RESEARCH ARTICLE

A method to improve the accuracy between the presumed depth of excision and the actual depth of excision in women receiving LLETZ cervical treatment; a single-center, two-operator experience

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Abstract

Background: We aimed to determine whether continuous auditing of the presumed depth of excision and comparing with the actual depth of excision in women having large loop excision of the transformation zone (LLETZ) improves the ability to acquire the desired depth of excision.

Methods: This was a prospective study of women submitted to a single LLETZ treatment between 2017-2018. Two senior colposcopists recorded what they presumed was the depth of excision at the time of treatment and the subsequent histopathology report provided the actual excised depth. Multiple linear regression identified independently associated parameters with the difference between presumed and actual excision depth. Non-linear regression determined the learning plateau defined as the theoretical minimal score of difference one could achieve with infinite practice.

Results: There were significant differences in practices with the first colposcopist using an 18-mm loop and the second colposcopist a 15-mm loop in the majority of cases. The median absolute and percentage difference between the presumed and actual excised depth was 2 mm and 16.6 % and 3.5 mm and 35.4 % for the two colposcopists, respectively. A learning plateau was identified only for the first colposcopist. We found that auditing consecutive excisions decreased significantly the difference between the presumed and actual depth of excision with a learning plateau at 2.2 mm of absolute difference and 22.6 % of percentage difference and with a learning rate of 13 cervical excisions.

Conclusion: There might be a benefit in auditing our treatment practice as there seems to be a learning plateau through this method. HIPPOKRATIA 2018, 22(3): 113-121.

Keywords: large loop excision of the transformation zone, LLETZ, intraepithelial neoplasia, CIN, learning plateau, learning curve, audit

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Introduction

In the United Kingdom, women with cervical intraepithelial neoplasia (CIN) are usually treated with large loop excision of the transformation zone (LLETZ), with only a small number of colposcopy units offering ablative treatment as an alternative[1,2]. Since its first introduction in 1990, the LLETZ method is amongst the most popular excisional cervical treatment techniques as it allows for the histopathological examination of the removed cervical tissue with a precise assessment of the margin status[3]. It has been reported in the literature that when performing LLETZ cervical treatment, the depth of cervical excision represents a significant risk factor associated with both the risk of future preterm birth and the risk of recurrence of CIN disease.

A nested case-control study has reported that small cervical excisions of less than 10 mm conferred no additional risk of preterm birth, however deeper and repeated excisions progressively increased the frequency and severity of preterm birth[4]. Another study demonstrated that the risk of preterm birth increased three-fold when the length of excision exceeded 12 mm when compared to those that measured less[5]. Moreover, a large population-based study estimated that the risk of preterm birth increased by 6 % for every mm of the depth of excision[6].

In an attempt to remove less cervical tissue during excisional treatment so as to decrease the theoretical risk of preterm birth, there are reports that this might increase the oncological risk of disease recurrence. According to the National Health Service Cervical Screening Programme (NHS-CSP) guidance, excisional techniques for treating ectocervical lesions should remove tissue to a depth of more than 7 mm given the fact that endocervical crypts involved by CIN2 or CIN3 may traverse to a

maximum depth of 5.22 mm from the surface of the cervix[7-9]. There are reports that in women of young age, the optimal cut-off depth for the complete excision of CIN lesions is 10 mm[10,11]. If margins are incompletely excised it has been shown that this increases by six-fold the risk of high-grade cervical disease recurrence at follow-up[12].

It has been suggested that when considering treatment in young women of reproductive age, treatment should always be tailored to treat the disease effectively and at the same time to minimize the potential risk of future adverse obstetric morbidity[2]. Nevertheless, there is scarce data in the literature as to how to achieve this and therefore, to improve the surgical performance of LLETZ treatment. Even though the optimal cut-off depth for complete excision of CIN has been reported to be 10 mm[10], nevertheless more than half of women in that study had a cone length that exceeded 11 mm. There have been several reports of training models designed to improve the surgical skills and performance during LLETZ excision, but none have addressed the issue of how to improve the accuracy between the desired depth of excision at the time of treatment when compared to the actual depth that has been ultimately excised[13,14].

