



Mini Review

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Trans-Cervical Resection of the Endometrium in Early Endometrial Cancer: An Alternative Surgical Management Technique in the Setting of Morbid Obesity

EF Craig^{1*}, Al- Rawahi¹, McCluggage WG² and McClelland HR

¹Department of Gynaecological Oncology, Belfast Health & Social Care Trust, North Island

²Department of Pathology, Belfast Health & Social Care Trust, North Island

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***Corresponding author:** EF Craig, Department of Gynaecological Oncology, Belfast Health & Social Care Trust, Belfast City Hospital BT9 7AB, North Island, Email: e_f_craig@hotmail.com

Abstract

Obesity is a risk for endometrial cancer. Morbidly obese patients with early endometrial cancer can present a formidable surgical challenge. Most patients have a low grade, early stage endometrioid endometrial adenocarcinoma which carries an excellent prognosis after hysterectomy. A small proportion of patients have such extensive obesity and related co-morbidities that definitive hysterectomy and anaesthetic are a major mortality risk. The treatment represents a greater risk than the oncolytic process. Our institution has been managing this challenging subset in a novel and previously unpublished manner.

Materials and methods: This study examines the experience of Trans-cervical resection of the endometrium (TCRE) in early stage low grade endometrial cancer associated with severe obesity. Retrospective cohort study from a specialist, tertiary referral gynaecological oncology centre of 12 patients with morbid obesity and early endometrial cancer. We describe the "Two-layer" technique of systematic endometrial resection that allows a clear resection margin of myometrium.

Results: We present demographic and clinico-pathological information of patients with morbid and super obesity with BMIs ranging between 42- 69 (mean 54±7.92SD) all with significant co-existing comorbidities. Complete operative and oncological outcomes including follow up data >70 months is shown. No peri or postoperative complications occurred. No recurrences have been observed.

Conclusion: There is no sign of the obesity epidemic abating, the gynaecological oncologist must adapt in this advancing era of personalised medicine to the challenges of morbid obesity. We present a valuable and safe alternative to hysterectomy when conventional management poses too great a risk.

Introduction

Obesity is the modern epidemic of westernised society and is now a public health crisis, the World Health Organisation has coined the phrase 'Globesity' to describe the scale of the problem [1]. Obesity is an acknowledged risk for endometrial cancer. A small proportion of morbidly obese patients have such extensive obesity related co-morbidities that definitive hysterectomy and associated anaesthetic pose a major mortality risk. These patients will likely suffer more morbidity and eventually die from a disease process unrelated to the uterine cancer [2]. Our institution has been managing this challenging subset of patients in a novel manner. This paper demonstrates a safe and feasible technique for managing early stage endometrial cancer in a certain selected subset of patients whose treatment options are limited by morbid obesity and extensive co-morbidities.

Endometrial cancer (EC) is the most common gynaecological tumour in developed countries [3]. It is the fourth most common malignancy in women with an estimated 46,470 new cases in 2011. Women have a 2.6% lifetime risk of developing this malignancy [2].

In general, EC is diagnosed at an early stage (80% Stage I) and prognosis is favorable, with a five-year survival rate over 95% [4]. EC incidence and mortality rates are on the rise. Over the past 20 years the incidence has risen by 40% and the mortality 20% despite improved survival rates and increasing obesity levels are linked to this [5-6]. Endometrial adenocarcinoma comprises the overwhelming majority of uterine malignancies (approximately 80%) followed by serous carcinoma (approximately 10-15%).

Endometrioid adenocarcinomas are generally low grade (grade 1 or 2), clinically indolent neoplasms and are related to oestrogenic stimulation; they are referred to as 'type 1 cancers'. In contrast, serous carcinomas are typically clinically aggressive and are referred to as type 2 cancer [7].

EC is a hormone-driven cancer, with approximately 80% of endometrial cancers arising attributable to either an excess of oestrogen or a lack of progesterone [8]. ECs have a well described set of risk factors, with obesity being the most common independent and modifiable risk factor. Nulliparity, unopposed oestrogen therapy, Polycystic Ovarian Syndrome and Diabetes Mellitus have also been implicated and often coexist with in the same patient.

Currently the best therapeutic approach in low grade, early disease is a total laparoscopic hysterectomy (TLH) and bilateral salpingo-oophorectomy (BSO). Adjuvant radiotherapy may be indicated based on final histopathological staging, if higher grade or more advanced disease is detected.

Given the escalating global health problem of obesity and its co-morbidities, the need to re- appraise its management is more compelling than ever. In the recent Gynecologic Cancer Inter Group (GCIg) Endometrial Cancer Clinical Trials Planning Meeting the group highlighted strategies for conservative management of endometrial cancer as a priority in an effort to personalize management for patients for high risk patients with obesity [9]. This study introduces the concept of individualising treatment for high risk surgical patients using adaptive techniques to tailor management which is important in this burgeoning era of personalised medicine.

