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## Hysteroscopic endometrial laser ablation – A novel approach for palliative management of endometrial cancer in inoperable patients

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#### ABSTRACT

Background: Endometrial cancer, the most common gynecologic malignancy in developed nations, poses substantial treatment challenges, particularly in patients with significant comorbidities or advanced obesity. Purpose: This manuscript introduces an innovative method that employs awake hysteroscopic endometrial laser ablation (HEA) as a palliative treatment for patients with endometrial cancer who were either inoperable or medically unfit to undergo general or regional anaesthesia for conventional therapies.

*Methods*: A retrospective evaluation of patients diagnosed with endometrial cancer at a tertiary center from 2019 to 2024, focusing on those with symptomatic uterine bleeding, who failed previous treatment options and could not undergo surgical or standard palliative interventions due to high surgical risk.

Results: In our study, three patients (n=3) with severe medical conditions—high BMI and poor performance status—underwent awake HEA using a vaginoscopic approach, treating symptomatic vaginal bleeding effectively. The procedure allowed for rapid treatment, minimal recovery time, and enhanced quality of life. Histological analyses post-ablation indicated satisfactory outcomes, contributing to symptom relief and stabilization of patients' conditions.

Conclusion: Our findings highlight the potential of conscious HEA as a palliative management strategy in highrisk patient populations, emphasizing its role when conventional therapies fail. This study underscores the importance of personalized treatment plans and multidisciplinary approaches in managing endometrial cancer, paving the way for further research into the safety and efficacy of HEA in similar cohorts.

#### 1. Introduction

Endometrial cancer is the most common gynecologic malignancy in the developed world and was the first to be recognized as being related to obesity. The percentage of endometrial cancer cases attributed to excess body weight is growing and is higher in western cultures, where the prevalence of obesity is rising, along with obesity driven comorbidities including Type II diabetes, hypertension, heart disease, and pulmonary disease (Crosbie et al., 2022). Early-stage endometrial cancer presents significant treatment challenges, particularly for patients deemed inoperable due to medical comorbidities or morbid obesity. While minimally invasive surgical staging that includes hysterectomy with bilateral salpingo-oophorectomy and lymph node assessment, remain the gold standard of treatment, this approach may

not be feasible for some patients due to pre-existing health risks (Laskov et al., 2023; Laskov et al., 2021; Pitakkarnkul et al., 2022; Nikolopoulos et al., 2020; Chao et al., 1996).

The management of inoperable endometrial cancer and treatment options for medically unfit patients with early-stage endometrial cancer involve several approaches, including radiation therapy, hormonal therapy, and the use of the levonorgestrel-releasing intrauterine system (LNG-IUD) (Pitakkarnkul et al., 2022; Nikolopoulos et al., 2020; Chao et al., 1996; Mittermeier et al., 2020; Baker et al., 2017).

Hysteroscopic endometrial resection, especially when combined with hormonal therapy, has also been shown as a safe and effective fertility-preserving treatment for both selected patients with early-stage endometrial cancer (Vitale et al., 2020; Arendas et al., 2015; Zhao et al., 2024), and in selected cases of endometrial cancer that are unfit for

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surgery (Vilos et al., 2007). However, hysteroscopic endometrial resection typically requires anaesthesia, which can be general or regional depending on the patient's condition, the extent of the procedure, and the surgeon's preference (Goldenberg et al., 2001).

Hysteroscopic endometrial laser ablation (HEA) has emerged as a minimally invasive procedure traditionally used to address abnormal uterine bleeding related to benign conditions. However, its application in the palliative management of endometrial cancer, especially among inoperable patients with low-performance status, is gaining recognition (Pinion et al., 1994; Vitale et al., 2023) HEA has been shown to provide symptomatic relief for patients experiencing severe vaginal bleeding, by alleviating symptoms and enhancing their quality of life (Pinion et al., 1994; Vitale et al., 2023). Unlike endometrial resection, HEA can be performed in conscious patients, using a vaginoscopic approach, without anaesthesia or by using local anaesthesia, often with a paracervical block, and sometimes with additional oral anxiolysis or minimal sedation which allows treatment in selected cased of very high surgical risk patients, unfit for general or regional anaesthesia (Chapa, 2008; Reinders et al., 2017).

