

The management of obstructive GI cancer: A modern approach

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Introduction

Gastrointestinal obstruction (GIO) is a very serious and life-threatening condition which commonly affects people with abdominal and pelvic malignancies. The pathophysiology of malignant bowel obstruction is often multi-factorial and involves: (a) mechanical block (intraluminal, within the wall or extrinsic compression); (b) post-radiation fibrosis; (c) motility/functional block from malignant involvement of autonomic nerves or intestinal muscle; (d) metastatic deposits (advanced stages); and (e) other factors such as oedema, faecal impaction, fibrosis, fatigues muscle and constipating drugs. Once the gastrointestinal (GI) tract is obstructed it distends proximal to the obstruction, resulting in a blockage of blood supply to the bowel wall which leads to necrosis and perforation with fatal consequences.

The Oxford-educated British physician, Sir William Heneage Ogilvie (1887–1971), stated: “In the acute abdominal emergencies the difference between the best and the worst surgery is infinitely less than between early and late surgery, and the greatest sacrifice of all is the sacrifice of time”. But Ogilvie was a war surgeon, serving in World War I (1914–1918), the Royal Army Medical Corps (1917–1920), World War II (Consulting Surgeon, Major General [1940–1940], East Africa Command [1940–1942], Middle East Land Forces [1942–1944], and Eastern Command [1944–1945]). In circumstances of war we all agree that time and facilities are limited to investigate the differential diagnosis, and optimise treatment management. However this sort of ethos is still prevalent in today’s surgical environment and the quickest option of surgery with minimal investigations is still routinely practised. However, the time has come to revisit the outdated management of GIO, in view of recent advancements in the treatment of critically ill surgical patients and the availability of the state of art diagnostic facilities, such as CT and MRI, to name but two.

The first objective of GIO treatment is to relieve the blockage and decompress the tract proximal to the obstruction, thus resolving the abdominal distention, pain, jaundice, vomiting, and so on. To achieve decompression either for curative or palliation purposes several options are available:

- surgery
- stenting
- laser debulking
- a pure palliative approach: decompression with a NGT, pharmacological intervention (morphine) and hydration.

Before attempting to construct a framework to optimise the treatment plan, it might be useful to define the targets that need to be achieved when dealing with the patient’s condition. The relief of the obstruction is the prime objective, but it might be appropriate to discuss other issues such as quality of life (QoL), and cost effectiveness, which are as important as cancer-related survival. This is because approximately 40–50% of patients with gastrointestinal tumours are not candidates for curative surgery due to locally advanced or metastatic disease [1]. Alternative options therefore must be taken into consideration to strike a balance between an aggressive surgical management for those patients with a more favourable prognosis, and a rational palliative approach for the ones whose life expectancy is limited. The complexity of this decision is further complicated by the urgency of the situation, the lack of time to complete investigations and thorough cancer staging, the lack of scoring tools to predict the operative risk, and the lack of any clinical trial providing hard evidence in favour of any specific treatment plan. On one hand there is a risk of overtreating malignant GIO, while on the other hand, it is unethical not to offer a potentially curative option when feasible.

Although surgical resection and removal of the blockage is the commonly practised treatment option (at the price of a high operative mortality, especially in elderly patients undergoing emergency operations, at times in suboptimal conditions), several pitfalls have

been documented, such as a lack of proof of any QoL improvement, excessively high incidence of stomas (unlikely to be reversed) and lengthy hospital stay.

The following predicaments should be taken into account to justify the lack of knowledge:

- difficulty in defining the nature, site(s), cause(s) and degree of GIO
- problems in staging patients within an urgent context
- personal prejudices to an individual approach
- ethical dilemmas related to patient information and consenting in emergency conditions
- standardisation of treatment
- barriers related to curative and palliative surgery
- definition of outcomes
- QoL appraisal
- pain control
- nutritional aspects

Management decisions for these complex problems are daunting and requires a multi-disciplinary approach (surgery, gastroenterology, traditional and interventional radiology, anaesthesiology, palliative care) to achieve the best possible outcome at the price of minimal morbidity and mortality.

