

ORIGINAL RESEARCH

A United Kingdom national survey of pre-operative imaging and lymph node staging practices in early-stage endometrioid endometrial carcinoma

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Abstract

Background: The molecular classification system for endometrial carcinoma has been recently introduced, offering a new framework for diagnosis and management. This study aims to evaluate variations in clinical practice concerning pre-operative imaging and determine whether the adoption of molecular classification has influenced surgical staging practices. **Methods:** A peer-reviewed online survey was distributed to members of the British Gynaecological Cancer Society (BGCS) using Microsoft Forms. The survey was conducted from 26 January 2024, to 02 August 2024. Data from the responses were analyzed using Microsoft Excel (Version 16.89.1, 2024). **Results:** The survey received 69 responses, representing 82% of cancer centres in the United Kingdom (UK). For grade 1 endometrial carcinomas, 68 out of 69 respondents (99%) reported performing pelvic imaging (ultrasound or magnetic resonance imaging (MRI)) for pre-operative staging, with 32 out of 69 (46%) performing pelvic imaging exclusively. Among cases of grade 2 carcinomas, 27 out of 69 respondents (39%) relied solely on pelvic imaging. For grade 3 endometrial carcinomas, 68 out of 69 respondents (99%) reported conducting chest, abdomen, and pelvis Computerised Tomography (CT) scans. Notable variations were observed in lymph node staging practices. The majority of centres do not perform lymph node excision for grade 1–2, stage 1A carcinomas. Sentinel lymph node biopsy is typically employed for grade 1–2, stage 1B or higher and for all grade 3 carcinomas. **Conclusions:** There is significant variability in the approaches to pre-operative imaging and lymph node staging for grade 1 and grade 2 endometrioid endometrial carcinomas across the UK. Enhancing adherence to guidelines could increase the use of pre-operative chest X-rays while reducing the frequency of CT scans, thereby minimising radiation exposure for patients with low-risk endometrial carcinomas. Expanding access to sentinel lymph node biopsies will have substantial implications for provision of services, particularly cancer units, in the UK.

Keywords

Gynaecological cancer; Endometrial cancer; Pre-operative imaging; Lymph node staging; Molecular classification

1. Introduction

Endometrial cancer is the sixth most prevalent cancer among women worldwide [1] and the fifth most common in the UK [2]. Initial evaluation typically involves a tissue biopsy, with histological grading playing a crucial role in guiding subsequent pre-operative investigations and treatment planning. Pre-operative pelvic magnetic resonance imaging (MRI) or ultrasound scan (USS) is recommended to assess the depth of myometrial and cervical stromal invasion, as these factors influence the surgical approach [3, 4]. The British Gynaecological Cancer Society (BGCS) guidelines recommend a chest X-ray for low-risk endometrial carcinoma and a computed tomography (CT) scan of the chest, abdomen, and pelvis for

high-risk cases due to the potential for extra-uterine disease [5]. Imaging plays a vital role in informing decisions about lymphadenectomy and identifying palliative cases where surgery may be avoided [6].

Sentinel lymph node biopsy has been introduced as an alternative to full pelvic lymphadenectomy in the surgical staging of endometrial carcinoma, offering the advantage of reduced morbidity while providing reliable information to guide adjuvant treatment decisions [6]. The European Society of Gynaecological Oncology (ESGO) guidelines recommend the use of sentinel lymph node staging for all patients with high-intermediate and high-risk disease, and it may also be considered for those with low and intermediate-risk disease [6]. In contrast, the BGCS guidelines suggest that sentinel lymph

node biopsy may be appropriate for women with disease exceeding low risk and strongly recommend it for those with high-grade disease [5].

Endometrial carcinoma has been surgically staged since 1988 [7]. Recent advancements include the incorporation of molecular classification, which utilizes three immunohistochemical markers—p53, MutS Homolog 6 (MSH6), and Postmeiotic Segregation Increased 2 (PMS2)—along with one molecular test, Polymerase Epsilon (POLE) [8]. These surrogate assays should be performed collectively, as a combination of positive tests can be observed in approximately 5% of patients [6]. Patients with p53 mutations generally have a poorer prognosis and are typically offered additional adjuvant treatments, including external beam radiotherapy with concurrent chemotherapy. This approach is supported by the molecular classification of the Adjuvant Chemoradiotherapy Versus Radiotherapy Alone in Women With High-Risk Endometrial Cancer (PORTEC-3) trial which demonstrated a five-year survival rate of 36% for patients with p53 mutations treated with radiotherapy alone, compared to 59% for those receiving concurrent chemoradiotherapy [9].

In contrast, patients with stage 1–2 endometrial cancer and POLE mutations exhibit improved prognostic outcomes, allowing for a reduction in the intensity of adjuvant therapy in early-stage disease [10]. However, for the rare cases of stage 3–4 POLE-mutated endometrial carcinoma, there is currently no available outcome data regarding the omission of adjuvant treatment. POLE sequencing remains the most costly and time-consuming test, with delays in obtaining results potentially impacting the timely initiation of adjuvant treatment and leading to increased costs for the National Health Service (NHS).

