Annals of *Research* in *Oncology*
Vol. 3(4), 147-154, 2023

RESEARCH ARTICLE

INCIDENCE AND CLINICAL OUTCOME OF ENDOMETRIAL CANCER: A POPULATION-BASED CANCER-REGISTRY STUDY

Lucia **Mangone** [1,*], Francesco **Marinelli** [1], Isabella **Bisceglia** [1], Maria Barbara **Braghiroli** [1], Valentina **Mastrofilippo** [2], Fortunato **Morabito** [3], Antonino **Neri** [4], Lorenzo **Aguzzoli** [2], Vincenzo Dario **Mandato** [2]

[1] Reggio Emilia Cancer Registry, Epidemiology Unit, Azienda Unità Sanitaria Locale - IRCCS di Reggio Emilia, Reggio Emilia, Italy
[2] Obstetrics and Gynaecology Unit, Azienda Unità Sanitaria Locale - IRCCS di Reggio Emilia, Reggio Emilia, Italy
[3] Biotechnology Research Unit, AO di Cosenza, Aprigliano, Cosenza, Italy
[4] Scientific Directorate, Azienda Unità Sanitaria Locale - IRCCS di Reggio Emilia, Reggio Emilia, Italy
* Correspondence to: mangone.lucia@ausl.re.it, https://orcid.org/0000-0002-5089-5178.

ABSTRACT: This study aimed to assess the incidence and patient characteristics of Endometrial cancer (EC) in an Italian Cancer Registry and identify those factors that may have an impact on the diagnosis and prognosis.
The three outcomes investigated were disease-free survival (DFS), recurrence, and overall survival (OS), by age and stage in the Reggio Emilia province from 2013 to 2015.
234 cases were registered: over 90% were over 50 years old, 69% were classified as stage I, nearly 86% had surgery, and 14.5% received chemotherapy. There were 21 recurrences, 10 were in stage III, 8 in stage I, and only 2 in stage II. Stage III presents a 53% recurrence rate in the first year, decreasing however in the following years.
DFS length increased at 1 and 3 years after diagnosis, rising from 60% to close to 86% for stage II and from more than 23% to 57% for stage III. The 5-year OS rate was about 79%, with values of 96.1%, 59.2%, 44%, and 17.3 % for stages I, II, III, and IV respectively a 100% 89.4% and 64.9% for age <59, 50-65 and 65+, respectively. Multivariate analysis confirms an increased stage-related risk for both DFS and OS, but the age-related risk disappears.
Even though most EC are stage I, there remains an increased risk of recurrence for stage III tumors; age does not seem to represent an important determinant, confirming the importance of good *ab initio* management of patients.

Doi: 10.48286/aro.2023.77

Impact statement: This population-based study, based on cancer registry data, shows that most endometrial cancers are stage I, but the risk of recurrence remains high for stage III cancers.

Key words: *endometrial cancer; stage; age; recurrence; disease-free survival; death.*

Received: Sept 5, 2023/**Accepted**: Nov 2, 2023
Published: Dec 22, 2023

INTRODUCTION

Endometrial cancer (EC) is the sixth most common cancer in women and the thirteenth most lethal, accounting for nearly 97,000 deaths worldwide each year (1). In Italy, approximately 10-200 new cases of EC (5.5% of all female cancers) are diagnosed annually, representing the third most frequent neoplasm among women aged 50 to 69 years, with regrettably 3,100 deaths (2). In Italy, the