This paper presents our single center experience in patients with endometrial cancer who were un-eligible for both surgical and standard conservative treatment, that were treated using hysteroscopic endometrial laser ablation without anaesthesia. This was done as a "last resort" after all other treatments were discouraged as a palliative management of endometrial cancer in low-performance status, inoperable patients, highlighting recent studies and clinical experiences.

#### 2. Methods

After Institutional Review Board approval (TLV-0964-20), we retrospectively evaluated all the patients who presented to a single center, university affiliated, tertiary hospital with new onset diagnosis of endometrial cancer that were considered for surgical staging. The majority of patients are referred to either laparoscopic or robotic-assisted surgery, in regard with surgeon discretion, with basal metabolic index (BMI) over 40 is a major consideration for the robotic approach. Prior to surgery all patients were referred to an anaesthesiologist evaluation. Both surgical, adjuvant and palliative treatment plans for all patients were discussed in our local multi-disciplinary Tumor —board meetings prior to treatment selection.

Most common palliative treatments were use of a hormonal IUD, Operative hysteroscopic resection or palliative radiation. However, some patients were still unfit for these procedures as they were not able to undergo general or regional anaesthesia. For these patients, hysteroscopic endometrial laser ablation using a vaginoscopic approach (using Bettocchi® hysteroscope, 4 mm diameter, by Karl-Storz $^{TM}$ ). This was done in conscious patients based on the clinical setting. The uterine cavity was visualized and whole endometrial ablation was done by using Holmium: YAG (Ho:YAG) laser for vaporization.

Histologic type, grade, clinical staging using imaging (CT/ PET-CT) and Clinical data such as age, BMI, ECOG (Eastern Cooperative Oncology Group) performance status and comorbidities were analysed. A review of the literature was also performed.

#### 3. Results

From 2019 to 2024, 513 newly diagnosed endometrial cancer patients were refereed for staging surgery. The vast majority underwent minimally invasive surgery (439/495, 89.0 %), while the remaining underwent upfront laparotomy (54/495, 10.9 %). 18 patients were deemed medically unfit for surgery (3.5 %) after multi-disciplinary discussion and were selected for standard palliative care. Of these, we encountered several patients who were unfit for both surgical and standard conservative palliative care, presenting a significant clinical challenge. 3 patients continued to have recurrent symptomatic uterine bleeding, failed conservative hormonal treatment, and were deemed

unfit for other palliative therapy by the anaesthesiologists or failed a trial of anaesthesia, as seen on Fig. 1.

In the following section, we will detail the cases of these patients, exploring their specific circumstances and the approach we took using endometrial laser ablation to address their needs.

#### 4. Case presentations

#### 4.1. Case 1

A 69-year-old patient presented with postmenopausal bleeding (PMB). Histopathology revealed endometrial adenocarcinoma Grade1 (G1). Her medical history included significant obesity (BMI 53), muscular dystrophy, respiratory failure, diabetes, and hypertension. ECOG performance status 4. Deemed as a very high surgical risk (inability to ventilate the patient using Trendelenburg manoeuvre), a trial of LNG-IUD was made. Follow-up hysteroscopy after six months showed persistent G1 endometrial CA. Oral progestin (megestrol acetate) were started but than halted due to adverse effects. Following treatment, abnormal uterine bleeding continued, with need of monthly hospitalization and blood product administration. Thus, treatment with HEA laser evaporation of the endometrium was performed while conscious with the use of sedation (Picture 1).

A year later, pathology indicated secretory endometrium without malignancy. Six months later a pancreatic mass was diagnosed as primary pancreatic cancer. The patient succumbed to the disease six months after diagnosis.

#### 4.2. Case 2

A 67-year-old patient with morbid obesity (BMI 60) and type 2 diabetes presented with PMB. A diagnostic hysteroscopy confirmed endometrioid adenocarcinoma, grade 2 (G2). Her surgical history included complications from an open cholecystectomy and a small bowel resection for obstruction. ECOG performance status 4.

After multidisciplinary team determined her ineligible for surgery, she was referred for radiation therapy but was unable to withstand brachytherapy or external beam radiotherapy, as not being able to fit into the radiation machine. An LNG-IUD was used, but 6 months later, follow-up hysteroscopy showed treatment failure, with pathology confirming endometrioid adenocarcinoma G1. Another attempt for palliative surgery was planned, but ventilation issues under the steep Trendelenburg position needed during the robotic assisted surgery led to its cancellation. Instead, hysteroscopy for endometrial ablation was performed while fully awake. Subsequent imaging indicated no active disease. A repeat hysteroscopy revealed endometrial intraepithelial neoplasia (EIN), prompting continued oral progestin-based treatment. As of the last follow-up in (58 month post endometrial ablation), the patient remains alive, undergoing conservative therapy without disease progression.