For the small subset of patients with both POLE mutations and mutant p53, survival data indicate that their prognosis is comparable to that of patients with POLE mutations alone [10]. As a result, these patients can be assigned to prognostic groups based on their POLE mutation status alone. Patients with Mismatch Repair deficiency (MMRd) or Non-specific Molecular Profile (NSMP), which constitute approximately two-thirds of endometrial carcinoma cases, exhibit an intermediate prognosis. This risk group is determined by their pathological features, which may also include results from sentinel lymph node biopsies [6].

The management of endometrial carcinoma is a rapidly evolving area of clinical practice in the UK. Consequently, the aim of this survey is to examine variations in practice concerning pre-operative imaging, surgical staging with sentinel lymph node biopsy, and the impact of molecular classification on surgical staging procedures.

2. Materials and methods

An online, peer-reviewed survey was distributed to all members of the BGCS via Microsoft Forms. The survey was conducted from 26 January 2024 to 02 August 2024 and comprised 24 questions. It was designed to be anonymous, with the first three questions gathering demographic information, including the respondent's current institution, type of hospital, and job role. The subsequent three multiple-choice questions focused on the choice of imaging for each grade of endometrioid

endometrial carcinoma. To minimize the respondent burden and encourage higher completion rates, the authors opted to restrict the survey to endometrioid endometrial carcinomas only.

The survey included branching questions based on respondents' use of molecular classifications (p53 and POLE) to guide operative staging decisions. For those who do not currently use molecular classification pre-operatively, follow-up multiple-choice questions were asked to explore their reasons for not doing so and whether they would consider using it if pre-operative results were available. Respondents were then presented with nine additional multiple-choice questions regarding their choice of lymph node staging procedure for each grade and stage of early-stage endometrioid endometrial cancer. The results were analyzed using Microsoft Excel Version 16.89.1, 2024 (Microsoft Corporation, Redmond, WA, USA).

3. Results

3.1 Demographics

The online survey received 69 responses, representing 82% of cancer centres in the UK. Of these, 57 responses (83%) were from cancer centres, while 11 responses (16%) were from cancer units. Responses were gathered from a diverse range of clinical professions and grades, with the majority, 42 responses (61%), coming from consultant gynaecological oncologists.

3.2 Pre-operative imaging

For grade 1 endometrial carcinomas, the vast majority of respondents (68/69, 99%) perform pelvic imaging (USS/MRI) for pre-operative staging, as shown in Fig. 1. Among these, 32/69 (46%) conduct pelvic imaging (USS/MRI) without concurrent chest imaging, 19/69 (28%) combine pelvic imaging with chest X-ray, and 17/69 (25%) routinely perform CT chest imaging in conjunction with pelvic MRI or USS.

Fig. 1 further illustrates that, for grade 2 endometrial carcinomas, the majority of respondents (63/69, 91%) perform pelvic imaging (USS/MRI) for pre-operative staging. Of these, 27/69 (39%) perform pelvic imaging (USS/MRI) only, without concurrent chest imaging, 13/69 (19%) combine pelvic imaging with chest X-ray, and 28/69 (40%) routinely conduct CT imaging either in isolation (5/69, 7%) or in combination with pelvic MRI or USS (23/69, 33%).

For grade 3 endometrial carcinomas, 68/69 (99%) of respondents perform CT imaging of the chest, abdomen and pelvis.

3.3 Molecular classification

Of the respondents, 44/69 (64%) do not use molecular classification to guide their choice of surgical staging procedure, while 15/69 (22%) sometimes use it, and 10/69 (14%) use it routinely. Among those who do not routinely use molecular classification for surgical staging, 36/44 (82%) indicated that they do not have access to the results pre-operatively. Other reasons for not using molecular classification include a lack of high-quality evidence, the absence of current departmental protocols, and the perceived complexity that the classification

