

# Influences of Uterine Adenomyosis On Pathologic Prognostic Characteristics and Survival Time in Patients with Endometrial Cancer

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## ABSTRACT

**Objective:** The first aim of the present study was to investigate whether the presence of adenomyosis (AM) had an effect on pathologic prognostic characteristics and survival time in patients with endometrial carcinoma (EC). The second aim was to evaluate the association of AM for each subtype grouping as low-grade endometrioid carcinoma, high-grade endometrioid carcinoma, and high-grade non-endometrioid carcinoma.

**Methods:** The present retrospective observational cohort study was conducted using the institution's database of patients with EC who underwent staging surgery. The cohort was divided into two groups according to the presence or absence of AM. Additionally, EC subtypes were grouped into low-grade endometrioid, high-grade endometrioid, and high-grade non-endometrioid tumors according to the presence or absence of AM as well. The survival outcomes and pathologic prognostic characteristics were compared between the groups.

**Results:** A total of 518 endometrial cancer patients were analyzed. Overall survival (OS) was similar between patients with and without AM (Cox regression Wald=0.654, p=0.419). In multivariate Cox regression analysis, the presence of AM was not associated with survival time (p=0.378). However, histologic type with grade, lymph vascular space invasion, and metastasis were significant factors predicting the survival time (endometrioid low grade vs endometrioid high grade, p1=0.075 and endometrioid low grade vs non-endometrioid high grade, p2=0.020; p=0.001 and p=0.001, respectively). Survival means for survival time in patients with and without AM in different histologic types with grade was similar for each subgroup (p>0.005 for each group).

**Conclusion:** Our findings indicated that the presence of AM with EC is not an independent prognostic factor for OS.

## INTRODUCTION

Uterine cancer is the most common gynecologic malignancy in developed countries. In 2022, 65 950 women were diagnosed with endometrial carcinoma (EC) in the United States.<sup>[1]</sup> The International Federation of Gynecology and Obstetrics (FIGO) staging system, which is based on surgical pathology, has been structured to represent

major prognostic factors in predicting patient outcomes and to guide surgical management.<sup>[2]</sup> However, it has been observed that the clinical features of patients with similar stages may differ.

Researchers have investigated the influence of various tumor characteristics and behaviors, such as histologic subtype and FIGO stage, grade, depth of myometrial invasion, and vascular invasion, to clarify the different clinical con-

ditions between patients with the same cancer stage.<sup>[3,4]</sup> Conversely, based on histopathology, EC has been classified into two major types. Type I neoplasms are typically low grade, estrogen sensitive, usually have a good prognosis, and are detected at an early stage. Type II neoplasms tend to develop in older women in an estrogen-independent manner, and they are associated with poor prognosis.<sup>[5,6]</sup>

Adenomyosis (AM) is a benign gynecologic disorder in which ectopic endometrial stroma and glands invade the myometrium of the uterus.<sup>[7]</sup> The presence of AM at high rates in hysterectomy specimens obtained from patients with EC has become the subject of many studies to illuminate the possible influence of AM on the prognosis of patients with EC.<sup>[8,9]</sup> Previous studies evaluating ECs associated with AM revealed that AM tended to occur in younger patients, are early FIGO stage with low-grade, well-differentiated, Type I endometrioid, estrogen-sensitive adenocarcinomas, and had a good prognosis.<sup>[9,10]</sup> Another study observed that the presence of AM was a protective factor associated with better outcomes of patients, through its protective barrier effect to the myometrial invasion of the tumor.<sup>[11]</sup> By contrast, other studies suggested that the presence of AM increased the contact area with the myometrium, which allowed malignant cells to invade the myometrium.<sup>[12,13]</sup> According to our knowledge, there is no clear study reporting the impact of co-existent AM on outcomes of patients with endometrial adenocarcinoma histopathologic subtypes.

The first aim of the present study was to investigate whether the presence of AM had an effect on pathologic prognostic characteristics and survival time in patients with EC. The second aim was to evaluate the association of AM for each subtype grouping as low-grade endometrioid carcinoma (Type I EC), high-grade endometrioid carcinoma (Type II EC), and high-grade non-endometrioid carcinoma (Type II EC), unlike previous studies, which mainly investigated the association of AM with endometrioid-type EC. Additionally, a number of prognostic factors were evaluated in patients with EC, other than AM.

