EJGO European Journal of Gynaecological Oncology

A retrospective study of clinicopathological characteristics, treatment, and outcomes of Chinese uterine and ovarian carcinosarcoma patients

Jun Zhu[1,2], Hao Wen[1,2], Rui Bi[2], Xiaohua Wu[1,2]

[1]Department of Gynecologic Oncology, Fudan University Shanghai Cancer Center, Shanghai; [2]Department of Oncology, Shanghai Medical College, Fudan University, Shanghai; [3]Department of Pathology, Fudan University Shanghai Cancer Center, Shanghai (China)

Summary

This study aimed to determine the clinicopathological and prognostic factors, and to assess the impact of cytoreduction to complete gross resection in Chinese uterine and ovarian carcinosarcoma patients. *Materials and Methods:* The authors reviewed 86 consecutive patients treated for uterine (n=60) or ovarian (n=26) carcinosarcomas between February 2006 and August 2013 at Fudan University Shanghai Cancer Center. *Results:* The median follow-up time was 24.0 months [interquartile range (IQR): 12.4 to 48.7]. The median age was 59 years (IQR: 53 to 66). The three- and five-year overall survival rates were 60.1% and 42.8%, respectively. Extent of tumor dissemination, mesenchymal component, and adjuvant therapy were predictive of overall survival. Among advanced carcinosarcoma patients, complete gross resection (R_0) had a three-year overall survival rate of 52.5%, *vs*. 38.9% and 20.8% in patients with gross residual disease ≤ 1cm and > 1cm ($p = 0.004$). On multivariate analysis, only heterologous mesenchymal component (HR=4.8; 95% CI, 1.4-16.7; $p = 0.015$) and gross residual disease (HR=2.6, 95% CI: 1.2-5.9; $p = 0.019$) were predictors of increased mortality. *Conclusions:* Heterologous tumor and incomplete gross resection were significantly predictive of a poor overall survival in carcinosarcoma patients. We recommend cytoreduction to R_0 for upfront treatment in CS patients.

Key words: Ovarian carcinosarcoma; uterine carcinosarcoma; prognostic factors; cytoreduction

Introduction

Carcinosarcomas, also called malignant mixed Müllerian tumors, are rare but aggressive tumors which are widely thought to be metaplastic carcinomas, where the mesenchymal part retains epithelial features [1]. Uterine carcinosarcomas (UCS) account for 2% to 5% of uterine carcinomas and ovarian carcinosarcomas (OCS) only account for 1 to 2% of all ovarian malignancies [2, 3]. Both UCS and OCS have relatively poor survival, with a median overall survival of approximately 21 months for UCS [4] and less than 18 months for OCS [5, 6].

Carcinosarcomas contain both malignant epithelial and mesenchymal elements. The mesenchymal component is either homologous or heterologous. Homologous sarcoma contains tissue that is native to the Müllerian duct, such as endometrial stromal sarcoma, fibrosarcoma or leiomyosarcoma. Cartilaginous, osteosarcomatous, liposarcomatous, and rhabdomyosarcomatous differentiations are commonly seen in heterologous elements.

Given their rarity and pathological diversity, there is no standard treatment modality for UCS or OCS at present. Surgery is still the mainstay therapy for these tumors. Meanwhile, the literature reports that adjuvant therapies, including radiotherapy and chemotherapy, have a role in minimizing both the pelvic and extrapelvic failure, whereas other studies have not validated this advantage [7, 8]. Current knowledge of the predictive/prognostic factors of UCS and OCS is largely based on a few retrospective studies with limited cases carried out in Western countries. The objective of this study was to determine the prognostic factors of UCS and OCS in Chinese patients. To the best of the authors' knowledge, this study included the largest number of carcinosarcoma patients in the Chinese mainland to date.

Materials and Methods

The authors performed a retrospective analysis in 86 consecutive patients diagnosed with UCS (n=60) and OCS (n=26) who underwent primary surgery between February 2006 and August 2013 at Fudan University Shanghai Cancer Center. Patients who underwent secondary cytoreductive surgery were excluded. Informed consent was obtained from all individual participants included in this study and procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (Institutional or regional) and with the Helsinki Declaration of 1975, as revised in 1983. All pathological slides were reviewed by gynecological pathologists to confirm the diagnosis.

