Submitted: 16 December, 2023 Accepted: 16 January, 2024 Published: 15 August, 2024 DOI:10.22514/ejgo.2024.078

ORIGINAL RESEARCH

European Journal of Gynaecological Oncology

The COVID-19 pandemic's ripple effects: investigating the impact of COVID-19 on endometrial cancer in a large UK regional cancer centre

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Abstract

COVID-19 has had a significant impact on the management of gynaecological malignancies globally. Despite the extensive work investigating the impact of the COVID-19 pandemic on gynaecological cancer care as a whole, little is known with regard to the specific management of endometrial cancer. The aim of this retrospective cohort study was to assess the impact of the COVID-19 pandemic on patients diagnosed with endometrial cancer in Northern Ireland (NI). All patients with endometrial cancer in NI between April 2019–March 2022 were included, divided into three cohorts: pre-COVID, COVID-Year 1 and COVID-Year 2. The median was used to express data that was not normally distributed. Students *t*-test and Mann-Whitney U test were used to compare means with and without normal distribution respectively. Statistical analysis of count data included the chi-squared test. The p-value < 0.05 was considered statistically significant. 683 patients were included with a similar distribution of age, histology and length of stay. There was a 22% decrease in new endometrial cancer diagnoses in COVID-Year 1 (n = 195) compared to Pre-COVID (n = 249), with evidence of recovery by year 2 (n = 241). In COVID-Year 1 there was a 29% decrease in surgical resections. During COVID-Year 2 there was an increase in symptom duration of >6 months (21%) compared to Pre-COVID (11% (p = 0.03)). By COVID-Year 2 there was an increase in Stage III disease (19%) compared to Pre-COVID (12% (p = 0.02)). In COVID-Year 1 and 2 there was an increase in the use of adjuvant oncological treatment, with a significant increase in the use of chemoradiotherapy in COVID-Year 2. In conclusion, COVID-19 has significantly impacted the treatment pathways of endometrial cancer patients in NI. There was a significant increase in symptom duration and stage III disease requiring increased use of adjuvant oncological treatments.

Keywords

COVID-19 pandemic; Endometrial cancer; Surgical oncology; Adjuvant treatment

1. Introduction

Endometrial cancer remains the 4th most common cancer in women in the UK [1] and the most common gynaecological malignancy in high income countries [2]. The SARS-CoV-2 (COVID-19) virus originated in Hubei, China and was declared a pandemic by the World Health Organisation (WHO) in March 2020 [3, 4]. During the COVID-19 pandemic many of the leading professional bodies developed guidelines for the management of gynaecological conditions during the pandemic. Some recommended the suspension of routine gynaecological services with the exception of urgent care [5, 6]. In the UK, The Royal College of Obstetricians and Gynaecologists (RCOG), in collaboration with the British Gynaecological Cancer Society (BGCS) and the British Society of Gynaecological Endoscopy (BSGE), developed guidance on the management of abnormal uterine bleeding (AUB) during the COVID-19 pandemic [7]. Heavy menstrual bleeding (HMB) was advised to be managed remotely with a referral to secondary care only if there was associated severe anaemia, haemodynamic compromise was suspected, or if other risk factors for malignancy or endometrial hyperplasia were present [7]. The recommendations for post-menopausal bleeding (PMB) on the other hand included an initial review within 7 days, followed by a 2 week wait referral [7] with the knowledge that 5–10% will have endometrial cancer [8]. Hysteroscopy and an endometrial biopsy was recommended up to 4 weeks from presentation to facilitate a 28-day diagnosis

[7] whilst those with suspected acute COVID-19 infection were advised to avoid attending secondary care for review or treatment [6, 7]. The International Society of Gynaecological Endoscopy (ISGE) recommended the use of minimally invasive surgery during COVID-19, where possible, to facilitate earlier discharge, reduce post-operative complications and therefore hospital readmission rates and nosocomial infections [6]. However, intercollegiate general surgical advice in the UK highlighted the potential risk of viral transmission from surgical smoke and the need for risk mitigation strategies to safely proceed with a laparoscopic approach [9].