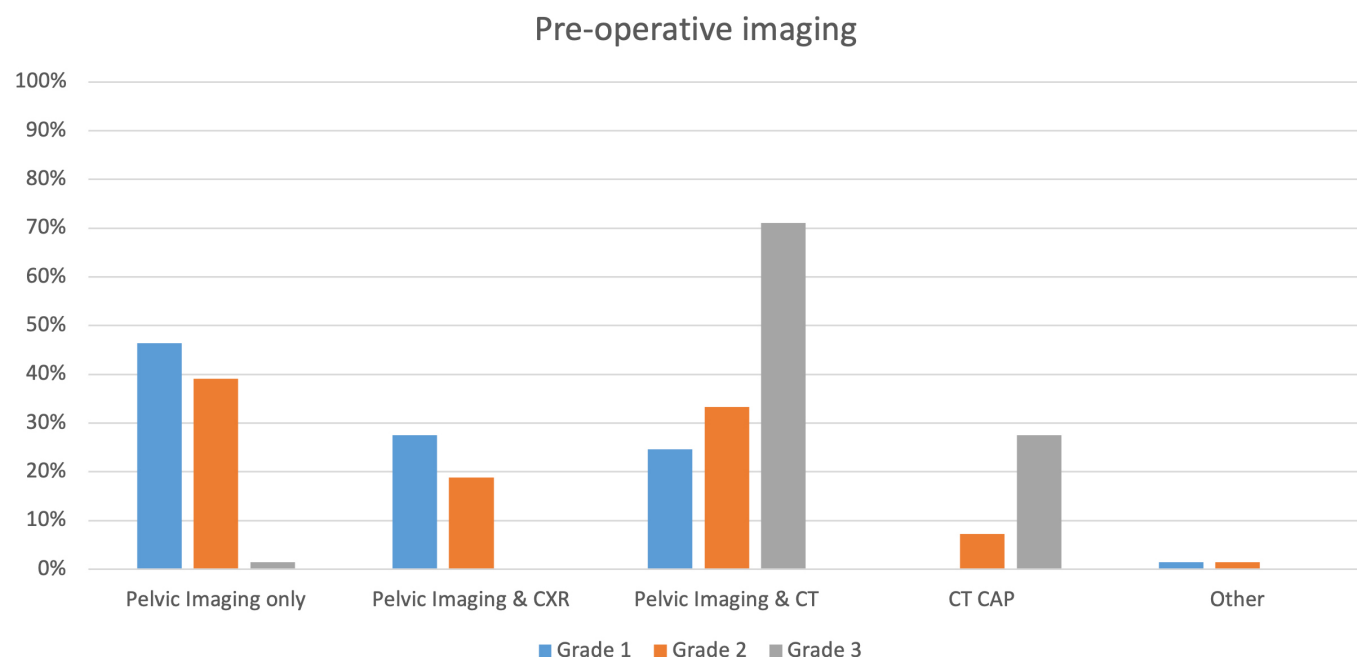


FIGURE 1. Pre-operative imaging of endometrial endometrioid adenocarcinoma by grade of tumour. CT: Computed Tomography; CAP: Chest Abdomen & Pelvis; CXR: Chest Xray.

results introduce into multidisciplinary team (MDT) decision-making. When asked whether they would use molecular classification if pre-operative results were available, 19/44 (43%) respondents indicated they would use it to guide surgical staging, while 16/44 (36%) stated they would not.

3.3.1 Lymph node staging for respondents not using molecular classification

A small proportion of respondents (8/44, 18%) report performing sentinel lymph node biopsies for grade 1 stage 1A endometrioid endometrial carcinomas. In contrast, the majority perform sentinel lymph node biopsies for grade 1 stage 1B (25/44, 57%) and stage 2 (25/42, 60%) carcinomas, as shown in Fig. 2. A higher number of respondents (14/43, 33%) perform sentinel lymph node biopsies for grade 2 stage 1A endometrioid endometrial carcinomas, while the majority perform sentinel lymph node biopsies for grade 2 stage 1B (26/43, 60%) and stage 2 (26/43, 60%) carcinomas. Fig. 2 also highlights that the vast majority of respondents (40/43, 93%) perform lymph node assessment for all early-stage grade 3 endometrioid endometrial carcinomas. Most of these respondents perform sentinel lymph node biopsies (28/43, 65% for stage 1A, 29/43, 67% for stage 1B, and 28/43, 65% for stage 2), with 5–8/43 (12–19%) performing bilateral pelvic lymphadenectomy, and two respondents performing bilateral pelvic and para-aortic lymphadenectomy for grade 3 stage 2 endometrioid endometrial carcinomas. A small minority (2–3/43, 5–7%) do not perform any lymph node staging.

3.3.2 Surgical staging for respondents using molecular classification

3.3.2.1 Grade 1

Fig. 3 illustrates that for grade 1 stage 1A carcinomas, few respondents perform sentinel lymph node biopsies for p53

wildtype cancers (2/25, 8% when POLE wildtype and 2/25, 8% when POLE mutant). However, there is a noticeable increase in the number of sentinel lymph node biopsies performed when p53 is mutant (12/25, 48% when POLE wildtype and 11/25, 44% when POLE mutant).

For stage 1B cancers, 9/24 (38%) of respondents perform sentinel lymph node biopsies regardless of molecular classification, although the number is still higher when p53 is mutant.

For stage 2 cancers, 11/24 (46%) of respondents perform sentinel lymph node biopsies regardless of molecular classification, with one respondent performing bilateral pelvic and para-aortic lymphadenectomy when p53 is mutant, and opting for no lymph node excision when both p53 and POLE mutations are present.

3.3.2.2 Grade 2

Fig. 4 illustrates that for grade 2, stage 1A carcinomas, approximately one-third of respondents perform sentinel lymph node biopsies for p53 wildtype cancers (9/25, 36% when POLE wildtype and 8/25, 32% when POLE mutant). In contrast, the majority of respondents perform sentinel lymph node biopsies for p53 mutant cancers (17/25, 68% when POLE wildtype and 16/25, 64% when POLE mutant).