## MATERIALS AND METHODS

The present retrospective observational cohort study was conducted using the institution's database of patients with EC who underwent staging surgery at the Kartal Dr. Lütfi Kırdar Hospital between August 2005 and November 2014. The Local Institutional Review Board approved the study design Kartal Dr. Lütfi Kırdar Hospital, Institutional Review Board (Approval number: 2019/514/156/13, Date: June 26, 2019), and informed consent was received from all patients using their medical data in the retrospective studies.

A total of 621 patients who were diagnosed as having EC on the final pathology report were identified. Of these, 518 patients were included if they had undergone optimal surgery and received chemotherapy and radiotherapy according to the final pathological stage. A total of 103 pa-

tients were excluded from the study based on the following criteria: the presence of synchronous tumors (n=7), involvement of AM by endometrial adenocarcinoma (n=9), incomplete surgical and/or medical treatments (n=52), having mucinous histologic type EC (n=12), and patients who died of causes other than EC (n=23). The flowchart of the study is shown in Figure 1.

The cohort was divided into two groups according to the presence or absence of AM. The demographic information and disease characteristics of patients with EC with and without AM were retrieved from the medical records, including age, survival time, type of surgical procedure, stage, tumor grade, depth of myometrial invasion, histology, tumor size, histologic grade of tumor, presence of lymph vascular space invasion, lymph node status, metastases, type of treatment, and overall survival (OS).

EC subtypes were grouped into low-grade endometrioid (Type I), high-grade endometrioid (Type II), and high-grade non-endometrioid (Type II). Grades 1 and 2 endometrioid tumors were considered low grade. Grade 3 endometrioid, serous, and clear-cell, mixed, carcinosarcoma, and undifferentiated tumors were grouped as high grade.

All surgical procedures were performed by a certified gynecologic oncology team. The pathology department at this institution defines "AM" as the presence of endometrial glands and stroma within the myometrium at a distance of at least one low power field (~2.5 mm) when measured from the lower border of the endometrium.<sup>[14]</sup> The histologic grading of the tumor with regard to the degree of differentiation was verified as low (grade I-II) and high (grade III).<sup>[15]</sup>

The date of the last follow-up entry was June 2016. Information about the survival status of the patients was confirmed by signing up the patients to the hospital database; alert messages appeared with the nonsurvival of patients. Also, death was confirmed through the National Death Notification System.

Statistical analysis was performed using SPSS statistics software for Windows version 25.0 (SPSS, Inc., Chicago, IL, USA). The normality of the distribution of numeric variables was assessed using the Kolmogorov–Smirnov test. Student's t-test or the Mann–Whitney U test was used for

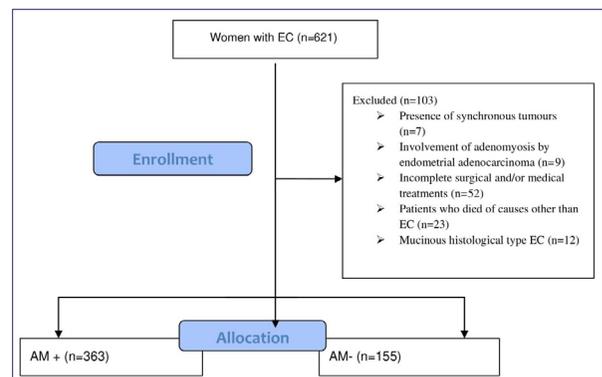


Figure 1. Flowchart of the study.

independent sample pairwise comparisons of numerical variables. Pairwise comparisons of categorical data were performed using the Chi-squared test. Survival was calculated using the method of Kaplan–Meier and compared using the log rank test. A multivariate Cox proportional hazards regression model was used to analyze the effect of risk factors on survival. A  $p$ -value  $<0.05$  was considered statistically significant. The sample size calculation was based on the main outcome variable “presence of AM.” The concurrent presence of EC and AM was previously reported as 28%.<sup>[16]</sup> To achieve a power of 80% for performing a survival analysis, given an alpha error of 5%,  $q_1$  (proportion of exposed subjects) of 28%, and a relative hazard of 0.75, a sample size of 470 patients was required.<sup>[17]</sup>