To expand awareness of the pivotal role of surgery even within a palliative context, the American College of Surgeons has recently required palliative care to be included in residency training program and developed a Surgical Palliative Care Task Force of the Division of Education [2]. "The task force was formed to facilitate introduction of the precepts and techniques of the palliative care to surgical practice and education in the United States and Canada. The task force endeavours to meet its goals by bringing together surgeons with demonstrated interest in palliative care to share resources, strategies and expertise, and in so doing, act as a catalyst for change" [3].

Diagnosis and staging

Initial diagnosis is often based on history, clinical examination and baseline investigations such as plain film of the abdomen, which easily reveals intestinal obstruction; however it is very difficult to underpin the real cause of GIO especially in malignancy. The obstruction may simply be due to benign causes such as adhesions, post-irradiation bowel damage, inflammatory disease, hernia etc. Some reports suggest a benign cause is responsible for GIO in 50% of colorectal cancer patients [4]. The small bowel is frequently involved as well, twice as commonly as the large bowel (61% vs 33%), while both are involved in over 20%.

Whatever the cause, GI symptoms are caused by the sequence 'distention-secretion-motor activity'. In the case of large bowel obstruction, every attempt should be made to define the site and number of obstructions, as this information is crucial in both formulating treatment strategy and predicting outcomes. For this purpose single contrast water-soluble enema is an inexpensive and quick investigation that can be performed by a radiographer. However, a CT scan is a better option, as it provides comprehensive information not just on the locality of the tumour but also on the local and distant spread of the disease. Such vital information on the presence or absence of synchronous metastasis (especially liver and lungs) has a direct bearing on the choice of treatment offered i.e. palliative or curative. About 20% of patients with carcinoma of the colon or rectum present with metastatic disease.

Surgeons are frequently asked to consider resection or other operative procedures in these patients for palliation [5]. A radical resection is of utmost importance for local control and prognosis, although T4 lesions of the rectum, and T3 tumours with a close relation to the margin should be considered as locally advanced [6].

However, how useful are imaging techniques in cancer staging? Several studies have been performed to compare MRI and CT in predicting the involvement of nearby structures. As far as rectal cancer is involved, MRI seems to be slightly superior (97% sensitivity, 98% specificity) [7] although CT was shown to be a better modality in predicting muscularis invasion in the lower T stages [8].

Endoscopic ultrasound has also been shown to be a useful diagnostic tool, particularly for rectal tumours as it provides a better T staging. However, the diagnostic work-up has changed in most centres of excellence, as a consequence of the recent advances in FDG-positron emission tomography (FDG-PET). Although FDG-PET cannot show tumour extension, its introduction has led to stage migration as a consequence of the detection of occult metastases. Use of this may alter the diagnosed cancer stage in one out of three patients [9], while this technique found 8% of occult liver metastases [10]. Interestingly, it has been possible to predict the effect of pre-operative chemoradiation with FDG-PET scan, and it is foreseeable that this technique might become an important tool in patient selection, although the European situation is different from North America and its availability is not comparable.

Apart from any interesting academic dissertation, GI obstruction is a surgical condition requiring urgent staging and well balanced treatment planning to

prevent its natural progression into acute peritonitis. Peritonitis on the other hand requires a rapid surgical intervention until and unless the patient is moribund.

Upper GI, biliary, or bowel obstructions represent a common complication in cancer patients. The reported frequency for small or large bowel obstruction ranges from 4% to 42%, depending on the series and site of the primary [11,12].

Histological diagnosis is also of paramount importance. A macroscopically inadequate resection, or a debulking procedure is a futile effort for most solid tumours as this does not change prognosis and causes more harm than good. However, the debulking procedure may be a useful adjuvant therapy if the patient is suffering from a large tumour burden, in the case of rare tumours such as carcinoid tumours [13]. It would be unwise and unethical to deny a surgical resection when a potentially curative operation can be performed. Moreover, even patients with metastatic carcinoids have been reported to be cured by resection of several tumour sites.