The authors retrospectively collected demographic and clinicopathologic data from medical records, which included age at

Revised manuscript accepted for publication January 19, 2017

Eur. J. Gynaecol. Oncol. - ISSN: 0392-2936
XXXIX, n. 3, 2018
doi: 10.12892/ejgo4043.2018

7847050 Canada Inc.
www.irog.net

diagnosis, parity, menopause state, body mass index (BMI), presence of ascitic fluid, tumor stage, family history of malignancy, mesenchymal component (homologous or heterologous), pretreatment serum level of CA125, and pathologic FIGO stage (postsurgical classification using the International Federation of Gynaecology and Obstetrics FIGO staging). In this study, OCS and UCS were considered as two different sites of tumorgenesis. Considering that UCS and ovarian OCS have disparities in their stage designation, the authors divided the patients into the following two groups: tumor limited to the pelvis (localized disease group) and tumor spread beyond the pelvis or with lymph node metastasis (disseminated disease group), according to the extent of tumor dissemination. Localized disease (n=50) included Stage I to IIIb UCS and Stage I and II OCS with disease confined to the pelvic cavity, and disseminated disease (n=36) included Stage IIIc to IVb UCS and Stage III to IV OCS.

Data on surgical procedures and adjuvant treatment (chemotherapy or radiotherapy for uterine carcinosarcoma) were also analyzed. Twenty-three OCS patients with Stage II-IV disease and 23 UCS patients with Stage III-IV disease received cytoreductive surgery. Optimal cytoreduction was defined as complete gross resection (R_0) at the primary operation. Overall survival was evaluated and defined as the interval between the date at diagnosis to the date when the patient died from the tumor or the last follow-up visit.

All procedures performed in studies involving human participants were in accordance with the ethical standards of Fudan University Shanghai Cancer Center research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Survival curves were calculated by the Kaplan-Meier method. Kaplan–Meier survival curves were generated and survival differences were quantified using the log-rank test (univariate analysis). A Cox regression model (multivariate analysis) was used for the multivariate analysis of overall survival. Statistical tests were considered significant at $p < 0.05$. All analyses were performed using SPSS statistical software.

Results

The authors enrolled 86 patients, among which 26 patients were OCS and the remaining 60 were UCS. The median age at diagnosis for all patients was 59 years (interquartile range (IQR): 53 to 66). The median follow-up period was 24.0 months (IQR: 12.4 to 48.7). In the complete series, the carcinosarcomas were fatal in 37 patients (43.0%). The three- and five-year overall survival rates were 60.1% and 42.8%, respectively. The overall survival of OCS was poorer than that of UCS, with a three- and five-year overall survival of 39.7% *vs*. 70.5% and 19.8% *vs*. 54.2%, respectively ($p = 0.005$, Figure 1). By Cox regression model, the authors found that tumor site was not an independently prognostic factor (HR=2.2; 95%CI, 0.5-10.6; $p = 0.329$).

In the present study, patients' age, parity, menopause state, BMI, family history of tumors, the serum CA-125 level before surgery, ascitic fluid, and other demographic factors were not correlated with the overall survival. However, the extent of tumor dissemination, the mesenchymal component, residual disease and postoperative adjuvant therapy were correlated with overall survival (Table 1).

Patients with OCS were more likely to be in Stage III/IV (18 *vs*. 8), whereas most UCS patients were in Stage I/II (37 *vs*. 23). By dividing the patients into a localized disease group and disseminated disease group, the authors found that patients with tumors confined to the pelvis had five-year overall survival rates of 64.8%, whereas patients with tumor spread beyond the pelvic cavity had a three-year overall survival rate of only 10.8% ($p < 0.001$, Figure 2a).

A heterologous mesenchymal component was observed in 25 patients (29.1%), and a homologous component was observed in 56 (65.1%) patients. The three- and five-year overall survival rate for patients with the homologous component were 79.4% and 58.1%, respectively, whereas these rates were 22.7% and 11.3%, respectively for patients with heterologous tumors ($p < 0.001$, Figure 2b).

Multivariate analysis confirmed that the heterologous component (HR=4.8; 95% CI, 1.4-16.7; $p = 0.015$) was significantly associated with a poor overall survival, which was shown to be an independent prognostic factor (Table 2).