The primary objective of our study was to determine whether the method of continuous auditing of the presumed depth of excision and comparing with the actual depth of excision in women who had LLETZ treatment, improves the accuracy and the ability of the colposcopist to acquire the desired depth of excision. To the best of our knowledge, this is a novel and innovative study in the literature reporting on ways to improve the colposcopist's performance and accuracy during a cervical excision.

Material and Method

This was a prospective study of women who were treated with LLETZ cervical treatment at the Shrewsbury and Telford Hospital NHS Trust between January 2017 and February 2018. The study received formal approval for the collection and management of women's data from the audit department of Shrewsbury and Telford Hospital NHS Trust [Reg. No: 4077/6-2018]. We included women who had a single LLETZ cervical treatment and whose cervical tissue was removed in a single fragment. Women with a previous excisional or previous ablative cervical treatment and those where the cervical lesion was removed in multiple fragments were excluded from the analysis.

The indications for excisional treatment included CIN2 or CIN3 on a pretreatment cervical punch biopsy, a see-and-treat policy at first visit, and other indications such as persistent low-grade cytological abnormalities and/or post-coital bleeding. The see-and-treat policy was offered to women who presented with a moderate or severe dyskaryosis cytology test, their colposcopic appearance was consistent with the cytology test, and the patient was informed ahead of the visit about the possibility of having excisional cervical treatment.

Prospective continuous auditing of cervical excision

Two senior British Society of Colposcopy and Cervical Pathology accredited colposcopists (DP, PK) performed all colposcopy examinations and cervical treatments. Their individual experience in colposcopy exceeded more than ten years at the commencement of the study, and they were performing on a monthly basis between five to ten cervical excisional treatments and more than 50 colposcopy examinations. All LLETZ treatments were performed in outpatient settings with the use of local anesthetic (1-3 vials of Citanest 3 % with Octapressin; 2.2 ml vials).

The colposcopist performed the LLETZ excision and at the time of treatment recorded in the woman's medical notes the visually presumed depth of excision (i.e. 12 mm). When the histopathology result was available from the histopathology laboratory two to four weeks later, then the actual depth of excision was noted (i.e. 14 mm), and the colposcopist who performed the treatment was informed of the result. The same colposcopist then continued with this process of continuous auditing of presumed and actual excision depth during consecutive excisional treatments. The loop sizes that were used had a depth that varied between 12 mm, 15 mm, 18 mm or 20 mm, and all had the same width of 13 mm (Meditech Systems Ltd., Dorset, UK).

Sample size

We calculated that a sample size of 60 cases of cervical excision would need to be included in the study in order to detect with a 90 % power a significant difference between presumed depth and actual excision depth at an effect size of 0.38 and level of significance of 0.05.

The first colposcopist performed 62 excisions over a twelve-month period, and the second colposcopist performed 19 excisions over a three-month period at the latter half of the time interval of the study. There were two women treated by colposcopist A that had multiple fragmentations of the cervical tissue specimen and were therefore excluded from the study. There was one woman treated by colposcopist B that was excluded from the study as she had a previous LLETZ cervical treatment. The recruitment of the second colposcopist was decided to be for only three months as this reflected a more pragmatic approach since we considered it difficult for colposcopists in other units to be able to carry on prospectively auditing their excision practice for more than three months.

Cervical treatment data collection

The data collected from the colposcopy and histopathology databases involved the demographic features of women, such as the age at cervical treatment, parity, and smoking status at cervical treatment. With regards to their treatment, we recorded the cytology tests of women prior to the treatment (normal, borderline nuclear changes in squamous cells, mild/moderate/severe dyskaryosis, glandular abnormalities), the histopathology result of any

pretreatment cervical punch biopsy (CIN1, CIN2, CIN3), and the pretreatment colposcopic impression of the lesion grade (normal, HPV-human papilloma virus changes/ inflammation/benign, low-grade, high-grade) in accordance to the International Federation for Cervical Pathology and Colposcopy nomenclature proposed in 2011[15]. We recorded the size of the loop that was used (depth in mm's) and the transformation zone type as determined within the national guidance[9]. We also recorded the excised cervical tissue features such as the depth (mm) and volume of excision (cm^3), the surface of the base of the excised tissue (mm^2), the histopathology result, and the margin status.