Debulking surgery, i.e. removal of part but not all of the tumour, has been advocated by some to decrease symptoms secondary to hormone secretion and relieve intestinal obstruction and ischemia (demonstrated by retrospective analysis of patient records), and prolong survival (less well substantiated). Surgery might be beneficial in prolonging survival if all gross tumour can be removed. Debulking procedures may improve quality but not quantity of life. Because of the potential benefits of surgery in the management of all patients with carcinoid tumours, a surgeon should be part of the team of physicians managing these complex patients [13,14].

Colorectal obstructions

While 10% of patients present with anaemia or bleeding, acute abdominal symptoms are responsible for 40% of the admissions for colorectal cancers at our Trust, and the remaining 50% patients have a mixed presentation. Unfortunately, even after radical surgery and adjuvant chemo/radiotherapy, 8–16% patients will present with recurrent disease [15,16] and most often present with an obstruction. At least 70% of obstructions occur on the left side of the colon, a location that is generally more amenable to colonic endo-luminal stenting [17].

A nihilistic approach is not acceptable in principle, as there is evidence that 25–50% of local recurrences represent limited disease and are amenable to surgical re-excision as proven through surgical and autopsy

studies. Both survival benefit and symptom relief have been shown to be associated with gross disease resection [18]. Therefore, an aggressive resective surgical approach should not be denied, as some authors have shown 25–30% long-term survival rates. However ‘locally advanced cancer’ is defined, a relatively large number of scientific papers advocate a vigorous resective approach based on the results achieved on selected series [19,20].

Nevertheless, a less aggressive approach should also be considered, as only one third of patients with a malignant bowel obstruction from peritoneal carcinomatosis will have prolonged palliation [21]. The majority of patients with locally recurrent rectal cancer will be excluded from consideration of resective surgery based on medical fitness, presence of metastatic deposits, locally unresectable disease, or unwillingness to consider the associated mortality and morbidity. These patients should be offered a comprehensive palliative treatment plan aimed at symptom control.

From the surgeon’s standpoint, therapy is palliative when resection of all known cancer sites is no longer feasible or appropriate. The goal of treatment here is no longer cure, rather symptom control and alleviation of suffering. The process of providing palliative care may be seen as a departure from traditional surgical satisfaction when the malignancy is completely excised, but surgeons excelling in palliative care will likely find this a rewarding endeavour [22].

In summary, CRC may be deemed incurable if [23]:

- the patient declines surgery (otherwise curable)
- the patient is not fit for surgery/general anaesthetics (co-morbidities)
- there is preoperative evidence of locally extensive cancer (R0 status cannot be achieved with resection)
- R0 can be achieved, at the price of extensive operative risk, or injury to abdominal structures
- there is distant metastatic spread (M1)

An alternative approach to surgical resection is managing colorectal obstructions primarily by means of endoscopic stenting or laser debulking [24]. Laser therapy can be used in conjunction with self-expandable metal stent (SEMS) toward recanalisation and decompression. Patients with unresectable disease may be able to avoid surgery altogether and achieve effective and durable palliation. This modality has an excellent risk/benefit profile, and is within the technical grasp of both gastroenterologists and interventional radiologists.

Colorectal stents are also increasingly used for palliation or as a 'bridge to surgery' in obstructing colorectal cancers. A systematic review of the published data on stenting for the treatment of colorectal obstruction was carried out by Khot and co-workers [25]. Technical and clinical success, complications and re-obstruction, both in palliation and as a 'bridge to surgery', were assessed. Technical success was achieved in 92% and clinical success in 88%. Palliation was achieved in 90%, while 85% succeeded as a 'bridge to surgery'. Operative death rate was 1% and perforation was induced in 4% cases. Interestingly, stent migration was reported in 10%, with a re-obstruction rate of 52%. The authors concluded that colorectal stents offer good palliation, and are safe and effective as a 'bridge to surgery', reducing the need for a stoma (especially when emergency surgery is avoided). Increased survival rates were also reported for Stage 4 patients with stenting (3.9 months non-stented vs 7.5 months stented) [26].

The survival advantage, however, was not confirmed when Stage 2–3 patients were treated with a stent (50% vs 48% at 3 yrs, 44% vs 40% at 5 years for surgery vs stenting, respectively), although postoperative complications were significantly lower for the stenting group, and fewer patients had stomas [27].