The rationale behind performing TCRE is that evidence suggests that in general the endometrial cancer observed in women with higher obesity levels tend to undergo a more indolent pathological process, as less aggressive disease at an earlier stage of presentation has been witnessed [7]. Also crucial to the rationale behind the endometrial resection management are the multiple reports have described the conservative treatment of this tumour in selected patients with the objective of preserving fertility [10-11].

It is essential that these women aren't under treated and whilst progestogen therapy has proved an effective technique, surgery remains the cornerstone of treatment. Surgical resection of a cancer focus is a longstanding oncological tenet, furthermore, major prognostic factors are determined from the pathological examination of the resection- usually hysterectomy specimens, to guide requirements for adjuvant treatment [9].

Materials and Methods

The purpose of this study is to ascertain the safety of TCRE in the treatment of morbidly obese patients with early stage, low grade EC in whom hysterectomy was contraindicated due to serious anaesthetic risk. Our experience and technique and

outcomes of a cohort of morbidly obese women treated with combined hysteroscopic resection and Levonorgestrel Intra uterine device (LNG-IUD.)

From March 2011 to January 2017, 12 patients were collected in this retrospective study. Patients were considered for selection when it was decided by the Regional Gynaecological Cancer Multi- Disciplinary group that the standard therapeutic approach posed too great a risk.

The inclusion criteria were early stage disease- absence of myometrial/ cervical invasion, pelvic- para aortic lymphadenopathy or any other concerning feature on MRI, and morbid obesity with significant medical comorbidities. All patients had to have confirmed Grade 1 or 2 disease on biopsy. In the case of patients referred with a diagnosis from elsewhere the pathology is reviewed by dedicated gynaecological pathologist (WGM) to confirm diagnosis. Those excluded from the treatment where those with disease outside uterus, unable to have MRI, adnexal disease, or patients not likely to be compliant with follow up.

Patient demographics and anthropometric data were collected. Further data concerning operative complications, significant outcomes and longitudinal review were gathered (Table 1). Anaesthetic opinions for each patient were sought, general anaesthetic was contraindicated due to medical co morbidity. The patients all gave written consent to the treatment and were counselled about long term follow up, specifically the requirement for six monthly hysteroscopic assessment and LNG IUD insertion. Each patient was appraised of the fact that this was a somewhat unprecedented treatment but the long term follow up should act as a potential safety net for any treatment failure or disease recurrence in this indolent disease. Each resection was performed by a Consultant Gynaecologist with considerable experience in the technique. All the biopsies and resection specimens were examined by one dedicated gynaecological pathologist.

Table 1: Demographic features, histopathology and clinical outcome. Characteristics of the patients selected for conservative surgery.

Clinical and Pathological Characteristics	
Mean age years	53 (range 36-78)
Mean BMI kg/m ²	52 (range 45- 69)
Histology	
Endometrioid Adenocarcinoma	12/12
Grade 1	11/12
Grade 2	1/12
Superficial Myometrial invasion	2/12

Clinical Features	
Hospital Stay (days)	mean 2(range 1-4) (rewarfinisation)
Medical Co- morbidities	Ischaemic Heart Disease
	Diabetes Mellitus
	Hypertension, Hypocholesteraemia
	Atrial Fibrillation
	Sleep Apnoea
	COPD
	Asthma
	Home Oxygen/CPAP Osteoarthritis
	mobility issues
	Previous colorectal cancer
Major abdominal surgery	
Oncological Outcomes	
Median Follow up (months)	mean 38 (range14- 66)
Disease evident at 2nd TCRE	2/12
Completion hysterectomy required	0/12
Adjuvant treatment	0/12

Operative Technique

Each patient was pre-assessed by the anaesthetic team. In general, the patients were admitted the night prior to inpatient surgery and routine bloods sent including a Group and Hold. Consideration for High dependency or intensive care beds were made. A low dose spinal anaesthetic was administered.

The uterine cervix is dilated to 10mm and a 9mm resectoscope introduced. 1.5% Glycine solution under gravity inflow of 80cm H2O pressure was used as the uterine distension medium. The Outflow valve is connected to suction pressure and fluid management system to allow accurate input/output measurement of the glycine fluid. A 5mm Monopolar resecting loop is used to remove strips of endometrium in a methodical fashion.

Systematic dissection of the endometrium is performed. The area with the most obvious tumour is resected first, this is a deep resection down to the level of the myometrium to ensure an oncological clear margin is achieved. Following this a second layer, deeper into the myometrium is performed. A LNG IUD is inserted in as standard in all patients before finishing. The average surgery time was 30 minutes.

The histopathology specimens must be recorded faithfully and an experienced pathologist must interpret them to build

up the best picture to ensure a clear oncological margin into the myometrium.

