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Original Research Article

Insight in the consistency of care pathway of patients newly diagnosed with stage 1A1 cervical cancer

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ABSTRACT

Background: This study aimed to assess the consistency of care pathway in patients diagnosed with stage 1A1 cervical cancer in our hospital.

Methods: Retrospective analysis of care pathway of patients with stage 1A1 cervical cancer over the last 5 years 2017-2022 by accessing their electronic records. Data collected were, information given to patients and their GP of cancer diagnosis, access to clinical nurse specialist, patient information leaflet, Multidisciplinary Team review, discussion of treatment following primary LLETZ and follow up.

Results: Total 45 patients were diagnosed with stage 1A1 cervical cancer. All patients and their GPs were sent letters about their diagnosis and plan for further management after multidisciplinary team discussion. Access to clinical nurse specialists noted in 16, and provision of patient information leaflet noted in 9 patient records. Regarding treatment 14 patients had a repeat LLETZ, 7 patients underwent hysterectomy, 5 patients had a second LLETZ procedure followed by hysterectomy and 19 had routine follow up (colposcopy and cervical smear). Follow up of the 33 patients who had LLETZ as definitive treatment, 1 patient had recurrence of cancer and 2 patients had low grade dyskaryosis. Histology post hysterectomy, 5 patients had no evidence of CIN, 6 patients showed CIN with complete excision, and no cases of CIN with incomplete excision. All vault smears were negative for malignancy.

Conclusions: The clinical standards of management were in par with expectations, however, to improve unmet holistic needs (access to information of support groups, clinical nurse specialists, patient information leaflets).

Keywords: Colposcopy, Follow up, Hysterectomy, LLETZ, LVSI, Stage 1A1 cervical cancer

INTRODUCTION

Worldwide about 570,000 new cases of cancer cervix and 311,000 cervical cancer related deaths occur annually.¹ 85% of these occur in the developing world.² There are approximately 3200 new cases of cervical cancer every year with an incidence of 12 per 100,000 in the UK.³

Despite the presence of well-organized cervical screening programmes in the UK and the introduction of HPV vaccination, cervical cancer incidence rates have increased

by around 4%. Every day nine women are diagnosed with cervical cancer, and it is currently the most common cancer in women under 35 years of age. Incidence rates are projected to rise by 43% in the UK between 2014 and 2035, to 17 cases per 100,000 women by 2035.⁴

Conisation (cold knife or LLETZ) is an acceptable treatment for stage IA1 squamous cell and adenocarcinoma of the cervix and hysterectomy offers no added survival advantage.⁴ With conisation becoming the standard treatment, there remains a small but definite

cancer recurrence risk, and these women need a dedicated follow up as well as need the reassurance to opt for this fertility sparing conservative treatment.

Over 49,000 women are living with or beyond cervical cancer in the UK today. Survival is high with over two thirds of women living 10 years or more however for those affected, diagnosis and treatment can have a significant impact on their quality of life and hence the importance of addressing unmet holistic concerns like access to information leaflets, support groups, clinical nurse specialists to mitigate the negative impact of cancer on quality of life.⁴

The primary objective of this study was to evaluate the performance of the current standard operative procedure in the diagnosis and follow up of newly diagnosed patients with Stage 1A1cervical cancer and address any lacunae/ areas for improvement and implement strategies to improve the Quality of Life of these women through their ‘cancer journey’.

METHODS

Retrospective analysis of the consistency of care pathway of patients newly diagnosed with stage 1A1 cervical cancer at the Nottingham University Hospital NHS Trust, over the last 5 years—from January 2017 to August 2022 by accessing their electronic records after obtaining approval from the hospital’s data protection committee. The selection criteria was histopathology diagnosis of stage 1 A1cervical cancer following LLETZ procedure done at our hospital.

