Palliative Cytoreductive Surgery in Advanced Ovarian Carcinoma

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ABSTRACT

Seventeen patients with advanced epithelial ovarian carcinoma underwent aggressive cytoreductive surgery ("Debulking") at King Abdulaziz University Hospital, Jeddah, Saudi Arabia. Thirteen patients (76.5%) had large bowel surgery, 5 (29.4%) had colostomy, and 2 (11.8%) had urinary tract segmental resection performed. All patients received postoperative chemotherapy in the form of cis-platinum and cyclophosphamide. The patients were divided into two groups: group 1 (N=9) consisted of those patients who died within 12 months of undergoing surgery, and group 2 (N=8) comprised of those who survived for more than 12 months following surgery. Data from these patients was analysed and eight factors including nationality, age, parity, menopausal status, ascitic fluid volume, stage and grade of the carcinoma, as well as its histological type were studied. However, except for the stage of the disease, none of these factors was found to be significant in predicting survival of more than 12 months following surgery. We conclude that cytoreductive surgery has a role in palliation, however, the variables presented cannot be utilised to predict survival in females with advanced carcinoma of the ovaries.

In the presence of advanced intra-abdominal tumours of stages III and IV, surgical procedures are often palliative and designed to relieve obstruction of the gastrointestinal and urinary tracts. These operations, such as excision of huge obstructing tumour masses which sometimes require hemicolectomy, small bowel resection, or diversionary procedures, are associated with a high degree of morbidity and mortality which commonly discourage surgeons from employing them as palliative measures for patients with advanced cancer disease.

In recent years, attempts to "debulk" large tumour masses, or more precisely, to accomplish effective surgical cytoreduction which is less involved than complete excision of the tumour has been a major goal of the gynaecological oncologist, in the hope that such procedures would help in improving the patient's response to chemotherapy due to the reduction of the tumour cell mass which might result in better palliation.

In our society, patients often present in late stages of ovarian carcinoma and are labelled as inoperable. In this paper, we review 17 patients in whom we adopted surgical "debulking" followed by chemotherapy, mainly for palliative purposes, and discuss the possible influence of various factors associated with the survival of patients.

METHODS

Seventeen patients were referred to King Abdulaziz University Hospital, Jeddah, Saudi Arabia, with the diagnosis of ovarian cancer of stages III and IV, who had either undergone previous operations or were considered to be clinically inoperable.

Complete blood count, serum creatinine and electrolytes, liver function tests, base line clotting studies and blood gases were performed for all patients. Chest X-ray, intravenous pyelogram, pelvic and upper abdominal ultrasound, CT scan and barium studies, if required, as well as cervical smear were also performed.

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Routine pre-operative management for all 17 patients included correction of acid-base imbalance and blood transfusion, if the haemoglobin was found to be less than 10 gm%, as well as mechanical and chemical bowel preparation. Prophylactic systemic antibodies were given 2 hours pre-operatively and for the first 24 hours postoperatively.

The surgical objectives were total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, appendicectomy, and removal of as much gross metastatic deposits as possible, which might include intestinal or urological surgery. It would be ideal to render the patient free of all macroscopic lesions, but if this was not feasible, an attempt was made to reduce all individual tumours to less than 1.5 cm. All 17 patients received 9 courses of chemotherapy postoperatively in the form of cyclophosphamide and cis-platinum.

For data analysis, we divided our patients into two groups: group 1 consisted of those patients who died within 12 months following surgery, and group 2 comprised of those who survived for more than 12 months after surgery, in an attempt to determine the important factors which might predict the survival of patients with advanced ovarian carcinoma (stage III and IV) for more than one year.

The means of age and parity in the two groups were compared by using the t-test. Several other factors, such as nationality (Saudi versus non-Saudi), age (less than 50 and more than 50 years), nullipara versus multipara, perimenopausal versus postmenopausal, presence of more than 1000 ml of ascitic fluid intra-operatively, stage of the disease, grade of the tumour, as well as its histopathological type were examined in the two groups in order to determine the statistical significance of each factor using Fisher's exact probability test.

Odds ratios were calculated for the aforementioned factors. Odds ratio estimates have a skewed distribution, therefore the usual method of representing accuracy in terms of standard error is inappropriate. For this reason, 95% confidence limits are given; their spread gives an indication of accuracy and the estimate is significant if the confidence limits are entirely below or above the value of 1, and do not include unity.

RESULTS

Out of 17 patients, 10 were of stage III and 7 of stage IV.

Table 1 shows the age distribution of all patients. The median age was 50 years and the mean age 48.2 years. The youngest patient was 20 years old and the oldest patient was 70 years old.

Table 1
The age groups of patients with advanced ovarian carcinoma (Stage III or IV)

Age Group	*Number*	*Percentage*
20 – 39 years	5	29.4
40 – 59 years	7	41.2
≥ 60 years	5	29.4
Total	17	100.0

Nine patients were postmenopausal and 8 were perimenopausal; 10 patients (58.8%) were Saudis and 7 (41.2%) were non-Saudis. The parity ranged from 0 to 7, with a median of 3 and a mean of 2.47 (SD 2.29). Five patients were nulliparous and 12 were multiparous. There were 8 (47.1%) serous, 4 (23.5%) mucinous, 2 (11.8%) endometroid and 3 (17.6%) undifferentiated carcinomas.

Table 2 shows the means of age and parity between the two groups, which were statistically not significant. Table 3 shows the procedures performed during laparotomy.

When the factors mentioned previously were cross-tabulated between the two groups, only the stage of the disease was found to be statistically significant (Table 4).

