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# Clinicopathological disparities between superficial and vanishing endometrial cancer

## Yüzeyel ve kaybolan endometrial kanser arasındaki klinikopatolojik farklılıklar

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## ABSTRACT

**Aim:** This study aims to compare the clinicopathological characteristics and oncologic outcomes of patients with vanishing endometrial cancer (VEC) and superficial endometrial cancer (SEC).

**Materials and Methods:** A retrospective analysis was conducted on 130 patients diagnosed with stage IA endometrial cancer who underwent surgery at Başkent University School of Medicine from 2007 to 2023. Data including age, body mass index (BMI), histopathological type, lymphovascular space invasion, and survival outcomes were collected. Statistical analyses were performed using IBM SPSS version 25.0.

**Results:** Among the 130 patients, 40 (30.8%) had VEC and 90 (69.2%) had SEC. The median age was 55 years, and the median follow-up was 74.5 months. The 5-year DFS and OS rates were 99.2% and 97.5%, respectively, with no significant differences between the groups. Patients with VEC were younger and had a lower mean BMI compared to those with SEC. Rates of endometrial intraepithelial neoplasia and hyperplasia were similar across the groups.

**Conclusion:** VEC is a rare entity that requires surgical intervention, as a significant proportion of patients exhibit hyperplasia or EIN in surgical specimens. The comparable survival outcomes for VEC and SEC suggest that current management strategies can yield favorable prognoses for both, emphasizing the need for careful monitoring to avoid undertreatment of VEC cases.

**Keywords:** Vanishing endometrial cancer, early-stage, superficial endometrial cancer, residual endometrial cancer, survival

## ÖZ

**Amaç:** Bu çalışmanın amacı, kaybolan endometrial kanser (KEK) ve yüzeyel endometrial kanser (YEK) hastalarının klinikopatolojik özelliklerini ve onkolojik sonuçlarını karşılaştırmaktır.

**Gereç ve Yöntemler:** 2007-2023 yılları arasında Başkent Üniversitesi Tıp Fakültesi'nde ameliyat olan evre IA endometrial kanser tanısı almış 130 hasta üzerine retrospektif olarak analiz edilmiştir. Yaş, vücut kütle indeksi (VKİ), histopatolojik tür, lenfovasküler alan invazyonu ve sağkalım sonuçları gibi veriler toplanmıştır. İstatistiksel analizler IBM SPSS sürüm 25.0 kullanılarak yapılmıştır.

**Bulgular:** Toplam 130 hastadan 40'ının (30.8%) KEK, 90'ının (69.2%) ise YEK olduğu tespit edilmiştir. Medyan yaş 55 yıl olup, medyan takip süresi 74.5 aydır. Beş yıllık hastalıksız sağkalım ve toplam sağkalım oranları sırasıyla %99.2 ve %97.5 olup, gruplar arasında anlamlı bir fark bulunmamıştır. KEK hastalarının, YEK hastalarına kıyasla daha genç ve daha düşük ortalama VKİ'ye sahip olduğu belirlenmiştir. Endometrial intraepitelyal neoplazi ve hiperplazi oranları gruplar arasında benzer orandadır.

**Sonuç:** KEK, cerrahi müdahale gerektiren nadir bir durumdur, çünkü hastaların önemli bir kısmında cerrahi örneklerde hiperplazi veya EIN tespit edilmektedir. KEK ve YEK için karşılaştırılabilir sağkalım sonuçları, mevcut yönetim stratejilerinin her iki grup için de olumlu prognoz sağladığını göstermektedir; bu nedenle, KEK vakalarında yetersiz tedaviden kaçınmak için yakın takip gerekmektedir.

**Anahtar Kelimeler:** Kaybolan endometrial kanser, erken evre, yüzeyel endometrial kanser, rezidüel endometrial kanser, sağkalım

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## INTRODUCTION

Endometrial cancer (EC) is the second most common gynecological cancer, following cervical carcinoma, according to GLOBOCAN 2022 (1). The incidence of EC rising due to factors such as obesity, age, and lifestyle changes. EC is broadly classified into two subtypes: type 1 and 2. Type 1 tumors primarily consist of endometrioid carcinoma and are associated with unopposed estrogen stimulation, while type 2 encompasses more aggressive histological forms, such as serous and clear cell carcinomas (2).