Endoscopic laser therapy using a neodymium:yttrium–aluminum–garnet (Nd:YAG) laser has been shown to be effective in palliating symptoms of obstruction, bleeding, and discharge in patients with colorectal cancer. Palliative laser therapy often involves multiple treatments over a period of weeks, and does have the advantage of effectively decreasing the occurrence of bleeding. The number of treatments received by each patient can vary (median 3; range 1–20 treatments), with a median interval between treatments of 10 weeks (range 1–25 weeks). Lifelong palliation of symptoms is reported to occur in 70–90% patients. Major complications are perforations and haemorrhage, with an overall complication rate of 4–7%. Procedure-related mortality is usually low in experienced hands (1–3%). In a report from St. George's Hospital, London, UK, the median survival of patients palliated completely by laser therapy was 8.5 (range, 0.6–52) months, with a probability of survival at 24 months of 1%. It was concluded that high-powered diode laser therapy is an effective method of providing palliation for obstruction, bleeding, and discharge in those patients with inoperable colorectal carcinoma. It produces results comparable to therapy with Nd:YAG laser and the equipment is cheaper, more compact, and portable [28].

Operable alternatives can be local or resective procedures. Transanal excision can be considered when advanced tumours preclude a local resection that may be inappropriate in consideration of widespread/unresectable metastases. The target here is to prevent impending obstruction by debulking the tumour or enlarging the channel for faecal passage [23].

Upper GI obstructions

Oesophageal cancer has a 5-year survival rate of 10% [29] and median survival rate cannot be expected to be longer than 6 months from diagnosis, regardless of the therapy [30]. Unfortunately, more than 50% oesophageal cancer patients are inoperable at presentation and progressive dysphagia is the most frequent and disabling symptom [31]. Palliation is achieved either with stenting, laser or brachytherapy [32]. The effects of single dose brachytherapy compare favourably to pure stenting (measures of dysphagia, eating, pain, physical function, global health status, self-related status).

Since surgery has been associated with considerable morbidity and mortality [33], a variety of palliative therapies have been proposed (i.e. radiation therapy, chemotherapy, endoscopic procedures, and their combinations [34].

Endoscopic techniques have proven effective. These include dilatation, laser vaporisation, and stent insertion. Nd:YAG laser therapy is a well established, rapid, and relatively safe method of palliating malignant dysphagia [35]; its major limitation is the frequent need for repeat treatments (median interval 8–12 weeks) [36,37].

Development and continuing improvements in self-expanding metal stents (SEMS) have been popularised (details in the following sections), with high technical success (90–100%) [38,39]. These devices can be inserted through small diameter delivery catheters and, once released, they can expand up to 25 mm in diameter. Significant improvement is achieved in 80–100% patients, at the price of a low complication rate (<3%). Haemorrhage and perforation are among the most serious complications, but there are reports of deployment and expansion problems as well as stent migration, chest pain, tumour over/in-growth, and gastroesophageal reflux).

A limited number of small trials do not allow evidence-based conclusions. For this reason the controversy between laser photocoagulation and stenting is still ongoing. Most recently, a pragmatic trial has

shown no difference in cost-effectiveness between SEMS and non-SEMS therapies; 18-mm SEMS had equal effectiveness to, but less associated pain than, 24-mm SEMS. Rigid intubation was associated with a worse quality of swallowing and increased late morbidity. Bipolar electro-coagulation and ethanol tumour necrosis lead to poor primary palliation. A survival advantage was found for non-stent therapies, but there was a significant delay to treatment. The length of stay accounts for the majority of the costs. A randomised controlled clinical trial of 18-mm SEMS versus non-stent therapies with survival and QoL end-points was advocated, as well as a study of delays in palliative radiotherapy treatment, with a view to implementing cycle-associated change to reduce waiting time [40].

Injection therapy, brachytherapy and bipolar probes are new developments still to be validated. Percutaneous endoscopic gastroenterostomy (PEG) should be mentioned as the last resource allowing enteral nutrition (either under endoscopic or radiological control, when other techniques have failed [41,42].

