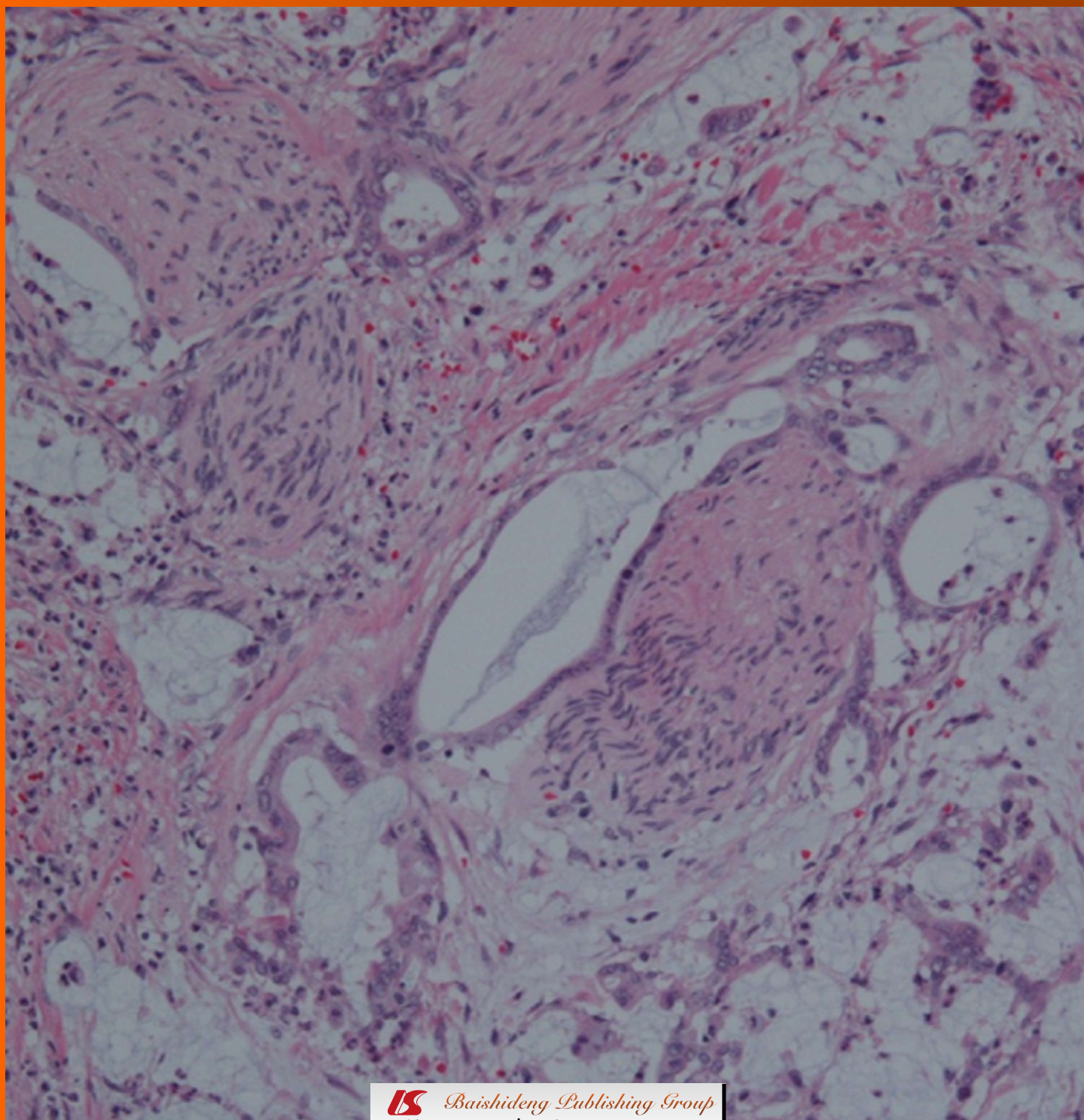


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Emergency laparotomy in octogenarians: A 5-year study of morbidity and mortality

Gemma Green, Irshad Shaikh, Roland Fernandes, Henk Wegstapel

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Author contributions: Green G and Shaikh I are joint first authors and contributed equally to this work; Green G collected and analysed data, drafted manuscript; Shaikh I conceived idea of study; Fernandes R collected data; Wegstapel H supervised study. Correspondence to: Dr. Irshad Shaikh, Department of Colorectal Surgery, Medway Maritime Hospital, Windmill Road, Gillingham, UK ME7 5NY, United Kingdom. i.shaikh@nhs.net

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Abstract

AIM: To determine the morbidity and mortality associated with emergency laparotomy for a clinically acute abdomen in patients aged ≥ 80 years.

