

HISTOLOGICAL TYPES OF UTERINE CANCER IN THE "DR. SALVATOR VUIA" CLINICAL OBSTETRICS AND GYNECOLOGY HOSPITAL ARAD DURING THE 2000-2009 PERIOD

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ABSTRACT. The purpose of this study is to examine the histological types of uterine cancer in our hospital during the 2000-2009 interval. The data was collected from the Histopathology Exams (HPE) registers. Uterine cancer was discovered in 392 cases, representing 31,46% of all genital cancers (1246 cases). Most cases (371 or 94,64%) were represented by carcinomas, sixteen patients (4,08%) had sarcomas and there were also four cases of carcinosarcoma (1,02%) and one case of carcinoma-carcinosarcoma combination (0,26%). Endometrioid carcinoma appeared in 87,33% of all carcinoma cases. Twelve cases of sarcoma were endometrial stromal sarcomas and four were leiomyosarcomas. The mean ages of the patients were $61,71 \pm 9,06$ years. After performing the t-test for mean ages of the patients, the statistically significant differences are those between the sarcoma cases and the entire uterine cancer group ($p < 0.000001$) and between the carcinosarcoma cases and the entire uterine cancer group ($p = 0.000002$). The results of our study are similar to those in previous researches regarding the frequency of different histological types and the median age. Uterine cancer, although less aggressive, still remains a serious public health issue in Romania as many cases are discovered too late.

INTRODUCTION

Tumors of the uterine corpus comprise the most common group of gynecologic malignancies (Jemal et al, 2007). The large number of survivors with uterine cancers reflects a disease characterized by early onset of symptoms, a long and slow evolution, and well-established diagnostic guidelines; uterine bleeding, the most frequent symptom, determines the patients to go to seek early medical attention. Nevertheless, women with high-risk or advanced disease have a poor prognosis and account for the most uterine cancer deaths (Zaino et al, 1991; Gusberg 1993).

Endometrial carcinoma is the most common malignancy of the female genital tract in the Western world and the fourth most common cancer in women after breast, lung, and colorectum. Developing countries and Japan have incidence rates four to five times lower than Western industrialized nations, with the lowest rates being in India and south Asia. Women have an approximately one in forty lifetime risk of being diagnosed with uterine cancer. The majority are stage I at diagnosis as most women present with postmenopausal bleeding. Approximately 90-95% of tumors arise within the epithelium of the uterine lining and are categorized as endometrial carcinomas; within this group, 75% to 80% are endometrioid adenocarcinomas (Zaino et al, 1991; Gusberg 1993; Parazzini et al, 1991); the remaining 5-10% of cases

being sarcomas. The median age of diagnosis for endometrioid cancer is 63 years and most patients are postmenopausal (Parazzini et al, 1991); also, most patients are between the ages of 50 and 59 years. Approximately 5% of women will have adenocarcinoma before the age of 40 years, and 20-25% will be diagnosed before the menopause (Creasman et al, 2007). About 70% are confined to the corpus at the time of diagnosis, with a 5-year survival of approximately 83% (Prat et al, 2007). The average age of patients with nonendometrioid cancer is 67 years, and at least half have already spread beyond the corpus at the time of diagnosis; their 5-year survival is approximately 62% for clear cell carcinomas and 53% for papillary serous cancers (Creasman et al, 2006). Two different clinical and pathological subtypes of endometrial cancer are recognized: the estrogen-related (type I or endometrioid), and the non-estrogen-related (type II or nonendometrioid). Each subtype has specific genetic alterations. Approximately 80% of newly diagnosed endometrial carcinomas in the Western world are endometrioid in type (Prat et al, 2007). Any factor that increases exposure to unopposed estrogen (e.g., estrogen-replacement therapy, obesity, anovulatory cycles, estrogen-secreting tumors) increases the risk of these tumors, whereas factors that decrease exposure to estrogens or increase progesterone levels (e.g., oral contraceptives or

