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LONG-TERM OUTCOME AND PROGNOSTIC FACTORS FOR YOLK SAC TUMOR OF THE OVARY

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ABSTRACT

Yolk sac tumors of the ovary (YST) are rare and highly malignant tumors occurring in children and young adults. Because of its rarity, YST prognostic factors remain unclear. Our purpose was to evaluate the prognostic factors in YST. We performed a retrospective review of 36 patients with pure YST from 1986 to 2006. The 5-year overall survival and progression-free survival were 66.6% and 68.8%, respectively. Patients with stage I–II disease had a more favorable prognosis than those with stage III–IV ($p < 0.05$). Those with an ascites volume of less than 100 ml or a residual tumor measuring less than 1 cm had improved to a relatively good prognosis. Neither serum AFP level nor age had any significant correlation with the prognosis in this study.

In conclusion, the FIGO (International Federation of Gynecology and Obstetrics) stage, ascites volume and residual tumor size tended to affect the prognosis of YST.

Key Words**:** Yolk sac tumor, Survival, Prognostic factor

INTRODUCTION

Malignant ovarian germ cell tumors (MOGCTs) are rare but aggressive, accounting for approximately 1% to 2% of all ovarian malignancies.[1)] The peak incidence is found in young women or adolescent girls. Yolk sac tumor (YST) is the second most common tumor in ovarian tumors of this group.[2)] YST is a highly malignant tumor that metastasizes early and invades all intraabdominal structures. Before the advent of combination chemotherapy, YST was almost universally fatal. At the end of the 1970s, the prognosis of YST dramatically improved with the introduction of novel chemotherapeutic regimens.[3)] Especially following the addition of cisplatin to combination regimens, survival rates reached excellent values, even for patients with advanced stage tumors. However, the prognosis for some patients still remains unsatisfactory. Although recent reports showed that the FIGO stage and tumor-reductive surgery strongly affected the prognosis of this disease.[4)] Other factors in the YST prognosis remain unclear. Therefore, this study evaluated the long-term outcome of pure YST in a larger series of patients and developed new prognostic parameters to predict relapse and survival.

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MATERIALS AND METHODS

Patients and management

Between January 1986 and December 2006, 36 patients with pure YST were registered and treated by the Tokai Ovarian Tumor Study Group consisting of Nagoya University Hospital and its affiliated hospitals. Clinical staging was performed according to the FIGO classification system. Histologic diagnosis was established after surgical resection or biopsy. Histologic classification of all tumors was performed by one of the authors in accordance with the system approved by the World Health Organization. Thirty-three patients were treated with primary surgery; unilateral salpingo-oophorectomy in 21 cases, bilateral salpingo-oophorectomy in 1 case, total abdominal hysterectomy with bilateral salpingo-oophorectomy in 10 cases, lymphadenectomy in 1 case, and 3 patients underwent probe laparotomy. All patients were treated with the following regimens of combination chemotherapy after primary surgery: 10 with a regimen of vincristine, actinomycin, and cyclophosphamide (VAC); 15 with vinblastine, bleomycin and cisplatin (PVB); 10 with etoposide, bleomycin and cisplatin (BEP); and one with etoposide, bleomycin and carboplatin. As a prognostic variable, age at the time of diagnosis, stage, residual tumor size, serum tumor markers AFP, and ascites volume were evaluated for significance.

Statistical analysis

Survival estimates were obtained via the Kaplan-Meier method. Progression-free survival (PFS) was calculated from the date of diagnosis to the date of recurrence or most recent follow-up. Overall survival (OS) was calculated from the date of diagnosis to the date of death from disease or most recent follow-up. Significance of differences was determined by Log-rank test and $\chi 2$ analysis. The results were considered significant at $p < 0.05$.

RESULTS

Thirty-six patients were enrolled and analyzed in this study. Characteristics of the patient population and parameters for prognosis are shown in Table 1. The 5-year overall survival and progression-free survival were 66.6% and 68.8%, respectively (Fig. 1A, B). Twenty-six patients were disease free, 9 died from the disease, and one from other causes. Of these patients, 21 were initially diagnosed as having the disease at stage I, 4 at stage II, 7 at stage III, and 4 at stage IV. There was a significant difference in the survival rate between stages I-II and III-IV ($p < 0.05$) (Fig. 1C). The 19 patients with an ascites volume of < 100 mL had a 5-year survival rate of 82.4%, while the 17 with an ascites volume of ≥ 100 mL had a rate of 63.2% (Fig. 1D). Although the ascites volume before initial surgery was not a significant prognostic factor, patients with an ascites volume of < 100 ml tended to have a better prognosis than those with a volume of ≥ 100 ml ($p = 0.12$). The 27 patients with a residual tumor measuring < 1 cm had a rate of 81.5%, while the 9 with a tumor measuring ≥ 1 cm had rate of 44.4% (Fig. 1D). Although a statistical analysis did not demonstrate a significant difference, patients with residual tumors measuring < 1 cm had a relatively good prognosis ($p = 0.07$). The serum AFP range level before initial surgery was 0–718740 U/ml (median, 24600 U/ml). We classified the patients into a < 25000 U/ml group and a ≥ 25000 U/ml group. The 5-year survival rate in these two groups was not significantly different. Thus, the serum AFP levels did not quality as prognostic factors in YST (Table 2). Patient ages ranged from 10 to 47 years (median, 20 years) and were classified into two groups (20 >, 20 ≤). There was no significant difference in the 5-year survival rate between the two groups. Similarly, patient age was not a prognostic factor (Table 2). In