Excised cervical tissue measurements after formalin fixation

In our study, the cervical tissue specimen was immediately placed after excision in a standard pot containing a 4 % solution of formaldehyde in water (10 % buffered formalin, GMAR™ Grade BF45, Genta Medical, Marston Business Park, York, UK). The specimen was transferred to the histopathology laboratory, and the diameters of the specimen were measured (in mm's) within 24-48 hours by the histopathologist prior to further processing and were reported in the histopathology report.

In the literature, it has been described that there is a 2.7 % of shrinkage to the longitudinal dimensions of the cervix due to formalin fixation when compared to a fresh specimen[16]. We did not, however, make any adjustments to the actual excision depth measurements in our analyses as we did not consider this degree of shrinkage to be clinically significant.

Definitions

The volume of excision was calculated from the formula of the ellipsoid: d1 x d2 x d3 x π/6, and the surface of the base of the excised tissue from the formula of the ellipse: d1 x d2 x π/4, where π =3.14 and d1, d2, and d3 were the three diameters of the tissue specimen as described in the histopathology report.

The absolute difference was calculated between the presumed by the colposcopist excision depth at the time of treatment and the actual excision depth recorded within the histopathology report two to four weeks later. The percentage (%) difference between presumed and actual excision depth was calculated as the ratio of absolute difference (numerator) to the actual excision depth (denominator).

To define the "learning curve" for excisional cervical treatment, non-linear regression was performed to fit an inverse curve with the case number used as the independent variable and the absolute difference between presumed depth and actual excision depth used as the dependent variable to yield an estimate of a (asymptote) and b (slope), according to the method described by Feldman et al[17]. The "learning plateau" was defined as the absolute difference between presumed depth and actual excision depth at the asymptote of the learning curve, and it represents the theoretical best score (minimal absolute difference) that a colposcopist could achieve with infinite cervical excision practice. The "learning rate" was then defined as the number of excisional procedures required to reach 90 % of the learning plateau potential. When the absolute difference between the presumed depth and the actual excision depth was a + 0.1 × (slowest difference - a), then the learning rate was the case number =10 × b / (slowest difference - a). We also performed this analysis on the percentage difference between the presumed depth and the actual excision depth.

We also performed consecutive groupings of women and divided the consecutive LLETZ excision procedures in groups of five. We compared the mean absolute difference between presumed and actual excision depth in each group with the subsequent group ("comparator group") to identify any possible reduction in the difference between presumed and actual excision depth with sequential cervical excisions.

Statistical analysis

Normally distributed variables were expressed as mean and standard deviation, whereas variables with a skewed distribution were expressed as a median and interquartile range (IQR). Qualitative variables were expressed as absolute and relative frequencies. Mann-Whitney and Kruskal-Wallis tests were used for the comparison of continuous variables between two or more groups, respectively. Spearman correlation coefficients were used to explore the association of two continuous variables. Wilcoxon signed rank test was used to perform paired comparisons between presumed and actual excision depth. Multiple linear regression analysis was conducted in a stepwise method (p for removal was set at 0.1 and p for entry was set at 0.05) in order to identify independently associated parameters with the absolute and percentage difference between the presumed depth and the actual cone depth. Adjusted regression coefficients (β) with standard errors were computed from the results of the linear regression analyses.

All reported p values were two-tailed. Statistical significance was set at $p < 0.05$ and analyses were conducted using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA).

Results

For the group of women who were treated by the first colposcopist and included in the study (n =60), the indication for treatment was CIN2 or CIN3 on pretreatment cervical punch biopsy in 23 women (38.3 %), a see-and-treat policy in 20 (33.3 %), and other indications such as persistent low-grade abnormalities and/or post-coital bleeding in 17 women (28.3 %). For the group of women who were treated by the second colposcopist and included in the study (n =18), the indication for treatment was CIN2 or CIN3 on pretreatment cervical punch biopsy in five women (27.8 %), a see-and-treat policy in nine (50 %), and other indications such as persistent low-grade abnormalities and/or post-coital bleeding in four women

(22.2 %).

There were no significant differences with regards to the age, parity, and smoking status of the two groups of women that were treated by the two colposcopists (Table 1). However, there were significant differences in the cervical excision practices between the two colposcopists (Table 2). The first colposcopist performed LLETZ cervical treatment in a total of 60 women and used an 18 mm loop size in the majority (81.7 %) of excisions. The second colposcopist performed LLETZ cervical treatment in a total of 18 women and used a 15 mm loop size in the majority (77.8 %) of excisions. There were no differences between the two colposcopists with regards to the excision margin status, the excised tissue histopathology result, and the excised cone volume or the base surface of the excised tissue.

