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The Role of Palliative Surgery in the Management of Acute Intestinal Obstruction Secondary to Peritoneal Carcinomatosis

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Rezumat

Rolul chirurgiei paliative în managementul ocluziei intestinale acute secundare carcinomatozei peritoneale

Introducere: Ocluzia intestinală acută secundară carcinomatozei peritoneale extinse este caracteristică stadiilor terminale de boală. La aceşti pacienți, rolul intervenției chirurgicale paliative este discutabil având în vedere complicațiile severe anticipate şi eficacitatea îndoielnică în obținerea unei paliări adecvate. Obiectivul principal al studiului nostru a fost de a evalua fezabilitatea şi capacitatea pacienților de a relua nutriția orală după chirurgia paliativă pentru ocluzia intestinală acută cauzată de carcinomatoza peritoneală.

Pacienți şi Metode: Acest studiu este observațional şi include datele a 40 de pacienți diagnosticați consecutiv cu ocluzie intestinală prin carcinomatoză peritoneală. Datele au fost extrase dintr-o bază de date clinică menținută prospectiv. Au fost urmărite variabile predefinite pre şi intraoperatorii. Au fost analizate variabile precum complicațiile postoperatorii, durata şederii în spital şi mortalitatea, dar şi consecințele acestora pe termen scurt la 3 luni sub forma supraviețuirii şi a capacității de a relua nutriția enterală.

Rezultate: Dintre cei 40 de pacienți, 18 au fost bărbați şi 22 femei. Cancerul ovarian a fost cel mai frecvent punct de plecare al carcinomatozei (27,5%). Doisprezece pacienți au avut ocluzie intestinală acută ca primă prezentare fără evenimente anterioare, iar 25 (62,5%) pacienți fuseseră operați anterior sau primiseră tratament sistemic adjuvant. Opțiunea chirurgicală paliativă a fost fezabilă tehnic la 37 (93,5%) pacienți. Şase (15%) pacienți au decedat în perioada postoperatorie. Durata medie de spitalizare pentru pacienții care au fost externați a fost de 10 zile, cu un interval de 6-18 zile. Complicații postoperatorii severe au fost

observate la 9 (26,4%) pacienți. Dintre pacienții (n=34) externați, 26 (76,4%) erau în viață la 3 luni. Dintre aceştia, 21 (80,7%) erau pe o formă de nutriție orală.
Concluzie: Chirurgia paliativă la pacienții cu ocluzie intestinală acută secundară carcinomatozei peritoneale este fezabilă, cu o morbiditate şi mortalitate acceptabile. Nutriția enterală poate fi restabilită la majoritatea acestor pacienți.

Cuvinte cheie: metastaze peritoneale, carcinomatoză peritoneală, chirurgie paliativă, ocluzie intestinală malignă acută

Abstract
Introduction: Acute intestinal obstruction secondary to extensive peritoneal carcinomatosis is an end stage event. The role of palliative surgery in these patients is debatable in view of the anticipated severe complications and its doubtful role in achieving adequate palliation. The primary objective of our study was to evaluate the feasibility and ability of patients to resume oral nutrition after palliative surgery for acute intestinal obstruction due to peritoneal carcinomatosis.
Patients and Methods: It is an observational study in which we retrospectively reviewed the data from a prospectively maintained clinical database of 40 patients. The predefined pre- and intraoperative variables were obtained. The immediate outcome variables like postoperative complications, length of hospital stay, and mortality were analyzed. The short-term outcomes at 3 months in the form of survival, ability to resume enteral nutrition were analyzed.
Results: Among the 40 patients 18 were males and 22 females. Ovarian cancer was the most common primary (27.5%) in the study. Twelve patients had acute intestinal obstruction as their first presentation without any past events and 25 (62.5%) patients had been operated on previously or received adjuvant systemic treatment. The palliative surgical option was technically feasible in 37 (93.5%) patients. The median length of hospitalization for the patients who were discharged was 10 days with a range of 6-18 days. Six (15%) patients died in the post-operative period. Severe post-operative complications were seen in 9 (26.4%) patients. Among the patients (n=34) discharged 26 (76.4%) were alive at 3 months. In those who were alive, 21 (80.7%) of them were on some form of oral nutrition at 3 months.
Conclusion: Palliative surgery in patients with acute intestinal obstruction secondary to peritoneal carcinomatosis is feasible with acceptable morbidity and mortality. The enteral nutrition can be restored in the majority of these patients.