Results

All patients presented with abnormal uterine bleeding either post-menopausal bleeding or heavy irregular menses.

BMI ranged from 47-69. All procedures were performed under spinal anaesthetic. No peri or postoperative complications occurred. Histopathological examination confirmed Grade 1-2 Stage 1A endometrioid adenocarcinoma. All patients had a LNG IUD inserted. Two patients required a further resection at 3 months because of incomplete primary resection.

Patients underwent strict six monthly review at outpatient clinic and underwent hysteroscopy and LNG IUD exchange under local anaesthetic.

All patients have had no evidence of malignancy at follow up hysteroscopy or on endometrial biopsy. The mean follow-up period is 39 months; maximum follow up has been 70 months. No recurrence/disease progression has been observed. No completion hysterectomy or adjuvant treatment has been required in any of the patients in the cohort.

Two Patients are Discussed in Detail

Case No. 1

58 year-old, nulliparous patient with morbid obesity (BMI 53kg/m²) presented with 6 months heavy post-menopausal bleeding. Existing medical co-morbidities included, cardiac disease involving severe congestive heart failure, hypertension, Type 2 Diabetes Mellitus and atrial fibrillation requiring warfarinisation.

Transvaginal ultrasound scan revealed a 1cm endometrial thickness and the histopathology of the office biopsy using pipelle confirmed grade 1 EC. An open MRI was performed given the arm- abdominal girth which confirmed FIGO stage 1A disease without myometrial invasion or other suspicious findings. A TCRE was performed under spinal anaesthesia. The hysteroscopic findings included an 8cm uterine cavity in a septate uterus with disease evident across the fundus. A deep layered resection of the endometrium was performed and each layer was sent separately for histopathological analysis. A LNG IUD was inserted in the cavity at the end of the procedure. The histopathology report showed the first layer to contain grade 1 endometrioid adenocarcinoma with a fragment of complex hyperplasia. The second and third submitted layers were comprised of myometrium with no evidence of malignancy. She has had follow up 5 hysteroscopy and biopsies at six month intervals during her follow up with LNG IUD in situ. There has been no evidence of malignancy in the follow up biopsies.

Case No.2

A 52 year-old nulliparous presented with heavy periods and intermenstrual bleeding with BMI of 60kg/m². Multiple medical

co morbidities included COPD, Sleep Apnoea, Diabetes and Cardiovascular disease. The histopathology of the pipelle biopsy revealed Grade 1EC within a background of atypical complex hyperplasia.

An open MRI was performed and was reported as stage 1A disease with no pelvic lymphadenopathy. She had a two-stepped interval TCRE procedures, both under regional anaesthesia. The first resection was performed in the layered technique described above.

The histopathology reported a grade 2 endometrioid adenocarcinoma in the first layer of endometrium and a small focus of invasion into the superficial myometrium with tumour free deep myometrium beneath. LNG IUD was inserted into the cavity at the end of the procedure, as before.

Given the small focus superficial myometrial invasion a Multidisciplinary team decision was made to repeat the TCRE in six months. The patient remained symptom free with the LNG IUD in situ in the interim. At the second resection, a further small focus of invasive adenocarcinoma was identified with clear myometrial margins beneath. At follow up six months later the histopathological examination reported an appearance of the endometrium in keeping with a hormonal effect with no evidence of malignancy.

It is important that patients remain on long term follow up and on hormonal treatment which provides a 'safety net' for disease recurrence. However, as our group's experience grew and the disease free follow up time lengthened the repeat hysteroscopy time was lengthened to yearly after the first-year disease free. In frail or medically complicated patients we moved to expectant management after some years with the knowledge that bleeding would herald the onset of disease recurrence.

Discussion

TCRE has been documented as a feasible technique for fertility preservation with early endometrial cancer and also in the management of atypical hyperplasia [12-14].

Medical management with progesterone treatment in the form of megestrol acetate has been shown to be an effective and relatively safe choice of treatment of women with well-differentiated endometrial adenocarcinoma who wish to preserve fertility [15-18].

It may be fair to comment based on the above evidence on fertility sparing and progestogen therapy whether a TCRE is necessary at all? However, our institution feel definitive treatment with surgical resection is important where possible and this technique provides evidence of a clear surgical myometrial margin. The recent feMMe trial study showed that 27 patients declined conservative management with progestogen therapy and opted for surgical treatment despite the risks posed, suggesting that hormonal management alone was not seen as an

acceptable management to some patients¹⁸. The concern with non-surgical treatments is if the cancer advances to later stage or higher grade on hormonal therapy the opportunity to use this valuable and highly acceptable technique has been missed.

Conclusion

Most morbid and even super obese patients will undergo hysterectomy with BSO usually by laparoscopic means however, endometrial resection may be an alternative in women with a high general anaesthetic risk who are compliant with regular long term follow up.