smoking) tend to be protective (Parazzini et al, 1991). Endometrial cancer may occasionally develop after radiation treatment for cervical cancer. In such cases, the majority are diagnosed at an advanced stage of disease and are high-risk histological subtypes. Their prognosis is poor but does not appear to be significantly worse when compared to patients with high-stage, high-grade sporadic cancers (Pothuri et al, 2006). Endometrial adenocarcinoma occurs during the reproductive and menopausal years. Variants of endometrioid adenocarcinoma include adenosquamous, villoglandular, ciliated, and secretory subtypes. About 10% of tumors are considered mixed histology; rare cell types, including papillary serous carcinoma, clear cell carcinoma, papillary endometrioid carcinoma, and mucinous carcinoma, account for the remaining cases. In general, all of these uncommon cell types are associated with a later age of onset, greater risk for extrauterine metastases, and poorer prognosis when compared with typical grade 1 adenocarcinomas (McMeekin et al, 2007; Hendrickson et al, 1982; Sutton et al, 1987).

Sarcomas arising within the uterus are relatively rare. According to the Surveillance, Epidemiology and End Results (SEER) data reported by Brooks and colleagues covering 2677 cases from 1989–1999, the age-adjusted incidence for all sarcomas (per 100,000 women age 35 and over) in US women was 2.68 for native American/Asian/ Hispanic, 3.58 for white, and 7.02 for black women. By comparison, the incidence for epithelial uterine cancers, per 100,000 women, is roughly 9 for black women and 20 for white women. Uterine sarcomas represented 8% of primary uterine malignancies in the most recent analysis of the SEER database. Harlow and coworkers had previously reported from SEER databases covering 1973–1981, which suggested an annual incidence of only 1.7 cases per 100,000 women. Sarcomas have been traditionally thought to represent only 3–5% of all uterine tumors. The increasing incidence of uterine sarcomas noted in the SEER studies may reflect better diagnosis, and perhaps a true increase in an aging population. Of the sarcomas, the most common, in order of decreasing incidence, are carcinosarcoma, leiomyosarcoma, endometrial stromal sarcoma, and adenosarcoma. Of the 1452 uterine sarcomas in Harlow's study, 86% were classified as carcinosarcoma (MMMT) or leiomyosarcoma. Sherman reporting on SEER data from 1992–1998 found that 53% of all sarcomas were carcinosarcomas (Holland, 2010).

Frequency of adenocarcinoma of the uterus

Type	Number (%)
Endometrioid	6231 (84%)
Adenosquamous	317 (4.2%)
Mucinous	74 (0.9%)
Papillary serous	335 (4.5%)
Clear cell	185 (2.5%)
Squamous cell	28 (0.04%)
Other	285 (3.8%) (Pecorelli, 1998)

Classification of uterine sarcomas

Non-Epithelioid Neoplasms

Leiomyosarcoma

Epithelioid

Myxoid

Endometrial stromal neoplasms

Stromal nodule

Low-grade stromal sarcoma

Undifferentiated stromal sarcoma

Smooth muscle tumor of uncertain malignant potential

(*STUMP*)

Mixed endometrial stromal and smooth muscle tumor

Leiomyoma

Histologic variants

Mitotically active variant

Cellular variant

Hemorrhagic cellular variant

Epithelioid variant

Myxoid

Atypical variant

Lipoleiomyoma variant

Mixed Epithelial and Non-Epithelial Tumors

Adenosarcoma

Homologous

Heterologous

Carcinosarcoma

Homologous

Heterologous

Adenofibroma

Carcinofibroma

Adenomyoma (Mendivil et al, 2010)

OBJECTIVES, MATERIAL AND METHOD

The purpose of this study is to examine the histological types of uterine cancer in our hospital during the 2000–2009 interval, the data being collected from the Histopathology Exams (HPE) registers. The bioptic material was obtained through curettage and from hysterectomy specimens.