incidence trend appears to be marginally decreasing between 2003 and 2014 with an Annual Percentage Change (APC) = -0.1%; (95% CI 0.4; -0.1), associated with a mortality slight decline in the period 2003-2017 (APC = -0.5%; 95% CI -2.1; 1.2) (2). EC has a favourable prognosis with a remarkable 5-year survival rate of 79% (2), but survival drops dramatically in advanced stages (3). Nulliparity, late menopause, obesity, diabetes, hypertension, and estrogen-based hormone replacement therapy, which is insufficiently counterbalanced by progestin therapy, are the main risk factors for hyperestrogenism-related forms (4). On the other hand, estrogen-independent neoplasms are linked to previous pelvic radiotherapy or tamoxifen use. Furthermore, they appear later in age (menopause), have serous or clear cell differentiations, and are unrelated to previous endometrial hyperplasia or dysplasia (5). EC is classified as low, intermediate, intermediate-high, and high-risk classes based on prognostic factors such as myometrial infiltration and differentiation, tumor size, the presence of vascular emboli and /or lymphatics, lymph node metastases, and histotype (6). The likelihood of recurrences is prominent in women who are deemed to be at high risk (7). In recent years, new risk factors and molecular features have been studied to profile EC (8) and the European Society of Medical Oncology guidelines have introduced a new classification of the recurrence risk based on The Cancer Genome Atlas results, with the aim of better-selecting patients to undergo to adjuvant therapy (9). Although it is not yet clear whether EC treatment should be centralized or not (10) it would seem reasonable to hypothesize that the multidisciplinary team (MDT) could improve the treatment of EC (11), as well as other female cancers (12-15). This study aimed to assess the incidence and patient characteristics of Endometrial cancer (EC) in an Italian Cancer Registry and the outcomes in terms of disease-free survival (DFS), recurrence, and overall survival (OS), by age and stage.

MATERIALS AND METHODS

The study includes all EC diagnosed between 2013 and 2015 in Reggio Emilia province. EC cases were classified as topography C54 in the International Classification of Diseases for Oncology, Third Edition (ICD-O-3) (16). The Reggio Emilia Cancer Registry (RE-CR) relies on three primary information sources: pathology reports, hospital discharge records, and mortality data, which are integrated with laboratory tests, diagnostic reports, and information from general practitioners. Consulting hospital medical records yielded Information on stage (TNM 8th edition) (17) as well as surgery and chemotherapy. All information was obtained from the Cancer Registry except for the variables on stage, surgery, chemotherapy, and recurrence which were retrieved from medical records since they are not routinely recalled from CRs. One-year, 3-year, and 5-year outcomes were defined as disease-free for the observation period, with a recurrence or death occurring within the specified time frame. To test the trends between these three periods, we used the Poisson regression model with the period as the independent continuous variable and the number of events from every category (disease-free, recurrence, and death) estimate for each period and the period-specific incident cases as exposed population. The 5-year survival was reported overall and by disease stage (I, II, III, IV, and unknown) and age (<50, 50-65, and >65). The time-to-event outcome, *i.e.*, disease-free survival (DFS) and overall survival (OS) were calculated by the Kaplan-Meier method. OS and DFS were adjusted for stage and age groups and performed by Cox proportional hazards multivariate models. Analyses were performed using STATA 16.1 software. In this study, we reported 95% confidence intervals (CI) and we defined a p-value <0.05 as statistically significant. The RE-CR covers a population of 532,000 inhabitants and is considered a high-quality CR due to its current extension until the end of 2020, a high percentage of microscopic confirmation (98.8% for EC), and a very low number of Death Certificate Only (DCO < 0,1%) (18). The Cancer Registry collects data and information by current flows to generate incidence, mortality, prevalence, and survival statistics for the resident population and demographic subgroups as required by the epidemiological report, defined by Law no. 29 of 03/22/2019 that regulates the cancer registries in Italy. The Law exempts the Registries from collecting informed consent. The procedures for conducting epidemiological analyses of the Reggio Emilia Cancer Registry data have been approved by the provincial Ethics Committee of Reggio Emilia (Protocol no. 2014/0019740 of 04/08/2014).

Table 1. *Reggio Emilia Cancer Registry. Endometrial cancers, Years 2013-2015. Distribution of cases by age, year of diagnosis, method of diagnosis, stage, treatment, and recurrence.*

	N	%
Overall	234	
Age at diagnosis		
<50	23	9.8
50-65	99	42.3
65+	112	47.9
Years		
2013	80	34.2
2014	82	35.0
2015	72	30.8
Method of diagnosis		
Histological	229	97.9
Clinical/instrumental	5	2.1
Stage		
I	162	69.2
II	13	5.6
III	26	11.1
IV	13	5.6
Unknown	20	8.5
Surgery		
Yes	201	85.9
No	24	10.3
Unknown	9	3.8
Chemotherapy		
Yes	34	14.5
No	186	79.5
Unknown	14	6.0