For the first colposcopist, the median presumed excision depth was 12 mm (IQR: 10-12), and the median actual excision depth was 11 mm (IQR: 8.5-12). The median absolute difference between presumed depth and actual excision depth was 2 mm (IQR:1-3) and the median percentage difference between presumed depth and actual excision depth was 16.6% (IQR:10.0-30.0). For the second colposcopist, the median presumed excision depth was 10 mm (IQR: 8-15), and the median actual excision depth was 14.5 mm (IQR: 11-16). The median absolute difference between presumed depth and actual excision depth was 3.5 mm (IQR: 1-5), and the median percentage difference between presumed depth and actual excision depth was 35.4 % (IQR: 10.0-50.0) (Table 2).

There was no significant difference between the presumed excision depth between the two colposcopists (Table 2). However, the median actual excision depth was deeper for the second colposcopist when compared to that of the first colposcopist. Moreover, the absolute and percentage difference between presumed excision depth and actual excision depth was greater for the second colposcopist when compared to the first colposcopist (Table 2). Also, the second colposcopist in 83.3 % of cases (15/18) underestimated the presumed excision depth, meaning that the actual excision depth was much greater (data not shown). For the first colposcopist, the underestimation of excision depth occurred in only 36.7 % of cases (22/60) (data not shown).

The association between the absolute difference and the percentage difference between presumed depth and actual excision depth with the categorical characteristics for the women treated by the first colposcopist (n =60) is shown in Table 3 and Table 4. The absolute and the percentage difference between presumed depth and actual excision depth was not found to be associated with smoking, parity, pretreatment cytology test, colposcopic appearance, the loop size used and the excised tissue histopathology.

The absolute and the percentage difference between presumed depth and actual excision depth were both found to be significantly and positively correlated with the d1 diameter of the excised tissue, the d2 diameter of the excised tissue, and the excised tissue base surface. Multiple linear regression analyses in a stepwise method revealed that the excised tissue base surface was the only independent factor associated with the absolute (β =0.006, SE =0.002, p =0.001) and the percentage difference (β =0.05, SE =0.02, p =0.003) between presumed depth and actual excision depth. We found that for every 10 mm^2 increase in the excised tissue base surface, the mean absolute difference increased about 0.06 mm, and the mean percentage difference about 0.50 %.

Learning plateau and learning rate

A learning plateau was identified only for the first colposcopist who performed 60 cervical excisions. The absolute difference between presumed depth and actual excision depth decreased significantly over the course of consecutive LLETZ cervical treatments when tested by inverse curve regression (R^2 =0.08, p =0.035) with a learning plateau at 2.2 mm and a learning rate of 13 cases (Figure 1). Similarly, the percentage difference between presumed depth and actual excision depth decreased significantly over the course of consecutive excision proce-

Table 1: Demographics of women treated by the two colposcopists with a single large loop excision of the transformation zone (LLETZ) cervical treatment between 2017-2018.

	Colposcopist A (n =60)	Colposcopist B (n =18)	p-values
Age at treatment, mean (SD)	36.5 (8.9)	33.2 (10.9)	0.195[a]
Smoking			
No	36 (69.2)	12 (66.7)	0.840[b]
Yes	16 (30.8)	6 (33.3)	
Parity			
0	12 (20.7)	6 (40)	0.230[c]
1	18 (31)	2 (13.3)	
≥2	28 (48.3)	7 (46.7)	

Values represent number of patients (with percentage in brackets) unless stated otherwise, [a]: Student's t-test, [b]: chi-square test, [c]: Fisher's exact test, SD: standard deviation, Numbers are provided based on available data. Eight women did not declare their smoking status and two women did not declare their parity status in the group of women treated by colposcopist A. Similarly, three women did not declare their parity status in the group of women treated by colposcopist B.

Table 2: Large loop excision of the transformation zone (LLETZ) treatment features of the two groups of women treated by the two colposcopists.