RESULTS

There were 1244 case of genital cancers diagnosed in our hospital during the 2000–2009 period, including cervical, uterine, ovarian, vaginal, and vulvar cancer; there were 392 cases of uterine cancer (Table 1). The fragments sent to the histopathology departments were obtained by biopsies in 239 cases (60,97%) and from surgical specimens in 153 cases (39,03%).

Of the uterine cancer cases, 371 were carcinomas (94,64%), sixteen were sarcomas (4,08%), four were a carcinosarcomas (1,02%) and there was a case of carcinoma combined with carcinosarcoma (0,26%) (Table 2, Figure 1). A total of 372 patients had carcinomas (94.90%), while five had carcinosarcomas (1.28%).

Type	Number	%
Cervical	731	58,76
Uterine	392	31,51
Ovarian	82	6,59
Vulvar + vaginal	39	3,14

Type	Number	%
Carcinoma	371	94,64
Sarcoma	16	4,08
Carcinosarcoma	4	1,02
Carcinoma+ carcinosarcoma	1	0,26

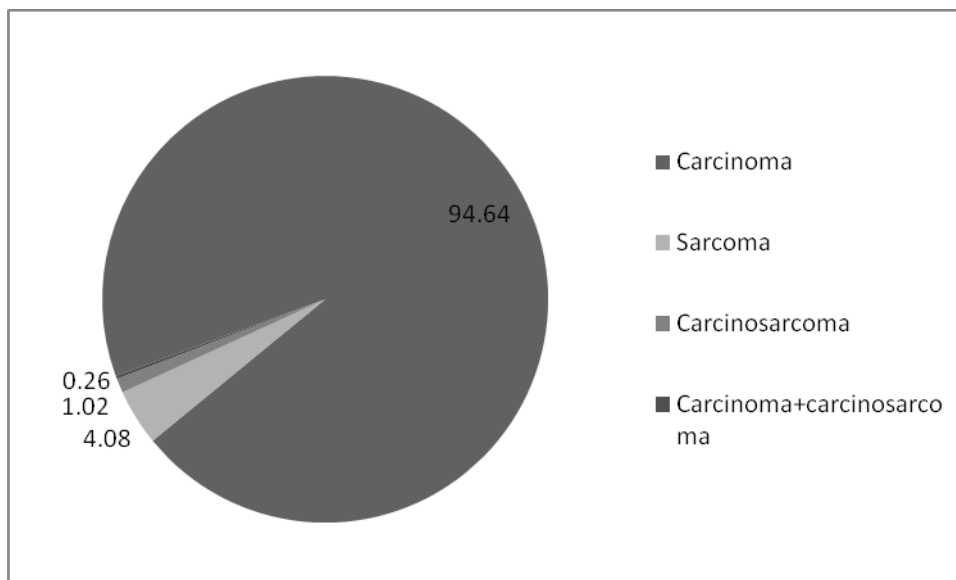


Figure 1 Types of uterine cancer (%)

The carcinoma cases had the following distribution: 266 endometrioid/endometrial, 28 clear cell carcinomas, 46 cases of combinations of the first two, seven adenosquamous, seven squamous+endometrial, four endometrial+serous, three squamous, two neuroendocrine, two clear cell+adenosquamous, two clear cell+squamous, one transitional, one clear cell+secretory, one secretory and one case of endometrial+secretory (Table 3); 63 patients had two types of carcinoma; as for the sarcomas, 12 were

endometrial stromal sarcomas (3.06 % of the 392 uterine cancer patients, 2.63% of the 456 different cancer types), 4 were leiomyosarcomas (1.02% of the 392 uterine cancer patients, 0.88% of the 456 different cancer types).

Endometrioid carcinoma appeared in 87,33% of all carcinoma cases, clear cell carcinoma in 21,29%, squamous carcinoma in 3,23%, and adenosquamous carcinoma in 2,43%. The 392 patients had 456 different types of cancers.

