



Original Article

Cytoreductive surgery including distal pancreatectomy with splenectomy in advanced stage ovarian cancer: Two centers analysis



Anil Erturk ^{a,*}, Oguzhan Kuru ^b, Utku Akgor ^b, Gokhan Boyraz ^b, Caner Cakir ^c,
Taner Turan ^c, Nejat Ozgul ^b, Coskun Salman ^b, Kunter Yuce ^b

^a Hacettepe University, Department of Gynecology and Obstetrics, Ankara, Turkey

^b Hacettepe University, Department of Gynecology and Obstetrics, Division of Gynecologic Oncology, Ankara, Turkey

^c Etlik Training and Research Hospital, Department of Gynecology and Obstetrics, Division of Gynecologic Oncology, Ankara, Turkey

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ABSTRACT

Objective: Complex procedures such as distal pancreatectomy and splenectomy (DPS) may be required for R0 resection in patients with ovarian cancer (OC). These procedures can increase survival and cause serious morbidity. We aimed to present our experience in this field.

Materials and methods: Thirteen patients who underwent DPS for OC between January 2004 and July 2018 in two centers (Hacettepe University Hospital, Etlik Hospital) were evaluated. Statistical analysis was performed using SPSS.

Results: The mean operative time was 310 min (220–570 min). None of the patients required transfusion. No perioperative mortality was observed. The mean postoperative hospital stay was 12 days (ranging from 8 to 33 days). The number of patients with early postoperative complications was four (30.7%). One of these patients was complicated by intestinal perforation, one with pancreatic fistula, one with pneumonia and the other with atelectasis. Other complications were observed conservatively. Ten patients underwent 6 cycles of platinum-based chemotherapy postoperatively. The median value of the postoperative chemotherapy period was 20 days (range 11–47 days). The median follow-up period was 46 months (2–144 months). Ten patients had recurrence. Eleven patients died of disease. Two patients are still alive. Disease-free (DFS) and overall (OS) survival were 16 and 63 months, respectively.

Conclusion: DPS for cytoreductive surgery is a procedure that increases morbidity, but most of the complications can be treated conservatively. Considering the increase in survival, it is considered to be a valuable procedure in upper abdominal disease.

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Introduction

Ovarian cancer (OC) is responsible for many of the deaths due to gynecological malignancies [1]. Most patients present with advanced disease. The most important factor that increases survival in advanced stage disease has been shown to be aggressive and optimal cytoreduction [2–4]. Many of the factors affecting overall survival are mentioned in this study.

In patients with limited tumor spread, optimal cytoreduction can easily be performed with a residual disease of less than 1 cm. However, the perspective of optimal surgical cytoreduction changed with no residual disease with maximum surgical effort. Aggressive surgical procedures have been shown to be appropriate for achieving maximum cytoreduction for OC treatment [5]. In

patients with diffuse upper abdominal disease, complex procedures such as distal pancreatectomy and splenectomy (DPS) may be required for zero residual disease (R0) defined as complete surgical cytoreduction in OC [6]. These procedures may be thought to increase survival, but it can be assumed that they cause serious morbidity in patients. In addition, there are publications that strongly support upper abdominal surgical procedures resulting in optimal cytoreduction for primary OC surgery [7,8].

This study presents the experience of two gynecological oncology centers with patients undergoing distal pancreatectomy and splenectomy due to diffuse upper abdominal disease in OC.

Materials and methods

After obtaining the local ethics committee approval, data from Hacettepe University Department of Gynecologic Oncology and Ankara Etlik Hospital Gynecologic Oncology Center were

* Corresponding author.

E-mail address: anilerturkmd@gmail.com (A. Erturk).

retrospectively screened between January 2004–July 2018 for patients who underwent surgery due to advanced stage and recurrent OC. Patients who underwent DPS for epithelial ovarian cancer (EOC) and who underwent R0 reduction were included in the study. Non-epithelial, mucinous, borderline tumors were excluded. Demographic characteristics and clinicopathologic features of patients, performed surgery, intraoperative findings, duration of surgery, duration of hospitalization, need for transfusion, postoperative complications and final pathology reports were recorded. The presence of tumoral invasion of the spleen and pancreas, if any, the extent of invasion were inscribed.

The disease stage was determined according to the 2014 International Federation of Gynecology and Obstetrics (FIGO) staging system. Optimal cytoreduction was defined as <1 cm residual tumor. Progression-free survival (PFS) and overall survival (OS) were analyzed using the Kaplan–Meier method. PFS was defined as the time between the cytoreductive surgery and the recurrence or progression of the disease. OS was defined as the time between surgery and death. Statistical analysis were performed with SPSS ver. 20.

