



Original Research Article

Analysis of Morbidity and Mortality Associated with Extensive Cytoreductive Surgeries for Advanced Ovarian cancer- Study in a Regional Cancer Centre

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ABSTRACT

Objective: To assess the morbidity and mortality associated with extensive cytoreductive procedures done for advanced carcinoma ovary.

Material and Methods: This is a retrospective study done from Jan 2009 to Dec 2010 .A total of 96 cases were included in the study who had undergone extensive cytoreductive surgeries including splenectomy, sub diaphragmatic stripping, bowel resections and others for advanced carcinoma ovary. Primary surgery was done in 70 patients, interval surgery in 9 patients and secondary cytoreductive surgery in 17 patients. Optimal surgery (≤ 1 cm) was done in 80/96(83.3%) patients.

Results: 13/67(19%) had bowel anastomotic leak and most of the leaks were after ileotransverse anastomosis (6/13). Of these four patients were managed conservatively while reexploration with diversion stoma was done in 9 patients. 12/96 (12.5%) had sepsis with respiratory infection, three patients had burst abdomen, 2 patients had deep vein thrombosis and one patient developed recto vaginal fistula. The total mortality was 6/96(6%), two due to anastomotic leak and sepsis, two due to pulmonary embolism, one due to severe OPSI and another due to recurrent gastric fistula and generalized sepsis.

Conclusion: Extensive cytoreductive surgery was associated with high optimal cytoreduction (83.3%) rates with slight increase in morbidity and mortality.

Keywords: Splenectomy, Bowel resection, Sub diaphragmatic stripping, Carcinoma ovary, Cytoreduction, Optimal.

INTRODUCTION

Carcinoma ovary is one of the leading causes of morbidity and mortality among gynecological cancers as more than 75% present with advanced stage (stage3/4). Optimal cytoreduction (< 1 cm) is one of the important prognostic factors for both overall survival and disease free survival (NBOCC, 2008). To achieve this bowel resection, sub diaphragmatic stripping (SDS),

splenectomy, peritonectomy, liver metastatectomy and other organ resection procedures may be required. It has been shown that these procedures can be done without increasing much morbidity while increasing survival (Zivanovic et al, 2008; Eisenhauer et al, 2008; Chi et al, 2009; Zivanovic et al, 2010).

This study is being done to assess the morbidity/mortality of extensive

cytoreductive surgeries at a tertiary regional cancer centre.

MATERIALS AND METHODS

This is a study done from Jan 2009 to Dec 2010 in a regional cancer centre. A total of 96 cases (70 primary, 9 interval, 17 secondary cytoreductive) out of 230 (41.7%) ovarian cases were included in the study who had undergone aggressive organ resection procedures resections, splenectomy, sub diaphragmatic stripping (SDS)] and other procedures as part of cytoreductive surgery along with hysterectomy, peritoneal tumor debulking, omentectomy and retroperitoneal lymph node dissection (table 1).

Case sheets were reviewed and analyzed for age, procedures done,

optimality of surgery, complications and mortality rate. Only advanced carcinoma ovary cases (stage3c and stage4) were included. Ultrasound abdomen and pelvis and CT scan were the investigation modality used in majority of patients. Patients with performance status 0 -2 (ECOG criteria) were considered fit for the surgery. The patient characteristics, the timing of surgery, optimality of surgery and pathology have been shown in table1. Optimal surgery was done in 80 out of 96 patients (which includes 58 out of 70 with primary surgery, 7 out of 9 with interval surgery and 15 out of 17 who underwent secondary cytoreduction)

All these surgical procedures were done by gynecologic oncologists with more than 10 years experience.

Table 1: Characteristics of patients

Total number of patients-96	
Age	Median 48 years (Range 13-70years)
Primary surgery (%)	70(73%), 58 optimal,12 suboptimal
Interval surgery (%)	9(9.3%), 7 optimal,2 suboptimal
Secondary cytoreductive surgery	17(17.7%), 15 optimal, 2 suboptimal
Optimal surgery	80(83.33%)
Sub optimal surgery	16(16.66%)
Grade of tumor	Grade 1—0, Grade 2—38, Grade 3--54
Pathology	Serous-70, Mucinous-10, Clear cell-3, Endometroid-4, Germ cell tumor-4, Un differentiated-5

RESULTS

The mean operating time was 220 mins (180-300mins). Mean blood loss was 750ml (500-2000ml).The hospital stay ranged from 10-35days (mean-16days).

Surgical Procedures

Splenectomy was done in 26 patients, sub diaphragmatic stripping in 29 patients, 72 bowel resections were done in 67 patients (including 5 double bowel resections), five patients had liver nodule excision(1-3cms), 4 patients had falciform ligament tumor removal (1-4cms), one

patient underwent partial gastrectomy, one had partial cystectomy (bladder) and one patient underwent celiac lymph node dissection .