RESULTS

Between 2013 and 2015, 234 incident cases were recorded in the RE-CR (**Table 1**): 90.2% of patients were over 50 years old, and 98% had histological confirmation. Most cases were in stage I (69.2%), while stages II, III, and IV accounted for 5.6%, 11.1%, and 5.6%, respectively. Moreover, 85.9% underwent surgery and 14.5% received chemotherapy. There were 21 recurrences in total, with an average of 2 years between cancer diagnosis and recurrence. The majority (77.1%) of the 201 patients who underwent surgery were in stage I, followed by 11.9% in stage III, 6.5% in stage II, and 2.5% in stage IV (**Table 2**). Only 34 women received chemotherapy, with 47.1% in stage III and 23.5% in stage I. Ten (47.6%) of the 21 recurrences were in stage III, 8 (38.1%) were in stage I, and only 2 (9.5%) were in stage II.

Table 3 summarizes the outcomes investigated, including DFS, recurrence, and death at 1, 3, and 5 years after diagnosis, according to the stage. In general, DFS improved over the years and in particular at 1 and 3 years after diagnosis it rises from 60% to 85.7% for stage II and from 23.5% to 57.1% for stage III. The greatest number of recurrences occur in the first year, fespecially for stage III (53%), followed by stage II (10%). The greatest number of deaths is observed within the first year of diagnosis for stage IV (50%), followed by stage II (30%) and stage III (23.5%).

Table 4 shows 5-year survival by stage and by age. The overall 5-year OS rate was 78.8%. In particular, all cases aged 50 were still alive after 5 years, while the 5-year rates for cases aged 50-65 and >65 were 89.4% and 64.9%, respectively. Similarly, the 5-year OS rates for stages I, II, III, and IV were 96.1%, 59.2%, 44%, and 17.3%, respectively (**Table 4**). When age and Stage were jointly introduced into the same multivariable model (**Figure 1**), stage II (HR = 3.8, 95% CI 1.6-8.9), stage III (HR = 532, 95% CI 2.9-9.6), and stage IV (HR = 9.2, 95% CI 4.4-19.2), remained independently associated with death. Conversely, only elderly age, *i.e.,* >65 years, showed a borderline significance (HR = 7.2, 95% CI 1.0-53.0), while age between 50 and 65 years

Table 2. *Reggio Emilia Cancer Registry. Endometrial cancers, Years 2013-2015. Distribution of surgery, chemotherapy, and recurrence by stage.*

STAGE	SURGERY		CHEMOTHERAPY		RECURRENCE	
	n	%	n	%	n	%
I	155	77.1	8	23.5	8	38.1
II	13	6.5	3	8.8	2	9.5
III	24	11.9	16	47.1	10	47.6
IV	5	2.5	4	11.8	0	0.0
Unknown	4	2.0	3	8.8	1	4.8
Total	201	100	34	100	21	100

Table 3. *Reggio Emilia Cancer Registry. Endometrial cancers, Years 2013-2015. Distribution of percentage at one, three, and five years after diagnosis of recurrence, DF, and death by stage.*

	1 YEAR	3 YEARS	5 YEARS	
	%	%	%	P-VALUE
Stage 1				
Disease-Free	81.5	84.8	89.5	0.46
Recurrence	3.8	3.3	2.8	n/a
Death	14.7	11.9	7.7	0.75
Stage 2				
Disease-Free	60.0	85.7	85.7	0.74
Recurrence	10.0	0.0	0.0	n/a
Death	30.0	14.3	14.3	0.98
Stage 3				
Disease-Free	23.5	57.1	66.7	0.33
Recurrence	53.0	14.3	0.0	n/a
Death	23.5	28.6	33.3	0.61
Stage 4				
Disease-Free	40.0	50.0	100	0.55
Recurrence	0.0	0.0	0.0	n/a
Death	60.0	50.0	0.0	n/a
All stages				
Disease-Free	72.7	82.6	89.1	0.12
Recurrence	8.0	3.4	2.4	0.78
Death	19.3	14.0	8.5	0.31