Key words: peritoneal metastasis, peritoneal carcinomatosis, palliative surgery, acute malignant intestinal obstruction

Introduction

Acute intestinal obstruction secondary to extensive peritoneal carcinomatosis is an end stage event in several intra-abdominal malignancies (1). The incidence of the malignant bowel obstruction due to peritoneal carcinomatosis is about 5-51% in gynecological cancer and 10-28% in advanced gastro-intestinal cancer (2). The peritoneal surface secondaries pose a challenge in the management of advanced cancer due to anatomical and technical difficulty. The protocols for the management of these advanced cancers have

evolved over time with the introduction of novel chemotherapy, targeted therapy, advanced surgical techniques, and hyperthermic intraperitoneal chemotherapy (HIPEC). However, a significant proportion of these patients develop sequelae like acute intestinal obstruction, perforation, fistulae, and ascites, further complicating the course (3).

The acute intestinal obstruction secondary to extensive peritoneal carcinomatosis is a challenging problem with complicated disease management. There are limited options available in these patients when conservative management fails. The literature on this topic has a considerable overlap, as most studies have included intestinal obstruction due to the primary tumour itself. We wanted to examine the benefits of the palliative surgical option in the cohort of patients who had acute intestinal obstruction due to the peritoneal deposits alone. These patients mostly have small intestinal obstruction with multiple sites involvement, making them unsuitable for lesser invasive options like endoscopic or radiological interventions. The option of palliative surgery is generally not offered in view of inherent technical difficulties of the procedure, possible intraoperative changes in decisions, anticipated severe complications and its doubtful role in providing adequate palliation (4,5).

We examined whether denying these patients an operation was correct and to identify those subsets of patients who benefited from a palliative procedure. The primary objective of the study was to evaluate the feasibility and ability of patients to resume oral nutrition after palliative surgery for acute intestinal obstruction due to peritoneal carcinomatosis.

Patients and Methods

We performed an observational study in which we retrospectively reviewed the data from a prospectively maintained clinical database of all patients with acute intestinal obstruction due to peritoneal carcinomatosis (*Fig. 1*) who were not suitable for endoscopic management and underwent palliative (*Chart 1*) surgery in the department of Surgical Gastroenterology and Liver Transplantation, Sir Ganga Ram Hospital, New Delhi between June 2010 to January 2022. The study was approved by the institutional ethical committee (EC/08/23/2336). We included all patients who underwent palliative surgery for acute intestinal obstruction secondary to extensive peritoneal carcinomatosis due to gynecological, genitourinary, and gastrointestinal cancers. We excluded patients who had peritoneal carcinomatosis with obstruction due to the primary tumour itself and those who received non-surgical or conservative management. The pre-operative variables collected were age, sex, site of the primary tumour, whether intestinal obstruction was the primary presentation, if they had received adjuvant chemotherapy and its duration, co-existent liver/lung metastases, haemoglobin level, serum creatinine level, presence of small or large bowel obstruction, and whether ascites was present /absent). Intraoperative variables like resection, anastomosis, stoma, bypass, adhesiolysis and biopsy alone were recorded. The immediate outcome variables analyzed were post-operative complications as evaluated by Clavien-Dindo grades, length of hospital stay, and mortality. Information was obtained on short-term outcomes at 3 months like survival, and ability to resume enteral nutrition.