Diagnosis of EC is based on pathological examination of endometrial samples. Occasionally, no EC is found in hysterectomy specimen despite a definitive diagnosis of cancer in endometrial biopsy specimen; this phenomenon is referred to as vanishing endometrial cancer (VEC) (3-5). Vanishing carcinoma is a rare entity characterized by significant cytological atypia with minimal tumor volume, first described in 1995 by Goldstein et al. in the context of prostate cancer (6). Additionally, superficial endometrial cancer (SEC) describes localized disease confined to the endometrium.

Despite the growing body of literature surrounding these malignancies, notable gaps exist in comparative studies that thoroughly investigate the clinical and pathological features influencing patient outcomes. Given the distinct trajectories of type 1 and 2 EC, understanding the differences between VEC and SEC could have significant implications for treatment and prognosis. Therefore, this study aimed to compare SEC and VEC in terms of clinicopathological factors and to demonstrate oncologic outcomes between the two groups.

## MATERIALS AND METHODS

Patients with EC who underwent surgery in Başkent University School of Medicine, Department of Obstetrics and Gynecology were retrospectively investigated from 2007 to 2023. The study was approved by Başkent University Institutional Review Board (KA23/192). Data including age, histopathological type, chemotherapy administration, comorbid diseases, parity, body mass index (BMI), menopausal status, presence of p53 mutation, lymphovascular space invasion (LVSI), recurrence and survival patterns were collected from the patient files and hospital data.

Preoperative endometrial samples for the diagnosis of EC were obtained via using 3 different instruments: dilatation and curettage (D&C), hysteroscopic biopsy, and pipelle biopsy. In D&C, the cervix is dilated, and uterus is scraped with a sharp curette and aspirated with a Karman cannula. In hysteroscopy, the tissue samples are collected using a thin, flexible telescope. The pipelle method employs a suction mechanism and requires no cervical dilation. Histopathological examinations were conducted by 2 gynecologic pathologists according to current guidelines.

Inclusion criteria consisted of patients who underwent total abdominal hysterectomy (TAH) and/or bilateral salpingo-oophorectomy (BSO) at Başkent University Ankara Hospital, with stage IA EC confined to the endometrium and no lymphatic metastasis. Both type 1 and type 2 EC patients were included, with type 1 referring to endometrioid adenocarcinoma and type 2 to serous, clear cell, and mixed carcinomas. Patients exhibiting myometrial invasion, cervical involvement, or distant metastasis were excluded. Additionally, those who received radiotherapy, chemotherapy, and fertility-sparing treatment between diagnosis and hysterectomy were also excluded.

Statistical analysis was conducted using IBM SPSS ver. 25.0 for Windows. Categorical variables were described as percentages, while continuous variables were presented as means and medians. Fisher's Exact test and Chi-Square tests were utilized when appropriate. The Kaplan-Meier survival test assessed disease-free survival (DFS) and overall survival (OS). A P-value less than 0.05 was deemed statistically significant.

## RESULTS

A total of 134 patients were investigated retrospectively, with 130 patients included in this study. The median age was 55.0 years (range:33-87). The median follow-up was 74.5 months (range:1-192). Forty patients (30.8%) had VEC, while 90 patients (69.2%) had SEC. Demographic characteristics of the patients between groups are presented in Table 1.

Seventy-three patients (56.2%) presented with postmenopausal bleeding, followed by abnormal uterine bleeding (n:39, 30.0%). Sixty-five patients (50.0%) had tumor arising in polyps. Disease characteristics of the patients between groups are summarized in Table 2.

A total of 121 patients (93.1%) underwent lymph node dissection, while 9 patients (6.9%) had only TAH-BSO. The mean number of lymph nodes extracted was 38.4 (range:8-73). Seven patients (5.4%) received adjuvant chemotherapy. Most patients in both groups had type 1 EC (85.0% and 82.2%, respectively; p: 0.317). Surgical and tumor characteristics between groups are detailed in Table 3. The 5-year DFS and OS were 99.2% and 97.5%, respectively, with no significant differences is DFS or OS noted between groups (p: 0.157 and 0.218, respectively). The Kaplan-Meier survival plots for DFS and OS are illustrated in Figure 1.