	Colposcopist A (n =60)	Colposcopist B (n =18)	p-values
Pretreatment cytology test (severe dyskaryosis + moderate dyskaryosis)			
No	20 (34.5)	1 (5.6)	**0.017**[c]
Yes	38 (65.5)	17 (94.4)	
Colposcopic appearance at treatment			
Normal/Low-grade/HPV/inflammation	24 (40)	12 (66.7)	**0.047**[b]
High-grade	36 (60)	6 (33.3)	
TZ type			
Type 1	58 (96.7)	14 (77.8)	**0.012**[c]
Type 2	2 (3.3)	2 (11.1)	
Type 3	0 (0)	2 (11.1)	
Loop size used			
12 mm	1 (1.7)	1 (5.6)	**<0.001**[c]
15 mm	10 (16.7)	14 (77.8)	
18 mm	49 (81.7)	2 (11.1)	
20 mm	0 (0)	1 (5.6)	
Presumed excised depth (mm), median (IQR)	12 (10-12)	10 (8-15)	0.174[a]
Actual excised depth (mm), median (IQR)	11 (8.5-12)	14.5 (11-16)	**0.002**[a]
Absolute difference between presumed and actual excised depth (mm), median (IQR)	2 (1-3)	3.5 (1-5)	0.100
Percentage difference between presumed and actual excised depth (%), median (IQR)	16.6 (10-30)	35.4 (10-50)	**0.041**[a]
Excised volume (cm^3), median (IQR)	1.5 (1-1.9)	1.7 (1-2.5)	0.217[a]
Excised tissue base surface (mm^2), median (IQR)	200.2 (153.5-282.6)	203.3 (153.1-247.3)	0.522[a]
d1 diameter of excised tissue (mm), median (IQR)	17.5 (15-20)	18 (15-21)	0.900[a]
d2 diameter of excised tissue (mm), median (IQR)	15 (13-18)	13.5 (13-15)	0.257[a]
Excised cervical tissue histopathology			
CIN1	10 (16.7)	2 (11.1)	0.900[c]
CIN2-CIN3	43 (71.6)	14 (77.8)	
HPV/inflammation/normal	7 (11.6)	2 (11.2)	
Excision margin status			
Incomplete endocervical margin	5 (8.6)	1 (6.3)	0.458[b]
Incomplete ectocervical margin	26 (44.8)	7 (43.8)	
Incomplete both margins	4 (6.9)	0 (0)	
Complete excision	23 (39.7)	8 (50)	

Values represent number of patients (with percentage in brackets) unless stated otherwise, [a]: Mann-Whitney test, [b]: chi-square test, [c]: Fisher's exact test, LLETZ: large loop excision of the transformation zone, TZ: transformation zone, IQR: interquartile range, CIN: cervical intraepithelial neoplasia, HPV: human papilloma virus. There are missing values for the pretreatment cytology test for women treated by colposcopist A, as two women were referred for a clinically suspicious cervix and therefore only a cervical punch biopsy was taken and not a cytology test. This means that the only cytology test available would be the one taken many years ago and therefore does not reflect the current pretreatment cytology status and for this reason it was not included.

dures when tested by inverse curve regression (R^2 =0.07, p =0.049) with a learning plateau at 22.6 % and a learning rate of 13 cases (Figure 2).

Consecutive groupings

The difference between the presumed depth and the actual excision depth was compared for every group of five sequential procedures and is shown graphically in Figure 3. No significant differences were found between the group of procedures 1-5 and the group of procedures 6-10 (p =0.841). The difference between the group of procedures 6-10 and the group of procedures 11-15 was significant (p =0.049) indicating a reduction of the difference between presumed depth and actual excision depth. The comparison of the other sequential groups was not significant.

Table 3: Association of absolute difference between presumed depth and actual excision depth with categorical characteristics for the women treated by colposcopist A (n =60).