METHODS: In this retrospective audit, octogenarians undergoing emergency laparotomy between 1st January 2005 and 1st January 2010 were identified using the Galaxy Theatre System. Patients undergoing abdominal surgery through groin crease incisions or Lanz or Gridiron incisions were excluded. Also simple appendectomies were excluded. All patients were aged 80 years or more at the time of their surgery. Data were obtained using casenote review with a standardised proforma to determine patient age, American Society of Anesthesiologists (ASA) grade, indications for surgery, early (within 30 d) and late (after 30 d) complications, mortality and length of stay. Data were inserted into a Microsoft Excel spreadsheet and analysed.

RESULTS: One hundred patients were identified from the database (Galaxy) as having undergone emergency laparotomy. Of those, 55 underwent the procedure for intestinal procedures and 37 for secondary peritonitis.

There was a 2:1 female predominance; average age 85 and ASA grade 3. Bowel resection was required in 51 out of the 100 patients and 22 (43%) died. Other procedures included appendicectomy, adhesiolysis, repair of AAA graft leak and colostomies for the pathological process resulting in an acute abdomen. Twelve of 100 patients (12%) suffered intra-operative complications, including splenic and bowel-serosal tears. Seventy patients (70%) had postoperative complications including myocardial infarction, wound infection, haematoma and sepsis. Overall mortality was 45/100 patients (45%). The major causes of death were sepsis (19/45 patients, 42%), underlying cancer (13/45 patients, 29%); with others including bowel obstruction (2/45 patients, 4%), myocardial and intestinal ischaemia and dementia.

CONCLUSION: Emergency laparotomy in octogenarians carries a significant morbidity and mortality. In particular, surgery requiring bowel resection has higher mortality than without resection.

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Key words: Laparotomy; Perioperative care; Aged; Mortality; Morbidity

Core tip: Aging is associated with an increase in operative and anaesthetic risk during emergency laparotomy. Literature addressing the outcomes following emergency laparotomy in the elderly is limited. The morbidity and mortality rates in this subgroup of patients were explored, and in our study we determined the mortality rate to be 45%.

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INTRODUCTION

An aging United Kingdom population has led to an increase in the number of emergency general surgical admissions in octogenarians; indeed 8739 patients over the age of 75 required emergency laparotomy in 2010-2011^[1]. This has significantly increased from 4486 patients in 2001 reflecting the increased life expectancy of today's population, with the average person living to 80 years compared with 74 years in 1983^[2].

Laparotomy is a major intervention. Given that it is a considerable surgery to undertake it is not surprising that laparotomy is associated with significant morbidity and mortality, especially in the emergency setting, with current literature quoting mortality figures of 10%-55%^[3-5].

Elderly patients present a higher risk for abdominal surgery owing to an increase in the number and severity of medical co-morbidities which may add to the complexity of both surgery and anaesthesia. The aging cardiovascular and immune systems predispose elderly patients to increased postoperative infection and cardiovascular events such as stroke, myocardial infarction and venous thromboembolism. Also older patients have a reduced physiological reserve to cope with longstanding hypotension secondary to anaesthesia and blood loss during surgery; and may take considerably longer to recuperate postoperatively although recent studies and scoring systems show that this is very subjective and that many older patients recover well postoperatively and return to function as well as their peers^[6,7].

MATERIALS AND METHODS

In this 5 year retrospective study, patients undergoing emergency laparotomy for intestinal conditions or secondary peritonitis between 1st January 2005 and 1st January 2010 were identified using the galaxy theatre management system used at Medway Maritime Hospital NHS trust (Galaxy Theatre System, Sanderson Ltd, 1-2 Venture Way, Aston Science Park, Birmingham, United Kingdom). Patients included in the study were those who were aged 80 years or over at the time of their operation. Laparoscopy alone without subsequent conversion to laparotomy and procedures involving inguinal incision for hernia repair were excluded from the study, as were other procedures such as simple appendicectomy if performed by Lanz incision. Medical records for the remaining relevant patients were sought and reviewed individually using the pro-forma shown in Figure 1. The American Society of Anesthesiologists (ASA) grade was determined from the anaesthetic pre-operative assessment chart and is shown in Table 1. Data was inserted into a spreadsheet and analysed using Microsoft Excel software.

RESULTS

Overall, 100 patients underwent emergency laparotomy for abdominal pathology between 1st January 2005 and 1st January 2010. Eight additional patients were excluded

from the study as these patients underwent laparoscopy, and local approaches for hernia repair rather than a mid-line laparotomy incision.

Patients

Data was collected from 100 patients who underwent emergency laparotomy between 1st January 2005 and 1st January 2010, all of whom were 80 years or over at the time of surgery. Overall, the mean age was 85 years (range 80-96 years); 2:1 female predominance and mean ASA grade of 3.08 (range 1-5).