The types of bowel resection were as shown in table 2. Elective prophylactic stoma was done in 12/67(18%) patients. All the anastomosis was hand sewn.

Sub optimal surgery was mainly due to tumor in porta-hepatis (not detected on pre-op ultrasound scan), bowel mesentery, densely matted and adherent lymph nodes to pelvic vessels and celiac lymph nodes.

Among the splenectomised patients, 12/26 (46%) patients had respiratory infection along with sepsis (OPSI, overwhelming postsplenectomy infection) and two of these patients died. Cultures of

blood, pus and or sputum were positive for gram negative organisms (E-coli, klebsiella, pseudomonas- usually ESBL)) and or Gram positive organisms (staphylococcus, enterococci).

Table -2 Types of bowel resections

Type of resection	Number(%)	Total-72
Anterior resection(AR)	31/72(43%)	
Right hemicolectomy with ileotransverse anastomosis	14/72(19.4%)	
Small bowel resection anastomosis	13/72(18%)	
Sigmoid colon resection anastomosis	3/72(4%)	
Left hemicolectomy	1/72(1.3%)	
Transverse colon resection anastomosis	6/72(8.33%)	
Hartmann's procedure	4/72(5.55%)	
Double bowel resection anastomosis	5/67(7.46%)	
Elective stoma	12/67 (18%)	

One of these patients died with multiorgan failure on the post operative day 3 and another patient died due to gastric fistula and sepsis with pneumonia on post-operative day 15. Pneumococcal vaccination was not given to any of our patients.

Subdiaphragmatic stripping (SDS) was done in 29 patients. The tumor deposits

ranged from 3-5 cms in size to complete plaque covering whole of subdiaphragmatic area (>1cm thick). Four patients had accidental opening of diaphragm which was repaired with or without intercostal drain. One of these patients died due to massive pulmonary embolism on post operative day 1.

Table-3. Types of bowel surgeries in patients with anastomotic leak

Type of resection	Number(%),total-13/72(18%)
Ileo transverse anastomosis	6/13 (46%)
Anterior resection	4/13 (30.7%)
Segmental sigmoid resection anastomosis	2/13 (15.38%)
Small bowel resection anastomosis	1/13 (7.69%)

Out of 72 bowel resection and anastomosis, 13 of 67 patients (19%) had anastomotic leak. Types of leak were as shown in Table-3. Of the 13 leaks, 9 required emergency laparotomy and diversion with stoma and others were managed conservatively.

Table -4 Comparison of splenectomy studies

Study	Year,durtn	No of pts	optimality	morbidity	mortality
Magtibay et al(2006)	2006	112	--NA-----	26/112, 23%	5.5% , p-0.058
Chen et al (2000)	2000,12 years	35	91.4%	25.7%	----NA-
Scott et al (2006)	2006	49	---NA-----	---NA-----	----NA-----
Bilgin et al (2005)	2005	13	--NA-----	2%	1/13,7.6%, p>0.05
KMIO	2010,2yrs	26	80.76%	12/26,46%	2/26,7.6%

NA-not available

Three of these patients had intra-operative and post operative hypotension due to tumor lysis syndrome. All patients with anastomotic leak had hypoproteinemia-albumin in the range of 1.5-2.5 g/dl, and total proteins in the range of 4.2-6g/dl in the post –op period which was managed with parenteral nutrition. Three of these patients died (3/67, 4.47%) –2 due to post-op sepsis (due to anastomotic leak) and one due to

embolism. The two patients with leak died on post op day 8 and day 10 respectively and the patient with embolism died on day 3.

Overall major morbidity was observed in 15/96 patients (15.6%) in the form of sepsis, deep vein thrombosis, rectovaginal fistula and burst abdomen. The total mortality rate was 6/96(5.76%).

Table-5. Comparison of bowel resection studies as part of cytoreductive surgeries.

Studies	Yr, duration	No	Leak rate	Optimality rate	Morbidity rate	Death
Nora et al (1998)	1998, 5yrs	31	0	19/31, 61%	0,---18 stoma	0
Cloven et al (2001)	2001, 12 yrs	105	4/105, 3.8%	33/105, 33%	10/105, 9.5%	6/105, 5.7%, NS , p-0.37
Bridges et al (2002)	1993, 5yrs	43	0	70%	0	0
Chia et al (2003)	2003, 5yrs	38	1/38, 2.6%	71%, 61% stoma	4/38, 10.5%	3/38, 7.89%, NS, p-0.30
Mourton et al (2005)	2005, 10 yrs	70	1/70, 1.7%	--NA----	7/70,10%	0
Estes et al (2006)	2006, 6yrs	48	1/48, 2.08%	25/48, 52%	5/48, 10.41%	2/48,4%, NS , p-0.39
Park et al (2006)	2006, 5 yrs	60	1/60, 1.6%	85%	3/60, 5%	--NA--
Cai et al (2007)	2007, 3yrs	95	-NA-	67%	--NA--	--NA--
Bristow et al (2009)	2009, 7yrs #	56	5.4%	85.7%	23.2%	1.8% ,NS, p-0.28
Kidwai MIO	2010, 2yrs	67	13/67, 19%	80.59%, 54/67	11/67, 16%	3/67, 4.5%

NA-not available, NS-not significant.