	Absolute difference (mm)		
	Mean (SD)	Median (IQR)	p-values
Smoking			
No	2.4 (1.7)	2 (1-3)	0.482[a]
Yes	2.5 (1.2)	2 (2-3)	
Parity			
0	2.6 (1.8)	2.5 (1-3.5)	0.447[b]
1	2.6 (1.8)	2 (2-4)	
≥2	1.9 (1.3)	2 (1-3)	
Pretreatment cytology test (severe dyskaryosis + moderate dyskaryosis)			
No	2.3 (1.7)	2 (1-3)	0.860
Yes	2.3 (1.5)	2 (1-3)	
Colposcopic appearance at treatment			
Normal/Low-grade/HPV/Inflammation	2 (1.4)	2 (1-2.5)	0.300[a]
High-grade	2.4 (1.6)	2 (1-4)	
Loop size used			
<18 mm	1.7 (1.5)	1 (1-3)	0.164[a]
18 mm	2.4 (1.6)	2 (1-3)	
Excised cervical tissue histopathology			
CIN1	1.9 (1.5)	2.5 (0-3)	0.975[b]
CIN2	2.4 (1.5)	2 (1-3)	
CIN3	2.3 (1.6)	2 (1-3)	
Other	2.3 (1.7)	2 (1-4)	

[a]: Mann-Whitney test, [b]: Kruskal-Wallis test, SD: standard deviation, IQR: interquartile range, CIN: cervical intraepithelial neoplasia, HPV: human papilloma virus.

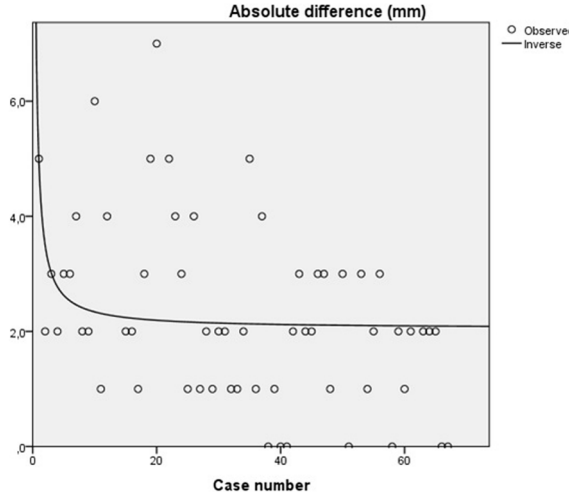

Figure 1: Inverse curve for the absolute difference between presumed depth and actual excised depth for the first colposcopist (n =60).

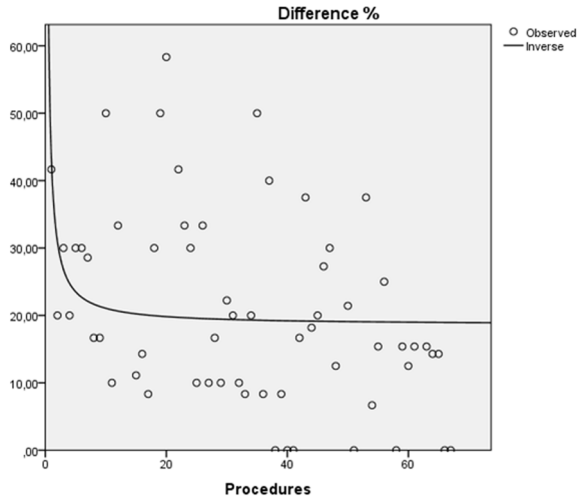

Figure 2: Inverse curve for the percentage difference between presumed depth and actual excised depth for the first colposcopist (n =60).

Discussion

There are reports that tissue specimens shrink after formalin fixation and that the type and composition of the tissue might influence the overall degree of shrinkage[18].

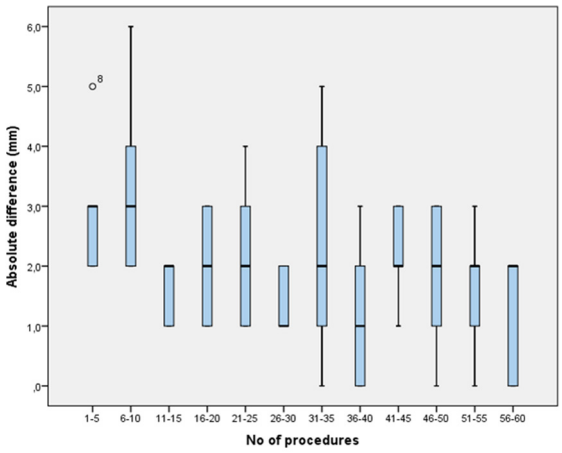

Figure 3: Box plots for the absolute difference between presumed depth and actual excised depth according to sequential groups of five procedures for the first colposcopist (n =60).