Indications for surgery

The indications for surgery and their corresponding patient numbers are shown in Table 2. Thirty seven of 100 patients underwent laparotomy for secondary peritonitis; of which 14/37 had lower gastrointestinal (GI) perforation including perforated diverticulitis and perforated appendicitis; 16/37 had upper GI perforation including perforated gastric and duodenal ulcers; and the remaining 7/37 had perforation of unknown or undocumented site. Twenty of 37 patients died, of which 10/37 had a upper GI perforation, and 9/20 had lower GI perforation. There was no statistically significant difference in mortality by the site of perforation.

Laparotomy to relieve colonic obstruction secondary to malignancy or adhesions was performed in 40/100 patients. The mortality in this group of patients was 17/40 patients (42.5%).

The mortality by indication for surgery is shown in Figure 2.

Procedures

Bowel resection was required in 51/100, patients with the main indication being malignancy, or ischaemia of the bowel secondary to adhesions. Of the 51 patients requiring bowel resection, 23/51 died (mortality 45%). Thirty one of 51 patients required bowel resection secondary to obstruction, with a mortality of 13/31 (42%). Seventeen of 51 patients required bowel resection from the complications of GI perforation and secondary peritonitis. Of these patients, 14/17 had lower GI perforation (*i.e.*, perforated diverticulitis) and 2/17 had upper GI perforation. No patients undergoing laparotomy for peptic ulcer perforation required resection. Nine of 17 patients with secondary peritonitis died, giving a mortality of 53%.

Mortality

The overall mortality for emergency laparotomy in octogenarians in this study is 44/100 (44%). There is a 2:1 female predominance. Sepsis represented the most frequent cause of death (19/45 patients, 42%), closely followed by death due to the underlying disease process, chiefly colonic cancer (12/45 patients, 27%). Other causes were myocardial infarction (2/45 patients, 4%), cerebrovascular disease (2/45 patients, 4%), death due to medical co-morbidities such as exacerbation of chronic

Name: _____
 Age: _____
 PAS: _____
 Diagnosis: _____
 Date of operation: _____
 Operation: _____
 ASA: _____
 Pre-op complications: _____
 Intra-op complications: _____
 Post-op complications: _____
 Date of admission: _____
 Date of discharge: _____
 Date of death: _____
 Cause of death: _____

Figure 1 Proforma for data collection.

Table 1 American Society of Anesthesiologist's pre-operative risk classification

ASA grade	Description
I	Normal healthy patient
II	Mild systemic disease – no functional limitation
III	Severe systemic disease – definite functional limitation
IV	Severe systemic disease which is a constant threat to life
V	Moribund patient who is unlikely to survive > 24 h with or without surgery

Reproduced from^[8]. ASA: American Society of Anesthesiologist.

airways disease (4/45 patients, 8%). Two of 44 (4%) patients died due to ischaemic bowel postoperatively and 2/44 patients (4%) had an unknown cause of death. One further patient was deemed to have died of inanition and dementia. Pictorial representation of mortality by cause of death is shown in Figure 3.

Sepsis represented 42% of the mortality. There were 2 sources of infection in these patients: 8/19 (42%) patients had abdominal sepsis and 8/19 (42%) had respiratory sepsis. The remaining 3/19 (16%) had sepsis of unknown origin.

The survival curve shown in Figure 4 shows that procedure associated mortality occurs early, with 50% of deaths occurring within 2 wk of surgery. The majority of patients who leave hospital following laparotomy survive more than 30 d. Twelve of 44 (27%) patients died following discharge from hospital, all of these deaths were unrelated to the operation but to the underlying illness or to unrelated acute problems which occurred more than 1 year later.

Twelve of 100 patients (12%) suffered intra-operative complications, including splenic and bowel-serosal tears, and abandonment for futility. Seventy patients (70%) had postoperative complications including myocardial infar-

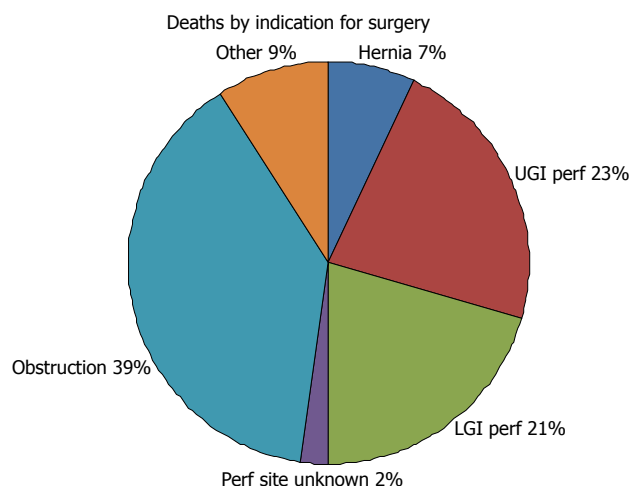


Figure 2 Absolute mortality by indication for surgery (excel chart). UGI: Upper gastrointestinal; LGI: Lower gastrointestinal tract.

tion (4/70, 5%), wound infection (6/70, 7.5%) and sepsis (32/70, 46%) which was largely of respiratory origin. Multi-organ failure occurred in 2 patients (2.5%). Other complications include cardiovascular problems including atrial fibrillation (AF) and congestive cardiac failure (8/70, 10%). The other causes of morbidity making up the remaining 39% included cardiovascular accident (CVA), scrotal oedema, stoma problems, rectal bleeding and acute renal failure.