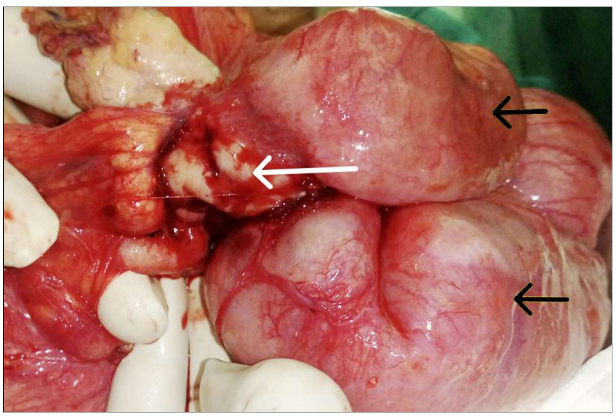
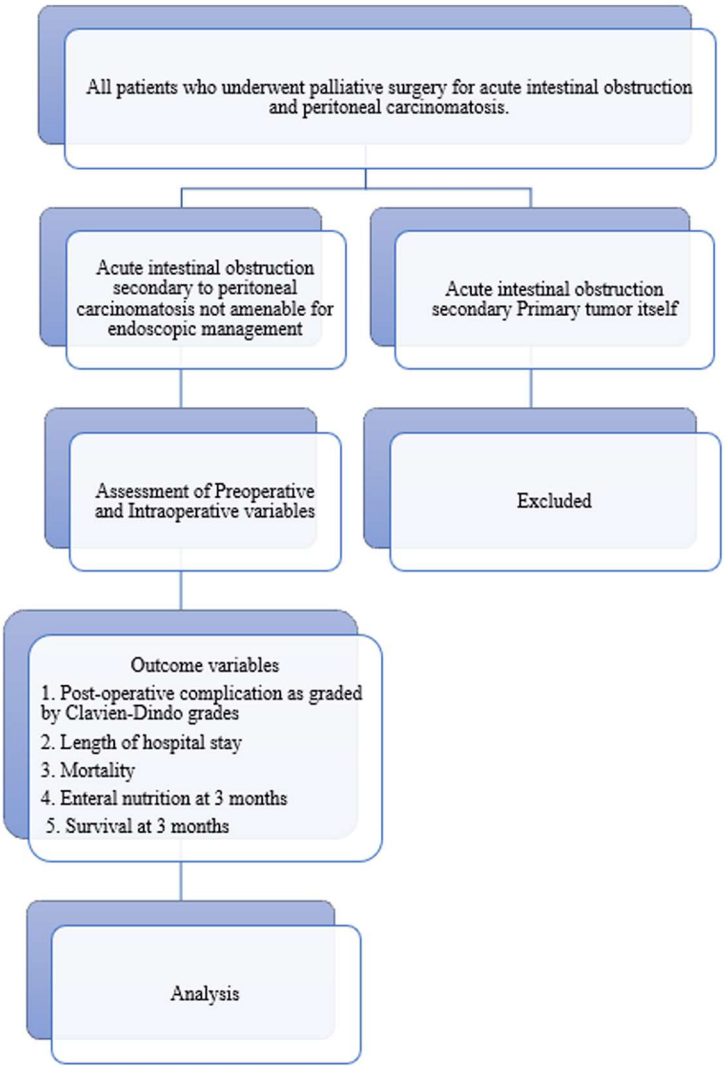


Figure 1. Intraoperative photograph showing peritoneal deposit (white arrow) resulting in obstruction and proximal small intestinal loops dilatation (black arrows).

Chart 1. Methodology of the study



Statistical Analysis

The continuous variables are presented with medians and standard deviations. Categorical variables are presented as numbers and percentages. Univariate logistic regression was performed to calculate unadjusted odds ratio. Clavien-Dindo grade and feasibility of enteral nutrition were used as dependent variable and other parameters were covariates. For all statistical tests, a p value less than 0.05 was taken to indicate a significant difference.