Head and neck cancer specimens have been reported to shrink after formalin fixation by 4.1 %[18], whereas liver tissue specimens by 10 %[19]. Prostate tissue specimens have been shown to decrease after formalin fixation by 4.5 %[20], lower lip tissue specimens derived from craniofacial cancer surgery up to 47.5 %[21], and lung tissue specimens by 28 %[22]. In contrast, other studies are reporting no change in size after formalin fixation of breast tissue[23] and palatal tonsils[24] after tumor surgery. Due to this variation in tissue shrinkage, it has been proposed that morphometric studies addressing changes in dimensions should be organ-specific and account for tissue composition[18]. Moreover, to avoid tissue shrinkage after fixation and during histopathological processing, different fixative protocols other than formalin have also been suggested in the literature[25,26].

In our study, the cervical tissue specimen was immediately placed after excision in a formalin solution, and there were no special fixatives used to reduce tissue shrinkage as this was a pragmatic study. Though the literature reports a 2.7 % of shrinkage to the longitudinal dimensions of the cervix due to formalin fixation when compared to a fresh specimen[16], we did not make any

Table 4: Association of percentage difference between presumed depth and actual excision depth with categorical characteristics for the women treated by colposcopist A (n =60).

	Percentage difference (%)		
	Mean (SD)	Median (IQR)	p-values
Smoking			
No	20.92 (14.86)	16.03(10-30)	0.197[a]
Yes	23.95 (12.34)	20.71(16.67-31.67)	
Parity			
0	25.07 (16.17)	25 (10-35.42)	0.261[b]
1	23.28 (15.79)	16.67 (14.29-37.5)	
≥2	16.73 (11.71)	15.38 (8.33-26.14)	
Pretreatment cytology test (severe dyskaryosis + moderate dyskaryosis)			
No	21.2 (15.7)	18.3 (9.2-30)	0.857
Yes	20.8 (13.4)	17.4 (12.5-30)	
Colposcopic appearance at treatment			
Normal/Low-grade/HPV/Inflammation	18.29 (13.3)	16.03 (10.56-23.61)	0.364[a]
High-grade	21.88 (14.73)	20 (10-31.67)	
Loop size used			
<18 mm	17.71 (15.77)	12.5 (6.67-30)	0.368[a]
18 mm	21.05 (13.89)	16.67 (11.11-30)	
Excised cervical tissue histopathology			
CIN1	19.67 (16.07)	25 (0-33.33)	0.999[b]
CIN2	20.71 (12.69)	15.38 (12.5-27.27)	
CIN3	20.93 (15.3)	16.67 (10-30)	
Other	19.08 (13.29)	16.67 (10-28.57)	

[a]: Mann-Whitney test, [b]: Kruskal-Wallis test, SD: standard deviation, IQR: interquartile range, CIN: cervical intraepithelial neoplasia, HPV: human papilloma virus.

adjustments in our analyses as we did not consider this degree of shrinkage to be significant and clinically meaningful. For example, if a cervical tissue specimen had an actual depth of excision of 10 mm, then a 2.7 % shrinkage would mean an absolute reduction in size by 0.27 mm. According to a large population-based study that has calculated that the risk of preterm birth increases by 6 % for every mm of the depth of excision, then this 2.7 % cervical tissue shrinkage would mean a miscalculation of increase in the theoretical risk of preterm birth by 1.6 %[6].

More importantly, whatever percentage magnitude of bias is ultimately introduced in our analyses due to the shrinkage of the cervical tissue after formalin fixation, our primary objective was to define the time trend of improvement in performance. This means that we aimed to calculate the time point (learning rate) when the colposcopist(s) had reached the minimal difference between presumed and actual excised depth and beyond which there was no further improvement. The bias due to the tissue shrinkage can affect the size of the difference between presumed and actual excised depth but cannot affect the time point when this difference becomes minimal.

We have found that even though both colposcopists aimed for essentially the same depth of excision (12 mm vs 10 mm; p =0.17), nevertheless the actual excised depth was different (11 mm vs 14.5 mm; p =0.002), with the second colposcopist excising the cervix at a significantly greater depth. We have also found that the percentage difference between the presumed depth and actual depth of excision was for the second colposcopist twice as great as that of the first colposcopist (35.4 % vs 16.6 %; p =0.04).