COVID-19 has had a significant impact on the management of gynaecological malignancies globally [10]. Cancer patients were identified as particularly high risk for COVID-19 infection with increased morbidity, admission to intensive care, and mortality [10]. Gynaecological cancer care was therefore reconfigured to avoid contact in this cohort of patients, including initial remote consultations followed by ultrasound or hysteroscopy in PMB [7]. There was maximisation of outpatient hysteroscopy with opportunistic levonorgestrel-releasing intrauterine system (LNG-IUS) if abnormal findings were identified and the use of laparoscopy where possible [10]. In a survey of gynaecological oncologists in the UK, Oxley *et al.* [11] demonstrated a 40% reduction in theatre capacity, 30% postponement of planned procedures and 75% of outpatient consultations conducted virtually during the first wave of the COVID-19 pandemic. There was evidence of some recovery by the second and third wave [11]. The COVIDSurg-Gynecologic Oncology Cancer Study [12] also demonstrated that 1 in 5 gynaecological cancer patients experienced an adjustment to the standard of care with 11.2% having a significant delay (>8 weeks) in treatment. 1 in 13 patients did not receive their planned procedure with 5% and 20% of those patients dying or showing disease progression respectively within 3 months [12]. In addition, with the peak age at diagnosis for endometrial cancer being 75–79 years [13] and a mortality rate from COVID-19 50 times higher for those between 70–79 years [14], it is widely accepted that older people felt very vulnerable during the COVID-19 pandemic. Older people, especially those with pre-existing comorbidities, were less likely to attend their general practitioners [15], allied with a 92.5% reduction in face to face primary care consultations during the first wave of the COVID-19 pandemic [16].

There is evidence to suggest that endometrial cancer diagnoses reduced during the initial phase of the COVID-19 pandemic [2, 17]. Despite the extensive work investigating the impact of the COVID-19 pandemic on gynaecological cancer care as a whole, little is known with regard to the specific management of endometrial cancer which relies heavily on timely investigation of AUB. Endometrial cancer caries a favourable prognostic profile with a 1 year and 5 years survival of 89.5% and 78.6% respectively, according to the Northern Ireland Cancer Registry [18]. This relies on timely diagnosis and management, which in most cases includes a minimally invasive hysterectomy, bilateral salping-oopherectomy and/or bilateral sentinel pelvic lymph node biopsy. The aim of this study was to assess the impact of the COVID-19 pandemic on the diagnostic and treatment pathways of patients diagnosed with endometrial cancer in Northern Ireland (NI).

2. Materials and methods

2.1 Study design

This retrospective cohort study was conducted on all patients diagnosed with endometrial carcinoma in Northern Ireland (NI) between 01 April 2019 and 31 March 2022. The study setting was the Northern Ireland Regional Cancer Centre, which is the tertiary gynaecological oncology centre for all patients diagnosed with endometrial carcinoma in N.I. The study period included a pre-COVID analysis followed by the two years, during the COVID-19 pandemic, and can be further defined as pre-COVID (01 April 2019–31 March 2020), COVID-Year 1 (01 April 2020–31 March 2021), and COVID-Year 2 (01 April 2021–31 March 2022). All years included in the study were analysed exclusively as separate cohorts. Patients diagnosed with myometrial sarcoma, other myometrial tumours or recurrences were excluded from the study.

2.2 Patient and tumour characteristics

Data items collected for analysis included: age, parity, symptom duration, histological subtype & grade, FIGO stage, magnetic resonance imaging (MRI) stage, surgical approach and type, location of surgery (cancer centre *vs.* cancer unit) length of stay (LOS) and adjuvant oncological treatments.