Results

There were 40 patients, 18 males and 22 females, whose age ranged from 16 to 78 (mean 55) years. *Table 1* shows their demographic, clinical and biochemical parameters. Twelve patients had acute intestinal obstruction as their first presentation without any past events and 25 (62.5%) patients had been operated on previously or received adjuvant systemic treatment. The median duration between the adjuvant chemotherapy to onset of the acute obstruction was 6 (SD 18.67) months. Two patients had not received any

Table 1. Clinical & preoperative biochemical parameters

Clinical Parameter	
Obstruction as first presentation, n (%)	12 (30)
Co-existing liver/ lung metastasis, n (%)	4 (10)
Co-existing ascites, n (%)	22 (55)
Level of obstruction, n (%)	
Small Bowel	38 (95)
Large bowel	2 (5)
Preoperative biochemical parameters	
Haemoglobin (g/dl, mean ± SD)	10.24 ± 1.77
Serum Albumin (g/dl, mean ± SD)	2.86 ± 0.61
Serum creatinine (mg/dl, mean ± SD)	0.92 ± 0.61

Table 2. Site of primary cancer

Site	n (%)
Ovary	11 (27.5)
Stomach	9 (22.5)
Colon	6 (15)
Rectum	5 (12.5)
Gallbladder	5 (12.5)
Pancreas	2 (5)
Esophagus	1 (2.5)
Genitourinary	1 (2.5)

adjuvant treatment and one was on neo-adjuvant treatment at presentation.

The distribution of the site of primary is shown in *Table 2* with ovarian cancer being the most common site.

Thirty-seven patients (n=37) received one or other palliative surgical option except for three, in whom it was not technically feasible. The palliative surgical options performed are as shown in *Chart 2*.

Six (15%) patients died in the post operative period, and severe post-operative complications were seen in 9 (26.4%) patients. The severe complications were mostly secondary to high output from the proximal stoma resulting in acute kidney injury, post-operative ventilator associated pulmonary complications, ascites, or wound complications. One of our patients had a midline retracted stoma which required revision under anesthesia. The outcome variables of our study are tabulated in *Table 3*.

The median length of hospitalization for the patients who were discharged was 10 days with a range of 6-18 days.

Among the patients (n=34) discharged, 26 (76.4%) were alive at 3 months. Out of the eight patients who died within 3-month post-discharge only 1 patient died due to recurrent obstruction.

In those who were alive, 21 (80.7%) were on some form of oral nutrition. Nine were tolerating solid food at the end of 3 months and were among those who received some sort of systemic therapy post-surgery. However, five patients developed recurrent episodes of obstruction requiring multiple admissions, two of whom required exploration and the rest were managed conservatively.

The univariate logistic regression analysis (*Table 4*) in our study has not identified any statistically significant preop or intra op indicators for predicting severe complications

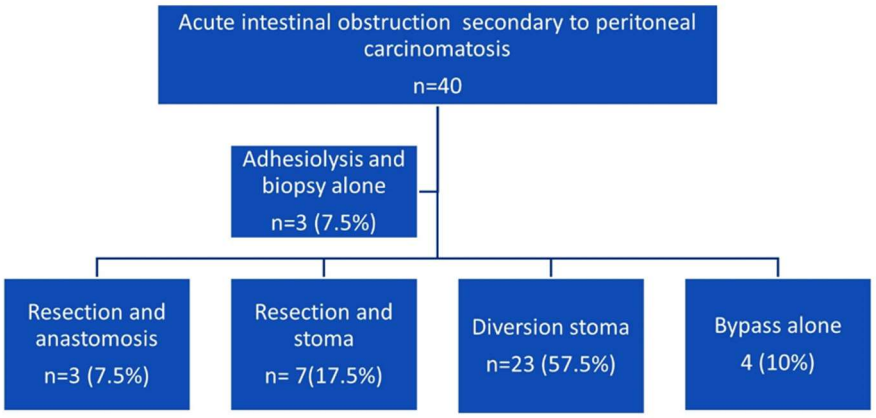


Chart 2. Distribution of the palliative surgical options

Table 3. Outcome variables

Outcome variables	n (%)
Complications (≥ Grade 3)	9 (26.4)
Operative Mortality	6 (15)
Alive among discharged at 3 months	26 (76.5)
Able to take oral nutrition (solid or liquid) at 3 months	21 (80.7)
Able to take solid food at 3 months	9 (42.8)
Received Systemic therapy after surgery	9 (34.6)

or death. However, a trend towards severe complications or death is seen in patients with higher serum creatinine level, low serum albumin level, and in patients who underwent laparotomy or bypass alone group.