Furthermore, Fig. 4 shows that for grade 2 stage 1B and stage 2 cancers, 12/25 (48%) of respondents perform sentinel lymph node biopsies regardless of molecular classification. However, a higher proportion of sentinel lymph node biopsies are performed when p53 is mutant.

3.3.2.3 Grade 3

Fig. 5 highlights that 15/24 (63%) of respondents perform sentinel lymph node biopsies for all early-stage, grade 3 endometrioid endometrial carcinomas, regardless of molecular classification.

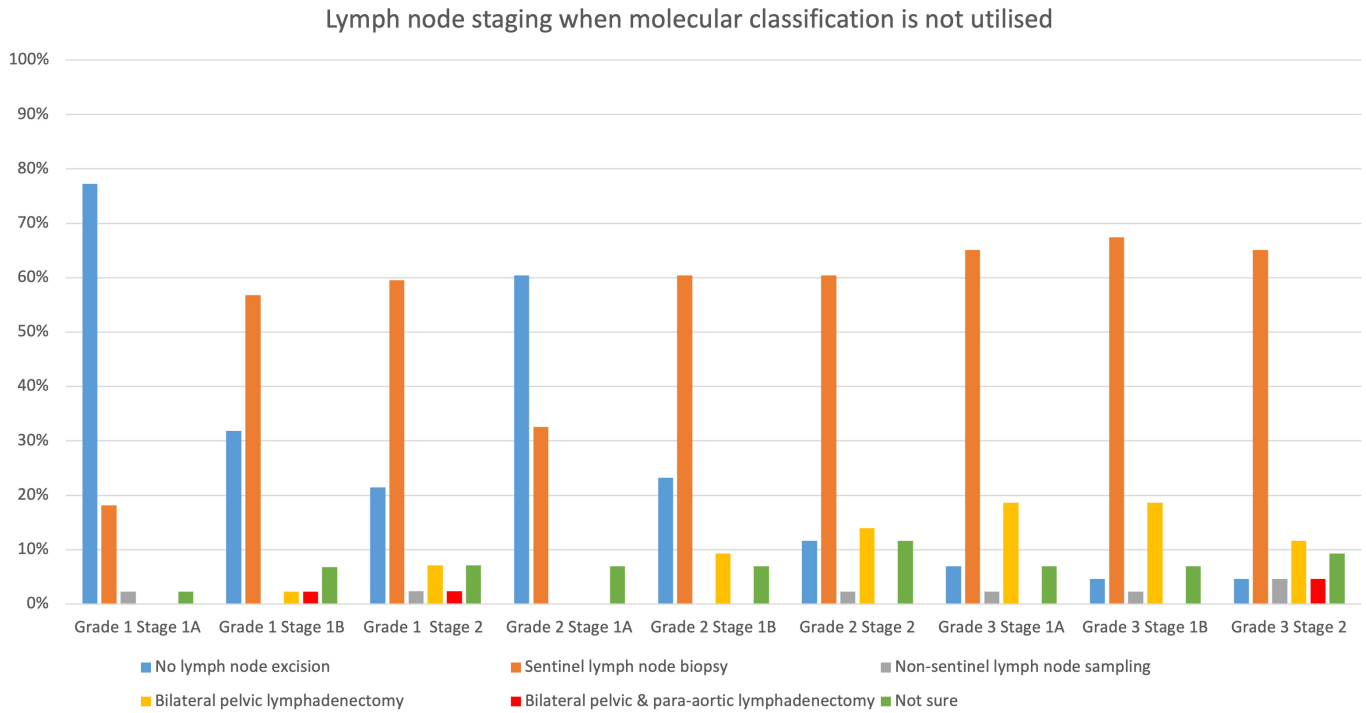


FIGURE 2. Lymph node staging when molecular classification is not used.

