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Survival benefit for patients with advanced-stage transitional cell carcinomas vs. other subtypes of ovarian carcinoma after chemotherapy with platinum and paclitaxel

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Abstract

Objective. Transitional cell carcinoma (TCC) of the ovary is a less well recognized histological type of ovarian carcinoma resembling TCC of the urinary bladder. A better prognosis due to a better chemosensitivity of ovarian TCC has been suggested. It was the aim of the present retrospective study to compare incidence and outcome of patients with TCCs and other subtypes of ovarian carcinoma from a large homogeneous collective of patients with primary advanced-stage ovarian carcinoma.

Methods. H&E-stained sections from a total of 302 cases from a prospective randomized, multi-center, phase III study of patients with ovarian cancer, FIGO-stages IIB–IV, comparing cisplatin plus paclitaxel (PT) with paclitaxel plus carboplatin (TC) were available for histological retyping of ovarian carcinomas applying current WHO criteria. Kaplan–Meier survival analysis was performed.

Results. 16 of 302 tumors (5.3%) were diagnosed as TCC. Only 1 of the 16 TCCs had been previously diagnosed as such by referring pathologists. TCCs were associated with smaller preoperative extraovarian tumor and with smaller postoperative residual tumor. 5-year survival of patients with TCC was 57% as compared to 31% for patients with ovarian carcinomas of other types ($P = 0.03$).

Conclusion. TCC of the ovary seems to be a less well recognized entity. In the current series, TCCs had a significantly better prognosis as compared to all other types of ovarian carcinomas after standardized chemotherapy. A propensity for micronodular rather than macronodular extraovarian spread and better surgical resectability of TCC might contribute to the survival benefit.

Keywords: Ovarian carcinoma; Histological type; Transitional cell carcinoma; Chemotherapy; Prognosis

Introduction

Transitional cell carcinoma (TCC) of the ovary is a less well recognized histological type of ovarian carcinoma resembling TCC of the urinary bladder. It was added to the World Health Organization (WHO) histological classification of ovarian tumors, where it is placed among other transitional cell tumors including Brenner tumors [1,2]. Recent interest has focused on whether the transitional type of ovarian carcinoma has independent prognostic significance. It was suggested that TCC of the ovary may have a better prognosis as compared to other types of

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ovarian carcinomas, possibly due to a better response to chemotherapy [3–7]. It was the aim of the present retrospective study to compare incidence and outcome of patients with TCCs and other subtypes of ovarian carcinoma from a large homogeneous collective of patients with primary advanced-stage ovarian carcinoma treated with platinum and paclitaxel-containing standardized chemotherapy [8].

Materials and methods

Study material

This study was planned as a subprotocol of the prospective randomized, multi-center, phase III study AGO-OVAR-3 which enrolled a total of 798 patients with ovarian cancer, FIGO-stages IIB-IV, comparing cisplatin 75 mg/m^2 plus paclitaxel 185 mg/m^2 (PT) with paclitaxel 185 mg/m^2 plus carboplatin (TC) [8]. After completion of recruitment and treatment, tissue blocks were requested from participating centers for scientific analysis. Between 1 and 53 paraffin blocks per case were received from a total of 334 study cases. Selection of these patients did obviously not follow any rule but was mainly based on both availability of material and willingness to cooperate. An explorative comparison of patient characteristics between patients with or without available paraffin blocks was performed. Paraffin sections were cut from all blocks and stained with Hematoxylin and Eosin. After review of all slides and exclusion of material which contained no tumor tissues or was insufficient for adequate histopathological analysis (32 cases), between 1 and 9 stained sections each from a total of 302 cases of primary invasive epithelial ovarian carcinomas were available for further study. All slides were reviewed by two gynecopathologists (FK, DS) who were blinded for the outside diagnoses. All ovarian carcinomas were typed according to the current WHO criteria and classified as either serous, mucinous, endometrioid, clear cell, transitional cell, or undifferentiated carcinoma [1,2]. A diagnostic consensus was reached in each case.

Histological criteria of TCC

TCC of the ovary was diagnosed if one or more of the typical transitional cell patterns (excluding malignant Brenner tumor) were present exclusively or in at least 90% of the tumor tissue present on the available slides. As was recently described in detail by Eichhorn and Young [9], TCCs typically showed undulating, diffuse, insular, and trabecular growth patterns. Cystic spaces of varying size and blunt papillae were present in most cases (Fig. 1). Minor foci (<10%) of serous or endometrioid carcinoma were consistent with a diagnosis of TCC. The tumor cell nuclei were oblong or round, often exhibiting nucleoli or longitudinal grooves (Fig. 2). The cytoplasm was often pale and granular, rarely clear, or eosinophilic.

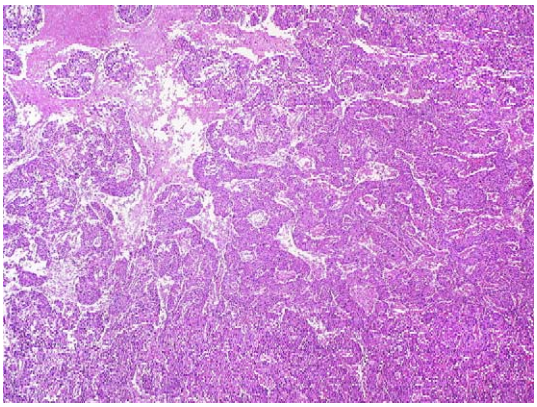

Fig. 1. Transitional cell carcinoma of the ovary, low-power magnification. Blunt papillae are lined by a multilayered epithelium with eosinophilic cytoplasm. Cystic spaces are also present (Hematoxylin and Eosin).

Statistical analysis

The exploratory analysis of possible selection bias of the study population was performed by the Chi-square test. Survival analysis was performed according to the method of Kaplan and Meier [10], survival times were compared using the log rank test [11] applying SSPS12 software.

Results

No significant selection bias was found after explorative analysis of patient characteristics (patient age, ECOG clinical performance, FIGO stage, preoperative extraovarian tumor, and postoperative residual tumor) comparing patients with and without available paraffin blocks by Chi-square analysis (data not shown). There was a similar distribution of patient characteristics age, ECOG performance status, and FIGO stage among TCCs and non-TCCs. However, in patients with TCC, preoperative extraovarian tumor size <1 cm and postoperative residual tumor <1 cm were represented significantly more often (Table 1). Only 1 out of 16 TCCs had been previously diagnosed as such by outside pathologists. A comparison between outside and central review histopathological diagnoses is given in Table 2.

The distribution of histological types of 302 ovarian carcinomas according to current WHO criteria after central review of H&E stained recuts from all available paraffin blocks is shown in Table 3. Overall, 16 patients with TCC were diagnosed representing 5.3% of the study population. The 5-year survival and median survival rates of all types of ovarian carcinoma are also given in Table 3. Five-year survival of patients with TCC was 57.14% as compared to 30.68% for patients with non-TCCs of the ovary. Kaplan–Meier analysis showed a better survival of patients with TCCs as compared to each individual non-TCC subtype