#### 4.3. Case 3

A 75-year-old presented with PMB. Diagnostic hysteroscopy confirmed grade 2 endometrioid adenocarcinoma. The patient suffered from morbid obesity (BMI 62), hypertension, atrial fibrillation, type 2 diabetes mellitus, hypothyroidism, and aortic + mitral valve stenosis. ECOG performance status 4. Due to the patient's substantial weight and associated anaesthetic risks, staging surgery was deemed inadvisable, leading to a recommendation for conservative management, with a trial of LNG-IUD. However, four months later, symptomatic bleeding persisted leading to recurrent hospitalizations and severe anemia (hemoglobin 7 g/dL). Subsequently, a HEA laser evaporation was conducted, followed by a LNG-IUD insertion under local cervical anaesthesia. Follow-up of 12 months indicated no further bleeding, haemoglobin levels stabilized, with plans for a repeat diagnostic hysteroscopy for

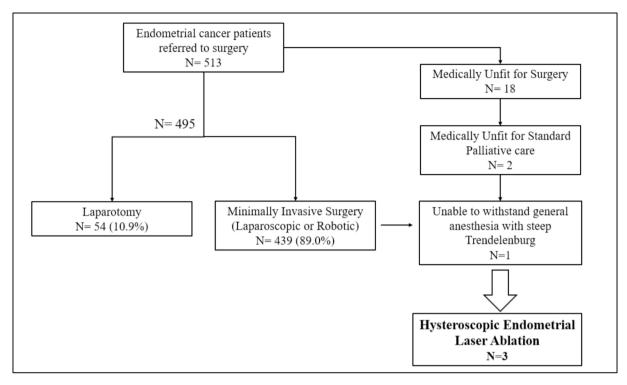
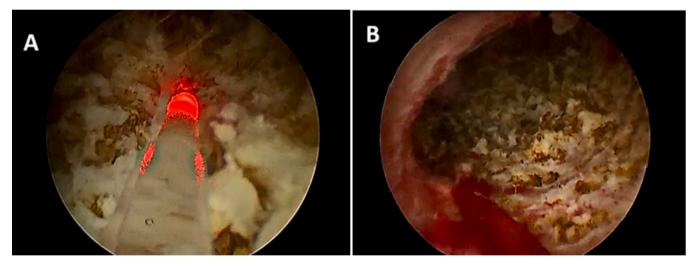


Fig. 1. Schemic representation of endometrial cancer patients treated in our centre.



**Picture 1.** Endometrial Laser Ablation for case1. Picture A – endometrial appearance at the beginning of the procedure. Picture B – Endometrial appearance at the end of the procedure.

ongoing monitoring.

#### 4.4. Summary of cases

Table 1 summarizes the characteristics of three cases, critical demographic, clinical, and treatment-related factors. The average age of the patients was 70 years, with severe comorbidities and BMI averaging approximately 58.3, that precluded their ability to undergo any form of anaesthesia or radiation treatment. All patients utilized conservative measures such as LNG-IUD prior to HEA treatment. All patients underwent the HEA laser endometrial ablation without the use of anaesthesia and were discharged the day after procedure. They all reported no recurrent symptomatic bleeding and were clinically stable after intervention.

#### 5. Discussion

For patients with non-operable endometrial cancer who have a very high surgical risk, current conservative treatment options include radiation therapy (particularly image-guided brachytherapy), systemic hormonal therapy, and the use of the levonorgestrel-releasing intrauterine device (LNG-IUD) (Schwarz et al., 2015; Abu-Rustum et al., 2023; Corzo et al., 2018).

Regarding our patients, brachytherapy was not an option due to the difficulty in obtaining regional anaesthesia in extreme morbidly obese patients. and the inability to ventilate during general anaesthesia. The above other conservative treatments such as Hormonal or IUD treatments were tried and failed to produce proper symptomatic relief of the bleeding.