## RESULTS

A total of 518 women with EC were included in the analysis. The average age of the participants was 60.9 (min–max: 25–98) years. Some features of patients related to their diseases are presented in Table 1. Tumor histology was mostly of endometrioid histotype (89.8%). Most of the non-endometrioid tumors were serous carcinoma (52.8%). At diagnosis, 60.0% of the patients were stage IA and 79.5% had low-grade tumors. A small number of patients developed metastases (3.3%). Tumor size was equal to or greater than 2 cm in 57.7% of patients. Lymph vascular space invasion was detected in 17.8% of the patients and endocervical involvement in 17.6%. In 32.2% of patients, myometrial invasion depth was greater than one-half, and AM was found in 29.9% of the cases (Table 1).

As shown in Table 1, lymph node resection was not required in 28% of the patients. Both pelvic and paraaortic lymph nodes were removed during surgery in 41.5% of patients, as well as performing total abdominal hysterectomy and bilateral salpingo-oophorectomy. Both pelvic and paraaortic lymph nodes were found to be negative in 77.6% of patients with pelvic and paraaortic lymph nodes removed. Only 92.4% of 158 patients whose paraaortic lymph nodes were removed had negative lymph nodes. Some 15.6% of patients received chemotherapy and 47.3% received radiotherapy. It was determined that 14% of the participants died. The mean life expectancy was calculated as  $4.9 \pm 2.3$  years.

As shown in Table 2, the depth of myometrial invasion was lower in those with AM than in those without AM ( $p=0.004$ ). Similarly, tumor size in those with AM was smaller than in those without AM ( $p=0.015$ ). However, this difference was not reflected in the survival time. The mean survival time was similar in patients with and without AM ( $p=0.399$ ).

Lymph nodal status was classified into three groups as not assessed, negative nodal metastasis, and positive nodal metastasis and was found different in those with and without AM ( $p=0.031$ ).

The mean survival time was  $164.7 \pm 4.2$  (standard error) months (95% CI: 156.4–172.9) in patients with AM and

**Table 1.** Clinicopathological characteristics of endometrial cancer patients

Variables	Number of patients (n=518)	%
Surgical approach		
TAH + BSO	145	28.0
TAH + BSO + PLND	158	30.5
TAH + BSO + PPLND	215	41.5
Presence of adenomyosis	155	29.9
Histologic subtype		
Endometrioid	465	89.8
Non-endometrioid	53	10.2
Tumor grade		
Low (1–2)	412	79.5
High (3)	106	20.5
Tumor size		
<2 cm	219	42.3
$\geq 2$ cm	299	57.7
Myometrial invasion depth		
$\leq 50\%$	351	67.8
$>50\%$	167	32.2
Lymphovascular invasion	92	17.8
Lymph node status		
Not assigned	145	28.0
Positive	60	11.6
Chemotherapy	81	15.6
Radiotherapy	245	47.3
Endometrial cancer-related death	75	14.5

TAH: Total abdominal hysterectomy; BSO: Bilateral salpingo-oophorectomy; PLND: Pelvic lymph node dissection; PPLND: Pelvic and paraaortic lymph node dissection.

$98.1 \pm 2.5$  months (95% CI: 93.1–103.0) in those without AM. OS was similar between patients with and without AM (Cox regression Wald=0.654,  $p=0.419$ ). The Kaplan–Meier survival plot is given in Figure 2a.

The mean survival time was  $172.4 \pm 4.1$  months (95% CI: 164.4–180.4) in patients with less than 0.5 cm myometrial invasion depth and  $90.1 \pm 3.1$  months (95% CI: 83.9–96.2) in those with 0.5 cm or greater myometrial invasion depth. OS was similar between patients with and without AM (Cox regression Wald=18.8,  $p<0.001$ ) (Fig. 2b).

Multivariate Cox regression analysis was performed by adjusting the variables for patients whose survival times were significantly different in univariate analysis (Table 3). Although AM was not significant in univariate analysis, it was included in the model due to its clinical significance. The overall significance of the model was  $<0.001$ . The presence of AM was not associated with survival time ( $p=0.378$ ).