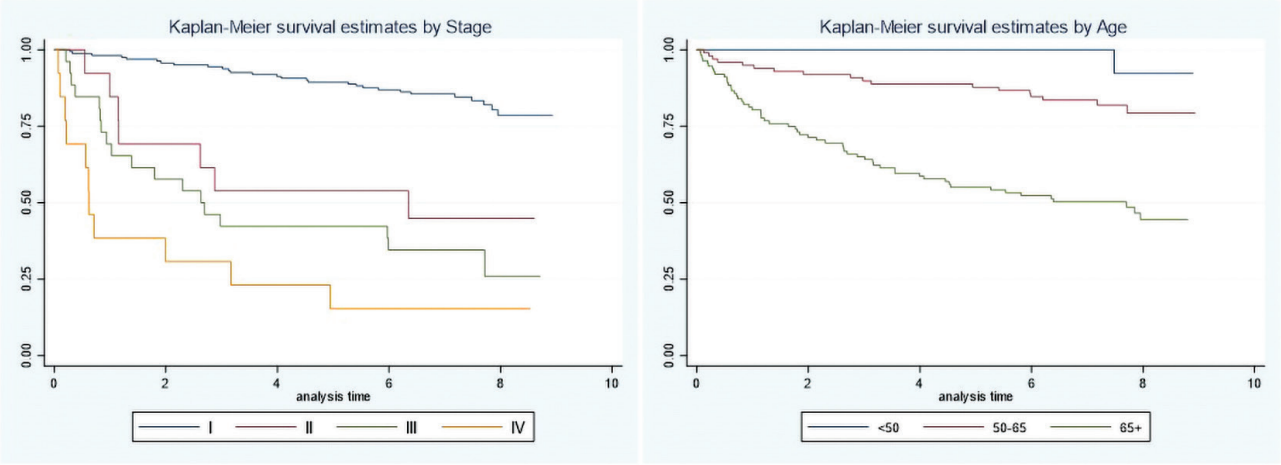
p-value: test for trend; n/a: not applicable.

Table 4. *5-year relative survival of endometrial cancer by age and stage.*

	N	%	95% CI
Overall	234	78.8	71.1–84.6
Age			
<50	23	100	99.5–100
50-65	99	89.4	80.5–94.4
65+	112	64.9	51.7–75.3
Stage			
I	162	96.1	83.2–99.2
II	13	59.2	22.5–83.2
III	26	44.0	24.7–61.9
IV	13	17.3	2.8–42.2

CI: confidence interval.

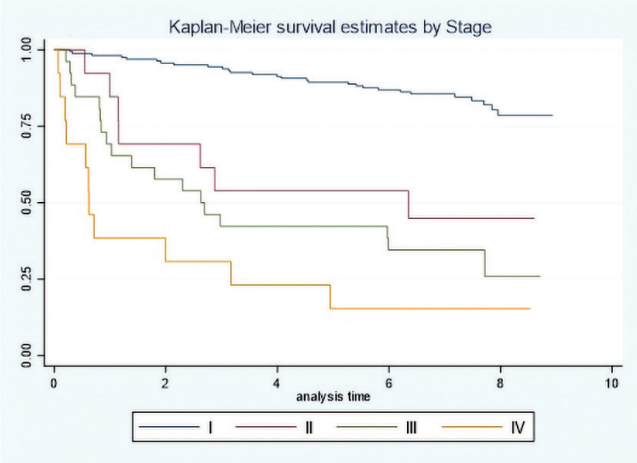
failed to maintain its independent prognostic role on OS after data adjustments (HR = 3.4, 95% CI 0.4-25.9). However, a multivariate model identified the clinical stage as the unique variable significantly predicting DFS. Stage IV, in particular, showed a nine-fold higher risk of progression than stage I (HR=1, reference group), while stages III (HR 7.7, 95% CI 4.4-13.6) and II (HR 3.5, 95% CI 1.5-8.0) had an intermediate risk of progression (**Figure 2**).