Similar to oesophageal cancer, most gastric cancer patients present with disease that is too advanced for radical surgery [43] and approximately 80% of the 13,175 gastric cancer patients reported by Hallissey, et al., could not receive a radical resection, with a median survival of less than 2 years [44]. Palliative gastrectomy or gastroenterostomy have often been advocated, and should be considered. The former is advisable for patients with bleeding and obstruction, although the relatively high morbidity and mortality rates and certainly no survival advantage discourage most surgeons from performing a total gastrectomy in asymptomatic patients with advanced systemic disease. The latter is often associated with recurrent and uncontrollable bleeding episodes, hence its real role has not been established. On the other hand, the data from the Birmingham Cancer Registry has shown how the 30-day mortality was significantly less for patients receiving palliative resection or by-pass surgery, and survival was significantly improved.

Confirmatory data from the Dutch Gastric Cancer Trial confirm a survival advantage for resected patients with less than two metastatic sites [45]. One could speculate that surgical resection may be the most appropriate method of palliation, however the patient's general conditions, his/her willingness to undergo surgery, and the extent of systemic spread must be taken into account.

When dealing with antro-pyloric strictures, endoscopic stenting has been shown to be superior to gastroenterostomy in a randomised trial. A shorter

hospital stay, shorter length of the procedure and time to oral intake and gastric emptying favouring a non-surgical management [46].

Malignant jaundice

Only 10% to 20% of pancreatic tumours are resectable at the time of diagnosis. Patients with advanced disease have a median survival of 4.9 months. Palliation is often required for biliary or duodenal obstruction, or both.

More than two-thirds of pancreatic cancers arise in the head of the pancreas, at the level of the intrapancreatic portion of the common bile duct. Hence, at the time of diagnosis jaundice is present in 70–80% of patients, while 90% of bile duct malignancies present with obstructive jaundice.

Ultrasound initially is considered the diagnostic modality of choice. Several other imaging techniques commonly used for diagnostic purpose include contrast enhanced spiral CT, MRI and MR cholangio-pancreatography (MRCP), endoscopic ultrasound (EUS), percutaneous transhepatic cholangiography (PTC) and intraductal ultrasound (IDUS). After a diagnosis is reached, a combination of these techniques is useful in appraising the extent of spread (duodenal invasion, vascular involvement, nodal involvement, liver metastases, carcinomatosis and ascitis) and resectability of the lesion. The role of preoperatively staging laparoscopy and laparoscopic ultrasound is still hotly debated as the real impact in sparing patients unnecessary laparotomy for an unresectable disease is as yet not established.

Optimal palliation should guarantee the shortest possible hospital stay and an acceptable survival period with a good QoL. In recent years, treatment options for palliation of biliary and duodenal obstruction due to pancreatic cancer have broadened. Endoscopic and percutaneous biliary stenting have been shown to be successful tools for safe palliation of high-risk and older patients. Nevertheless, fit younger patients with unresectable pancreatic cancer benefit from surgery, which allows long-lasting biliary and gastric drainage. While laparoscopic cholecystojejunostomy and gastroenterostomy in patients with advanced pancreatic cancer have been widely used, laparoscopic hepaticojejunostomy is also feasible [47]. A randomised phase III trial comparing open cholecystoenterostomy vs choledochoenterostomy (for malignant as well as benign disease) seemed to favour the latter technique, in view of higher post-operative complication rate, increased drainage failure and higher recurrence of jaundice [48].

Palliative management concentrates primarily on symptom relief of biliary and duodenal obstruction, as well as pain. The treatment chosen is influenced by several factors: severity of symptoms, overall health status of the patient, expected survival rate, and mortality/morbidity of the chosen procedures. The expected survival is difficult to predict: distant metastases, pre-op endocrine insufficiency, low Karnofsky score, pain, weight loss, tumour size >30 mm have been associated with a decreased survival rate. Terwee, *et al.* [49] developed a prognostic score chart that can be used to select patients with relatively low expectation of survival for endoscopic palliation, and patients with relatively high expectation of survival for surgical palliation.