Patient’s electronic records were accessed using the hospital’s data storage records (DHR and NOTIS) of their clinic appointments, treatment and follow ups and the following data were collected: age of patients, HPV changes at colposcopy, histopathology of cervical cancer, involvement of margins needing repeat LLETZ, presence of lymph vascular space invasion (LVSI), information given to patients viz-access to clinical nurse specialist, patient information leaflet, outcome of multidisciplinary team review, information to GP, and details of follow up and percentage of results derived by number of patients for a particular result (cited above) divided by the total patients multiplied by 100.

RESULTS

Total 45 patients were diagnosed with stage 1A1 cervical cancer during the study period. 43 patients (97.7%) except 2 (4.6%) were referred after detection of abnormal screening cytology. One was a 69-year old lady referred following postmenopausal and postcoital bleeding. The other was a 34-years old referred after histology of products of conception after surgical management of miscarriage revealed endometrioid type of endocervical carcinoma.

Table 1: Age at diagnosis.

Age (years)	N	%
<25	0	0
26-30	15	33.3
31-35	8	17.8
36-40	10	22.2
41-45	4	8.95
46-50	3	6.7
51-55	2	4.4
56 and above	3	6.7

Most common age group was 26-30yrs, (n=15;33.3%) followed by 36-40yrs (n=10;22.2%). The oldest patient was 69-years, this patient was referred for post-menopausal and post coital bleeding

In this cohort of patients 36 (80%) were positive for high-risk HPV. 3 patients (6.7%) were HPV negative aged 26, 28 and 69-yrs. HPV status was not documented in 6 (13.3%) patients.

Table 2: HPV changes visualised at colposcopy.

HPV changes	N	%
SEEN +HR HPV+	36	80
HPV negative	3	6.7
Not documented	6	13.3

Of the 3 patients (n=3;6.7%) who were HPV negative 1 had co existing Lichen sclerosus (aged 69yrs) and the other 2 HPV negative pts. were 26 and 28yrs of age. The latter had endocervical adenocarcinoma which has a lesser correlation with HPV than squamous cell carcinoma of cervix.

There was no lymph vascular space invasion (LVSI) in 39 (86.7%) of patients and LVSI was not documented in 6 (13.3%) patients.

Table 3: LVSI on histopathology of LLETZ (n=45).

LVSI negative (%)	LVSI positive (%)	LVSI not documented (%)
39 (86.7)	0 (0)	6 (13.3)

Most of the tumours were squamous cell cancers (n=35;77.8%) followed by adenocarcinomas (n=7; 15.6%) neuroendocrine small cell cancer was found in one patient (2.2%).

Total 43 patients (95.6%) were informed of their cancer diagnosis by face-to-face clinic appointment and 2 (4.4%) patients were informed by telephone.

Provision of patient information leaflets and access to clinical nurse specialists were documented in (n=9;20%) and (n=16;35.6%) respectively.

Table 4: Histopathology total cases (n=45).

Histology	N	%
Squamous cell carcinoma	35	77.8
Adenocarcinoma	7	15.6
Aden squamous carcinoma	2	4.4
Small cell-neuroendocrine tumour	1	2.2
Sarcoma	Nil	0
Malignant melanoma	Nil	0

Table 5: Provision of patient information leaflet and access to nurse specialist.

Pt. information leaflet	N	%
Given	9	20
Not documented	36	80
Access to nurse specialist		
Given	16	35.6
Not documented	29	64.4

All patients were discussed in the multidisciplinary team (MDT) and all patients, and their GPs received letters of the MDT outcome.

Treatment following primary LLETZ procedure

In 19 patients (42.2%) the primary LLETZ procedure was adequate as the definitive treatment, hence required routine follow up by colposcopy and cervical smear testing, 19 patients (42.2%) underwent a repeat LLETZ of which (n=5;11.1%) underwent hysterectomy following the repeat LLETZ procedure and 7patients (15.6%) underwent hysterectomy.

Table 6: Treatment following primary LLETZ procedure.