All of the 86 patients underwent surgery as the initial treatment at our institution (Table 3). A total of 83 patients (96.5%) received hysterectomy and bilateral salpingo-oophorectomy, two patients received hysterectomy and resection of the right attachment due to a history of the right ovarian cyst, and another patient received only bilateral salpingo-oophorectomy with a history of hysterectomy due to hysteromyoma. Pelvic and/or para-aortic lymphadenectomy was performed in 46 patients, and omentectomy was performed in 80 (93.0%) patients. Among all of the patients, 23 (88.5%) OCS patients had Stage II-IV disease and 23 (38.3%) UCS patients had Stage IIIc-IVb disease. All 46 patients with advanced stage disease received additional cytoreductive surgery. Eleven (23.9%) had a bowel resection, nine (19.6%) had peritoneal stripping, and two (4.3%) had diaphragm peritonectomy. R_0 was achieved in 17 (37.0 %) patients, 16 (34.8%) were left with residual disease of no more than 1 cm, and 13 (28.3%) patients were left with residual disease of more than 1 cm. Patients that accepted complete gross resection had a three-year overall survival of 60.6%, and those with gross residual diseases ≤ 1 cm and > 1 cm had a three-year overall survival of 35.2% and 16.9% ($p = 0.004$), respectively (Figure 2c). Multivariate analysis confirmed that incomplete gross resection (HR=2.6, 95% CI: 1.2-5.9; $p = 0.019$) was significantly associated with a poor overall survival.

Adjuvant therapy was found to be predictive of overall survival in both UCS and OCS patients. Chemotherapy was given to all but 11 patients and the initial regimens consisted of platinum-involved (n=75), ifosfamide-involved (n=15) or doxorubicin-involved chemotherapy (n=11, 14.7%). No significant survival outcome was found after comparing the overall survival between the platinum-involved and non-platinum-involved group ($p = 0.448$) and

Table 1. — *Univariate analysis of factors associated with overall survival in uterine and ovarian carcinosarcomas.*

Factor	N.	Death (%)	*p*-value
Age at diagnosis			
≤ 60	52	23 (44.2)	0.875
> 60	34	14 (41.2)	
Family history of malignancy			
Yes	28	14 (50.0)	0.265
None	58	23 (39.7)	
Menopause			
Premenopausal	18	6 (33.3)	0.918
Postmenopausal	68	31 (45.6)	
BMI			
< 25	47	19 (40.4)	0.407
≥ 25	39	18 (46.2)	
Pretreatment CA125 level			
≤ 200 U/ml	51	21 (41.2)	0.055
> 200 U/ml	25	15 (60.0)	
Ascites			
Negative	36	14 (38.9)	0.950
Positive	50	23 (46.0)	
Extent of tumor dissemination			
Localized	50	13 (26.0)	<0.001
Disseminated	36	24 (66.7)	
Mesenchymal component			
Homologous	56	16 (28.6)	<0.001
Heterologous	25	16 (64.0)	
Residual disease			
R_0	17	6 (35.3)	0.004
≤ 1 cm	16	10 (62.5)	
> 1 cm	13	12 (92.3)	
Adjuvant therapy			
CT/RT	79	33 (41.8)	0.033
None CT/RT	7	4 (57.1)	
Adjuvant chemotherapy			
Paclitaxel+carboplatin	42	16 (39.1)	0.081
Ifosfamide+cisplatinum	15	8 (53.3)	

R_0= complete gross resection; CT= chemotherapy; RT= radiotherapy.

Table 2. — *Multivariate survival analysis in uterine and ovarian carcinosarcomas.*

Variables	Hazard ratio	95% confidence interval	*p*-value
Tumor site*	2.195	0.453-10.629	0.329
Pretreatment CA125 level	2.886	0.736-11.318	0.128
Residual disease	2.624	1.168-5.893	0.019
Extent of tumor dissemination	1.667	0.359-7.737	0.514
Mesenchymal component	4.756	1.350-16.764	0.015

* *Uterine carcinosarcoma compared with ovarian carcinosarcoma.*

Table 3. — *Surgical procedures performed and surgical outcomes (n=86)*

Surgical procedures	N (%)
Abdominal hysterectomy	85 (98.8)
Hysterectomy+bilateral salpingo-oophorectomy	83 (96.5)
Hysterectomy+resection of the right attachment	2 (2.3)
Bilateral salpingo-oophorectomy	1 (1.2)
Lymphadenectomy	46 (53.5)
Pelvic alone	10 (11.6)
Pelvic and para-aortic	38 (44.2)
Inguinal	2 (2.3)
Other procedures	
Omentectomy	80 (93.0)
Appendectomy	38 (44.2)
Peritoneal stripping	9 (10.5)
Rectosigmoid resection	11 (12.8)
Diaphragm peritonectomy	2 (2.3)
Residual disease*	
No gross residual disease (R_0)	17 (37.0)
Gross residual disease ≤ 1 cm	16 (34.8)
Gross residual disease > 1 cm	13 (28.3)

* *Forty-six patients with advanced disease received additional cytoreductive surgery.*

the ifosfamide-involved and non-ifosfamide-involved group ($p = 0.055$). Patients that received carboplatin-paclitaxel (PC) and ifosfamide-cisplatin had a median overall survival of 45.7 months (95% CI, 38.9-52.5) and 18.6 months (95% CI, 8.2-28.9), respectively, but no significant difference was found ($p = 0.081$).