2.3 Data collection

Data was collected using three regional electronic sources; The N.I Regional Cancer Patient Pathway System (CaPPS), The N.I Electronic Care Record (NIECR) and the N.I Regional Information System for Oncology & Haematology (RISOH).

2.4 Statistical analysis

Data was collected electronically and statistical analysis performed using XLSTAT (Version 2021.3.1, Addinsoft, Paris, France) software. The median was used to express data that was not normally distributed. Count data were expressed by frequency and percentage. Statistical analysis of count data was done using the chi-squared test. The students *t*-test was used to compare means for normally distributed variables while the Mann-Whitney U test was used for variables without normal distribution. The *p*-value less than 0.05 was considered significant.

3. Results

3.1 Study population

A total of 683 patients were included in the study with 249, 195 and 239 in the pre-COVID, COVID-Year 1 & COVID-Year 2 respectively (Table 1). The age, histological type and grade were similarly distributed across the three periods.

The median age at diagnosis was relatively unchanged across the three years studied (Table 1). There was a 22% decrease in new diagnoses of endometrial cancer in COVID-Year 1, as shown in Table 1, with 249 new diagnoses pre-COVID compared to 195 in COVID-Year 1 (p = 0.007) with evidence of recovery by COVID-Year 2 (n = 239).

TABLE 1. Endometrial cancer: patient and tumour characteristics.

	Pre-COVID	COVID-Year 1	COVID-Year 2	Total
Patients	249	195	239	683
Median Age (Range)	67 (34–93)	68 (25–92)	66 (33–91)	
Histological subtype				
Endometrioid carcinoma	194 (78%)	141 (72%)	175 (73%)	510 (75%)
Serous carcinoma	32 (13%)	28 (14%)	30 (13%)	90 (13%)
Clear cell carcinoma	6 (2%)	9 (5%)	15 (6%)	30 (4%)
Carcinosarcoma	12 (4%)	7 (4%)	10 (4%)	29 (4%)
Endometrial stromal sarcoma	1 (<1%)	2 (1%)	1 (<1%)	4
Undifferentiated carcinoma	1 (<1%)	4 (2%)	3 (1%)	8
Other	3 (<1%)	4 (2%)	5 (2%)	12
Histological Grade				
FIGO Grade 1	122 (49%)	87 (45%)	130 (54%)	339 (50%)
FIGO Grade 2	54 (22%)	30 (15%)	30 (12%)	114 (17%)
FIGO Grade 3	71 (28%)	73 (37%)	77 (32%)	221 (32%)
Ungraded	2 (<1%)	5 (3%)	2 (<1%)	9 (1%)
Symptom Duration				
<3 mon	160 (64%)	128 (65%)	132 (55%)	420 (61%)
3–6 mon	48 (20%)	30 (15%)	42 (18%)	120 (18%)
>6 mon	28 (11%)	28 (14%)	50 (21%)	106 (16%)
Missing/asymptomatic	13 (5%)	9 (5%)	15 (6%)	37 (5%)
FIGO Stage				
I	188 (75%)	133 (68%)	159 (67%)	480 (70%)
II	7 (3%)	9 (5%)	11 (5%)	27 (4%)
III	29 (12%)	32 (16%)	46 (19%)	107 (16%)
IV	22 (9%)	19 (10%)	20 (8%)	61 (9%)
Unknown	3 (1%)	2 (1%)	3 (1%)	8 (1%)

FIGO: International Federation of Gynecology and Obstetrics.

3.2 Symptom duration

Symptom duration was very well recorded (95%) in all three cohorts. There was an increase in the number/percentage of patients with a symptom duration of more than 6 months in COVID-Year 2 50/239 (21%) compared to pre-COVID (28/249 11%). This increase, as shown in Fig. 1, was statistically significant ($p = 0.03$).