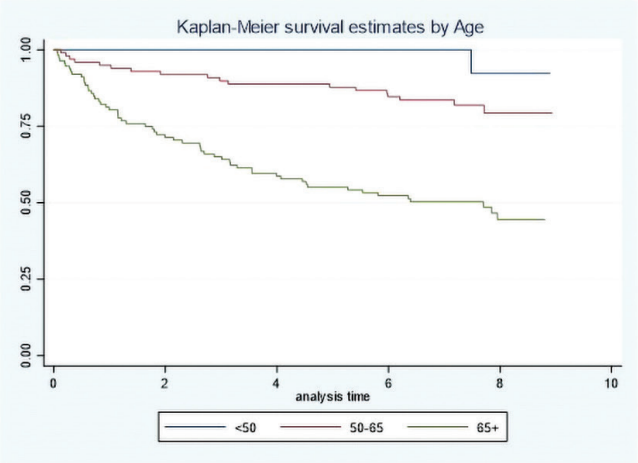


Cox proportional hazards model

Stage	HR	95%CI	Age	HR	95%CI
I	1.0		<50	1.0	
II	3.8	1.6-8.9	50-65	3.4	0.4-25.9
III	5.3	2.9-9.6	65+	7.2	1.0-53.0
IV	9.2	4.4-19.2			

Figure 1. *Overall survival probabilities by stage and age. Cox proportional hazards model adjusted for age and stage.*





Cox proportional hazards model

Stage	HR	95%CI	Age	HR	95%CI
I	1.0		<50	1.0	
II	3.8	1.6-8.9	50-65	3.4	0.4-25.9
III	5.3	2.9-9.6	65+	7.2	1.0-53.0
IV	9.2	4.4-19.2			

Figure 2. *Disease-free survival probabilities by stage and age. Cox proportional hazards model adjusted for age and stage.*

DISCUSSION

Endometrial cancer is common in adult and elderly women and the 5-year survival rate is around 84% (19). The excellent 5-year survival rate is largely due to the high number of tumors diagnosed at an early stage. According to the American SEER data, the survival rate is 96% for localized forms and 72% for regional cases, but it falls dramatically to 20% for distant metastatic cases (19). Siegel et al. published a similar figure, showing an overall 5-year survival rate of 81%, with only 17% and 15% for stages IVA and IVB, respectively (20). According to our data, the OS rate was around 79% with values ranging from 96.1% for the early to 17.3% for the metastatic forms. Age was a key prognostic factor in our study, as the proportion of alive patients at 5 years was inversely related to age. Elderly women (>65 years) showed the worst 5-year survival rate (64.9%), while all young patients (<50 years) were still alive, and cases in middle age had an intermediate survival rate (89.4%). This poorer outcome is most likely due to a strong link between older age and more prognostically adverse disease features, as well as an expected limited approach to surgery and adjuvant treatment (21). Thus, it is reasonable that age results an independent significant predictor for recurrence (HR = 1.75, P = .007), cancer-associated death (HR = 1.89, P = .003), and overall death (HR = 2.4, P < .001) on multivariable analysis (22). In our study, age lost its independent prognostic power in the DFS multivariate analysis, while remaining borderline significant in the OS multivariate model. This finding, which appears to contradict the literature data (21, 22), could be explained by the introduction of a Multidisciplinary Team, which can improve adherence to treatments and guidelines, patient management, and surgical technique strategy (11, 23, 24). According to our findings, 69.2% of EC were classified as stage I. This incidence is comparable to that reported by in the United States (25) and Italy cohorts (26), where nearly 70% and 80% of women, respectively, are diagnosed with early-stage uterine cancer. This data is not surprising since early bleeding which represents the first symptom of EC, allows for a very timely diagnosis of the disease (27). Nonetheless, because advanced cases harm clinical outcomes, staging remains a key prognostic factor in EC, influencing therapeutic algorithms. In this regard, surgery represents the cornerstone of EC treatment (28), whereas adjuvant radiation therapy has been shown to reduce pelvic recurrence (7, 8). Adjuvant chemotherapy is mainly reserved for patients in stage III (29) (also confirmed in our study), since it has been shown to improve OS in these high-risk recurrence cases (30, 31). Endometrial Cancer recurrence remains a significant clinical challenge, despite its generally favourable prognosis at primary diagnosis. In general, the median