Treatment	Number	Percentage
Repeat LLETZ	14	31.1
Hysterectomy	7	15.6
Repeat LLETZ +hysterectomy	5	11.1
Trachelectomy	0	0
Routine follow up by colposcopy+smear	19	42.2

Of the 19 patients needing repeat LLETZ the most common indication for repeat LLETZ was CIN3 involving the ectocervix-followed by incomplete excision and CIN3 involving the endocervix.

Of the 19 patients who had repeat LLETZ-9 patients (47.4%) were positive for high-risk HPV subtypes but had no CIN, 5 patients (26.3%) had -CIN1 and were positive for high-risk HPV subtypes, and another 5 (26.3%) CIN3 and were positive for high-risk HPV subtypes.

Table 7: Number of patients needing repeat LLETZ – [(n=19) (42.2%)].

Indication	N	%
CIN3 with possible invasion	1	5.26
CGIN involving ecto cervix	1	5.26
CIN3 involving ecto cervix	8	42.1
Incomplete excision	3	15.78
CIN3 close to margin (2mm)	1	5.26
Multifocal tumour	1	5.26
CIN3 involving endo cervix	3	15.78
CIN3+CGIN involving margin	1	5.26

Table 8: Histo-pathology and high-risk HPV @ repeat LLETZ (n=19).

CIN	Hr HPV	N	%
No CIN	Positive	9	47.4
No CIN	Negative	0	0
CIN1	Positive	5	26.3
CIN1	Negative	0	0
CIN2	Positive	0	0
CIN2	Negative	0	0
CIN3	Positive	5	26.3
CIN3	Negative	0	0

Follow up after LLETZ

Of the 45 patients diagnosed with stage 1A1 cervical cancer 33 patients (73.3%) were treated LLETZ alone (primary LLETZ in 19 patients and repeat LLETZ in 14 patients) and 12 patients underwent hysterectomy.

Of the 33 patients all except one had completed their first follow up at 6months post procedure. 3 patients were from other counties and were referred there.

Of the 29 patients who had follow up at after LLETZ treatment-25patients (86.2%) were normal (normal colposcopy, smear and high-risk HPV negative). 1 patient was found to have recurrence of squamous cell carcinoma (Hr HPV negative) and was referred for radical chemoradiation as she was high risk for surgery. (69-year-old with previous h/o pulmonary embolism, myocardial infarction, had 4 coronary stents, had atrial fibrillation and was on rivaroxaban, had type 2 DM.) One patient (3.45%) had normal cervical smear but was positive for high-risk HPV subtypes. The 2 patients with low grade dyskaryosis and HR HPV positive had cervical biopsies of which 1 patient had no CIN, the other had CIN1 (LSIL).

Total 25 patients had had annual follow-ups, of which 23 patients (92%) were normal (normal colposcopy, smear, and high-risk HPV negative) 2 patients (8%) had normal smears but were positive for high-risk HPV, and the same 1 patient (4%) continued to have low grade dyskaryosis

and HR HPV positive. She had cervical biopsy which showed CIN1.

Table 9: Colposcopy smear and Hr HPV @6months (n=29).

Recurrence of cancer (%)	Normal smear and HPV negative	Normal smear and HPV positive	Low grade dyskaryosis and HPV positive
1 (3.45)	25 (86.2)	1 (3.45)	2 (6.9)

Follow up after hysterectomy

Of the 12 patients (n=12), 1 patient (8.3%) who had open radical hysterectomy +5cycles of vaginal vault brachytherapy was discharged from follow up. She had her treatment in Poland and there were no records regarding

the histopathological assessment of CIN post hysterectomy. Of the 11 patients done at NUH 5 patients (41.6%) had no evidence of CIN and 6 patients (50%) had CIN which was completely excised on histopathological assessment of cervix post hysterectomy and there were no cases with of CIN with incomplete excision.