In the present study, although the univariate analysis (*Table 5*) of the preoperative parameters and surgical options did not yield any statistically significant predictor for feasibility of enteral nutrition at 3 months, those who underwent resection rather than stoma alone were likely to resume enteral nutrition at 3 months.

Discussion

We aimed to identify the usefulness of palliative surgery in restoring enteral nutrition in acute intestinal obstruction secondary to peritoneal carcinomatosis, thereby exploring the possibility of further treatment and care in these patients with end stage cancers. Most of these patients have multiple level of obstruction which makes them unsuitable for the endoscopic mode of treatment. In our study, 95% of patients had small bowel obstruction leaving no option but to opt for palliative surgery for relief. The data on patients with acute intestinal obstruction secondary to peritoneal carcinomatosis are limited. High quality evidence discussing the approach and options available in these patients is less. In most developing countries, the approach towards such patients is generally nihilistic. The reason for such management is due to lack of financial support since most of these patients have already exhausted their resources for managing the primary cancer. Also, the surgical options are not always

Table 4. Univariate analysis of preoperative and intraoperative variables for severe complications or death

Demographic parameter	Clavien-Dindo grade < 3 N=25	Clavien-Dindo grade more than or equal to grade 3 N=15	P value
Age in years, Mean±SD	51.40 ± 16.53	56.73 ± 12.91	0.288
Gender			0.870
Male	11 (44 %)	7 (46.7%)	
Female	14 (56 %)	8 (53.3%)	
Obstruction as first presentation, n (%)			0.722
Yes	8 (32%)	4(26.7%)	
No	17 (68 %)	11(73.3 %)	
Co-existing liver/ lung metastasis, n (%)			0.138
Yes	1 (4 %)	3(20%)	
No	24 (96.0 %)	12(80%)	
Co-existing Ascites, n (%)	12 (48 %)	10 (66.7%)	0.254
Level of obstruction, n (%)			0.711
Small Bowel	24 (96 %)	14(93.3%)	
Large bowel	1 (4 %)	1 (6.7%)	
Hemoglobin in g/dL, mean	10.36±1.70	10.03 ±1.91	0.564
Serum Albumin in g/dL, mean	2.89 ± 0.51	2.80 ± 0.77	0.658
Serum creatinine in mg/dL, mean	0.74±0.16	1.22 ± 0.90	0.071
Site of Primary			
Ovary	7 (28 %)	4(26.7%)	0.591
Stomach	7 (28 %)	2(13.3%)	
Colon	4 (16 %)	2(13.3%)	
Rectum	4 (16 %)	1 (6.7%)	
Gallbladder	2 (8%)	3(20%)	
Pancreas	-	2 (13.3%)	
Esophagus	1 (4%)	-	
Genitourinary	-	1 (6.7%)	
Surgery			
Resection and anastomosis	2 (8.0 %)	1 (6.7%)	0.620
Resection and stoma	5 (20%)	2 (13.3%)	
Diversion stoma	16 (64%)	7 (42.9%)	
Bypass alone	1 (4.0 %)	3 (20 %)	
Adhesiolysis alone	1 (4.0%)	2 (13.3%)	

Table 5. Univariate analysis of pre- and intraoperative variables for the feasibility of enteral nutrition in patients who were alive at 3 months