time to first recurrence was 16 months (32), slightly lower compared with the 24 months of our study. The number of recurrences at 3 years after diagnosis, is around 10-15% (33), regardless of whether the surgery is laparoscopic or laparotomy (34), with no impact on the 5-year survival rate of 89%. In our experience, stage III cancer has the highest recurrence rate, with 53% of women developing a recurrence within 12 months of diagnosis and 14.3% within 3 years. Adding adjuvant radiotherapy to adjuvant chemotherapy after radical surgery may reduce significantly the risk of local and overall recurrence improving the stage III EC Overall Survival (35). Also in our experience, stage III patients have a comparable DFS to stage IV patients, but the overall survival is clearly detached, allowing these women a moderate survival even 8 years after diagnosis. On the other hand, nothing influences survival by age which has very similar values both in terms of DFS and OS.

In conclusion, based on 234 Endometrial cancers registered at RE-CR, this study confirmed the high incidence rate for the early disease Stage, which showed the best clinical outcome, with a significantly reduced risk of progression and death through to the appropriate surgical approach. Age, which represents another important risk factor, loses its negative effect in the multivariate analysis, probably because patient management has changed.

The introduction of a multidisciplinary approach over the years may have allowed for a better selection of women destined for surgery and subsequent treatment, based on the personalized characteristics of the patient. Among the study's strengths must be mentioned the population-based strategy, which makes it less susceptible to selection bias. Furthermore, the evaluated variables have high-quality data, and missing values are almost always minor and always pertain to recent years.

The small size of the cohort under study and the lack of molecular profiles which in fact have become important to guide treatment could be two important limiting factors of the study. Furthermore, we worked on the 2013-2015 case series to have 5 years of follow-up that would allow both the evaluation of the number of recurrences and deaths and the 5-year survival. However, it would be important to evaluate the trend also in subsequent years, so our objective is to update this work with more recent years.

COMPLIANCE WITH ETHICAL STANDARDS

Fundings

This study was partially supported by the Italian Ministry of Health - Ricerca Corrente Annual Program 2024.

Conflicts of Interests

The Authors have declared no conflict of interests.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' Contributions

LM: conceptualization, investigation, writing - original draft, visualization, supervision; FM: formal analysis, visualization, supervision; IB: writing-review and editing, and visualization, investigation, supervision; MBB: investigation, supervision; VM: investigation, supervision: FM: supervision; AN: supervision; LA: supervision; VDM: conceptualization, writing-original draft, investigation, and management. All authors have read and agreed to the published version of the manuscript.

Ethical approval

Human studies and subjects

This population-based cohort study uses data from the Reggio Emilia Cancer Registry, approved by the Provincial Ethics Committee of Reggio Emilia (ref. no. 2014/0019740 of 4 August 2014). The Ethics Committee authorized, even in the absence of consent, the processing of personal data, including those suitable for revealing the state of health of patients who are deceased or untraceable for the execution of the study.

Animal studies

N/A.

Publication ethics

Plagiarism

The contents of the article are original and any overlaps with other articles are by the Authors themselves and appropriately cited.