this study, the difference in overall survival rates with and without a cisplatin-based regimen was not significant (data not shown).

Table 1 Clinical characteristics of 36 patients with yolk sac tumor

Characteristic	Number of patients
Age	
20 >	18 (50.0%)
20 ≤	18 (50.0%)
FIGO stage	
I	21 (58.3%)
II	4 (11.1%)
III	7 (19.4%)
IV	4 (11.1%)
AFP (U/ml)	
25000 >	18 (50.0%)
25000 ≤	18 (50.0%)
Ascitic fluid volume	
100 ml >	19 (52.8%)
100 ml ≤	17 (47.2%)
Residual tumor size	
1 cm >	27 (75.0%)
1 cm ≤	9 (25.0%)

Table 2 Univariate analysis for several clinical parameters in relation to survival

Variable	Number	5-year survival rate	*p* value
Age			
20 >	18	70.6%	0.681
20 ≤	18	77.8%	
AFP (U/ml)			
25000 >	18	77.8%	0.291
25000 ≤	18	66.7%	
FIGO stage			
I–II	25	80.0%	< 0.05
III–IV	11	54.5%	
Ascitic fluid volume			
100 ml >	17	82.4%	0.12
100 ml ≤	19	63.2%	
Residual tumor size			
1 cm >	27	81.5%	0.07
1 cm ≤	9	44.4%	