All the 5 patients with absence of CIN at hysterectomy had vaginal vault assessment post hysterectomy at 6months in the Colp clinic and had started their annual colposcopy assessment of the vaginal vault. Among the 6 patients who had CIN which was completely excised on histopathological assessment of hysterectomy, all had completed vaginal vault assessment post hysterectomy at 6months in the Colp clinic and 5 had started their annual colposcopy assessment of the vaginal vault. There was no case of recurrence in either group of patients at follow up.

Table 10: Follow up after hysterectomy.

Serial#	CIN @HPE	Number	Percentage
1.	NO CIN	5	41.6
6/12 @COLP		5	41.6
2.	CIN complete excision	6	50
6/12 @COLP		6	50
3.	Discharged from follow up	1	8.3
4.	CIN with incomplete excision	NIL	0

DISCUSSION

In this study 43 patients (95.4%) were referred after detection of abnormal screening cytology. Which is like the results of retrospective review done at greater Glasgow and Clyde health board between 2007-2011, where 90% of stage 1A1 cervical cancers were detected following abnormal screening cytology.⁵

With regards to histology squamous cell cancers were the most frequent-35 patients (77.8%) followed by adenocarcinomas in 9 patients (20%) and small cell neuroendocrine were the least (1 patient) 2.2%. This was consistent with the prevalence of cervical cancer histology reported in the SEER data for cancer 2003-2007 and by Alfsen et al viz the most common being squamous cell (70 percent). Adenocarcinoma in 25 percent of cases, and cervical neuroendocrine (mainly small cell) tumours in about 2 percent of cervical malignancies.^{6,7}

Treatment planning should be made on a multidisciplinary basis (at a specialist gynaecological cancer multidisciplinary team meeting (SMDT) and based upon predictive factors for oncological outcome, presence of comorbidities and impact on quality of life.^{4,8} All patients in our study (n=45,100%) were discussed in the

multidisciplinary team (MDT) and all of them and their GPs received letters of the MDT outcome. It is commendable of the effective communication within the health care team and with the patient and their GPs and service within the NHS, despite the restrictions imposed during the C-19 pandemic in 2020 and 2021.

Conisation can be considered a definitive treatment as hysterectomy does not improve outcome.⁸ Conisation for stage 1A1 cervical cancer has been recommended by established guidelines and by numerous authors as acceptable treatment for stage 1A1 squamous cell and adenocarcinoma of the cervix.^{4,8,9,5,10-12} The aim of conisation was to achieve negative margins to both cancer and dysplasia. For patients in whom margins are negative, no further treatment is necessary; however, simple hysterectomy may be an acceptable alternative for patients who desire definitive treatment and have completed childbearing as it benefits with less intense cytological follow up and reduced psychological stress of cancer recurrence. Re-conisation is recommended if there are positive margins to intra-epithelial neoplasia or if the specimen cannot be orientated, is fragmented.⁴

In our cohort of, 19 patients (42.2%) the primary LLETZ procedure was adequate as the definitive treatment; yet

another 19 patients (42.2%) underwent a repeat LLETZ of which (5 patients;11.1%) underwent hysterectomy following the repeat LLETZ procedure and 7 patients (15.6%) underwent hysterectomy. Of the 19 patients who underwent repeat conization CIN3 involving the ectocervix- (8;42.1%) was the most common indication followed by incomplete excision and CIN3 involving the endocervix each 3 patients -(15.78%) for repeat LLETZ. Persistence of high-risk HPV subtypes was seen at histopathology in all the 19 patients who had repeat LLETZ and histopathology of repeat LLETZ showed no CIN in 9 patients (47.4%), CIN1 in 5 patients (26.3%), and CIN3 in 5 patients (26.3%). All post hysterectomy vault smears were normal.

Patients with stage IA1 disease have an extremely low risk of recurrence. In literature reviews by Mota et al and Ostor.^{14,13} Among patients with stromal invasion <1 mm and 1 to 3 mm, lymph node metastases were present in 0.1 percent (3 of 2274) and 0.4 percent (5 of 1324) of patients, respectively.^{13,14} The rate of recurrence was also low (0.4 and 1.7 percent,). In our cohort 1 patient had recurrence of cervical cancer.