Radiotherapy treatment was performed only in UCS patients. Among 57 UCS patients accepting adjuvant therapy, three (5.3%) received adjuvant radiation therapy, 28 patients (49.1%) received adjuvant chemotherapy, and 26 patients (45.6%) received adjuvant chemotherapy with radiotherapy. The three- and five-year overall survival in patients with multimodal therapy were 78.8% and 71.0%, respectively, compared to 59.7% and 35.8% in patients who received adjuvant radiotherapy or chemotherapy alone, respectively ($p = 0.028$).

Discussion

Female genital tract carcinosarcomas are aggressive tumors and have high possibility of recurrence. Previous studies involved only a small number of patients due to its rare morbidity, limiting statistical analysis to robust prognostic factors. Recent studies from SEER analysis, which involved a large number of patients, have confirmed that the survival of OCS and UCS is worse than that of advanced epithelial ovarian carcinoma and endometrial cancer [9-11]. However, detailed information from the SEER database was limited. Few studies involving Asian patients exist in the literature. Thus, the present study included the largest case series evaluating the demographic and clinicopathological factors that predict the survival of UCS and OCS patients in China.

FIGO stage is an important prognostic factor. The present authors found that both in UCS and OCS patients, patients with early-stage disease had a better survival than those with advanced stage disease. Numerous studies

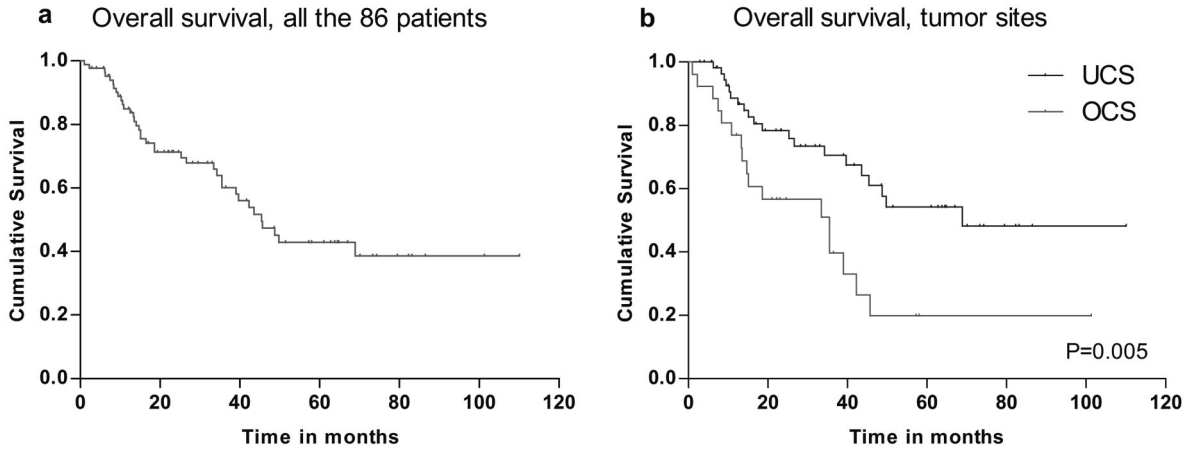

Figure1. — (a) Overall survival curve of 86 uterine and ovarian carcinosarcomas patients. The three- and five-year overall survival rates were 60.1% and 42.8%, respectively. (b) Overall survival according to sites of carcinosarcomas. UCS (blue line) median OS: 68.9 months and OCS (red line) median OS: 35.5 months, $p = 0.005$.