Demographic parameter	Enteral nutrition not feasible N=5	Enteral nutrition feasible N=21	P value
Age in years, median (Range)	55.00±20.95	52.57 ± 13.13	0.716
Gender			
Male	2 (40%)	11 (52.4%)	0.326
Female	3 (60%)	10 (47.6%)	
Haemoglobin in g/dL, mean	11.14 ± 1.24	10.39 ±1.80	0.569
Serum Albumin in g/dL, mean	3.06 ± 0.314	3.02 ±0.64	0.093
Serum creatinine in mg/dL, mean	0.87 ± 0.311	0.73 ± 0.18	0.098
Surgery			
Resection and anastomosis	-	3 (14.3%)	0.138
Resection and stoma	-	6 (28.6%)	
Diversion stoma	5 (100%)	11 (52.4%)	
Bypass alone	-	1 (4.8%)	

rewarding. In a retrospective study by de Boer et al. in 12 years, where they performed palliative surgery for patients with acute intestinal obstruction due to peritoneal carcinomatosis, the study identified that the surgical option in these patients is associated with post-operative complications in 58.1% of patients. More than one fourth of them had 2 or more complications. However, they demonstrated better survival in patients with neuroendocrine tumors. The study drew a conclusion that best supportive care was a better option than surgery (6).

Acute intestinal obstruction may be the first presentation in some cases (in the present study 30% patients had peritoneal carcinomatosis with intestinal obstruction as their first clinical presentation), responsiveness to the advanced systemic therapy may not have been determined. Advances in oncology with systemic therapy demand a striking balance in planning for such patients. In a recent case control study by A. Razzaq et al., 80% of patients who underwent palliative surgery tolerated enteral nutrition following discharge and nearly half of them received systemic chemotherapy. The study also demonstrated the survival advantage in patients who received surgical palliation than the best supportive care alone (5).

Chen et al. studied 46 patients with primary colorectal cancer with extensive peritoneal carcinomatosis. The symptom control was achievable in 76.1 % of patients. Their subgroup analysis identified that the relief of symptoms in the debulking group (91.3%) was higher than in the bypass cohort (69%). The study revealed that fewer than 10% of patients developed severe (grade 3 or more) Clavien-Dindo complications. The study also looked at the number of patients who received chemotherapy following palliative surgery. It reported that out of the total 24 patients, 10 in the stoma/bypass group and 14 in the debulking group, received systemic therapy after surgery (7).

To examine the benefit of surgical palliation for intestinal obstruction, Blair et al., in their retrospective study of 63 patients observed that palliation was best achieved with surgery and about 76% of patients were on regular diet at their last follow up. The study identified that patients with colorectal primary, absence of ascites, serum albumin level >3 gm/dl in the pre-operative period and obstruction not involving the small bowel show better response to surgical palliation (8).

In their large series of 254 patients over 10 years, Wong et al. reported that 30-day post-operative morbidity was seen in 43% and death in 21 % of patients. The study also developed a predictive model for better prognosis. They identified age, pre-operative albumin, and performance status as predictor of 30-day post-operative morbidity (9).

In a systematic review of 17 studies on palliative surgery for malignant obstruction by Olson et al., palliation in the form of relief of obstruction was achieved in 32-100% patients, 45-75% were able to eat, and 34-87% of patients were discharged. The review showed similar results in terms of the outcomes and it also highlights the increased morbidity and mortality with palliative surgery (10).

A systematic review in elderly patients with malignant bowel obstruction by Santengelo et al. identified the factors like poor performance status, diffuse carcinomatosis, previous radiotherapy, and small bowel obstruction as contributor to the surgical failure. The studies suggested that symptomatic relief was achieved in 26-100% of patients. The complications reported in 7-44% with a mortality of 6-22% (11).

Observational studies on this topic have reported a wide range of morbidity (5-44%) and mortality rates (5-32%) following palliative surgery. The wide spectrum of primary and lack of uniformity in the presentation makes it difficult to establish a management protocol for these patients, which may explain the variations in the results of these studies (9-12). Studies published before the 2000s reported a morbidity of 16-45% and mortality of 17-35% (13-17). Recent studies have shown a reduction in post operative mortality. This may be attributed to the improved surgical,

ICU and critical care facilities. However, the studies have reported a higher morbidity and highlighted their concerns of prolonged hospitalization or re-admissions (5,9,18,19).