Despite the diverging survival curves, myometrial invasion depth was not significant (Fig. 2b). However, age, histologic type with grade (Fig. 2c), lymph vascular space in-

**Table 2.** Demographic and disease characteristics of endometrial cancer patients with adenomyosis versus those without adenomyosis

		Adenomyosis				Test	p
		Absent (n=363)		Present (n=155)			
		Mean (n)	SD (%)	Mean (n)	SD (%)		
Age at diagnosis (years)		61.3	11.2	60.1	8.8	-1.260 <sup>†</sup>	0.208
Survival time (months)		59.3	29.5	57.2	26.9	-0.843 <sup>†</sup>	0.399
Tumor grade	Low (1–2)	285	69.2	127	30.8	0.782 <sup>‡</sup>	0.377
	High (3)	78	73.6	28	26.4		
MI depth	<1/2	232	66.1	119	33.9	8.226 <sup>‡</sup>	0.004
	≥1/2	131	78.4	36	21.6		
Histologic subtype	Endometrioid	325	69.9	140	30.1	0.074 <sup>‡</sup>	0.786
	Non-endometrioid	38	71.7	15	28.3		
Tumor size	<2 cm	141	64.4	78	35.6	5.866 <sup>‡</sup>	0.015
	≥2 cm	222	74.2	77	25.8		
Lymph node status	Not assessed	90	62.1	55	37.9	6.963 <sup>‡</sup>	0.031
	Negative nodal metastasis	232	74.1	81	25.9		
	Positive nodal metastasis	41	68.3	19	31.7		
Metastasis	No	351	70.1	150	29.9	0.013 <sup>‡</sup>	0.910
	Yes	11	68.8	5	31.3		
ECR death	Yes	307	69.3	136	30.7	0.881 <sup>‡</sup>	0.348
	No	56	74.7	19	25.3		

<sup>†</sup>Mann–Whitney U test. <sup>‡</sup>Chi-squared test; ECR: Endometrial cancer related; MI: Myometrial invasion depth; SD: Standard deviation.

**Table 3.** Multivariate analysis for survival time in patients with endometrial cancer

Variable	B	Wald	p	exp(B)	95% CI for exp(B)	
					Lower	Upper
Age at diagnosis (years)	0.098	83.014	0.000	1.103	1.080	1.127
Adenomyosis (absence vs presence) <sup>†</sup>	0.254	0.778	0.378	1.289	0.734	2.263
Histologic subtype and tumor grade						
Endometrioid high grade <sup>‡</sup>	0.640	3.161	0.075	1.897	0.937	3.841
Non-endometrioid high grade <sup>‡</sup>	0.773	5.380	0.020	2.167	1.127	4.166
Myometrial invasion depth (<1/2 vs ≥1/2 cm)	0.169	0.344	0.558	1.184	0.673	2.082
Lymphovascular invasion (absence vs presence)	1.041	11.088	0.001	2.832	1.535	5.227
Metastasis (absence vs presence)	1.666	18.222	0.000	5.291	2.462	11.368
Lymph node positivity						
Negative nodal metastasis <sup>§</sup>	-0.568	2.569	0.109	0.567	0.283	1.135
Positive nodal metastasis <sup>§</sup>	0.767	2.911	0.088	2.153	0.892	5.197