3.3 FIGO stage

When comparing advanced (stage III + IV) and non-advanced (stage I + II) disease, there was no significant difference seen ($p = 0.16$). However, when analysed separately, there was an increase in number/percentage of patients with FIGO Stage III disease compared to non-advanced disease (stage I–II) in COVID Year 2 (46/246 19%) compared to pre-COVID (29/246 12%) which was statistically significant ($p = 0.02$), as shown in Fig. 2.

3.4 Treatment

3.4.1 Surgery

In COVID-Year 1 there was a 29% decrease ($p = 0.009$) in surgical resections in keeping with reduced number of diagnoses and restricted surgical access (Table 2). There was a 36% reduction in surgical procedures performed in the NI regional cancer centre compared to a 23% reduction in local cancer units. Laparoscopic procedures performed in COVID-Year 1 were reduced by 33% in keeping with overall reduction in surgical resections ($p = 0.076$). Length of stay in hospital was similar across the three periods.

3.4.2 Adjuvant oncological treatment

There was an increase in the use of external beam radiotherapy (EBRT) with brachytherapy in COVID-Year 1 & 2. There was a significant increase in use of combined EBRT & brachytherapy *vs.* no adjuvant therapy in COVID Year-2 compared to Pre-COVID ($p = 0.007$). There was also a significant increase ($p \leq 0.0001$) in the number/percentage of patients having triple therapy (EBRT + brachytherapy + chemotherapy) *vs.* no adjuvant therapy in COVID year-2 compared to Pre-COVID (Table 2 & Fig. 3).

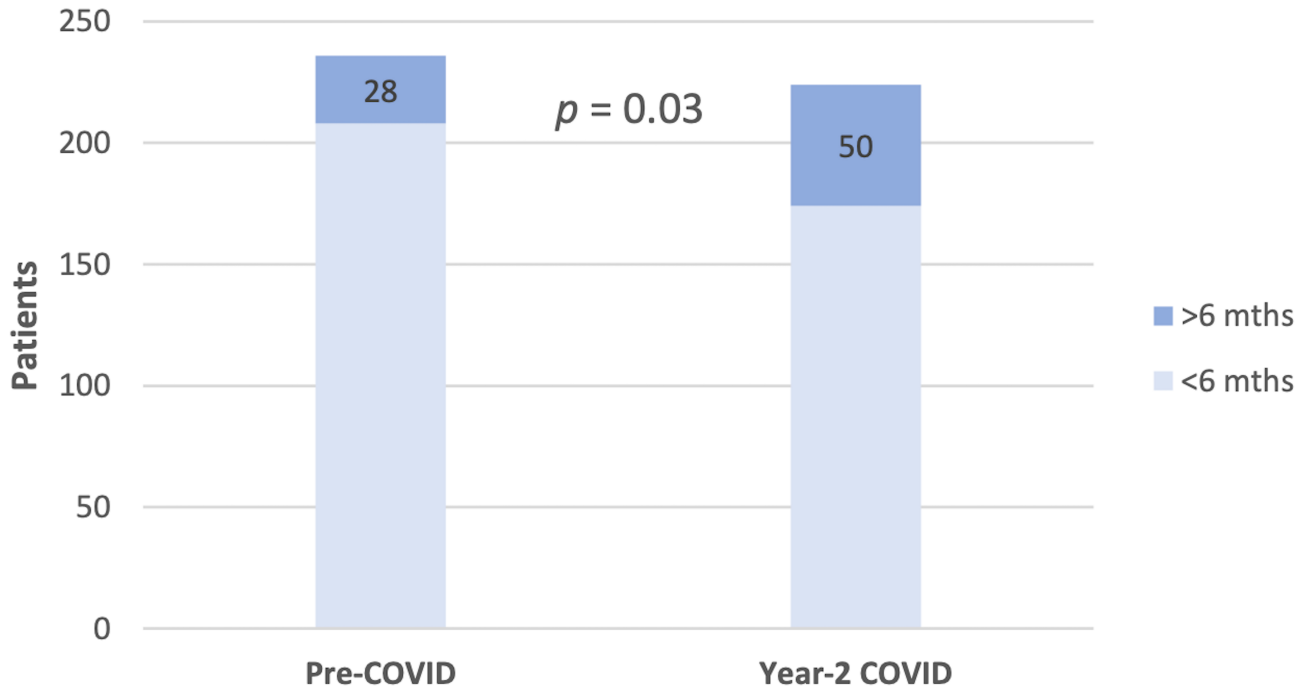

FIGURE 1. Endometrial cancers: symptom duration Pre-COVID *vs.* COVID-Year 2.