Data falsification and fabrication

All the data correspond to the real.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424. doi: 10.3322/caac.21492.
2. AIOM, AIRTUM, Fondazione AIOM, Osservatorio Nazionale Screening, PASSI, Passi d'Argento, SIAPEC-IAP. I numeri del cancro in Italia 2022. Intermedia editore, September 2022.
3. Survival Rates for Endometrial Cancer. Available from: https://www.cancer.org/cancer/types/endometrial-cancer/detection-diagnosis-staging/survival-rates.html. Accessed: November 06, 2023.
4. Tavassoli FA, Devilee P (Eds.). World Health Organization Classification of Tumours. Pathology and genetics of tumours of the breast and female genital organs. IARC Press, Lyon, 2003.
5. Cirisano FD Jr, Robboy SJ, Dodge RK, Bentley RC, Krigman HR, Synan IS, et al. The outcome of stage I-II clinically and surgically staged papillary serous and clear cell endometrial cancers when compared with endometrioid carcinoma. Gynecol Oncol. 2000;77(1):55-65. doi: 10.1006/gyno.2000.5737.
6. Kasius JC, Pijnenborg JMA, Lindemann K, Forsse D, van Zwol J, Kristensen GB, et al. Risk Stratification of Endometrial Cancer Patients: FIGO Stage, Biomarkers and Molecular Classification. Cancers (Basel). 2021;13(22):5848. doi: 10.3390/cancers13225848.
7. Mariani A, Dowdy SC, Keeney GL, Long HJ, Lesnick TG, Podratz KC. High-risk endometrial cancer subgroups: candidates for target-based adjuvant therapy. Gynecol Oncol. 2004;95(1):120-6. doi: 10.1016/j.ygyno.2004.06.042.
8. Torricelli F, Nicoli D, Bellazzi R, Ciarrocchi A, Farnetti E, Mastrofilippo V, et al. Computational development of a molecular-based approach to improve risk stratification of endometrial cancer patients. Oncotarget. 2018;9(39):25517-28. doi: 10.18632/oncotarget.25354.
9. Oaknin A, Bosse TJ, Creutzberg CL, Giornelli G, Harter P, Joly F, et al. Endometrial cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol. 2022;33(9):860-877. doi: 10.1016/j.annonc.2022.05.009.
10. Mandato VD, Palicelli A, Torricelli F, Mastrofilippo V, Leone C, Dicarlo V, et al. Should Endometrial Cancer Treatment Be Centralized? Biology (Basel). 2022;11(5):768. doi: 10.3390/biology11050768.
11. Torrent A, Amengual J, Sampol CM, Ruiz M, Rioja J, Matheu G, et al. Sentinel Lymph Node Biopsy in Endometrial Cancer: Dual Injection, Dual Tracer-A Multidisciplinary Exhaustive Approach to Nodal Staging. Cancers (Basel). 2022;14(4):929. doi: 10.3390/cancers14040929.
12. Menon A, Khalil H, Naidu B, Bishay E, Steyn R, Kalkat MS. Chest wall resection and reconstruction for recurrent breast cancer - A multidisciplinary approach. Surgeon. 2020;18(4):208-13. doi: 10.1016/j.surge.2019.10.001.
13. Voinea SC, Sandru A, Blidaru A. Management of Breast Cancer Locoregional Recurrence. Chirurgia (Bucur). 2017;112(4):429-35. doi: 10.21614/chirurgia.112.4.429.
14. Scott R, Hawarden A, Russell B, Edmondson RJ. Decision-Making in Gynaecological Oncology Multidisciplinary Team Meetings: A Cross-Sectional, Observational Study of Ovarian Cancer Cases. Oncol Res Treat. 2020;43(3):70-7. doi: 10.1159/000504260.
15. Mangone L, Marinelli F, Bisceglia I, Braghiroli MB, Mastrofilippo V, Cerullo L, et al. Ovarian Cancer in a Northern Italian Province and the Multidisciplinary Team. Cancers (Basel). 2022;15(1):299. doi: 10.3390/cancers15010299.
16. Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM, Whelan S. International Classification of disease for Oncology, 3rd edition. World Health Organization, 2013.
17. Sobin L, Gospodarowicz M, Wittekind C. TNM Classification of Malignant Tumours. UICC, 8th edition. Wiley-Blackwell, 2016.
18. Mangone L, Borciani E, Michiara M, et al. I tumori nelle province dell'Area Vasta Emilia Nord: Piacenza, Parma, Reggio Emilia e Modena: Anni 2013-2014. I Registri Tumori, 2015.
19. Cosgrove CM, Backes FJ, O'Malley D, Bixel KL, Suarez AA, Fowler JM, Copeland LJ, Goodfellow PJ, Cohn DE. Endometrial Cancer: Who Lives, Who Dies, Can We Improve Their Story? Oncologist. 2021 Dec;26(12):1044-1051.
20. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin. 2018;68(1):7-30. doi: 10.3322/caac.21442.