The advantages of the endometrial resection include avoidance of general anaesthesia, quicker recovery, less complications and shorter hospital stay. This technique also provides an oncologically safe alternative as no patient has shown disease recurrence in our long follow up series.

This study includes the largest and to the best of our knowledge only series of hysteroscopic resection for early EC in the obese population. Although small in numbers and insufficiently powered to draw major conclusions from, this is an important study that provides convincing evidence for the role of trans-cervical resection of the endometrium in early low grade EC that provides a safe management for a carefully selected subset of patients.

The long median follow-up of this study makes our results reliable. Larger numbers and further research in the form of a randomised prospective trial are required to reinforce our early, favourable results

There are relatively few challenging patients like this in our population currently, however should the tide of obesity not turn these patients may become more common place and this is a very useful therapeutic strategy.

1. HO (2015) Global Database on Body Mass Index.
2. Fader AN, Arriba LN, Frasure HE, von Gruenigen VE (2009) Endometrial cancer and obesity: Epidemiology, biomarkers, prevention and survivorship. *Gynecol Oncol* 114: 121-127.
3. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, et al. (2013) Cancer Incidence and Mortality Worldwide: IARC Cancer Base. *GLOBOCAN* 2012. *Int J Cancer* 136(5): E359-386.
4. Colombo N, Creutzberg C, Amant F, Bosse T, González-Martín A, et al. (2015) ESMO-ESGO-ESTRO Consensus Conference on Endometrial Cancer. *Ann Oncol* 00: 1-26 .
5. Cancer Research UK (2012) Cancer Statistics. UK.
6. Mackintosh ML, Crosbie EJ (2013) Obesity-driven endometrial cancer: is weight loss the answer? *BJOG* 120(7): 791-794.
7. Mc Cluggage WG (2006) My approach to the interpretation of endometrial biopsies and curettings. *J Clin Pathol* 59(8): 801-812 .
8. Carlson MJ, Thiel KW, Yang S, Leslie KK (2012) Catch it before it kills: progesterone, obesity, and the prevention of endometrial cancer. *Discov Med* 14(76): 215-222.
9. Creutzberg CL, Kitchener HC, Birrer MJ, Landoni F, Lu KH, et al. (2013)

Gynecologic Cancer Inter Group (GCIG) Endometrial Cancer Clinical Trials Planning Meeting. *Int J Gynecol Cancer* 23(8): 1528-1534.

10. Alonso S, Castellanos T, Lapuente F, Chiva L (2015) Hysteroscopic surgery for conservative management in endometrial cancer: a review of the literature. *Ecancermedicalsience* 9: 505.
11. De Marzi P, Bergamini A, Luchini S, Petrone M, Taccagni GL, et al. (2015) Hysteroscopic Resection in Fertility-Sparing Surgery for Atypical Hyperplasia and Endometrial Cancer: Safety and Efficacy. *J Minim Invasive Gynecol* 22(7): 1178-1182.
12. Vilos GA, Harding PG, Ettler HC (2002) Resectoscopic surgery in 10 women with abnormal uterine bleeding and atypical endometrial hyperplasia. *J Am Assoc Gynecol Laparosc* 9(2): 138-144 .
13. Sui L, Xie F, Cao B (2006) Management of abnormal uterine hemorrhage with atypical endometrial hyperplasia by transcervical resection of endometrium. *Int J Gynecol Cancer* 16(3) : 1482-1486.
14. Mazzon I, Corrado G, Masciullo V, Morricone D, Ferrandina G, et al. (2010) Conservative surgical management of stage IA endometrial carcinoma for fertility preservation. *Fertil Steril* 93(4): 1286-1289.
15. Eftekhari Z1, Izadi-Mood N, Yarandi F, Shojaei H, Rezaei Z, et al. (2009) Efficacy of Megestrol Acetate (Megace) in the Treatment of Patients With Early Endometrial Adenocarcinoma. *Int J Gynecol Cancer* 19(2): 249-252.
16. Ramirez PT, Frumovitz M, Bodurka DC, Sun CC, Levenback C (2004) Hormonal therapy for the management of grade 1 endometrial adenocarcinoma: a literature review. *Gynecol Oncol* 95: 133-138.
17. Qin Y, Yu Z, Yang J, Cao D, Yu M, et al. (2016) Oral Progestin Treatment for Early-Stage Endometrial Cancer. *Int J Gynecol Cancer* 26(6): 1081-1091.
18. Obermair A, Brennan DJ2, Baxter E3, Armes JE, Gebiski V, et al. (2016) Surgical safety and personal costs in morbidly obese, multimorbid patients diagnosed with early-stage endometrial cancer having a hysterectomy. *Gynecol Oncol Res Pract* 3: 1.



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