Carcinoma type	Number	% of all carcinomas (434)	% of all uterine carcinoma patients (371)	% of all cancers (456)	% of all uterine cancer patients (392)
Endometrial/endometrioid	324	74.65	87.33	71.05	82.65
Clear cell	79	18.20	21.29	17.32	20.15
Squamous	12	2.76	3.23	2.63	3.06
Adenosquamous	9	2.07	2.43	1.97	2.30
Serous	4	0.92	1.08	0.88	1.02
Secretory	3	0.69	0.81	0.66	0.77
Neuroendocrine	2	0.46	0.54	0.44	0.51
Transitional	1	0.23	0.27	0.22	0.26

The mean ages of the patients were $61,71 \pm 9,06$ years for all cases of uterine cancer (age range 38 to 85 years), $61,89 \pm 9,13$ years for carcinomas (age range 38 to 85 years), $57,69 \pm 7,56$ years for the sarcoma cases (age range 48 to 77 years), $59,50 \pm 5,26$ years for the four patients with carcinosarcomas (age range 55 to 65

years), while the patient with a carcinoma-carcinosarcoma combination was 67 years old. A number of 149 patients belonged to the 51-60 year age group, representing 38,01% of all uterine cancer cases. (Table 4, Figures 2-5)

Table 4 Age groups				
Age group (years)	Carcinoma (%)	Sarcoma (%)	Carcinosarcoma (%)	Total (%)
31-40	4 (1.08)	-	-	4 (1.02)
41-50	33 (8.89)	4 (25)	-	37 (9.44)
51-60	139 (37.47)	8 (50)	2 (50)	149 (38,01)
61-70	124 (33.42)	3 (18.25)	2 (50)	130* (33.16)
71-80	65 (17.52)	1 (6.25)	-	66 (16.84)
81-90	6 (1.62)	-	-	6 (1.53)