21. Duska L, Shahrokni A, Powell M. Treatment of Older Women With Endometrial Cancer: Improving Outcomes With Personalized Care. Am Soc Clin Oncol Educ Book. 2016;35:164-74. doi: 10.1200/EDBK_158668.
22. Hag-Yahia N, Gemer O, Eitan R, Raban O, Vaknin Z, Levy T, et al. Age is an independent predictor of outcome in endometrial cancer patients: An Israeli Gynecology Oncology Group cohort study. Acta Obstet Gynecol Scand. 2021;100(3):444-52. doi: 10.1111/aogs.14015.
23. Aviki EM, Gordhandas SB, Velzen J, Riley M, Manning-Geist B, Rice J, et al. Implementation of Evidence-Based Presurgical Testing Guidelines in Patients Undergoing Ambulatory Surgery for Endometrial Cancer. JCO Oncol Pract. 2022;18(1):e219-e224. doi: 10.1200/OP.21.00247.
24. Davidson BA, Puechl AM, Watson CH, Lim S, Gatta L, Monuszko K, et al. Promoting timely goals of care conversations between gynecologic cancer patients at high-risk of death and their providers. Gynecol Oncol. 2022;164(2):288-94. doi: 10.1016/j.ygyno.2021.12.009.
25. Stages of Uterine (Endometrial) Cancer. Available from: https://www.mskcc.org/cancer-care/types/uterine-endometrial/diagnosis/stages. Accessed: November 06, 2023.
26. Trojano G, Olivieri C, Tinelli R, Damiani GR, Pellegrino A, Cicinelli E. Conservative treatment in early stage endometrial cancer: a review. Acta Biomed. 2019;90(4):405-10. doi: 10.23750/abm.v90i4.7800.
27. Signs and symptoms of uterine cancer. Available from: https://www.cancercenter.com/cancer-types/uterine-cancer/symptoms. Accessed: November 06, 2023.
28. Amant F, Moerman P, Neven P, Timmerman D, Van Limbergen E, Vergote I. Endometrial cancer. Lancet. 2005;366(9484):491-505.
29. Tong N, Kumar A, Gelowitz G, Tinker A, Holloway C, Ko J. Impact of the adjuvant management and risk factors on survival in FIGO stage 3 endometrial cancer patients. Front Oncol. 2023;13:1035511. doi: 10.3389/fonc.2023.1035511.
30. Johnson N, Bryant A, Miles T, Hogberg T, Cornes P. Adjuvant chemotherapy for endometrial cancer after hysterectomy. Cochrane Database Syst Rev. 2011;2011(10):CD003175. doi: 10.1002/14651858.CD003175.pub2.
31. de Boer SM, Powell ME, Mileshkin L, Katsaros D, Bessette P, Haie-Meder C, et al. Adjuvant chemoradiotherapy versus radiotherapy alone in women with high-risk endometrial cancer (PORTEC-3): patterns of recurrence and post-hoc survival analysis of a randomised phase 3 trial. Lancet Oncol. 2019;20(9):1273-85. doi: 10.1016/S1470-2045(19)30395-X.
32. Siegenthaler F, Lindemann K, Epstein E, Rau TT, Nastic D, Ghaderi M, et al. Time to first recurrence, pattern of recurrence, and survival after recurrence in endometrial cancer according to the molecular classification. Gynecol Oncol. 2022;165(2):230-8. doi: 10.1016/j.ygyno.2022.02.024.
33. Sorbe B, Juresta C, Ahlin C. Natural history of recurrences in endometrial carcinoma. Oncol Lett. 2014;8(4):1800-6. doi: 10.3892/ol.2014.2362.
34. Palomba S, Ghezzi F, Falbo A, Mandato VD, Annunziata G, Lucia E, et al. Laparoscopic versus abdominal approach to endometrial cancer: a 10-year retrospective multicenter analysis. Int J Gynecol Cancer. 2012;22(3):425-33. doi: 10.1097/IGC.0b013e318244248c.
35. Cao SY, Fan Y, Zhang YF, Ruan JY, Mu Y, Li JK. Recurrence and survival of patients with stage III endometrial cancer after radical surgery followed by adjuvant chemo- or chemoradiotherapy: a systematic review and meta-analysis. BMC Cancer. 2023;23(1):31. doi: 10.1186/s12885-022-10482-x.