Results

Median age of 13 patients was 63 years (range 53–75 years). Distal pancreatectomy and splenectomy (DPS) were performed for primary EOC in 11 patients, and for recurrent EOC in 2 patients. All of the patients had serous tumors. The clinicopathologic features of patients, CA-125 levels are shown in Table 1.

DPS was performed in each patient. Each patient underwent R0 resection. Table 2 describes the postoperative characteristics of DPS patients. The median duration of surgery was 310 min (ranges 220–570 min). There were no patients with blood loss above 1000 ml. Transfusion was not needed in any patients. Five patients underwent postoperative intensive care. There was no perioperative mortality. The median duration of hospitalization after surgery was 12 days (ranges 8–33days).

The number of patients with pancreatic parenchymal invasion according to the pathology report was three. The average tumor size in these patients was 1,3 cm. The number of patients with splenic parenchymal invasion was five. The average tumor size of these patients was 1,6 cm. The number of patients who had any early postoperative complications (within 4 weeks following surgery) was four (30.7%). One of these patients complicated with bowel perforation, one with pancreatic fistula, one with pneumonia and one with atelectasis (Table 3). Fistula and intestinal perforation were treated with re-operation and other complications were treated conservatively. Ten of the patients received postoperative 6 cycles of platinum-based chemotherapy. The median time for chemotherapy after surgery was 20 days (ranges 11 to 47).

Table 1
The clinicopathologic features of patients.

Variable	Number	%
Median age (range)	63 (53–75)	
Median BMI (kg/m ²) (range)	30 (19–42)	
Comorbidities (HT, DM, HF)	8	61.5
Preoperative median serum CA-125 (mU/l) (range)	1380 (147–4743)	
Disease status		
Primary disease	11	84.7
Recurrent disease	2	15.3
Stage of disease		
IIIC	8	61.5
IV	5	38.5
Histologic Type		
Serous	13	100

BMI: body mass index, HT: hypertension, DM: Diabetes mellitus, HF: heart failure.

Table 2
Intraoperative findings and postoperative characteristics of patients with DPS.

Variable	Value
Ascites volume (ml)	2000 (200–4600)
Duration of surgery (min)	310 (220–570)
Patients with	
Pancreatic parenchymal invasion	3 (23)
Splenic parenchymal invasion	5 (38.4)
Need for intensive care unit	5 (38.4)
Duration of hospitalization (day)	12 (8–33)
Interval from surgery to chemotherapy (day)	20 (11–47)
Postoperative complications	4 (30.7)

Values are given number (%) or median (range). Min: minutes.

The median follow-up period of the patients was 46 months (ranges 2–144 months). Ten patients experienced recurrence after DPS. Eleven patients died due to the disease. Two patients are still alive. The median of PFS and OS were 16 and 63 months, respectively.

Discussion

In advanced stage OC, surgical cytoreduction is associated with increased survival rates [3]. Optimal cytoreduction was defined by Gynecologic Oncology Group (GOG) as the maximum tumor size <1 cm residual disease [9]. Previously, it was acceptable to have the residual tumor below 1 cm optimally, while the current approach is maximal cytoreduction [5]. Therefore, maximal surgical effort should be exercised to improve survival in patients. Thus, distal pancreatectomy and splenectomy may be necessary for optimal cytoreduction in OC in the presence of upper abdominal disease. Most publications on distal pancreatectomy and splenectomy are based on general surgery literature. Gynecologic oncological studies on the subject are limited. Existing studies consist of case series and retrospective data.

In a limited number of studies, Xiang et al. retrospectively examined 18 patients who underwent distal pancreatectomy and splenectomy with splenic metastasis and found postoperative morbidity to be 44% and interpreted this rate as high. However, postoperative mortality was not observed [10]. Because of the aggressive surgery applied to the patient, the possibility of revision due to early complications may be a problem. Furthermore, Xiang et al. needed relaparotomy for a patient due to splenic venous hemorrhage [10]. In our series, relaparotomy was needed in the early postoperative period due to intestinal perforation and pancreatic fistula closure.

In addition, it can be predicted that blood loss may be higher in DPS patients. Chi et al. compared the standard primer cytoreductive surgery and the extensive upper abdominal procedure in their studies, showing that blood loss and transfusion need are greater in the extensive surgery group [1]. Conversely, there was no excessive blood loss in our patients and no transfusion was needed.