**Table 1.** Characteristics of the Patients

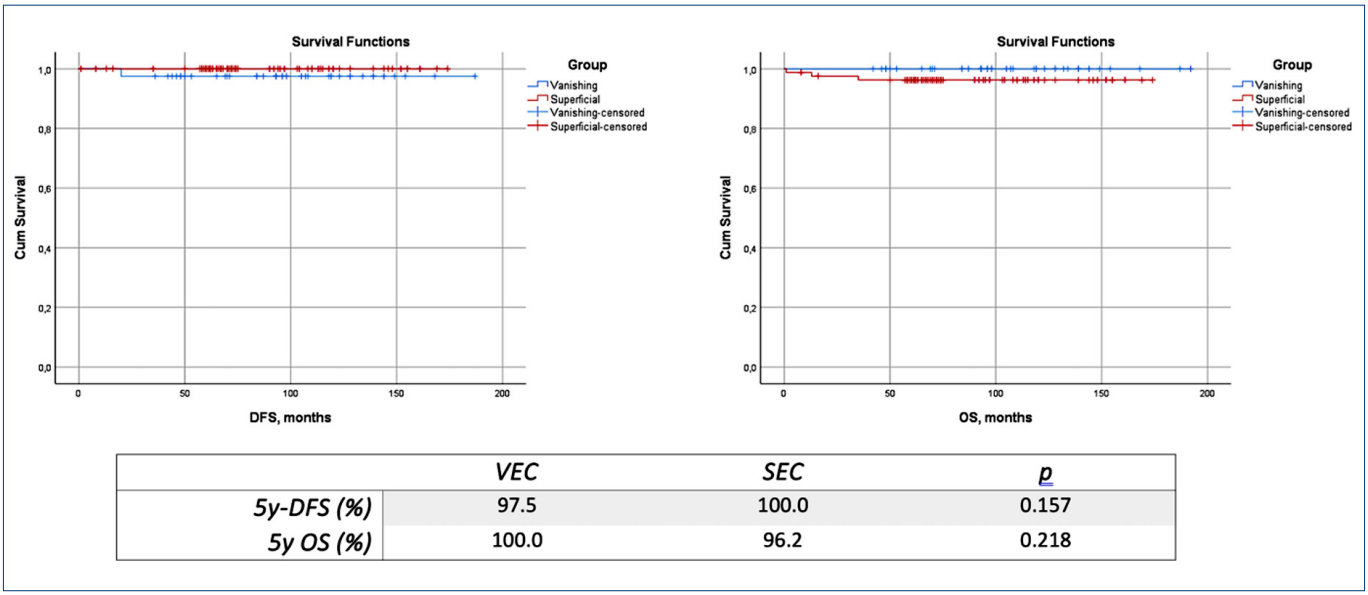
| | Vanishing (n:40) | Superficial (n:90) | P |
|---|---|---|---|
| **Age, median (years)** | 55.5 (33-77) | 57.0 (34-87) | **0.036** |
| **Parity, mean** | 2.84 (0-9) | 2.78 (0-11) | 0.899 |
| **Menopausal Status** | | | |
| Yes (%) | 16 (40.0) | 23 (25.6) | 0.103 |
| No (%) | 24 (60.0) | 67 (74.4) | |
| **BMI, mean (kg/m²)** | 30.3 (22.2-47.3) | 34.0 (19.6-68.1) | **0.046** |
| **Follow-up, median (months)** | 98.0 (42-192) | 71.0 (1-174) | **0.007** |