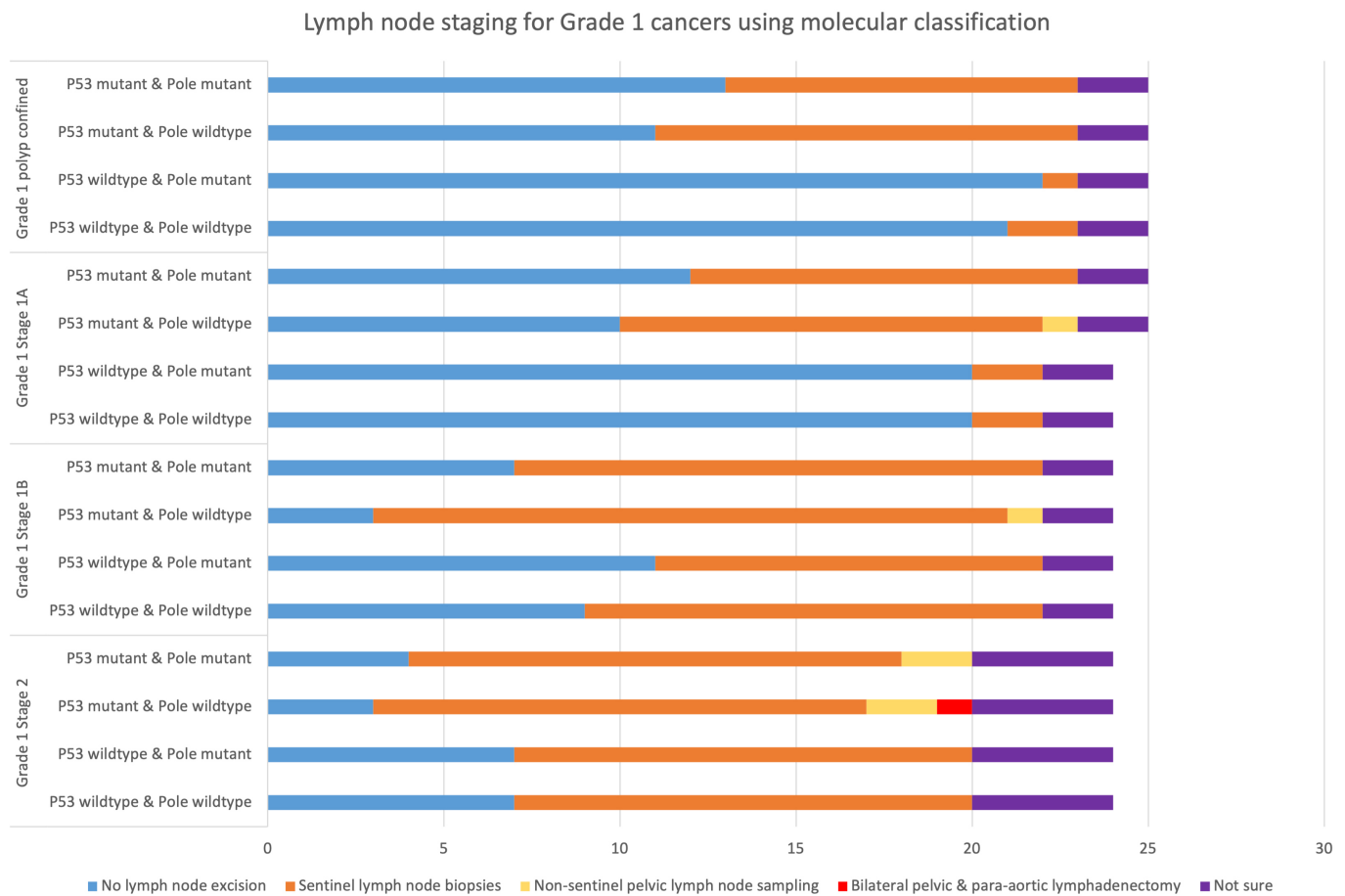


FIGURE 3. Lymph node staging for Grade 1 endometrial endometrioid carcinomas using molecular classification.