In fact, the complications of distal pancreatectomy are better evaluated in general surgery literature. It is seen that pancreatic leakage may occur in these patients [11]. Kehoe et al. reported that the rate of pancreatic leakage in patients who underwent extensive cytoreductive surgery due to OC was 24%. They stated that the mean time after surgery for pancreatic leakage diagnosis was 9

Table 3
Complications related to DPS.

Postoperative complication	Number	Treatment
Pancreatic fistula	1	Re-laparotomy
Bowel perforation	1	Re-laparotomy
Atelectasis	1	Observation
Pneumonia	1	Antibiotics

Table 4

Summary of the literature about patients underwent DPS for EOC.

Study(ref)	No. of patients	Patient's Age (range)	Complication	Mortality	Follow-up period (range)	Survival rate
Chi et al. [1]	19	60 (36–88)	N/A	N/A	N/A	N/A
Eisenhauer et al. [12]	6	N/A	N/A	N/A	N/A	N/A
Kehoe et al. [10]	17	63 (43–76)	4 patients (pancreatic leakage)	N/A	N/A	N/A
Yildirim et al. [13]	6	52 (41–68)	4 patients	0 (perioperative)	27 m (9–36)	2 years 66.7%
Bacalbasa et al. [11]	4 (secondary cytoreduction)	N/A (49–56)	2 patients	0 (for 30 days)	N/A	Median DFS: 32 m Median OS: 36.38 m
Xiang et al. [8]	18	54.5 (39–75)	8 patients	0	25 m (3–68)	2 years PFS: 40.2%/OS:84.8%
Current Study	13	63 (53–75)	4 patients	0 (perioperative)	46 m (2–144)	Median DFS: 16 m Median OS: 63 m

Ref: reference, no: number, m: months. N/A: not applicable. DFS: disease free survival, OS: overall survival, PFS: progression free survival.

days. The mean hospitalization time for patients with somatostatin analogue treatment and drainage was 32 days. None of their patients needed reoperation and this condition is thought to be associated with effective intraabdominal drainage [12]. Bacalbasa et al. reported a pancreatic fistula rate of 33.3% (2/6) in a series of 6 patients. One of the patients was reopened for fistula closure. The hospitalization period of the patient who received relaparotomy was 32 days. In patients without pancreatic fistula, chemotherapy was given within 30 days after surgery, whereas in patients with fistula, chemotherapy was postponed for 1 month [13]. Unlike the literature, the rate of pancreatic fistula in our patients was low, 7.6% (1/13). Despite effective intraabdominal drainage and somatostatin analogue therapy, this patient was reopened for fistula closure. Similar to other studies, the duration of hospital stay for this patient was 33 days.

In a retrospective study involving 262 patients, stage IIIC–4 patients were divided into three groups: extensive upper abdominal, standard and suboptimal cytoreductive surgery, and no significant differences were found between the groups in terms of major surgical complications. Nevertheless, the time to chemotherapy was found to be significantly higher in the aggressive cytoreductive group than in the other groups [8]. At that rate, despite the benefits of survival, the use of chemotherapy may be delayed in aggressive cytoreduction procedures. Our median time between surgery and chemotherapy was 20 days, less than the mentioned study. In the Eisenhauer et al. study, it was also noted that although the initial onset of chemotherapy was delayed, the response to chemotherapy in patients undergoing aggressive surgery was better [8].

Upper abdominal surgery in advanced stage OC can improve survival rates, despite complications. In a study of patients follow-up of 31 months, PFS was calculated to be 24 months in excessive surgery and was reported to be higher when compared with suboptimal cytoreduction [8]. Yildirim et al. reported a 2-year survival rate of 66.7% in six patients with DPS followed for 27 months [14]. Xiang et al. reported that PFS was 40.2% and OS was 84.2% in the study of eighteen patients who underwent DPS and the median follow-up period was 25 months [10]. In our study, the survival rate was 15%. The survival rate seems to be low, but the follow-up period of our patients (46 months) was longer than the literature and the our complication rate was lower (Table 4).

Patient number and retrospective nature of the data were limitations of our study. On the other hand, summing data from Turkey's two gynecologic oncology referral centers for advanced surgery in OC was the superiority of our study.

In summary, DPS for cytoreductive surgery is a procedure that increases morbidity. But most of the complications can be treated conservatively. Given the increased survival, it is anticipated as a viable procedure in upper abdominal disease. Prospective studies are needed.

Declaration of competing interest

Authors declare that they have no conflict of interest.

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