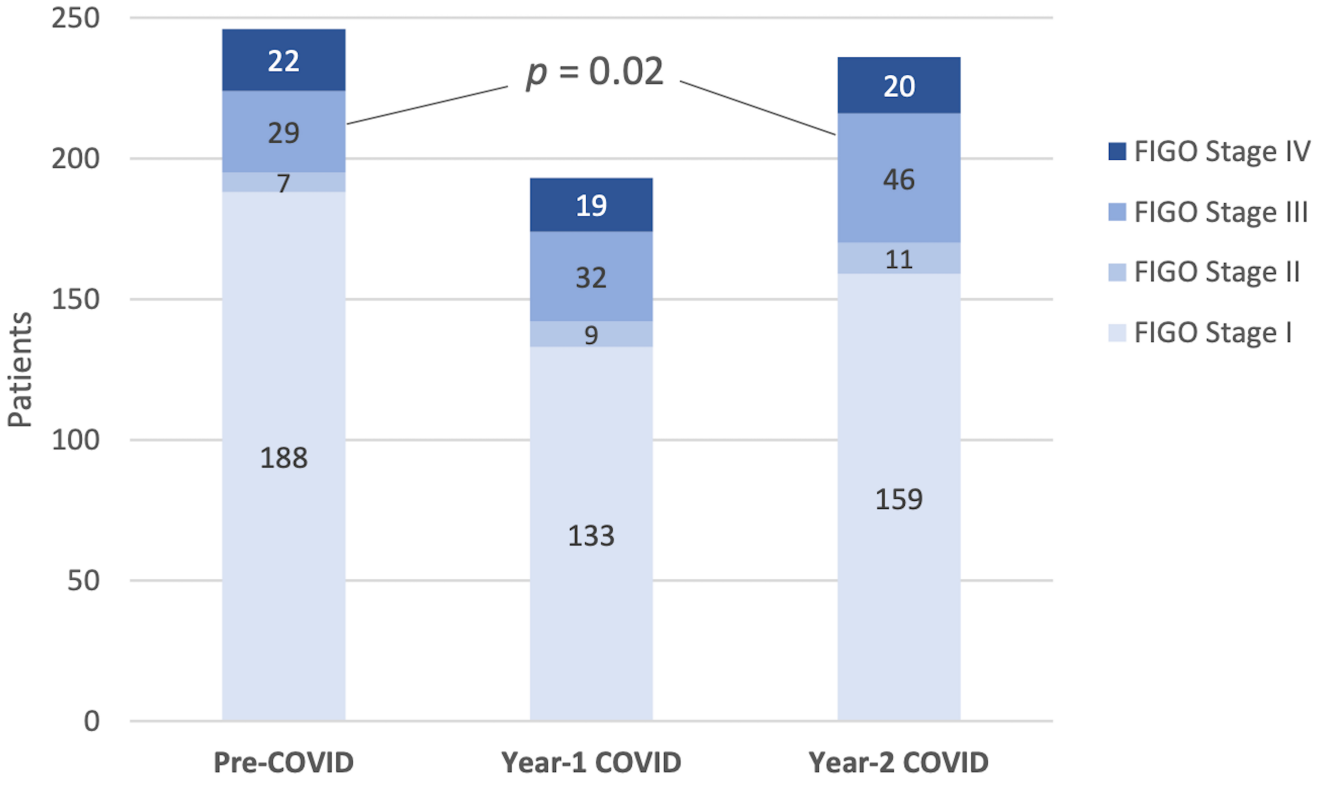

FIGURE 2. FIGO Stage Pre-COVID, COVID-Year 1 & 2. FIGO: International Federation of Gynecology and Obstetrics.