With regards to follow up after treatment of stage 1A1 cancer cervix in a retrospective review of 78 patients with stage 1A1 cancer cervix by Wendy Susan et al 43 patients (55%) had LLETZ as primary treatment, 86% cytology post LLETZ was negative, 1 patient (1.3%) had recurrence and all post hysterectomy vault smears were normal.⁵

In a retrospective study of 75 patients by Lee et al 22 patients (29.3%) had LLETZ as their definitive treatment for stage 1 A1 cervical cancer and 53 patients (70.7%) had hysterectomy after diagnostic LLETZ 10 patients (13.3%) had a repeat LLETZ procedure and 2 patients (2.7%) had hysterectomy following their 2nd LLETZ.¹⁰

Histopathology analysis of repeat conization showed no residual tumour in 4 patients (40%), 1 patient (10%) had CIN 2, 3 patients (30%) had CIN 3 and 2 (20%) patients had microinvasive carcinoma with negative resection margins. In this study 59.1% of patients who were treated with conization had normal cytology in their 1st follow up and 31.8% had normal cytology in their subsequent follow ups. Histopathology results in the 53 patients who underwent hysterectomy were as follows: no residual tumour in 30 patients (56.6%) CIN3 in 11 patients (20.8%) microinvasive carcinoma in 9 patients (17%) CIN 1 in 1 patient (1.9%) and invasive carcinoma in 1 patient (1.9%). No patient developed recurrent disease following either conization or hysterectomy. Furthermore, there was no correlation between LVSI and resection margin status on follow up cytology results.

In a study of 82 stage 1A1 cervical carcinoma patients by Bekkers et al 77 patients (94%) were treated by LEEP (single and repeat); of which 15 patients (19.5%) had no residual disease or recurrence after their 1st LEEP, 30 patients (39%) had no residual CIN, 18 patients (23.4%)

had residual CIN 1/2, and 14 patients (18.2%) had residual CIN3/microinvasive carcinoma necessitating a second LEEP and were disease free after it.¹⁵ Of the 5 patients who underwent hysterectomy 4 patients (4.9%) had persistent microinvasive carcinoma/CIN3 after a second LEEP and 1 patient (1.2%) had recurrence of cancer following primary LEEP. There was no correlation between pathology results and endocervical resection margin or LVSI in this study.

Emotional and psychological impact of the problem...

The emotional impact of diagnosis and treatment of patients with early cancer cervix is also often neglected. Unmet needs were reported among women of all ages, however, was greater among younger women. While women were more positive about the physical impacts being addressed, only 30% reported their emotional needs had been addressed and 20% stating they had not been addressed at all.

Following completion of treatment, patients will have significantly reduced contact with their care team. For some women it is a difficult transition leaving them feeling vulnerable.

Clinical Nurse Specialist (CNS) and support groups can be pivotal in reducing isolation increase psychological and emotional wellbeing and alleviate pressure on those working within primary and secondary care to be the sole source of information and support. Increased awareness of long-term consequences will enable women to identify symptoms, seek early intervention and better self-manage their care.⁴

CONCLUSION

Cervical cancer is commonly detected in women in their prime of life. Prognosis and survival following conization is excellent but however mandates long-term follow up secondary to a small but definite cancer recurrence risk. It is also imperative to address the significant impact on the quality of life the cancer diagnosis, treatment and follow up entail. Though the clinical standards of management of these women are in par with expectations, there is significant room for improvement to address the unmet holistic needs (access to information in the form of support groups, clinical nurse specialists,) for these women.

Recommendations

Draft and implement a checklist for all staff performing Colposcopy that includes Post loop excision management, provision of patient information sheet, contact details of clinical nurse specialist, and support groups.

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