Hysteroscopic treatment followed by hormonal therapy is another

**Table 1**Cases characteristics: demographic, clinical, and treatment-related factors.

| Cases | Age | Histology                                       | ВМІ | Co-Morbidities   | Time of follow-up              |
|-------|-----|---|-----|--|--------------------------------|
| 1     | 69  | Endometrioid<br>adenocarcinoma,<br>FIGO grade 1 | 53  | Obesity, muscular<br>dystrophy,<br>respiratory failure,<br>DM type 2, HTN                | 18 months<br>post<br>treatment |
| 2     | 67  | Endometrioid<br>adenocarcinoma,<br>FIGO grade 1 | 60  | Obesity, DM type 2, cardiac pacemaker  | 58 months<br>post<br>treatment |
| 3     | 75  | Endometrioid<br>adenocarcinoma,<br>FIGO G2      | 62  | Obesity, DM type2,<br>atrial fibrillation,<br>HTN,<br>hypothyroidism,<br>Aortic stenosis | 6 months<br>post-<br>treatment |

Abbreviations (DM - diabetes mellitus, HTN - Hypertension).

conservative approach, with promising results in reproductive aged women and for early endometrial cancer/atypical hyperplasia (Török et al., 2020; Atallah et al., 2021). Hysteroscopic endometrial resection in patients with endometrial cancer defined as high surgical risk was also reported (Casadio et al., 2019), showing regression of lesions after six months, with no intra- or post-operative complications, and no recurrence of cancer during five years of follow-up.

In this study, we used a novel approach of awake hysteroscopic laser endometrial ablation. This resembles endometrial resection in being minimally invasive hysteroscopic procedure, however this was done in a vaginoscopic approach in conscious patients, offering precision in targeting endometrial tissue, resulting in reduced blood loss and a shorter recovery time (Practice Committee of American Society for Reproductive Medicine, 2008; Li et al., 2017). Endometrial resection is more effective for removing larger or more extensive lesions. However, it carries a higher risk of complications such as uterine perforation and injury to adjacent organs and generally has a longer operative time (Corzo et al., 2018; Török et al., 2020).

The findings from our pilot study contribute to the existing body of literature, highlighting the potential benefits of laser ablation as an effective treatment modality for managing this patient population of frail patients.

This method allows for rapid treatment, ease of execution, quick hospital discharge, and does not require general anaesthesia. However, it is important to acknowledge several limitations within our study. The small number of patients limits our ability to conclusively assess safety and oncological significance. Additionally, it is essential to note that the treatment was primarily palliative due to persistent vaginal bleeding, which was understood by both patients and their families. Although office hysteroscopy has a growing role in routine gynecologic care and utilization, it is important to note that those ablative procedures were performed by a highly skilled hysteroscopic expert.

In summary, while hysteroscopic resection followed by progestin therapy may be a viable conservative management option for early-stage endometrial cancer and atypical hyperplasia—especially in frail patients who cannot undergo surgery—our findings underscore the need for further investigation to establish the safety and effectiveness of this innovative treatment approach.

#### 6. Conclusion

Endometrial cancer in patients with significant comorbidities presents unique challenges and highlights the need for a conservative yet effective approach. These cases illustrate the complexities of surgical intervention in individuals with severe obesity and other medical conditions that elevate surgical risk. Despite the application of conservative measures, such as the LNG-IUD, persistent or progressive disease warranted additional intervention with hysteroscopic endometrial laser ablation.

Collectively, these cases illustrate the complexities of managing endometrial conditions in patients with significant comorbidities. They underscore the importance of multidisciplinary approaches, individualized treatment plans, and the utilization of conservative methods when surgical risks are prohibitively high. Overall, these experiences reinforce the necessity for individualized patient care to navigate the complexities of endometrial disease in the setting of significant health challenges, allowing for effective management even when surgical options are limited.

#### CRediT authorship contribution statement

Michael Lavie: Writing – review & editing, Writing – original draft, Data curation, Conceptualization. Gilad Rattan: Writing – review & editing, Data curation. Dana Englander: Formal analysis, Data curation. Shai Ram: Data curation. Neta Solomon: Writing – review & editing, Data curation. Nadav Michaan: Writing – review & editing, Validation. Dan Grisaru: Writing – review & editing, Supervision. Ido Laskov: Writing – review & editing, Methodology, Conceptualization.

#### **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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