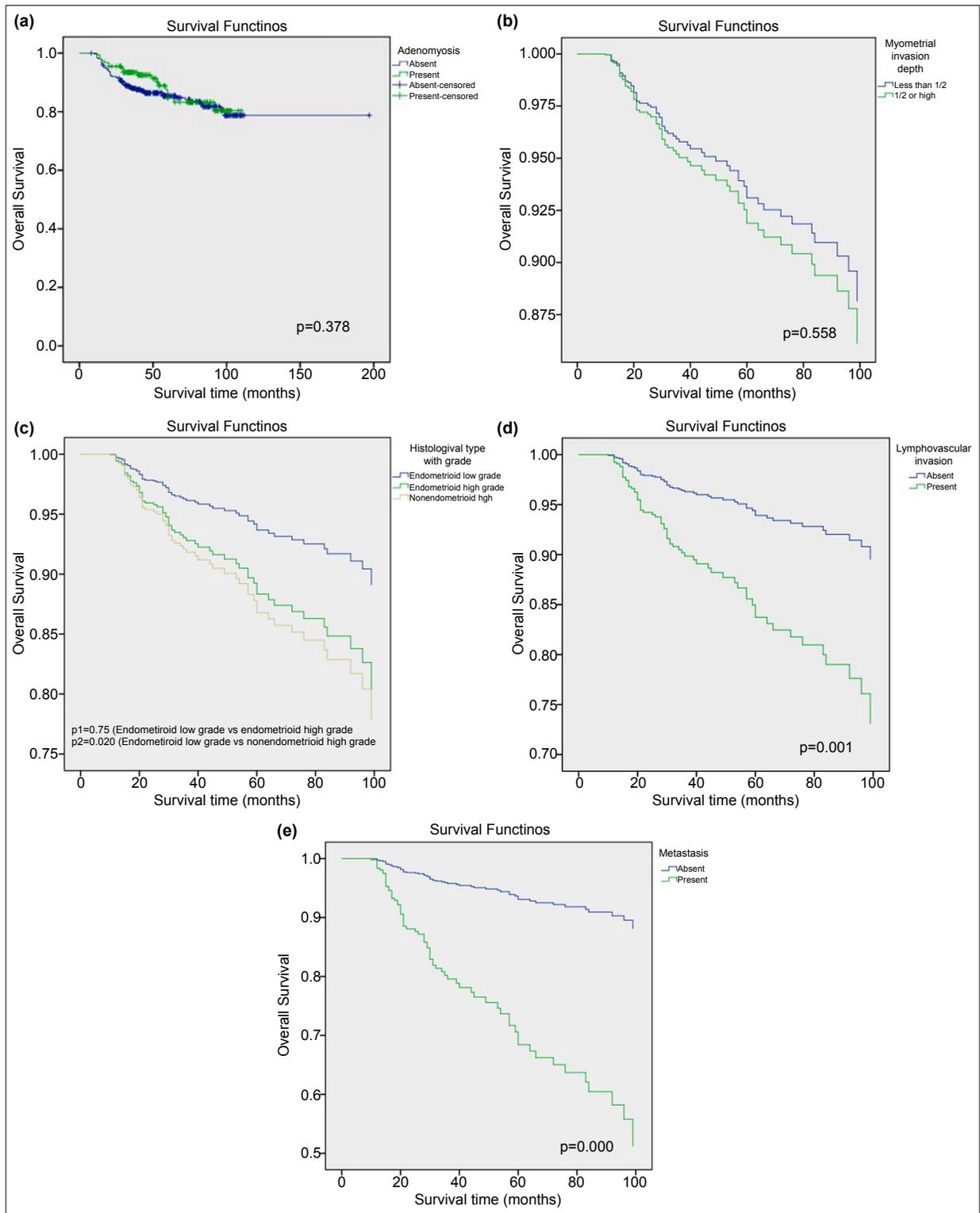
<sup>†</sup>Although adenomyosis was not significant in univariate analysis, it was included in the model due to its clinical significance; <sup>‡</sup>Reference category, endometrioid low-grade; <sup>§</sup>Reference category, no lymph nodes assessed; Cox proportional hazard regression test for p-values (significant variables with p<0.05 are bold); 95% CI: 95% confidence interval; exp(B): Exponential bound.

vasion (Fig. 2d), and metastasis (Fig. 2e) were significant factors predicting the survival time (Table 2). The hazard ratio (HR) was the largest for metastasis with 5.3 (95% CI: 2.4–11.4).

Survival means for survival time in patients with and without AM in different histologic types was similar for each subgroup consisting of endometrioid low grade, endometrioid high grade, and non-endometrioid histologic type of EC (p>0.005 for each group) (Table 4).