DISCUSSION

Recent studies have shown improved progression-free and overall survival in advanced ovarian cancer as a result of a change in surgical paradigm (Eisenhauer et al, 2008; Chi et al, 2009; Zivanovic et al, 2010). Treating advanced carcinoma ovary is very challenging as they require extensive organ resection procedures to achieve optimality and a good ICU care. Studies (Ibeanu & Bristow, 2010) have shown that Surgeon's skill is one of the important factors which contribute to optimality of surgery. 35% of cases which were considered as difficult to achieve optimality

on radiology (CT scan based on meyer's scoring) were optimally reduced.

Studies (Eisenhauer et al, 2006; Park et al, 2006) have shown that bowel resections and extensive upper abdominal surgeries done to achieve optimal cytoreduction have improved both disease free survival and overall survival without increasing morbidity. They have shown that benefits of increased survival outweigh the morbidity.

Magtibay et al (2006) has shown that splenectomy can be included as part of cytoreductive surgery without increasing much morbidity. Table-4 shows comparison of the various studies with our morbidity

and mortality (Chen et al, 2000; Bilgin et al, 2005; Magtibay et al 2006; Scott et al 2006).

Overwhelming post splenectomy infection (OPSI) is one of the important complications after splenectomy which can occur from post surgery from 1 week to many years later (Okabayashi & Hanazaki, 2008). Studies (Okabayashi & Hanazaki, 2008; Thomsen et al, 2009) have clearly shown the reasons and the prevention. They are usually treated with antibiotics and supportive treatment.

Vaccination after splenectomy is controversial. There is only level-3 evidence for this (Post-Splenectomy Vaccine Prophylaxis, 2006). Thomson et al (2009) did a population based study on splenectomised patients. It was found out that only 4 % of infections are caused by pneumococci and majority are by gram negative organisms. In the present study there were no pneumococcal infections. Few centers and countries routinely practice vaccination according to their respective guidelines.

Park et al (2006) and other studies have clearly shown the benefits of low anterior en bloc resection in both advanced primary and recurrent ovarian cancers. Other bowel resections done to achieve optimality have shown to increase survival. (Cloven et al, 2001; Park et al, 2006; Cai et al, 2007). Table-5 shows other studies in comparison with our study (Bridges et al,1993; Nora et al, 1998; Chia et al, 2003; Mourton et al, 2005; Estes et al, 2006; Bristow et al, 2009).

In the present study 12/67 (18%) had prophylactic elective stoma and maximum leak rate was with ileotransverse anastomosis while it should have been the least. There may be several factors involved-prolonged duration of surgery, extensive deposits, anemia, hypoproteinemia and surgical skill. The morbidity due to

anastomotic leak in the present study was seen in 13/67(19%) patients.

In the study done by Nora et al(1998) ,18 prophylactic elective stomas were done out of 31 anastomosis (58%), and in the study done by Chia et al(2003), 61% stoma was done. So morbidity and mortality was 0 in previous study and leak rate was 1/38, death rate was 3/38 in the latter study. The morbidity in the present study was much higher which may be due to the fact that less number of patients had elective prophylactic stomas.

Urinary bladder cystectomy as part of cytoreductive surgeries have been described during secondary cytoreductive surgeries (Bristow et al, 2009). The same principal has been applied in the present study, since optimal cytoreduction could be easily achieved without injuring trigone.

The mortality per se due to bowel surgeries was 3/67 (4.47%) which is on par with international standards.(p value>0.05), while the overall mortality was 6/96(6%) which is more in comparison with international standards.

Three of these patients died of severe sepsis with resistant ESBL organisms. Survival of patients with severe sepsis is only 10% in a level 3 ICU, but ours is level 2(Intensive care society, 2009).

CONCLUSION

Extensive cytoreductive surgery was associated with high optimal cytoreduction (83.3%) rates with slight increase in morbidity and mortality. In developing countries the surgeries for advanced ovarian cancer should be individualized depending on patient's age, nutrition, socio-economic factors, surgical skill and critical care available.

Declaration of Interest: The authors report no declaration of interest.

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