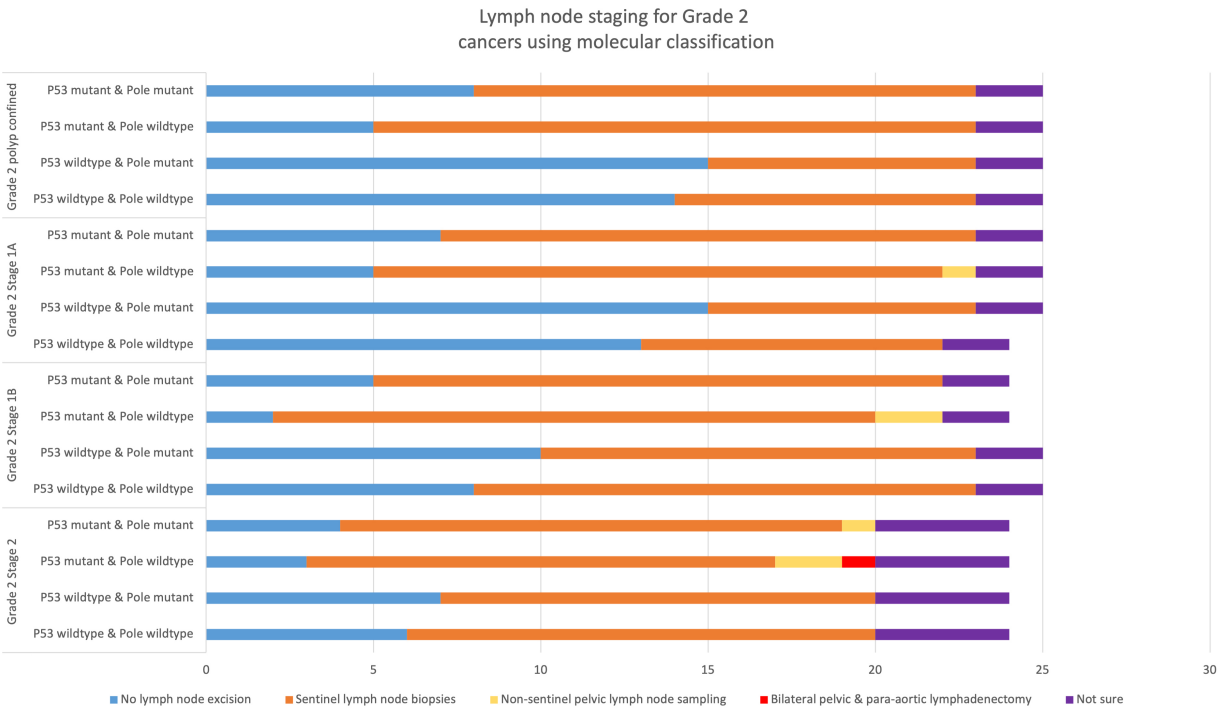


FIGURE 4. Lymph node staging for Grade 2 endometrial endometrioid carcinomas using molecular classification.

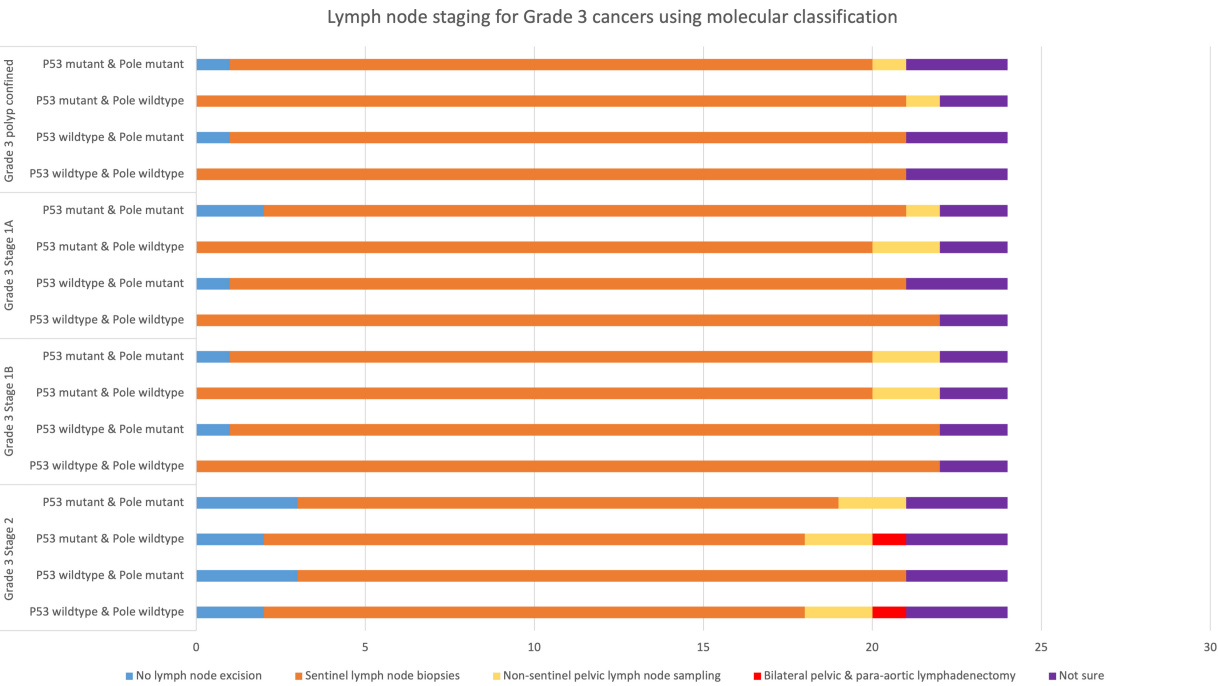


FIGURE 5. Lymph node staging for Grade 3 endometrial endometrioid carcinomas using molecular classification.

3.3.3 Route of sentinel lymph node biopsies

Overall, 37/57 (65%) of cancer centres perform sentinel lymph node biopsies laparoscopically, 33/57 (58%) robotically, 13/57 (23%) via open surgery, and 6/57 (11%) do not perform sentinel lymph node biopsies. The six responses indicating no sentinel lymph node biopsies correspond to five cancer centres: two of these centres perform pelvic lymph node lymphadenectomy in selected cases, two are unsure, and one centre does not perform any lymph node excision for early-stage endometrioid endometrial cancers.