## DISCUSSION

The key findings of our results are that (i) EC with coexisting AM was associated with lesser myometrial invasion, and the size of the tumor was smaller than in those without AM; (ii) no survival difference was seen in patients with endometrial adenocarcinoma with or without AM; and (iii) the presence of AM was not associated with the survival time between subgroups, including low-grade endometrioid, high-grade



**Figure 2.** Overall survival (OS) curve (a) according to the presence or absence of adenomyosis, (b) myometrial invasion depth, (c) histologic type with grade, (d) lymphovascular invasion status, (e) presence or absence of metastasis in patients with endometrial cancer who underwent staging surgery.

endometrioid, and the high-grade non-endometrioid adenocarcinomas. Additionally, (iv) although non-endometrioid high-grade histologic type, presence of lymphovascular invasion, and nodal metastasis were independent prognostic

factors, AM and myometrial invasion depth were not significant factors predicting the survival time for EC.

As mentioned in a literature review, adenomyotic uteri contain associated endometrial and myometrial lesions

**Table 4.** Means for survival time in patients with and those without adenomyosis in different histologic subtype and tumor grade

Histologic subtype with tumor grade	Adenomyosis	Means for survival time (months)				p
		Mean	SD	95% CI interval		
				Lower	Upper	
Endometrioid low grade	Absent	177.304	4.136	169.197	185.410	0.383
	Present	98.307	2.517	93.375	103.240	
	Overall	175.342	3.643	168.201	182.483	
Endometrioid high grade	Absent	82.652	6.264	70.375	94.929	0.136
	Present	100.667	8.520	83.967	117.366	
	Overall	88.815	5.388	78.255	99.376	
Non-endometrioid high grade	Absent	46.275	4.854	36.761	55.789	0.097
	Present	71.422	9.429	52.942	89.902	
	Overall	58.256	5.375	47.721	68.791	

\*Kaplan–Meier test (log rank test).

consisting of endometrial polyps, hyperplasia, leiomyoma, endometriosis, and EC in up to 80% of the resected hysterectomy materials.<sup>[7,10,18]</sup> Even though the relationship between AM and EC has been reported in many studies, the exact prevalence of this coexistence is still inconsistent.<sup>[19]</sup> In this present study, AM coexisted in 140 out of 325 (30.1%) patients with endometrioid and 15 out of 38 (28.3%) with non-endometrioid histologic types. Our study supports previous observations where 64 out of 229 (28%) patients with EC had coexisting AM.<sup>[16]</sup> However, according to the results of the present study, the prevalence of AM was higher than in a study by Mao et al.,<sup>[20]</sup> who observed that 25 patients out of 127 (18.9%) with EC had AM. Consequently, the reported prevalence of AM in patients with EC is variable. This observation may support the hypothesis that sampling of hysterectomy specimens lacks standardization, and within this context, histopathologic analysis of AM may differ from pathologist to pathologist, which may account for the different rates in the literature.<sup>[8]</sup> Another possible explanation is that the diagnosis of AM may be neglected when EC is detected by pathologists. Research on the subject has mostly advocated that endometrial adenocarcinomas associated with AM tend to occur in Type I endometrioid, hormone-sensitive adenocarcinomas.<sup>[7,8]</sup> However, we observed that AM was found with both endometrioid and non-endometrioid adenocarcinomas at similar rates. This result may be explained by the fact that AM, which is a hormone-dependent disease, also accompanies the non-endometrioid subtype due to the high serum levels of estrogen caused by the peripheral conversion of androgen to estrogen. The high frequency of coexistent of AM with non-endometrioid EC, which frequently affects older women, may be explained by the peripheral conversion of androgen to estrogen in patients with EC.<sup>[21]</sup>

On the basis of the present data, we analyzed prognostic factors including less than 50% myometrial invasion, tumor size  $\leq 2$  cm, and negative lymph node involvement, which are also known to be associated with better survival in EC.<sup>[22,23]</sup> We reported that the presence of AM was associ-

ated with a low incidence of outer-half uterine myometrial invasion (33.9% vs 66.1%,  $p=0.004$ ), a high incidence of less than 2 mm tumor size (64.4% vs 25.8%,  $p=0.015$ ), and less lymph node involvement (25.9% vs 74.1%,  $p=0.031$ ) in patients with EC. This finding is consistent with other studies,<sup>[9,24,25]</sup> unlike Taneichi et al.,<sup>[26]</sup> who suggested that AM was related to deep myometrial invasion in stage I endometrioid adenocarcinoma without any influence on the prognosis of endometrioid adenocarcinoma.

