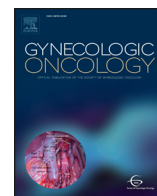




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Surgical management of cardiophrenic lymph nodes in patients with advanced ovarian cancer

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HIGHLIGHTS

- Importance of complete resection in primary ovarian cancer
- Excision of suspicious cardiophrenic lymph nodes via a transdiaphragmatic approach
- Feasibility, management and complications of resection

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ABSTRACT

Objective. Debulking surgery for advanced ovarian cancer does not routinely include opening of the thorax. Even systematic lymphadenectomy does not commonly extend to lymph nodes above the diaphragm. We evaluated the outcome of systematic resection of suspicious cardiophrenic lymph nodes detected on preoperative CT-scan in patients with advanced epithelial ovarian cancer (EOC).

Methods. Single-center, prospective series of 196 consecutive patients with EOC undergoing primary debulking surgery between June 2013 and June 2015. Suspicious cardiophrenic lymph nodes were defined as ≥ 10 mm on the short axis diagnosed in pre-operative CT-scan and were removed if intra-abdominal debulking resulted in complete resection or residual tumor < 10 mm and the patients' performance status allowed this additional procedure. Removal of suspicious cardiophrenic lymph nodes was performed via a trans-diaphragmatic approach.

Results. Thirty (15%) out of 196 EOC patients had radiologically suspicious cardiophrenic lymph nodes ≥ 10 mm and complete resection or residual tumor < 10 mm. Twenty-seven out of the thirty patients had at least one confirmed metastatic cardiophrenic lymph node. Metastatic cardiophrenic lymph nodes were associated with extensive intra-abdominal tumor spread in the upper abdomen.

Conclusions. Patients with suspicious cardiophrenic lymph nodes detected by preoperative CT-scan had histologically confirmed metastasis in 90% of cases. The surgical procedure is feasible without major complications if performed by experienced gynecologic oncologists. The prognostic value of this procedure should be evaluated in larger controlled studies.

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1. Introduction

Epithelial ovarian, fallopian and peritoneal cancer (EOC) is the second most common gynecologic malignancy in the Western World and

the most common cause of death due to gynecologic malignancies [1]. Approximately 75% of patients with ovarian cancer are diagnosed with advanced stage (FIGO III–IV) (Fédération Internationale de Gynécologie et d'Obstétrique, [2]) disease. The most important prognostic factor next to FIGO stage is debulking surgery leaving no macroscopic residual disease [3]. The latter often requires extensive surgical procedures such as diaphragmatic stripping, splenectomy, atypical

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liver resection, excision of bulky lymph nodes and bowel resection. These procedures improve complete resection rate and subsequent survival of patients with advanced EOC [4]. The prognostic impact of systematic paraaortic and pelvic lymphadenectomy in optimally debulked patients with radiologically and clinically negative lymph nodes is unclear at the moment. In contrast, removal of bulky lymph nodes is indicated if complete resection can be achieved elsewhere in the abdomen [3].

Terminology for lymph nodes at the low anterior mediastinum is not yet uniform, as they are frequently described as precordial, paracardial, mediastinal, retrosternal, epiphrenic, supradiaphragmatic, or cardiophrenic-angle lymph nodes. In the present study these lymph nodes are referred to as *cardiophrenic lymph nodes*. Cardiophrenic lymph nodes have been described in patients with lung, esophageal and colorectal cancer and in patients with lymphoma [5]. In patients with EOC, enlarged cardiophrenic lymph nodes have been described as a possible predictive parameter for the failure of optimal debulking surgery [6] and are associated with impaired overall survival [7].

We report on our experiences with surgical evaluation of cardiophrenic lymph nodes in patients undergoing upfront debulking surgery for advanced EOC.

2. Patients and methods

A consecutive series of 196 patients with advanced EOC treated between 6/2013 and 6/2015 at the Department of Gynecology and Gynecologic Oncology, Kliniken Essen-Mitte, Germany was investigated. Data were retrieved from the prospectively maintained clinical tumor database. Patients with non-invasive, non-epithelial ovarian cancer or borderline tumors, as well as patients who had undergone surgery other than upfront debulking and/or received pre-operative chemotherapy and patients with parenchymal metastases, were excluded. All patients had a routinely performed preoperative CT-scan, in which the cardiophrenic region was evaluated and described. CT-scans were performed with oral and intravenous contrast and a slice thickness of 5 mm. All CT-scans were discussed in the multidisciplinary preoperative tumor conference including gynecologic oncologists as well as radiologists. According to RECIST (Response Evaluation Criteria in Solid Tumors) criteria 1.1 [8] cardiophrenic lymph nodes ≥ 10 mm on short axis are defined as suspicious (Fig. 1). All patients had given written informed consent for all surgical procedures necessary to achieve complete resection (= no macroscopic residuals) and for documentation and scientific analysis of their data entered in our clinical tumor database [5].