TABLE 2. Endometrial cancer treatment Pre-COVID, COVID-Year 1 & 2.

	Pre-COVID	COVID-Year 1	COVID-Year 2	Total
Primary Treatment modality (n = 682*)				
Surgery	221/249 (89%)	158/195 (81%)	205/239 (86%)	584/682 (86%)
Chemotherapy +/− Radiotherapy +/− Brachytherapy	7/249 (3%)	17/195 (9%)	14/239 (6%)	38/682 (6%)
Hormone therapy	8/249 (3%)	15/195 (8%)	9/239 (<4%)	32/682 (5%)
Best supportive care	13/249 (5%)	5/195 (3%)	10/239 (4%)	29/682 (4%)
Surgery Location (n = 581***)				
Cancer Centre	90/221 (41%)	58/158 (37%)	91/205 (44%)	239/584 (41%)
Cancer Unit	130/221 (59%)	100/158 (63%)	112/205 (55%)	342/584 (59%)
Surgical Approach (n = 583***)				
Laparoscopic	107/221 (49%)	72/158 (46%)	88/205 (43%)	267/584 (46%)
Converted	4/221 (2%)	6/158 (4%)	6/205 (3%)	16/584 (3%)
Open	70/221 (32%)	50/158 (32%)	87/205 (42%)	207/584 (35%)
Vaginal	40/221 (18%)	30/158 (19%)	23/205 (11%)	93/584 (16%)
Length of Stay (n = 581***)				
<5 d	159 (72%)	121 (77%)	39/205 (68%)	420/584 (72%)
5–9 d	48 (22%)	32 (20%)	50/205 (24%)	131/584 (22%)
>10 d	13 (6%)	5 (3%)	14/205 (7%)	32/584 (6%)
Adjuvant Treatment (n = 250/584)				
Adjuvant EBRT** + Brachytherapy	41/221 (19%)	55/158 (35%)	62/205 (30%)	158/584 (27%)
Adjuvant EBRT**, Brachytherapy + chemotherapy	14/221 (6%)	25/158 (16%)	39/205 (19%)	78/584 (13%)
Adjuvant chemotherapy +/− EBRT/Brachytherapy	26/221 (12%)	33/158 (21%)	48/205 (23%)	107/584 (18%)
Any adjuvant treatment	77/221 (35%)	83/158 (53%)*	90/205 (44%)	250/584 (43%)
No adjuvant treatment	144/221 (65%)	75/158 (47%)	115/205 (56%)	334/584 (57%)

**One patient referred to centre outside N.I (treatment details incomplete).*
***External beam radiotherapy.*
****3 patients had surgery performed outside HSCNI.*