**Abbreviations:** BMI: Body-mass index

**Table 2.** Disease Characteristics of the Patients

| | Vanishing (n:40) (%) | Superficial (n:90) (%) | P |
|---|---|---|---|
| **Complaint** | | | |
| PMB | 16 (40.0) | 57 (63.3) | **0.000** |
| AUB | 14 (35.0) | 25 (27.8) | |
| Pain | 1 (2.5) | 2 (2.2) | |
| Discharge | 0 (0.0) | 4 (4.4) | |
| None | 7 (17.5) | 0 (0.0) | |
| Missing | 2 (5.0) | 2 (2.2) | |
| **Tumor Size, mean cm** | 1.72 (0.3-4.8) | 2.47 (0.0-8.5) | 0.117 |
| **Tumor Arising in Polyp** | | | |
| Yes | 20 (50.0) | 45 (50.0) | 0.145 |
| No | 20 (50.0) | 40 (44.4) | |
| Missing | 0 (0.0) | 5 (5.6) | |
| **Non-tumor Endometrium** | | | |
| Normal | 13 (32.5) | 44 (48.9) | 0.727 |
| EIN | 8 (20.0) | 27 (30.0) | |
| Non-atypical Hyperplasia | 3 (7.5) | 17 (18.9) | |
| Missing | 16 (40.0) | 2 (2.2) | |
| **Time Interval*, median, days** | 16.0 | 18.0 | 0.55 |

**Abbreviations:** EIN: Endometrial intraepithelial neoplasia
*Time interval between biopsy and surgery.




| | VEC | SEC | p |
|---|---|---|---|
| 5y-DFS (%) | 97.5 | 100.0 | 0.157 |
| 5y OS (%) | 100.0 | 96.2 | 0.218 |

**Figure 1.** DFS and OS plots of VEC vs SEC
Abbreviations: DFS: Disease-free survival, OS: Overall survival, VEC: Vanishing endometrial cancer, SEC: Superficial endometrial cancer

**Table 3.** Surgical and Tumoral Characteristics of the Patients

| | Vanishing (n:40) (%) | Superficial (n:90) (%) | P |
|---|---|---|---|
| **Surgery** | | | |
| TAH-BSO | 2 (5.0) | 7 (7.8) | 0.630 |
| TAH-BSO+LND | 38 (95.0) | 83 (92.2) | |
| **Histology** | | | |
| Endometrioid | 34 (85.0) | 74 (82.5) | 0.612 |
| Serous | 3 (7.5) | 10 (11.1) | |
| Clear | 1 (2.5) | 3 (3.3) | |
| Carcinosarcoma | 1 (2.5) | 0 (0.0) | |
| Mixed | 1 (2.5) | 2 (2.2) | |
| Undifferentiated | 0 (0.0) | 1 (1.1) | |
| **Adjuvant Treatment** | | | |
| Yes | 1 (2.5) | 6 (6.7) | 0.603 |
| No | 39 (97.5) | 84 (93.3) | |
| **Type** | | | |
| I (Endometrioid) | 34 (85.0) | 74 (82.2) | 0.317 |
| II (Serous, Clear cell, Mixed) | 6 (15.0) | 16 (17.8) | |
| **P53 mutation** | | | |
| Negative | 2 (5.0) | 2 (2.2) | 0.520 |
| Positive | 2 (5.0) | 9 (10.0) | |
| Wild type | 1 (2.5) | 5 (5.6) | |
| Missing | 35 (87.5) | 74 (82.2) | |
| **LVSI** | | | |
| Negative | 40 (100.0) | 89 (98.9) | 1.000 |
| Positive | 0 (0.0) | 1 (1.1) | |
| **No of LNs, mean (range)** | 39.7 (12-71) | 37.7 (8-73) | 0.425 |

**Abbreviations:** TAH: Total abdominal hysterectomy, BSO: Bilateral salpingooophorectomy, LND: Lymph node dissection, No of LNs: Number of lymph nodes

## DISCUSSION

This study presents a comprehensive retrospective analysis of 130 patients diagnosed with stage IA EC, comprised of 40 with VEC and 90 with SEC. The demographic and disease characteristics demonstrate a significant cohort with varied presentations, predominantly experiencing postmenopausal and abnormal uterine bleeding, underscoring the need for vigilance in diagnosing EC among postmenopausal women. Patients in the VEC group were younger and exhibited lower BMI. Comparing the clinicopathological outcomes between the groups the tumor size, presence of polyp, and time interval between diagnosis and surgery were similar. Endometrial intraepithelial neoplasia (EIN) and hyperplasia rates were similar between groups. The 5-y DFS and OS were also similar between groups.

Patients in the VEC group were younger. This aligns with recent studies indicating that patients with vanishing cancer are often younger (3). Notably, the mean BMI in the VEC group was also lower, raising questions about the interplay between obesity, estrogen production, and cancer progression. As we know type 1 EC is estrogen dependent and being overweight may contribute to the invasion rate of cancer by causing excessive estrogen secretion from adipose tissue (2). This may be the cause of lower BMI value in VEC group.