Contrary to expectations, we observed that the presence of AM was associated with low-risk tumors; however, it was not associated with better survival time compared with those without AM ( $p=0.399$ ). After controlling for other significant variables in univariate analysis, in multivariate analysis, clinicopathologic factors including histologic type with grade, lymph vascular invasion, lymph node positivity, and metastasis were significant factors predicting survival time regardless of the presence of AM. On the other hand, the presence of AM did not remain an independent prognostic factor due to the OS (HR=1.289; 95% CI: 0.734–2.263;  $p=0.378$ ). Similarly, in a study that examined 314 patients with endometrioid EC, 79 (25.1%) of whom had AM, Aydin et al.<sup>[27]</sup> reported that coexistent AM in EC was not a prognostic factor and did not affect survival outcomes. In contrast, some studies found that coexisting AM was associated with less aggressive tumor behavior of EC with significantly better survival time. A recent study by Koshiyama et al.<sup>[28]</sup> found relatively better survival outcomes in 29 patients with ECs with AM uteri out of 179 patients with stage I adenocarcinoma. Matsuo et al.<sup>[29]</sup> found that EC coexisting with AM was associated with a better OS (91.8 vs 83.9%;  $p=0.004$ ), and AM was associated with a decreased risk of disease recurrence after surgery as an independent prognostic factor (HR=0.53; 95% CI: 0.30–0.92;  $p=0.023$ ) on multivariate analysis. Regarding these observations, researchers proposed that adenomyotic lesions promoted an inflammatory process, resulting in repeated cycles of tissue injury repair, constituting an environment conducive for fibrogenesis.<sup>[30]</sup> Additionally, they speculated

that the presence of AM positively affected progression-free survival and OS depending on the limiting effect of AM on the local and distant spread of endometrial cancer.<sup>[11,24,29]</sup>

Another surprising finding was that myometrial invasion depth did not remain an independent prognostic factor due to the OS (HR=1.184; 95% CI: 0.673–2.082; p=0.558). One possible explanation of this conflicting result could be related to the difficulty in distinguishing between an adenocarcinoma that spreads the myometrium and that of carcinoma with intramucosal invasion into foci of AM from the pathologic standpoint.<sup>[7]</sup> It has been suggested that preoperative frozen section analysis of AM might result in false-positive predictions of myometrial invasion and might result in inaccurate surgical staging, which drives management options. In our opinion, the staging accuracy of EC in assessing the depth of myometrial invasion might improve when pathologists are alert to the coexistence of AM and EC and have adequate information about findings obtained from preoperative diagnostic imaging modalities. Moreover, factors used to guide surgical decisions for lymphadenectomy are uncertain.<sup>[27]</sup> Routine prophylactic sentinel lymph node biopsy might be performed for surgical staging in cases with coexisting AM with early stage EC. In this instance, cancers classified as stage IA preoperatively might turn out to be stage 3 postoperatively.

Also, much-debated question has been raised, whether AM has a different effect on EC subtypes in terms of survival outcomes. With respect to the research question, we performed an analysis to evaluate whether there was any impact of AM in different histopathologic subtypes of EC. In multivariate analysis, the non-endometrioid histologic type was independently associated with worse survival (HR=2.167; 95% CI: 1.127–4.166; p=0.020). However, subgroup analysis of EC revealed no differences in means for survival time in patients with and without AM in different histologic types (p>0.005 for each group). Similar to our study, Erkilinç et al.<sup>[24]</sup> reported that the presence of AM had no effect on either disease-free survival (DFS) or EC-related death rates for patients with non-endometrioid-type cancers. Their multivariate analysis revealed the positive effect of AM and negative effect of tumor grade on OS. Therefore, they speculated that AM might be considered to be a prognostic factor along with histologic grade.

The strength of this study was the homogeneity between the two groups, with and without AM, in terms of median age at the time of diagnosis. Thus, length time bias was prevented. Although we designed a retrospective study, the case–control design was relatively large compared with the previous literature evaluating ECs in patients with and without AM. Another strength was that this was the first study comparing survival time in patients with and without AM in different histologic types. However, a limitation is that we were not able to analyze the DFS of patients with EC because our hospital is a tertiary hospital to which patients are admitted from distant cities, and some data were missing due to their irregular follow-up in the same hospital. Another weakness of the study is that this was a

retrospective study, which may miss potential confounding factors. Therefore, the optimal study to elucidate the association of coexistent AM and EC with different cancer subtypes would be a prospective study with a larger sample size to support our results.