Cardiophrenic lymph nodes were resected in patients in whom complete intra-abdominal resection was achieved and in patients with macroscopic residuals having a maximum diameter not exceeding 10 mm and suspicious bulky cardiophrenic lymph nodes ≥ 10 mm in smallest diameter. Resection of cardiophrenic lymph nodes usually followed diaphragmatic stripping \pm full thickness resection as described elsewhere [9]. Normally, cardiophrenic lymph nodes were in the anterior cardiophrenic region and if not already performed as part of the diaphragmatic procedure, the ventral diaphragm was incised with bipolar

scissors from the abdominal cavity starting at the anterior mediolateral margin of the centrum tendineum approximately 1–2 cm laterally to the midline to avoid damaging the hepatic vein and diaphragmatic vessels and nerve, following the direction of the muscle fibers to the ventral abdominal wall along a length of approximately 5 cm, pushing the mobilized liver caudally and posteriorly. The anesthesiologist was informed about open pleural cavity. Afterwards, the parietal and visceral pleura, including the interlobular space and the mediastinum, were inspected and palpated. If necessary, additional thoracoscopy was performed. If the supradiaphragmatic tumor was limited to enlarge cardiophrenic lymph nodes, suspicious nodules were resected by Ligasure® (Picture 1:1, 2), avoiding any damage to the pericardium. No lymphadenectomy was performed if pre- or intraoperative evaluation had revealed diffuse carcinomatosis or multiple enlarged additional bulky lymph nodes in the mid- or upper mediastinum not accessible by a transdiaphragmatic approach. The diaphragmatic defect was closed via continuous polydioxanone (PDS 2.0) sutures (Picture 1:3). Intraoperative placement of a thoracic chest tube was not performed routinely. A risk-adapted strategy was followed. In thirteen (43%) out of 30 patients with additional risk factors such as relevant preoperative pleural effusion or extensive pre- and intraoperative ascites ≥ 500 ml a thoracic chest tube was placed intraoperatively for drainage after removal of cardiophrenic lymph nodes. The thoracic chest tube was removed when daily effusion volume was <100 ml. Complications were documented according to the Clavien-Dindo classification [10].

Owing to the lack of a control arm in this exploratory series, only descriptive analyses without any comparisons were performed.

3. Results

During the two-year observation period, 196 patients with advanced EOC stage (FIGO IIIC/IV) who were fit for multivisceral surgery underwent upfront debulking. In 30 (15.3%) patients cardiophrenic lymph nodes were resected and histologically evaluated (Table 1). The median patient age was 59 years and all but one patient had an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0. Median operating time was 465 (240–660) minutes. Complete macroscopic tumor resection was achieved in 25 (83%) out of 30 patients. Five (16%) patients had macroscopic tumor residuals between 1 and 10 mm. All 30 patients underwent subtotal deperitonealization of all four quadrants of the abdomen including complete deperitonealization of the right diaphragm, and 28 (93%) underwent bowel resection (large and/or small bowel resection). Splenectomy was performed in 16 (53%) patients. Thirteen (43%) patients had more than 500 ml of ascites and 8 (26%) had preoperative pleural effusion (Table 2).

The median number of resected cardiophrenic lymph nodes was two (1–12), with a median number of one (0–5) positive cardiophrenic lymph node. Histological examination of the resected cardiophrenic lymph nodes revealed that 27 (90%) out of 30 patients with preoperatively diagnosed suspicious bulky cardiophrenic lymph nodes had histologically proven macroscopic metastatic disease, in 3 cases even with extracapsular involvement. The median histologic diameter of the

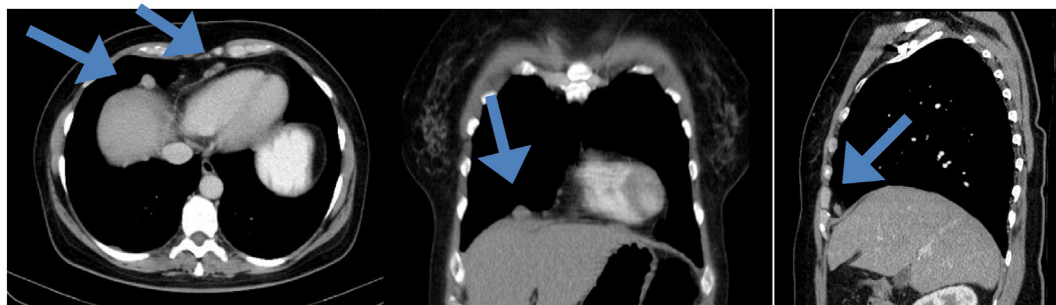


Fig. 1. CT-scan with cardiophrenic lymph node.

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