4. Discussion

There is considerable variation in the pre-operative imaging practices for grade 1 and grade 2 endometrioid endometrial carcinomas across the UK. Approximately two-fifths of respondents perform pelvic imaging alone, one-fifth combine pelvic imaging with a plain chest X-ray, and just under two-fifths employ CT imaging of the chest, abdomen, and pelvis, with or without additional pelvic imaging. The BGCS endometrial cancer guidelines recommend chest radiology—either CT

or plain X-ray, depending on tumor grade—as part of the staging process for all women with endometrial cancer [5]. In contrast, the ESGO guidelines advocate for expert transvaginal/transrectal ultrasound or pelvic MRI for all endometrial carcinomas, with additional imaging modalities, including CT, recommended based on clinical or pathological risk factors to assess for extra-uterine disease [6].

A study by Gordon *et al.* [11] compared chest X-ray findings with thoracic CT in 93 cases of endometrial carcinoma and found agreement between the two modalities in 98% (91/93) of cases. Of the two cases with discrepancies, both had negative chest X-rays and equivocal CT findings [11]. One patient did not receive further follow-up, while the other was found to have a stable granuloma. More recently, Hashimoto *et al.* [12] assessed the diagnostic accuracy of CT and MRI in endometrial cancer. They highlighted the low sensitivities of these imaging modalities for detecting myometrial and cervical invasion, as well as pelvic lymph node and para-aortic metastases, emphasising the limitations of preoperative diagnostic performance despite advances in imaging technology [12].

Further support of omission of chest imaging in grade 1 and 2 endometrial carcinoma can be found in a retrospective cross-sectional study by Amkreutz *et al.* [13]. They found no instances of pulmonary metastasis in pre-operatively staged grade 1–2 endometrial carcinoma patients at a single site, with 784 patients included in the analysis [13]. Therefore, reducing the 25% of grade 1 and 40% of grade 2 patients currently undergoing CT imaging could offer several benefits, including a reduction in patient exposure to ionising radiation, as well as a decrease in healthcare costs and waiting times within the NHS. CT imaging could be reserved exclusively for grade 3 endometrial carcinoma patients, as chest imaging for grade 1 and 2 tumors has not been shown to alter radiological staging or management. The fact that only a minority of cancer centres in this study perform such imaging in these groups suggests that the majority of centres have already adopted this approach.

Several studies have investigated the risk of nodal metastases in endometrial carcinoma. One of the earliest studies was conducted by Creasman *et al.* [14] in 1987, who evaluated 621 patients with stage 1 endometrial carcinoma. They found that the risk of pelvic nodal metastasis for grade 1 cancers was 2% for stage 1A and 4% for stage 1B. For grade 2 cancers, the risk was 8% for stage 1A and 10% for stage 1B, while for grade 3 carcinomas, the risk increased to 11% for stage 1A and 26% for stage 1B [14]. These findings were later updated by Praiss *et al.* [15], who used the 2009 International Federation of Gynecology and Obstetrics (FIGO) staging criteria and the National Cancer Database to retrospectively review 161,960 patients who underwent surgery for endometrial carcinoma between 2004 and 2016. Praiss *et al.* [15] found that for grade 1 endometrioid carcinomas, the risk of nodal metastases was 1.1% for stage 1A, 8.6% for stage 1B, and 11.9% for stage 2. For grade 2 carcinomas, the risk was 2.9% for stage 1A, 13.7% for stage 1B, and 19.5% for stage 2. Finally, for grade 3 carcinomas, the risk was 4.8% for stage 1A, 16.9% for stage 1B, and 28.5% for stage 2 [15].

Milam *et al.* [16] further contributed by analysing 971 low-risk endometrial carcinoma patients, where low-risk was defined as tumours with less than 50% invasion, tumour size

under 2 cm, and well or moderately differentiated histology, equivalent to grade 1–2, stage 1A. Their study found the risk of nodal metastasis to be only 0.8%. These studies collectively demonstrate that the risk of nodal metastasis is low for grade 1, stage 1A tumours, which supports the decision by most centres not to perform lymph node staging in such patients. However, the findings for grade 1 stage 1B (ranging from 4% to 8.6%) and grade 2 stage 1A (ranging from 0.8% to 8%) cancers are more variable, explaining the observed practice differences among UK centres.

The BGCS guidelines recommend sentinel lymph node biopsy for all but low-risk disease [5], while the ESGO guidelines strongly advocate its use for high-intermediate and high-risk diseases [6]. However, even for low-risk populations, the risk of nodal metastasis remains an important factor in guiding adjuvant treatment to reduce recurrence. Consequently, these guidelines permit consideration of lymph node biopsy in lower-risk groups, facilitating personalised medicine—a crucial approach in the era of molecular classification of cancers. Additionally, the increasing use of sentinel lymph node biopsy for p53-mutant grade 1, stage 1A carcinomas highlights the role of molecular classification in surgical management. Abnormal p53 expression is associated with higher-risk features, such as lymphovascular space invasion and nodal metastasis [17], underscoring the importance of incorporating molecular classification into decisions regarding surgical management.