In conclusion, although the presence of AM with EC is not an independent prognostic factor for OS, at the time that AM is suspected, preoperative and postoperative evaluations should be carefully made by both a gynecologist and a pathologist. Routine sentinel lymph node sampling may be an option as a part of staging surgery in patients with low-risk EC with accompanying AM. Thus, the surgical stage might change from low stage to high stage, which will determine postoperative medication. Further clinical studies are needed to evaluate the effect of AM on EC progression.

## Acknowledgments

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## Ethics Committee Approval

This study approved by the Martal Dr. Lutfi Kirdar Training and Research Hospital Clinical Research Ethics Committee (Date: 26.06.2019, Decision No: 2019/514/156/13).

## Informed Consent

Retrospective study.

## Peer-review

Internally peer-reviewed.

## Authorship Contributions

Concept: G.B.; Design: E.C.G.; Supervision: E.M.; Fundings: G.Y.; Materials: A.K.; Data: B.K., M.M.A.; Analysis: M.Y.; Literature search: M.G.; Writing: N.D.U., M.M.A.; Critical revision: T.A.U.

## Conflict of Interest

None declared.

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## Endometriyal Kanseri Hastalarda Adenomyozis Varlığının Patolojik Prognostik Özellikler ve Sağkalım Süresi Üzerine Etkileri

**Amaç:** Bu çalışmanın ilk amacı, endometrial kanserli (EK) hastalarda adenomyozis (AM) varlığının patolojik prognostik özellikler ve sağkalım süresi üzerine etkisinin olup olmadığını araştırmaktır. İkinci amaç, düşük dereceli endometrioid karsinom, yüksek dereceli endometrioid karsinom ve yüksek dereceli endometrioid olmayan karsinom olarak her bir alt tip gruplandırması için AM ilişkisini değerlendirmektir.

**Gereç ve Yöntem:** Mevcut geriye dönük gözlemsel kohort çalışması, Sağlık Bilimleri Üniversitesi, İstanbul Kartal Dr. Lütfi Kırdar Şehir Hastanesi'nde evreleme ameliyatı geçiren EK'lı hastalardan kurulum veri tabanı kullanılarak yapılmıştır. Kohort, AM varlığına veya yokluğuna göre iki gruba ayrıldı. Ek olarak, EK alt tipleri düşük dereceli endometrioid, yüksek dereceli endometrioid ve yüksek dereceli endometrioid olmayan tümörler olarak gruplandırıldı ve ayrıca AM'nin varlığına veya yokluğuna göre ayrıldı. Sağkalım sonuçları ve patolojik prognostik özellikler her grup arasında karşılaştırıldı.

**Bulgular:** Toplam 518 endometriyal kanser hastası analiz edildi. AM olan ve olmayan hastalar arasında genel sağkalım (OS) benzerdi (Cox regresyon Wald=0.654, p=0.419). Çok değişkenli Cox regresyon analizinde AM varlığı sağkalım süresi ile ilişkili değildi (p=0.378). Ancak histolojik tip ve grade, lenfovasküler invazyon ve metastaz sağkalım süresini öngören önemli faktörlerdi. (Endometrioid düşük dereceli ve endometrioid yüksek dereceli, p1=0.075, Endometrioid düşük dereceli ve endometrioid olmayan yüksek dereceli, p2=0.020; p=0.001 ve p=0.001). AM olan ve olmayan farklı grade ve histolojik tiplere sahip EK hastalarının sağ kalım süresi ortalamaları her alt grup için benzerdi. (her grup için p>0.005).

**Sonuç:** Bulgularımız, Ek ile AM varlığının OS için bağımsız bir prognostik faktör olmadığını gösterdi.

**Anahtar Sözcükler:** Adenomyosis; endometrial adenokarsinom; endometrioid karsinom; non-endometrioid karsinom; sağ kalım analizi.