Initial relief of jaundice is best achieved with endoscopic stenting (plastic stents if survival is <6 months; otherwise metallic stents). Surgical biliary decompression in the form of hepaticojejunostomy should only be attempted when endoscopic or radiological stenting fails. The preferred method for a surgical by-pass of the gastro-duodenal stricture is a simple gastro-jejunostomy. If a laparotomy is undertaken, chemical splanchnicectomy is recommended for pain control. Prophylactic gastric by-pass only has a historically relevance [50,51]. In summary, malignant jaundice has three main targets: relief of biliary obstruction, relief of duodenal obstruction and pain control. Endoscopic stenting accomplishes relief of obstructive jaundice, but patients with an expected longer life expectancy (>6 months) should be considered for surgical palliation. If a laparotomy is undertaken, a double bypass along with chemical splanchnicectomy achieves excellent palliation for both obstruction and pain. Prophylactic gastric by-pass is not advisable in the initial non-surgical decompression [52].

Palliative medical management

During the last two decades, evidence has been accumulated to support a correlation between the duration of survival with measures of health-related QoL; hence, health care professionals should focus on physical indicators such as nausea, dyspnoea and weakness. Psychosocial distress does not appear to have negative impact on survival; however, future studies should clarify the prognostic significance of 'positive attitudes', such as hope and optimism, in patients with advanced cancer [52].

When survival cannot be expanded, health carers should focus on its quality. QoL indicators should be assessed and monitored. Indicators such as nausea,

vomiting, dyspnoea and weakness will help gathering prognostic clues in patients with terminal cancer. These symptoms may reflect consequences of cancer cachexia and the progress of patients toward this terminal syndrome.

Proper and adequate pain control is an outcome that is increasingly expected by both the patient and relatives. First line treatment is usually oral opioids (morphine or diamorphine in the UK), which may also relieve colic. Fears regarding addiction and liability related to narcotic prescription are unfounded in the context of palliative care. The dose of analgesic has to be titrated for each individual patient until pain relief is achieved, as proposed by the Working Group of the European Association for Palliative Care [53]. Second line medications, when opioids fail to relieve the pain, are amitriptyline or gabapentin for neuropathic pain taken by mouth.

If colic persists, hyoscine butylbromide or hyoscine hydrobromide should be added [54]. Hyoscine butylbromide has low lipid solubility and unlike atropine and hyoscine hydrobromide, does not cross the blood-brain barrier hence it does not cause somnolence and hallucinations.

Epidural catheter placement may allow more effective pain control in selected patients. Finally, neuroablative techniques (i.e. cordotomy to block pain transmission through the spinothalamic tract of the spinal cord) may be considered for patients with the most refractory conditions.

Artificial hydration aims to correcting dehydration-related symptoms. Unfortunately, a high level of intravenous hydration may result in an excess of bowel secretion [55], hence a careful balance should be kept between efficacy of the treatment and side effects.

Conclusions

The role of surgery in malignant GI obstruction remains controversial, and no firm conclusion can be made from retrospective series. Careful evaluation is needed with the use of validated outcome measures.

This Educational Symposium aims to highlight the risk of targeting cancer-related survival, rather than using a holistic approach including symptom control and QoL.

The following articles within this section will discuss some of these options in greater detail, bearing in mind that QoL is as important as any increase in survival. There is definitive evidence that QoL can be monitored; these findings should be recorded and clearly reported [32].

The complexity of gastrointestinal obstruction requires multimodal management, where all treatment options are taken into consideration, and the treatment is specifically tailored accordingly following a multidisciplinary discussion. An extensive discussion with the patient, family and friends of options available is mandatory.

Few studies compare alternative management of GIO, hence no evidence-based guidelines can be drafted; moreover, the variables involved in comparative studies are numerous, and quantifying risks and benefits is almost impossible.

The lack of hard data regarding the management of this frequent medical condition is not likely to expand through prospective trials, given the circumstances of the acute setting.

This Educational Symposium is also intended to promote homogenisation of standards in reporting on management of GI obstructive series. We advocate the addition of the following information:

- clear pre-treatment definitions of the site and number of obstructions
- adequate staging
- short-term outcomes such as 30-day mortality/morbidity, length of hospitalisation, time to and persistence of symptom improvement, patient involvement and priorities and multimodal management

This will allow a meaningful comparison between series and improve our management of GI obstructions.

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