Additionally, the survey responses indicate that some centres are modifying lymph node staging procedures for POLE-mutant carcinomas, informed by the improved prognosis associated with POLE mutations, as evidenced by the molecular classification findings from the PORTEC-3 trial [9]. For patients with known POLE-mutant carcinomas identified pre-operatively, sentinel lymph node biopsy is particularly important to identify the small subset of stage III–IV patients, for whom the evidence supporting the omission of adjuvant treatment is currently insufficient. Accurate staging through sentinel node biopsy is therefore critical for tailoring treatment in this population.

In cases where a POLE mutation co-occurs with a p53 mutation, the POLE mutation takes precedence in determining subsequent adjuvant treatment strategies [18]. Ongoing clinical trials, such as PORTEC-4a (NCT03469674), are further investigating the safety and efficacy of treatment de-escalation in this context [18]. Consequently, it is essential to have both molecular classification results available pre-operatively to inform the most appropriate lymph node staging approach.

A recent survey conducted by George *et al.* [19] on endometrial cancer management was based on interviews from 2020–2021. It lacks clarity regarding the number of UK cancer centres represented, as participants were invited by an industry sponsor [19]. Furthermore, it provides no detailed information on the type of surgeries performed or how molecular classification influenced these surgical decisions. In contrast, our survey offers the most up-to-date insights into the surgical management practices of early-stage endometrial carcinoma in UK cancer centres. This study has several limitations that warrant consideration. Firstly, the results were constrained by the fact that some centres did not consistently have access to

molecular classification data preoperatively. This lack of information likely influenced surgical decision-making, making direct comparisons with centres that had preoperative molecular data more challenging. Additionally, the survey did not encompass all cancer centres within the UK, nor did it capture responses from every member of each multidisciplinary team. Furthermore, there may be variations in practice within individual centres that were not fully portrayed by this survey, potentially limiting the comprehensiveness of the findings.

There has been a paradigm shift in endometrial cancer staging, transitioning from full lymphadenectomy to sentinel lymph node biopsy, following the landmark FIRES (A comparison of sentinel lymph node biopsy to lymphadenectomy for endometrial cancer staging), SHREC (Pelvic Sentinel lymph node detection in High-Risk Endometrial Cancer) and SENTOR (Sentinel Lymph Node Biopsy *vs.* Lymphadenectomy for Intermediate- and High-Grade Endometrial Cancer Staging) studies [20–22]. With the recent FIGO 2023 staging update, it is imperative for the gynaecological oncology community to understand current trends and practices in light of these significant advancements [8]. This study offers valuable insights into how these significant advancements are being incorporated into clinical practice and highlights the need for the gynecological oncology community in the UK to enhance preoperative and surgical staging procedures to improve patient outcomes in cancer care.

5. Conclusions

Significant variation exists in pre-operative imaging and lymph node staging practices for grade 1 and grade 2 endometrioid endometrial carcinomas across the UK. There is an opportunity to improve compliance with established guidelines by increasing the use of plain chest X-rays for pre-operative imaging while simultaneously reducing the overutilisation of staging CT scans in patients with low-risk endometrial carcinomas. Furthermore, achieving greater consensus on the selection of lymph node staging procedures for grade 1, stage 1B, and grade 2, stage 1A endometrioid endometrial carcinomas could standardise practices and optimise patient care nationwide.

ABBREVIATIONS

BGCS, British Gynaecological Cancer Society; NHS, National Health Service, CT, Computerised Tomography; MRI, Magnetic Resonance Imaging; USS, Ultrasound scan; MMRd, Mismatch Repair deficiency; NSMP, Non-specific molecular profile; ESGO, European Society of Gynaecological Oncology; MSH6, MutS Homolog 6; PMS2, Postmeiotic Segregation Increased 2; POLE, Polymerase Epsilon; MDT, multidisciplinary team; FIGO, International Federation of Gynecology and Obstetrics; PORTEC-3, Adjuvant Chemoradiotherapy Versus Radiotherapy Alone in Women With High-Risk Endometrial Cancer; FIRES, A comparison of sentinel lymph node biopsy to lymphadenectomy for endometrial cancer staging; SHREC, Pelvic Sentinel lymph node detection in High-Risk Endometrial Cancer; SENTOR, Sentinel Lymph Node Biopsy *vs.* Lymphadenectomy for Intermediate- and High-

Grade Endometrial Cancer Staging.

AVAILABILITY OF DATA AND MATERIALS

The data are contained within this article.

AUTHOR CONTRIBUTIONS

HP and AM—were responsible for conceptualization, data curation, investigation, analysis, writing- original draft and writing-review and editing. CN—was responsible for conceptualisation, supervision and writing-review and editing. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This survey was promoted with a clear understanding that its results would be published in a peer-reviewed journal, thereby implying informed consent through participation. Ethics approval was not required for this survey because it did not involve randomization of participants, nor did it aim to alter treatment or care of any patients during the survey. According to the Health Research Authority (HRA) guidelines in the UK, studies that do not meet the definition of research—such as those that focus on understanding practice patterns without directly affecting patient care—do not require formal research ethics approval. Consequently, this study was classified as a service evaluation, and ethical approval was not sought.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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