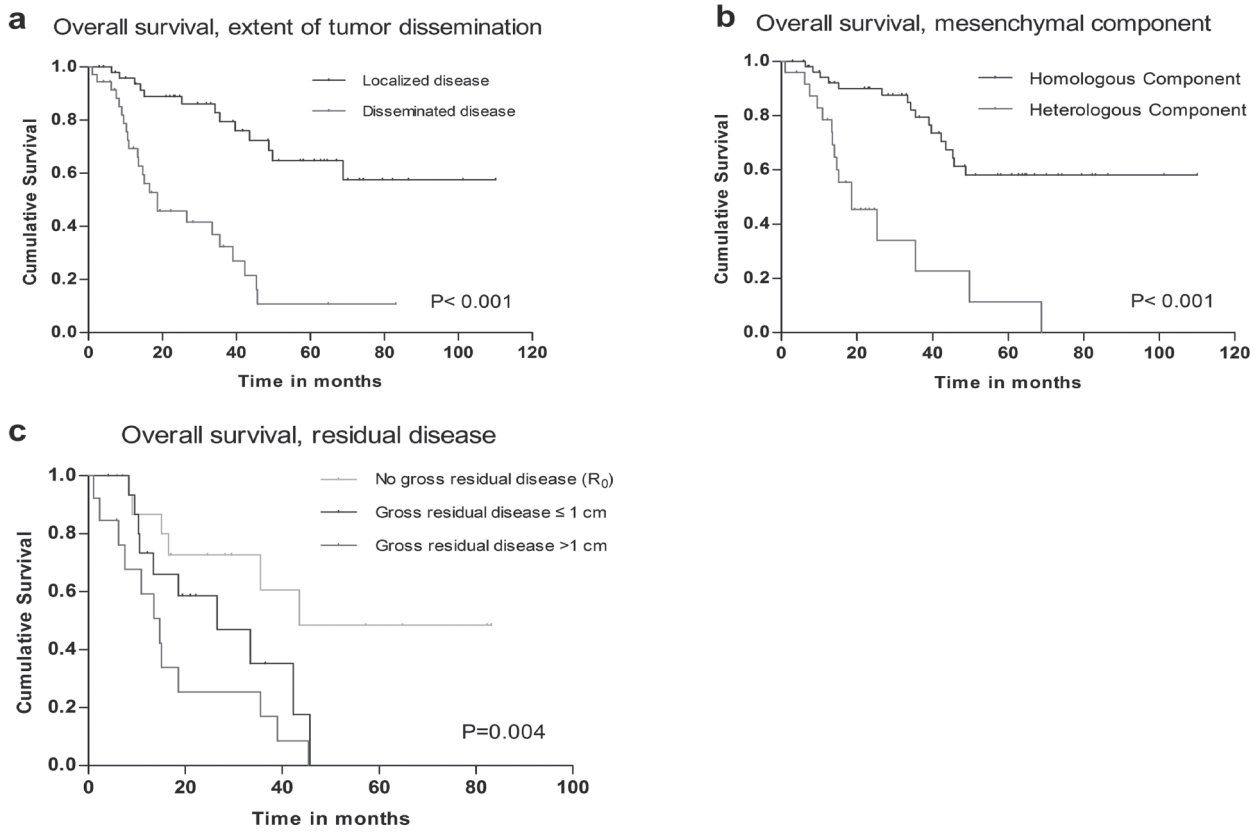

Figure 2 — Kaplan-Meier survival curves according to extent of tumor dissemination, mesenchymal component, residual disease and adjuvant therapy (UCS). CT= chemotherapy, RT= radiotherapy. (a) Localized disease (blue line), three- and five-year overall survival rate: 70.0% and 55.9%; disseminated disease (red line), three-year overall survival rate: 28.4%, $p < 0.001$; (b) Overall survival according to mesenchymal histological component. Homologous component (blue line), three- and five-year overall survival rate: 79.4% and 58.1%; Heterologous component (red line), three- and five-year overall survival rate: 22.7% and 11.3%, $p < 0.001$; (c) Complete gross resection (blue line), three-year overall survival rate: 52.5%; gross residual diseases ≤ 1cm (red line), three-year OS rate: 38.9%; gross residual diseases >1 cm (yellow line), three-year OS rate: 20.8%, $p = 0.038$; (d) Multimodal therapy (CT combined with RT, blue line), three-and five-year overall survival rate: 78.8% and 71.0%; Adjuvant CT/RT alone (red line), three- and five-year overall survival rate: 59.7% and 35.8%, $p = 0.028$.