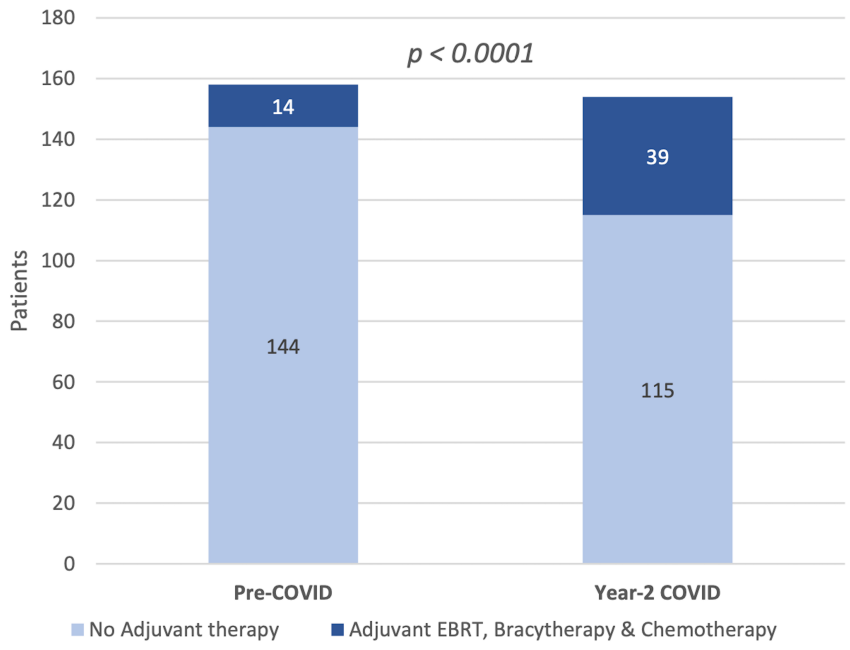

FIGURE 3. Adjuvant EBRT, Brachytherapy & Chemotherapy Pre-COVID and COVID-Year 2. EBRT: external beam radiotherapy.

4. Discussion

4.1 Summary of main results

In this study of 683 patients diagnosed with endometrial carcinoma we demonstrated a significant decrease in new diagnoses in COVID-Year 1 compared to Pre-COVID numbers with evidence of recovery by COVID-Year 2. This is in keeping with reduced access to primary care and diagnostic services at the start of the COVID-19 pandemic [7, 14, 16, 19, 20]. In COVID-Year 1 there was an overall 29% reduction in surgical resections ($p = 0.009$) and a 36% reduction in surgical procedures performed in the regional cancer centre compared to 23% reduction in the local cancer units. This is most likely a result of reduced diagnoses in combination with reduced theatre access and the development of the regional Nightingale Hospital at Belfast City Hospital (NI. Regional Cancer Centre) during COVID-19. In the UK, Nightingale hospitals were used to specifically manage COVID-19 related illness and other services were re-deployed to other nearby hospitals [20]. In NI, all surgical specialties in Belfast City Hospital were moved to the neighbouring Royal Victoria Hospital (RVH) and theatre time was divided between all surgical specialities. This contributed to the significant increase in elective waiting lists during the COVID-19 pandemic [21]. In addition, the number of minimal access hysterectomies fell by 33% in Covid-Year 1 which we attribute to the overall reduction in surgical resections as this was not statistically significant ($p = 0.076$). By COVID-Year 2 we see a significant increase in patients reporting symptoms for more than 6 months, significant increases in FIGO Stage III cancers and a significant increase in adjuvant chemoradiotherapy.

4.2 Results in the context of published literature

Wylie *et al.* [2] and Suh-Burgmann *et al.* [17] suggested a reduction of new endometrial carcinoma diagnoses of between 19–35% during the COVID-19 pandemic [2, 17]. The findings of these studies agree with our data with a 22% decrease in new endometrial carcinoma diagnoses in COVID-Year1, however we offer further insight into this with evidence of recovery in the number of new diagnoses by COVID-Year2. The 29% decrease in surgical resections overall, and 36% reduction in those performed in the regional cancer centre, may be attributable to the limited theatre access throughout the COVID-19 pandemic, as highlighted in the survey of gynaecological oncologists by Oxley *et al.* [11]. Despite international guidance advising the use of minimally invasive surgery (MIS), where possible [6], this study demonstrates a reduction in the MIS approach to surgery by one third in COVID-Year 1.

4.3 Strengths and weaknesses

To our knowledge this is the first and largest study to assess the impact of the COVID-19 pandemic on the management of endometrial cancer. Other strengths include the large cohort of patients included over an appropriate timeframe, capturing the changing landscape of management throughout the pandemic in comparison to a pre-COVID cohort of patients. Northern Ireland offers a unique opportunity to accurately assess this impact as all patients had their management discussed at a single, regional gynaecological oncology multi-disciplinary team (MDT) meeting, ensuring a standard approach of care for all patients and high homogeneity amongst the population. Weaknesses include the retrospective approach to data collection and the lack of data on survival outcomes.