The results indicate impressive survival rates, with a 5-year OS of 97.5% and a DFS of 99.2%, highlighting the favorable prognostic outlook for early-stage EC when managed through appropriate surgical interventions. Importantly, no significant differences in DFS or OS were noted between the two types. A recent study reported similar survival with our study (7). The lack of significant differences in DFS or OS between two types suggests that the current treatment paradigms for both VEC and SEC may yield comparable outcomes, which could challenge existing notions regarding the aggressiveness or treatment needs of VEC.

Our findings support existing literature regarding the efficacy of lymph node dissection in enhancing staging accuracy as evidenced by most patients undergoing this procedure (8). The low incidence of adjuvant chemotherapy (5.4%) reinforces the common management approach for early-stage diseases, which typically involves surgical intervention as the primary strategy.

The similar rates of endometrial intraepithelial neoplasia (EIN) and hyperplasia between groups – ranging from 30% to 50% in hysterectomy specimens – suggest that hysterectomy may be warranted even in patients classified as having vanishing tumors. This is further supported by findings from another study reporting high rates of endometrial hyperplasia with atypia among VEC patients (76.2% endometrial hyperplasia with atypia, and 4.8% endometrial hyperplasia without atypia) (3).

This study is subject to several limitations inherent in retrospective designs, including biases in patient selection and limited generalizability due to the single institution setting. Furthermore, the small sample size of VEC patients limits the statistical power to derive broader conclusions. The absence of molecular analysis in many cases is another drawback.

To the best of our knowledge, this study demonstrates one of the largest cohorts with over six years of median follow-up for VEC, allowing for a comparative evaluation of clinicopathological characteristics and and survival outcomes between VEC and SEC.

In conclusion, while vanishing endometrial cancer remains a rare entity, it necessitates hysterectomy due to the high incidence of hyperplasia or EIN in the surgical specimens. Furthermore, the absence of EC in these specimens may lead both clinicians and patients to underestimate the disease, potentially resulting in undertreatment or insufficient follow-up.

### Conflict Of Interest

The authors declare there is no conflicts of interest.

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None.

## REFERENCES

1. Filho AM, Laversanne M, Ferlay J, Colombet M, Pineros M, Znaor A, et al. The GLOBOCAN 2022 cancer estimates: Data sources, methods, and a snapshot of the cancer burden worldwide. Int J Cancer. 2024.
2. Setiawan VW, Yang HP, Pike MC, McCann SE, Yu H, Xiang YB, et al. Type I and II endometrial cancers: have they different risk factors? J Clin Oncol. 2013;31(20):2607-18.
3. Gorgulu G, Dogan Ozdas E, Ozdas E, Sayhan S, Kuru O, Gokcu M, et al. Analysis of vanishing endometrial cancer by pathological types. J Obstet Gynaecol Res. 2022;48(8):2175-9.
4. Kumtepe Y UP, Delibas I, Demirci E. Two cases of vanishing endometrial carcinoma. Research Journal of Medical Sciences. 2011(5):4.
5. Dube V, Macdonald D, Allingham-Hawkins DJ, Kamel-Reid S, Colgan TJ. Vanishing endometrial carcinoma. Int J Gynecol Pathol. 2007;26(3):271-7.
6. Goldstein NS, Begin LR, Grody WW, Novak JM, Qian J, Bostwick DG. Minimal or no cancer in radical prostatectomy specimens. Report of 13 cases of the "vanishing cancer phenomenon". Am J Surg Pathol. 1995;19(9):1002-9.
7. Ahmed QF, Gattoc L, Al-Wahab Z, Abdulfatah E, Ruterbusch JJ, Cote M, et al. Vanishing endometrial cancer in hysterectomy specimens: a myth or a fact. Am J Surg Pathol. 2015;39(2):221-6.
8. Bharani V, Rai B, Rajwanshi A, Gupta N, Dey P, Kalra J, et al. Evanescence of Endometrial Carcinomas in Hysterectomy Specimens: Observations on the "Vanishing Cancer" Phenomenon. Int J Surg Pathol. 2019;27(1):43-7.