	75%	78%	91%	100%	90%
PPV	75%	70%	25%	43%	44%	70%

Table 5: Comparative observation for CIN detection by Swede and Reid scores.

Considering all HSIL (CIN 2 and 3) cases to qualify for See-and-Treat approach, we should have a high sensitivity and specificity parameters accurately determined in order not to miss any treatment.

RCI showed better specificity and an average sensitivity with good PPV for both CIN 2 and 3. Swede showed better sensitivity and NPV over RCI.

In our practice, all case of CIN 1 were recalled for follow up, RCI scored well in terms of all the above parameters. RCI scored better as compared to Swede in terms of comparing overtreatment –RCI 24 % as compared to 42 % in swede. In our data of 84 samples the correlation between the scoring system of Swede and RCI was 0.65. However, the REID scoring was more correlated with

histopathology compared to Swede system (R = 0.71 between REID and HP and R = 0.65 between Swede and HP).

Discussion

Based on this study, we propose to use Swede score cut-off at ≥6 to detect about 94% of histopathologically confirmed CIN2+ cases. Likewise, in the case of Reid score a cut-off of at ≥4 the detection rate of CIN2+ cases was better (94%).

The purpose of scoring the lesions is to identify the high grade lesions and to treat them either by ablative or Excisional methods. Excisional method i.e. LEEP should be performed in c/0 Swede 8 and above and in c/o RCI-Lesions scoring 7 and 8. Thus the tissue can be sent for HP to ensure lesion free margins and in c/o Preclinical SCC further treatment can be provided.

Most rural India faces a stiff challenge of getting the qualified services of the histopathologists. Histopathology itself is not perfect and tends to be biased and influenced by the overt clinical findings. Many cases fail to come for follow up treatment. Hence using RCI scoring system provides an excellent method to analyse the lesions and to further treat all the high-grade lesions [7-9].

Difference of both scoring system	Modified RCI	Swede
About the scoring system	More descriptive, COLPOSCOPY IS AN ART	Art converted to Points.
Points included	Color, margins, BV, Lugols MAX- 8 POINTS	Color, Margin and surface configuration, BV, Lugols, Size of the lesion MAX-10 POINTS
Color	More descriptive 0--Snowy white, transparent- 1-Gray white, 2-Oyster white or persistent	0-No, Transparent, 1-Milky white but opaque,2-Distinct.
Margins-	0-Jagged, angular, diffuse, satellite lesions 1-Sharp distinct 2-Raised, rolled margin	No, diffuse Sharp, Jagged, Angular, satellite Sharp distinct, difference in levels

Lugols	0-Brown, Yellow if above score is <3,1-Variegated, Patchy 2-Yellow if above score->4	BROWN Patchy, Variegated Yellow
Our study of 650 cases, 84 lesion cases detected (12.9 %)	RCI	SWEDE
% concordance with HP co-relation with HP (R)	CIN 1-85, CIN 2-42, CIN 3-70 0.71	CIN 1-75, CIN 2-25, CIN 3-47 0.65
% Overtreatment	24 %	42%
Sensitivity Specificity	CIN1-63%, CIN 2-81% CIN 3-70% CIN 1-81%, CIN 2-63%, CIN 3-96%	CIN1-36%, CIN2-55%, CIN3-100% CIN 1-55%, CIN2-50%, CIN3-85%
NPV PPV	CIN1-66%, CIN2-91%, CIN3-96% CIN1-70%, CIN2-43%, CIN3-70%	CIN1-59%, CIN2-78%, CIN 3-100% CIN1-75%, CIN2-25%, CIN3-44%
Threshold for see and treat	4 =/> (97% of CIN2+on HP)	6 +/> (94% of CIN 2+ cases on HP)
Learning curve	HIGH	LOW

Table 6: Inference in nut shell.

Conclusion

RCI is a better scoring system to avoid unnecessary over treatment as compared with Swede system in “See and treat” programs adopted in rural areas and camp set up. As per our study, our recommendation will be to safely use Swede score cut-off at ≥6, in the case of Reid score a cut-off of at ≥4 in “See and Treat” program.

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