demonstrated that advanced FIGO stage was associated with poor overall survival [12]. Meanwhile, the present authors found that OCS was observed to have a worse overall survival compared with UCS. The present authors believed that the poorer overall survival of OCS was likely attributable to the advanced stage at diagnosis, and UCS was prone to diagnosis at a relatedly early stage. The earlier diagnosis in UCS patients is mainly due to the appearance of symptoms, such as vaginal bleeding, which can be easily detected by the patients themselves, whereas OCS tends to remain undiagnosed for a longer time period due to its invisible symptoms. Considering the inappropriateness of direct stage-to-stage comparison between OCS and UCS, the authors divided the patients into two groups: patients with tumors limited to the pelvis and those that spread beyond the pelvis, which ensured the consistency of comparisons between UCS and OCS. They found that patients with extrapelvic disease spread had a significantly poorer overall survival compared with patients with limited disease. These patients with disseminated diseases may have had early-stage disease. Meanwhile, the poor distribution in the number of cases between the disseminated group and the localized group might also account for the significant difference. Using multivariate analysis, the extent of tumor spread was not an independent prognostic factor for survival outcome. This might reflect the difference in the patterns of management, as well as the biological characteristics between OCS and UCS.

A notable finding of the present study was that the prognostic value of the tumor's mesenchymal component should receive closer attention. The authors found that in both OCS and UCS, a homologous tumor was associated with a prolonged OS, which correlated with the results of Hellstrom *et al.* [13]. A similar result was reported in a study of 42 Stage I UCS patients after primary surgery. The presence of heterologous sarcomatous elements appeared to be a powerful negative prognostic factor, and the three-year overall survival rates were 45% *vs*. 93% in women with heterologous compared with homologous Stage I UCS patients ($p < 0.001$) [14]. This may be relevant to the fact that most heterologous tumors were diagnosed at an advanced stage when compared to the homologous tumors, and tumors with different components might have worse sensitivity to chemotherapeutic agents. However, several studies did not validate this finding [15, 16].

Residual diseases were found to be an independent prognostic factor with survival of patients in both univariate and multivariate analysis in the present cohort. The authors found that among patients who received cytoreductive surgery, those with complete gross resection had a significantly better overall survival rate compared to those with gross residual disease. Garg *et al.* study [12] also clearly supported the beneficial effect of optimal cytoreductive surgery (no visual residual disease or residual disease ≤ 1 cm), and it was recommended in the upfront surgical strategy to improve patients' survival. In light of previous studies by Edward *et al.* [17], complete gross resection led to a better overall survival (52.3 months) compared to gross residual disease (8.6 months, $p < 0.0001$); complete gross resection was independently associated with overall survival in advanced USC patients on multivariate analysis ($p = 0.044$). Similarly, Doo *et al.* [18] also suggested that radical surgery to no visible disease appeared to correlate with better progressive free survival ($p = 0.036$) and overall survival ($p = 0.015$) in OCS. It appeared that optimal cytoreductive surgery would confirm a trend toward a better survival for advanced ovarian and uterine carcinosarcomas.

Chemotherapy is considered to be the standard adjuvant treatment for UCS and OCS patients; nevertheless, the optimal choice of chemotherapy regimen remains to be determined [19,20]. Given that tumors with a sarcomatous component may be more responsive to ifosfamide, ifosfamide-based chemotherapy was evaluated in several series. The combination of ifosfamide-cisplatin also exhibited superior progression free survival compared to single-agent ifosfamide; however, there was no significant difference in overall survival, at the cost of an increased toxicity, especially in terms of myelotoxicity, gastrointestinal toxicity, and asthenia. The recommendations of chemotherapeutic regimen, based on retrospective data, are platinum-based chemotherapy. Although the present authors were not able to demonstrate a significant difference between patients with platinum-involved and ifosfamide-involved regimens in overall survival, a slight advantage favoring the use of paclitaxel-carboplatin compared to the cisplatin-ifosfamide combination was shown in this cohort. The confounding result that adjuvant therapy did not effectively improve overall survival was mainly due to the retrospective and non-randomized nature of the analysis, the insufficient number of patient, and the lack of a standard chemotherapeutic regimen, which imposed restrictions on the statistical analysis. Several studies have found favorable outcomes in carcinosarcoma patients treated with carboplatin-paclitaxel and recommended this regimen as a first-line treatment [21, 22]. A Japanese phase II trial [23] with 51 patients with UCS showed a better overall survival with the combination of paclitaxel and carboplatin as an adjuvant therapy (four-year overall survival: 76.0%, 95% CI, 60.5%-86.1%). Additionally, the GOG is performing a randomized phase III trial to compare carboplatin-paclitaxel and paclitaxel-ifosfamide in chemotherapy-naïve patients with UCS and OCS. The present authors believe that paclitaxel with carboplatin could be an effective and feasible adjuvant chemotherapeutic regimen for carcinosarcoma patients.