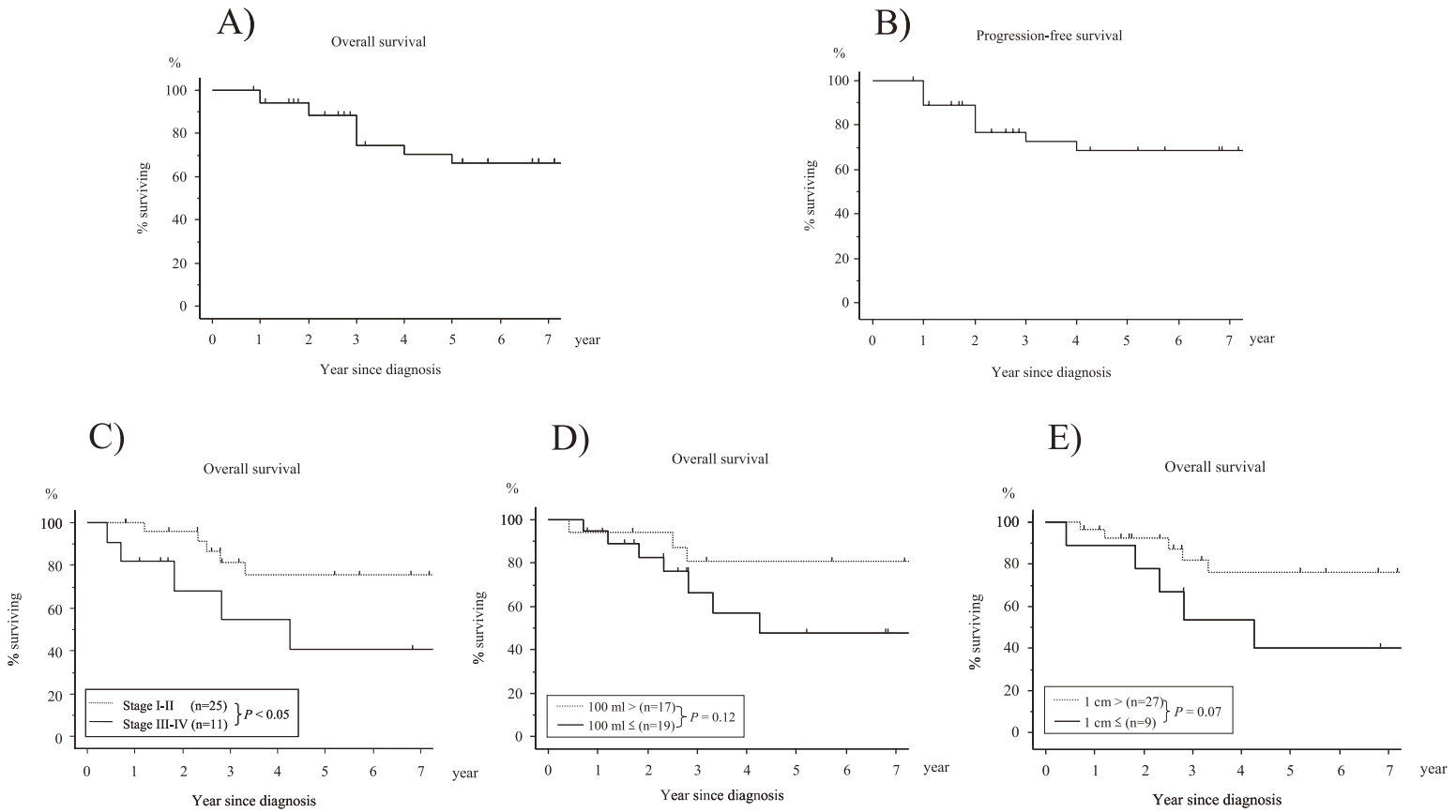

Fig. 1

A) Kaplan-Meier estimate of overall survival curve for YST.

B) Kaplan-Meier estimate of progression-free survival curve for YST.

C) Kaplan-Meier estimate of overall survival curve by initial stage of disease. Discontinuous line represents stage I-II (n=25). Continuous line represents stage III-IV (n=11). Stage III-IV patients had a significantly poor prognosis ($p < 0.05$).

D) Kaplan-Meier estimate of overall survival curve by volume of ascites. Discontinuous line represents 100 ml > (n=17). Continuous line represents 100 ml ≤ (n=19). Patients with ascites volume less than 100 ml tended to have a better prognosis (p = 0.12).

E) Kaplan-Meier estimate of overall survival curve by residual tumor. Discontinuous line represents 1 cm > (n=27). Continuous line represents 1 cm ≤ (n=9). Patients with residual tumor less than 1 cm tended to have a better prognosis (p = 0.07).

DISCUSSION

YST belongs to a group of MOGCTs. Several reports have suggested that the long-term outcomes of MOGCTs patients are excellent, with a 5-year survival rate of 87-97%.[5-8] However, our report demonstrated that the long-term outcome of YST is relatively poor, with a 5-year survival rate of 66.6%. This is probably due to the fact that most MOGCTs are diagnosed at an early stage. Stage I patients with MOGCTs accounted for up to 71%.[5-8] Stage I patients with YST comprised 58.3% in our report. Before the introduction of combination chemotherapy, the outcome of advanced YST was disastrous. Kurman and Norris reported that only nine of their 65 patients were long-term survivors, with a 3-year actuarial survival rate of 13%.[9] However, the majority of patients can now be cured with multimodality therapy including platinum-based chemotherapy. For instance, while the overall YST 5-year survival rate is 66.6%, that of epithelial ovarian cancer is 38.3%–59.6%.[10-12] Furthermore, the 10-year survival was also 66.6% in our study, suggesting that the likelihood of relapse after 5 years was extremely rare. In our study, tumor stage significantly affected survival. Additionally, the presence and quantity of ascites before initial surgery and the residual tumor size after surgery constitute prognostic factors. Previous reports showed that younger women with epithelial ovarian cancer have a survival advantage compared to older patients.[13,14] However in YST, age was not a significant prognostic factor. A recent study reported that an elevation of the serum markers β-human chorionic gonadotropin and AFP are independent poor prognostic factors in malignant ovarian germ cell tumors.[15] However, the serum AFP level was not a significant prognostic factor in YST. Our group previously reported several prognostic factors for YST of the ovary.[4] That previous study included patients with mixed types of YST, and the only cisplatin-based chemotherapy was “PVB.” In this study, we concentrated only on patients with pure type YST in order to assess originally prognostic factors of YST, and since 1999, our group has adopted the new “BEP” regimen. Thus, we evaluated the association of prognosis with chemotherapy-regimen. As a result, although prognostic factors with pure type of YST were almost the same as those in our previous report, the patients receiving “BEP” had a somewhat better but still insignificant prognosis compared to those receiving other regimens (data not shown). However, to better determine the efficiency of “BEP,” we would like to analyze a greater numbers of YST patients.

In conclusion, this study demonstrated that tumor stage, ascites volume before initial surgery, and residual tumor size were prognostic factors in YST. This is relevant for the management of YST since it facilitates the identification of patients who may require more intensive therapeutic strategies.

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