*including the carcinoma-carcinosarcoma case

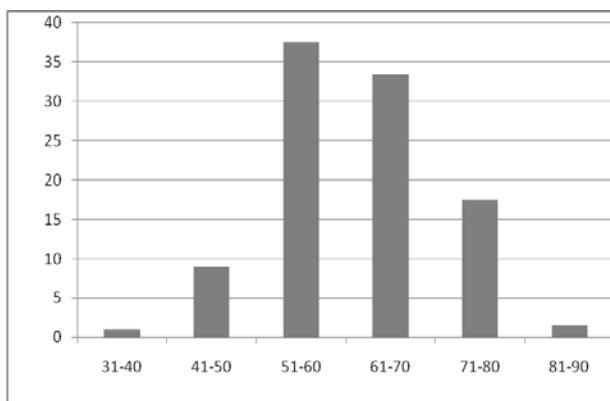


Figure 2 Carcinoma age groups

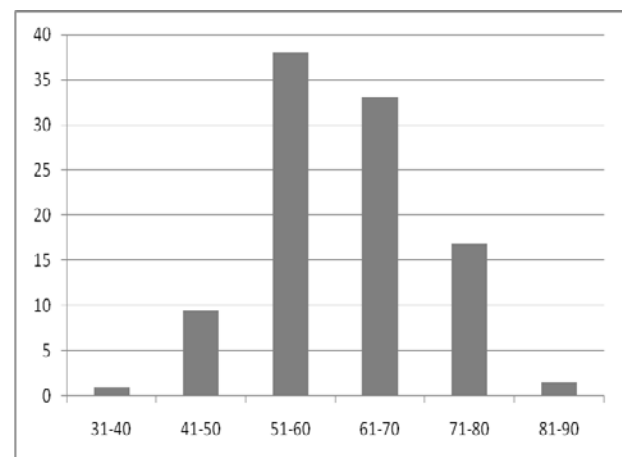


Figure 4 Uterine cancer age groups

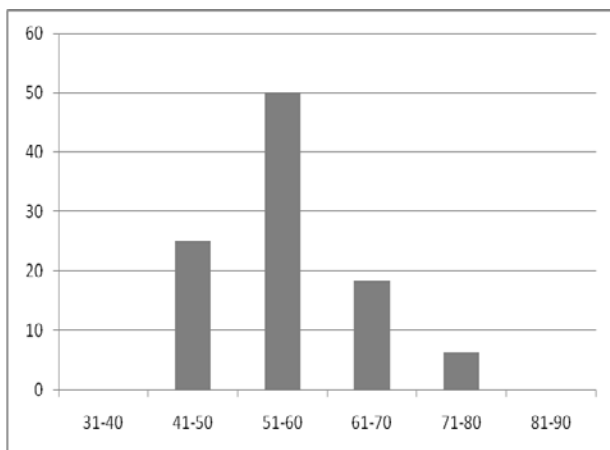


Figure 3 Sarcoma age groups

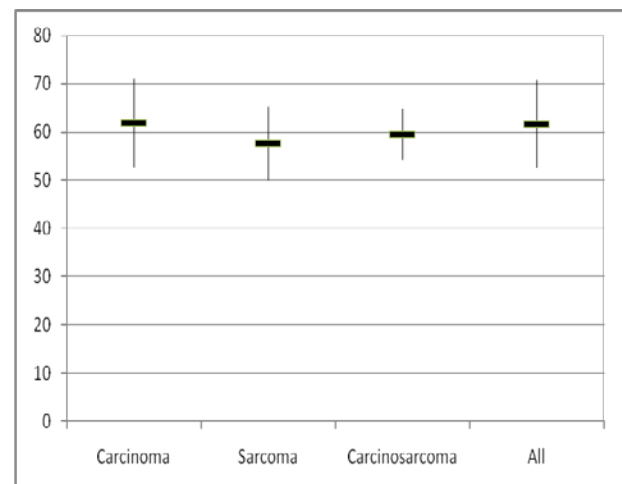


Figure 5 Mean age ± SD

After performing the t-test, we conclude that the only statistically significant differences between the mean ages of the patients are those between the sarcoma cases and the entire uterine cancer group ($p < 0.000001$) and between the carcinosarcoma cases

and the entire uterine cancer group ($p=0.000002$), all other values of p being >0.50 (Table 5).

Comparison	p value
Carcinoma vs. sarcoma	0.5010
Carcinoma vs. sarcoma	0.5995
Carcinoma vs. carcinosarcoma	0.6951
Carcinoma vs. all	0.6144
Sarcoma vs. all	<0.000001
Carcinosarcoma vs. all	0.000002

DISCUSSIONS, CONCLUSIONS

The frequency of the main histological types in our study differs more or less from those in literature, one of the reasons being the smaller number of cases in our research:

- Carcinomas
 - endometrioid+endometrial 71.05%
(<http://seer.cancer.gov>) versus 75.6% and 84% (Pecorelli, 1998)
 - squamous metaplasia 2.63% versus 2.4%
(<http://seer.cancer.gov>)
 - clear cell 17.32% versus 1.4%
(<http://seer.cancer.gov>) and 2.5% (Pecorelli, 1998)
 - adenosquamous 1.97% versus 2.6%
(<http://seer.cancer.gov>) and 4.2% (Pecorelli, 1998)
- Other
 - leiomyosarcoma 0.88% versus 1.9%
(<http://seer.cancer.gov>)
 - endometrial stromal sarcoma 2.63% versus 1.3%
(<http://seer.cancer.gov>)
 - carcinosarcoma 1.28% versus 1.5%
(<http://seer.cancer.gov>)

Uterine cancer, although less aggressive, still remains a serious public health issue in Romania as many cases are discovered too late because many patients ignore the symptoms or are afraid/ashamed to go to the physician.

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