The present authors found that adjuvant radiotherapy with chemotherapy was predictive of better survival in UCS patients compared with those receiving CT or RT alone. Gungorduk *et al.* [24] performed a retrospective review of three cancer centers involving 66 UCS patients and also noted that adjuvant chemotherapy with radiotherapy was associated with improved overall survival, compared with chemotherapy or radiotherapy alone (HR, 3.3; 95%CI,

0.7 to 15.0; $p = 0.01$), which was consistent with the present results. Makker *et al.* [25] compared chemotherapy with or without radiation to radiation alone in UCS and reported the improved progression free survival (35% *vs*. 9%) and overall survival (66% *vs*. 34%) for chemotherapy combined with radiotherapy. We await larger number of cases and prospective trials warranting the evaluation of the effectiveness of multimodal therapy in UCS patients.

In conclusion, the present study reports on the largest number of OCS and UCS patients in China to date and ensured the validity of results due to the similarity in the demographic information and quality assurance concerning surgery and follow-up data. The present authors recommend optimal debulking surgery to R_0 in combination with adjuvant chemotherapy (e.g., paclitaxel and carboplatin) for gynecologic carcinosarcoma, and radiotherapy combined with chemotherapy can be used as an additional adjuvant therapy for UCS. Although no significant benefit of molecular-targeted agents has been reported, we can still see the clinical potential in the management of carcinosarcoma patients. In the future, large and multi-centered studies should be performed to gather more data and gain a better understanding of the treatment of UCS and OCS.

Acknowledgements

This work was supported by the Science and Technology Commission of Shanghai Municipality (Grant No. 12411950300).

References

[1] Kernochan L.E., Garcia R.L.: "Carcinosarcomas (malignant mixed Mul-lerian tumor) of the uterus: advances in elucidation of biologic andclinical characteristics". *J. Natl. Compr. Canc. Netw.*, 2009, *7*, 550.

[2] Cimbaluk D., Rotmensch J., Scudiere J., Gown A., Bitterman P.: "Uterine carcinosarcoma: immunohistochemical studies on tissue microarrays with focus on potential therapeutic targets". *Gynecol. Oncol.*, 2007, *105*, 138.

[3] Siegel R., Ward E., Brawley O., Jemal A.: "Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths". *CA Cancer J. Clin.*, 2011, *61*, 212.

[4] Gadducci A., Sartori E., Landoni F., Zola P., Maggino T.,Cosio S., *et al.*: "The prognostic relevance of histological type in uterine sarcomas: a Cooperation Task Force (CTF) multivariate analysis of 249 cases". *Eur. J. Gynaecol. Oncol.*, 2002, *23*, 295.

[5] Barnholtz-Sloan J.S., Morris R., Malone J.M. Jr., Munkarah A.R.: "Survival of women diagnosed with malignant, mixed müllerian tumors of the ovary (OMMMT)". *Gynecol. Oncol.*, 2004, *93*, 506.

[6] Mano M.S., Rosa D.D., Azambuja E., Ismael G., Braga S., D'Hondt V., *et al.*: "Current management of ovarian carcinosarcoma". *Int. J. Gynecol. Cancer*, 2007, *17*, 316.

[7] Arend R., Doneza J.A., Wright J.D.: "Uterine carcinosarcoma". *Curr. Opin. Oncol.*, 2011, *23*, 531.

[8] Mano M.S., Rosa D.D., Azambuja E., Ismael G., Braga S., D'Hondt V., *et al.*: "Current management of ovarian carcinosarcoma". *Int. J. Gynecol. Cancer*, 2007, *17*, 316.

[9] Rauh-Hain J.A., Diver E.J., Clemmer J.T., Bradford L.S., Clark R.M., Growdon W.B., *et al.*: "Carcinosarcoma of the ovary compared to papillary serous ovarian carcinoma: a SEER analysis". *Gynecol. Oncol.*, 2013, *131*, 46.

[10] National Cancer Institute: Chapter 16 ovarian cancer" 2012. Available at: http://seer.cancer.gov/publications/survival/surv_ovary.pdf

[11] George E.M., Herzog T.J., Neugut A.I., Lu Y.S., Burke W.M., Lewin S.N., *et al.*: "Carcinosarcoma of the ovary: natural history, patterns of treatment, and outcome". *Gynecol. Oncol.*, 2013, *131*, 42.