4.4 Implications for practice and future research

This study highlights the potential impact of a reduced access to diagnostic services. A delay in investigation, resulting in a prolonged symptomatic period, led to a higher stage at diagnosis in COVID-Yr2. This study therefore justifies the rapid access and investigation of AUB and illustrates how delays in diagnosis can lead to upstaging of endometrial cancer and by inference may affect survival. It is therefore important to consider a further analysis of disease outcomes, including survival, of the patients in this study to assess the long-term impact of the COVID-19 pandemic. In the UK, early stage (Stage I), low grade (grade I) endometrial cancers receive surgical management in local cancer units, as opposed to a tertiary gynaecological oncology cancer centre. This usually includes a minimal access hysterectomy and bilateral salpingo-oopherectomy. This study therefore provides insight into the workload divided amongst the regional cancer centre and local cancer units as an overall assessment of the NI cancer network (NICaN). Further work is in development concentrating on gynaecological oncology diagnostics within local cancer units. The upstaging of disease as a result of a prolonged symptom duration, as seen during COVID-Yr2, will of course lead to a burden of cancer services with the NI regional cancer centre in Belfast. This will have led to a more complex surgical approach, requiring surgery in the regional cancer centre, which was more difficult to facilitate due to reduced theatre capacity. We also know that it led to an increase in the use of adjuvant oncological treatments, all of which are provided at the NI regional cancer centre, adding further burden to these services.

5. Conclusions

The COVID-19 pandemic, and the reduction of access to diagnostic services, led to an overall reduction of endometrial cancer diagnoses. There was, however, evidence of recovery by COVID-Year 2. More surprisingly, the reduction in surgical resections, which is the hallmark of treatment for these patients, was most significant in COVID-Year1 married with a significant upstage and an increase in the use of adjuvant treatment in COVID-Year 2. This may be explained by the reduced access to primary care, diagnostics and theatre capacity during the pandemic. Further work will establish if the COVID-19 pandemic has impacted progression free survival and overall survival in this cohort of patients.

AVAILABILITY OF DATA AND MATERIALS

The data are contained within this article.

AUTHOR CONTRIBUTIONS

JCM—conceptualisation, methodology, formal analysis, investigation, data curation, writing-original draft preparation/review and editing, visualization; EL, SW and FA—formal analysis, investigation, writing-review & editing; LR—methodology, validation, formal analysis, investigation, data curation, writing-original draft preparation/review and editing; IH, MM, EC and HN—methodology, investigation, writing-reviewing & editing; SD—conceptualisation, methodology, formal analysis, investigation, data curation, writing-original draft preparation/review and editing, visualisation, supervision.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The National Health Service (NHS) Health Research Authority decision tool was used. This study was assessed as a service evaluation of the N.I Regional Gynaecological Oncology Regional Multidisciplinary Team (MDT) on behalf of the N.I Cancer Network (NICaN). Therefore, no NHS research ethics committee review was necessary.

ACKNOWLEDGMENT

This work was completed on behalf of the NI regional gynaecological oncology Multidisciplinary Team (MDT) as part of the NI cancer network (NICaN), including the regional tertiary cancer centre in Belfast and four local cancer units in NI.

FUNDING

This research received no external funding.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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How to cite this article: Josh Courtney McMullan, Emily Leitch, Susan Wilson, Fatma AlWahaibi, Lisa Ranaghan, Ian J Harley, *et al*., On behalf of the N.I Regional Gynae-oncology Multidisciplinary Team (MDT). The COVID-19 pandemic's ripple effects: investigating the impact of COVID-19 on endometrial cancer in a large UK regional cancer centre. European Journal of Gynaecological Oncology. 2024; 45(4): 131-138. doi: 10.22514/ejgo.2024.078.