Odds ratio for patients who died within 12 months following cytoreduction of the ovarian carcinoma, are shown in Table 5. Except for the stage of the disease, none of these factors was found to be statistically significantly associated with death within 12 months after surgery.

DISCUSSION

Retrospective and prospective studies strongly suggest a role and benefit for cytoreductive surgery in the management of advanced ovarian cancer.[1-5] An attempt to "debulk" should be part of the management of ovarian cancer, which might include gastrointestinal and urological surgery.[4-8] It has been shown that optimal cytoreduction is possible in a high proportion of patients if the

Table 2
Age and parity of the two groups of patients with advanced ovarian carcinoma (Stage III or IV)

Variable	*Group 1 (N=9) Survival < 1 year*		*Group 2 (N=8) Survival > 1 year*		
	Mean ± SD	*Range*	*Mean ± SD*	*Range*	*P*
Age	50.9 ± 12.9	32-70	45.3 ± 17.3	20-70	0.46*
Parity	3.1 ± 2.7	0-7	1.8 ± 1.7	0-4	0.22*

* non-significant

operation is performed by a gynaecologist with a special interest in this field. Postoperative morbidity was acceptably low, whether or not bowel resection was required.[5] In the present study, a team consisting of a gynaecologist, a general surgeon and a urologist were involved in the surgical management of patients with ovarian cancer, which might be a way to overcome the lack of a gynaecological oncologist.

Table 3
Procedures performed during laparotomy in 17 patients with advanced ovarian carcinoma (Stage III or IV)

Procedure	*Number*	*Percentage*
Total abdominal hysterectomy	12	70.6
Bilateral salpingo-oophorectomy	17	100.0
Omentectomy	17	100.0
Small bowel resection	7	41.2
Large bowel resection	13	76.5
Resection of other metastases	8	47.1
Colostomy	5	29.4
Segmental urinary tract resection	2	11.8

In a series reported by Blythe and Wahl, 6 cytoreductive operations were performed in 19 patients, of whom 17 (89.5%) had bowel surgery and 13 (68.4%) had colostomies. Henitz et al[5] reported that in 70 patients who underwent cytoreductive operations, 45 (64.3%) had bowel surgery performed, and 6 (8.6%) had colostomies.[4] In our present study, among the 17 patients, we performed bowel surgery in 13 (76.5%) and colostomies in 5 (29.4%),

Table 4
Factors influencing survival in two groups of patients with advanced ovarian carcinoma

Factors	*Survival <12 months*	*Survival >12 months*	*P-Value*
Nationality			0.34
Saudi	4	6	
Non-Saudi	5	2	
Age			0.64
< 50 years	5	3	
> 50 years	4	5	
Parity			0.62
Nullipara	2	3	
Multipara	7	5	
Menopause			0.35
Perimenopausal	3	5	
Postmenopausal	6	3	
Ascitic Fluid			0.33
< 1000 ml	5	2	
> 1000 ml	4	6	
Stage			0.002
Stage III	2	8	(statistically
Stage IV	7	0	significant)
Grade			0.58
Otherwise	6	7	
Grade 3	3	1	
Histopathology			0.21
Otherwise	6	8	
Undifferentiated	3	0	

Table 5
Odds ratio and 95% confidence limits of patients who died within 12 months following surgery

Factor		*Odds ratio*	
Nationality		3.8	(0.5 – 29.8)
Saudi	= 0		
Non-Saudi	= 1		
Age		0.5	(0.1 – 3.35)
< 50 years	= 0		
> 50 years	= 1		
Parity		2.1	(0.3 – 17.6)
Nullipara	= 0		
Multipara	= 1		
Menopause		3.3	(0.5 – 24.4)
Perimenopausal	= 0		
Postmenopausal	= 1		
Ascitic Fluid		0.3	(0.03 – 2.1)
< 1000 ml	= 0		
> 1000 ml	= 1		
Stage .		107918.4	(*)
Stage III	= 0		
Stage IV	= 1		
Grade		1.9	(0.5 – 6.79)
Otherwise	= 0		
Grade 3	= 1		
Histopathology		1.8	(0.7 – 4.7)
Otherwise	= 0		
Undifferentiated	= 1		

* could not be obtained

2 of which were permanent and 3 were temporary dysfunctional colostomies.

Withshaw et al[9] reported, in a retrospective study, that out of 25 patients who underwent salvage surgery for ovarian cancer and whose ages ranged between 26 and 72 years, 18 had stage III and 7 had stage IV ovarian cancer; and the tumours were poorly differentiated in 9. It was also found that survival for more than one year depended on whether the patient's age was less than 55 years, the patient survived for more than 12 months from diagnosis to salvage surgery, the operation was performed by a spe-cialist, and the residual macroscopic lesion was between 0–2 cm at the end of salvage surgery.[9]

It has been shown that the factors which are associated in the resectability of tumours to optimal status include the diameter of less than 50 mm of the largest metastasis before cytoreductive surgery, ascites of less than 1000 ml and age of less than 70 years.[4]

In our study, all our patients had metastatic tumours larger than 50 mm and none of them were optimally "debulked". However, the survival of more than 12 months with good life quality was achieved in 8 out of the 17 patients. Except for the stage of the disease, none of the factors we studied was found to be significant in predicting the survival for more than one year following surgery.

CONCLUSION

Cytoreductive surgery plays an important role in the management of advanced ovarian cancer, whether optimal reduction is achieved or not. This study shows that an aggressive approach should be employed in the management of advanced ovarian cancer, with a lot of benefit in terms of symptomatic relief, so that longer survival can be achieved. Except for the stage of the disease, none of the factors we studied was found to be significant in predicting the duration of survival.

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