[12] Garg G., Shah J.P., Kumar S., Bryant C.S., Munkarah A., Morris RT..: "Ovarian and uterine carcinosarcomas: a comparative analysis of prognostic variables and survival outcomes". *Int. J. Gynecol. Cancer*, 2010, *20*, 888.

[13] Hellström A.C., Tegerstedt G., Silfverswärd C., Pettersson F.: "Malignant mixed müllerian tumors of the ovary: histopathologic and clinical review of 36 cases". *Int. J. Gynecol. Cancer*, 1999, *9*, 312.

[14] Ferguson S.E., Tornos C., Hummer A., Barakat R.R., Soslow R.A.: "Prognostic features of surgical stage I uterine carcinosarcoma". *Am. J. Surg. Pathol.*, 2007, *31*, 1653.

[15] Harris M.A., Delap L.M., Sengupta P.S., Wilkinson P.M., Welch R.S., Swindell R., *et al.*: "Carcinosarcoma of the ovary". *Br. J. Cancer*, 2003, *88*, 654.

[16] Pacaut C., Bourmaud A., Rivoirard R., Moriceau G., Guy J.B., Collard O., et al.: "Uterine and ovary carcinosarcomas: outcome, prognosis factors, and adjuvant therapy". *Am. J. Clin. Oncol.*, 2015, *38*, 272.

[17] Tanner E.J., Leitao M.M. Jr., Garg K., Chi D.S., Sonoda Y., Gardner G.J., et al.: "The role of cytoreductive surgery for newly diagnosed advanced-stage uterine carcinosarcoma". *Gynecol. Oncol.*, 2011, 123, 548.

[18] Doo D.W., Erickson B.K., Arend R.C., Conner M.G., Huh W.K., Leath C.A.: "Radical surgical cytoreduction in the treatment of ovarian carcinosarcoma". *Gynecol. Oncol.*, 2014, *133*, 234.

[19] Wolfson A.H., Brady M.F., Rocereto T., Mannel R.S., Lee Y.C., Futoran R.J., *et al.*: "A gynecologic oncology group randomized phase III trial of whole abdominal irradiation (WAI) versus cisplatin-ifosfamide and mesna (CIM) as post-surgical therapy in stage I-IV carcinosarcoma (CS) of the uterus". *Gynecol. Oncol.*, 2007, *107*, 177.

[20] Manolitsas T.P., Wain G.V., Williams K.E., Freidlander M., Hacker N.F.: "Multimodality therapy for patients with clinical stage I and II malignant mixed Müllerian tumors of the uterus". *Cancer*, 2001, *91*, 1437.

[21] Toyoshima M., Akahira J., Matsunaga G., Niikura H., Ito K., Yaegashi N., Tase T.: "Clinical experience with combination paclitaxel and carboplatin therapy for advanced or recurrent carcinosarcoma of the uterus". *Gynecol. Oncol.*, 2004, *94*, 774.

[22] Leiser A.L., Chi D.S., Ishill N.M., New W.P.: "Carcinosarcoma of the ovary treated with platinum and taxane: the memorial Sloan-Kettering Cancer Center experience". *Gynecol. Oncol.*, 2007, *105*, 657.

[23] Otsuki A., Watanabe Y., Nomura H., Futagami M., Yokoyama Y., Shibata K., et al.: "Paclitaxel and carboplatin in patients with completely or optimally resected carcinosarcoma of the uterus: a phase II trial by the Japanese Uterine Sarcoma Group and the Tohoku Gynecologic Cancer Unit". *Int. J. Gynecol. Cancer*, 2015, *25*, 92.

[24] Gungorduk K., Ozdemir A., Ertas I.E., Gokcu M., Telli E., Oge T., *et al.*: "Adjuvant treatment modalities, prognostic predictors and outcomes of uterine carcinosarcomas". *Cancer Res. Treat.*, 2015, *47*, 282.

[25] Makker V., Abu-Rustum N.R., Alektiar K.M., Aghajanian C.A., Zhou Q., Iasonos A., *et al.*: "A retrospective assessment of outcomes of chemotherapy-based versus radiation-only adjuvant treatment for completely resected stage I-IV uterine carcinosarcoma". *Gynecol. Oncol.*, 2008, *111*, 249.

Corresponding Author:
XIAOHUA WU, M.D.
Department of Gynecologic Oncology
Fudan University Shanghai Cancer Center
270 Dong-An Road
Shanghai, 200032 (China)
e-mail address: docwuxh@163.com