To the best of our knowledge, the evidence supporting the best supportive treatment guidelines in managing these study populations and making them suitable for receiving the established systemic therapy are lacking. The approaches like gastrostomy and parenteral nutrition fail to palliate symptoms and offer limited survival advantage (20). Non-operative interventions as a mode of palliation have been reported, however the ability to achieve enteral (to be precise oral) form of nutrition is barely possible (18,21,22).

Although palliative surgery seems to be a viable option, it cannot be denied that the complications in this group are considerable. In this setting, patient comfort is the primary goal. The patient's wishes should be respected, and patients should not be subjected to unnecessary treatment if not desired. The goals of surgery should be practical, and the limitations of surgery should be informed to the patient. There must be due considerations of the fact that these patients may end up spending a substantial portion of their remaining lives in the hospital recovering from the surgery instead of spending time with their loved ones (23-25). Nevertheless, these data supporting surgery can be used by the surgeon to frankly discuss the option of palliative surgery and also if it is in line with what the patient expects and desires. Similarly, it also illustrates to the patients what palliative surgery can accomplish for them in the scenario of peritoneal carcinomatosis causing intestinal obstruction. It is important that the patient understands that surgery does not entail cure.

In our study, we report a clinical success by restoring enteral nutrition in 80% of patients who were alive at 3 months (76.5%). Severe complications and mortality rates were 26.4 and 15% respectively. We came across failed laparotomies in only 3 patients and the rest received one or the other palliative surgical option proving the feasibility. A very few patients opted for systemic chemotherapy after surgery (although all were offered the option) to have a meaningful conclusion about its benefit. Further follow-up data were available for fewer than half of the patients rendering it difficult to draw any conclusions regarding their later survival.

Studies, as discussed above, have identified several parameters like pre-operative albumin, hemoglobin, performance status, co existent ascites, resectional surgery predict immediate post operative out comes. We could not establish any statistically significant correlation between pre- and intraoperative variables with severe complications, mortality and feasibility of enteral nutrition at 3 months. However, the biochemical parameters like low albumin, high serum creatinine level and failure to resect or bring a proximal stoma to the surface adequately has shown a trend towards severe post operative complications or mortality.

Conclusion

The surgical palliation for acute intestinal obstruction secondary to extensive peritoneal carcinomatosis is feasible. The centers equipped with multidisciplinary care involving intensive care unit, stoma therapist, other specialty services are essential for a better management. The clear goals of the management should be discussed with the patient and the family before offering the surgical option. The choice of procedure needs to be tailored on case-to-case basis. Patients with preserved preoperative health status having normal level of albumin and creatinine, technical feasibility for resection and/ or stoma tend to have better post-operative outcome. The role of further palliative chemotherapy in them needs to be established with further studies. There is a need to explore this option widely with rapid advancements in cancer treatment which is apt in the current world.

Limitations and Biases

Our study has some limitations, the study has only taken the set of patients who underwent

surgery, and there are no data available on comparative group who received only best supportive care. The study has a small number of patients with wide spectrum of primary cancers making it difficult to establish a protocol. A prospective study of selective primary, with a comparison group receiving best supportive care may establish a better management approach.

Author's Contributions

- Bharath Kumar Bhat - conceptualization, methodology, formal analysis, investigation, writing original draft, software, visualization;
- Amitabh Yadav - writing review and editing, visualization, supervision;
- Samiran Nundy - supervision, project administration, writing review and editing, final approval of the manuscript.

Acknowledgment

Miss. Roopa Gopal Poojari - Statistical analysis; Mr. Parmanand Tiwari - Data collection, technical assistance.

Conflicts of Interests and Source of Funding

None.

Ethics Statement

The study is approved by the institutional ethical committee (IEC) under vide no. (EC/08/23/2336). The consent was waivered by the IEC.

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