We cannot identify any obvious reason that could explain these findings. The two diameters and the surface of the base of the excised tissue were not different between the two colposcopists, meaning that the actual area surface that was excised on the surface of the ectocervix was similar for both practitioners. Moreover, the second colposcopist used in the majority of cases a loop size of 15 mm versus the loop size of 18 mm that was used by the first colposcopist. It seems that the use of a smaller loop size gave the false reassurance to the second colposcopist of excising a smaller depth of excision, leading to an underestimation in 83.3 % of cases of the presumed excision depth as the actual excision depth was much greater.

We have found that there is a learning plateau for only the first colposcopist through the method of continuous recording of practice that we have described. We have determined that there is a learning rate that can be attained at 13 cervical excisions and that with infinite cervical excision practice the absolute and percentage difference between presumed and actual excised depth can be decreased significantly to 2.2 mm and 22.6 %, respectively. There are reports in the literature of studies where attempts have been made to define learning curves in other surgical procedures and emerging technologies with the use of a study design similar to the study design we have utilized[17,27]. The fact that the second colposcopist did not achieve a learning plateau can be explained by the fact that learning curves vary among operators and are affected by factors such as innate ability, their previous experience, the task complexity, the case mix, and operative findings[28,29].

We have found that an independent factor that affects the accuracy of cervical excision is the surface of the base of the excised tissue. We have identified that the wider the piece of the cervix that is to be excised, the greater the inaccuracy that is observed between the presumed tissue depth and the actual tissue depth that has been removed. This has important clinical implications, especially in young women when the acetowhite staining area to be excised is widespread on the cervix. In this case, even though the colposcopist may be opting to be conservative with a presumed depth of excision between 7-10 mm as per national guidance[9], nevertheless the actual excised depth may be significantly greater thus exposing this woman to increased future obstetric morbidity[4].

In our study, the incomplete excision rates with involved endocervical margins were 8.6 % and 6.3 %, respectively, for the two colposcopists. This is much less when compared to the pooled rates of approximately 13.4 % (95 % confidence interval: 10.8-16.3) of incompletely excised endocervical margins that have been reported from a recent meta-analysis in women who underwent LLETZ treatment[30]. The incomplete excision rates with involved ectocervical margins in our study were 44.8 % and 43.8 %, respectively, for the two colposcopists. These rates even though higher than what has been quoted in other studies[30,31], nevertheless they have been reported before in the literature in much larger cohort sizes[10].

Limitations

There are certain limitations to our study. First, the result of the actual excised depth was made known to the colposcopist two to four weeks after the cervical excision through the histopathology report, thus not allowing instant feedback and real-time learning. Ideally, the optimal study design should have included feeding back the information of the actual excised depth immediately to the colposcopist once the excision was performed so as to compare with the presumed excised depth. This would have required the use of a ruler and an independent operator to measure the actual excised depth, thus probably increasing the procedure time for the patient by several minutes. Logistically this was not possible for the purposes of this prospective study.

Second, the method of continuous auditing of the presumed versus the actual excised tissue depth showed a learning plateau for only the first colposcopist but not the second colposcopist, and with a learning rate of 13 cases of cervical excision. Should the second colposcopist have continued with more cervical excisions, then perhaps a learning plateau might have been demonstrated but with a larger number of cases.

Conclusion

We have found that a learning plateau can be reached after 13 cervical excisions through the continuous auditing method described between presumed and actual excision depth. This means that the maximum potential of reducing the difference between what we believe we have excised as compared to the actual excised depth can be reached in a relatively short time interval and that continuous prospective auditing beyond this case number does not seem to improve performance further.

Further research is required with colposcopists of varying levels of prior experience and with perhaps larger numbers of cervical excisions to establish the learning plateau and learning rate in a greater population of colposcopists. Furthermore, it would be interesting to study the oncological outcome regarding the recurrence rates of CIN during follow-up in relation to the degree of accuracy between the presumed and actual depth of cervical excision. If a higher accuracy during cervical excision can lead to less recurrence at follow-up, then methods like the one we suggest to improve performance of excision can potentially gain significant clinical importance.

Conflict of interest

The authors declare no conflicts of interest.

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