Cost analysis

On average emergency laparotomy costs £10000 per patient, giving a total surgical cost for our cohort of £100000. Added to this the average length of stay was 27 d (range 1-192 d). Our patients on average spent 3 d in critical care. The cost of a critical care stay for 3 d is £4200 and the cost per day for an national health service (NHS) bed is £400. So the average cost of an emergency laparotomy per patient assuming 27 d stay with 3 d critical care admission is £23800. This gives a total cost for our cohort of £238000. Forty four percent of these patients died (*i.e.*, a loss of £104720) which limits the cost effectiveness of this procedure and highlights the importance of patient selection in terms of cost effectiveness and productivity.

DISCUSSION

A change in United Kingdom demographics has lead to an increasingly elderly population and prompted increased demand for acute surgical care in octogenarians^[9]. The catchment population of Medway Maritime hospital is generally of low socioeconomic status^[10], and patients tend to present to hospital late with extensive surgical disease and multiple medical and social co-morbidities. Given their poor physiological reserve for extensive surgery and anaesthesia, the decision to treat these patients operatively must be undertaken with extreme care and consideration; and must take into account the patient's

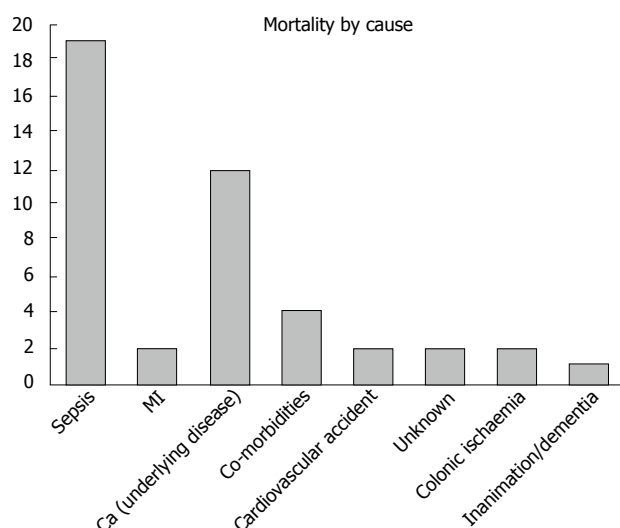


Figure 3 Bar chart depicting mortality by cause of death (excel chart).

s future quantity and quality of life and the health beliefs of patients and their relatives. Additionally in today's age of austerity surgeons are also urged increasingly to consider cost implications of emergency surgery in patients with a potentially limited prognosis^[11]. Thus the indications for surgery in this age group are often limited. Trends in management of elderly patients are inconsistent; previously there was a tendency towards conservative or palliative management of these patients, however with newer techniques and increased patient expectations these opinions are shifting towards increasingly operative intervention^[12].

Studies have shown that the number of octogenarians requiring admission to acute surgical wards and ICU beds has been increasing. Reiss *et al* showed 7.5% of general surgical admissions in their series were aged 80 years or over, and more recently a 5 year study in Bath showed that 8.8% of admissions to intensive care unit (ICU) in 5 years were in elderly patients and a Turkish study done in 2002 showed 19% of cases in their series to be aged over 80 years^[9,12,13].

Mortality rates in octogenarians have been documented as between 10% and 55%, with an increased risk in emergency as opposed to the elective setting^[3]. We show a mortality rate for emergency laparotomy only of 44% which is in keeping with previous studies. There is limited literature documenting morbidity data in the group of patients in our study. We show a morbidity rate of 70% within 30 d of operation. Mortality and morbidity are often inextricably linked and therefore may lead to increased numbers seen. 25/44 patients who died had morbidity postoperatively, however 12 of these had complications completely unrelated to their abdominal pathology such as hypertensive episodes, exacerbations of chronic obstructive pulmonary disease (COPD) and angina.

Surgical treatment of secondary peritonitis; which can be defined as the localized equivalent of the systemic inflammatory response within the peritoneal cavity secondary to contamination from another process for

Table 2 Indications for surgery

Indication for surgery	Number of patients
Hernia	12
Secondary peritonitis	37
Colonic obstruction	40
Leaking colonic anastomosis	1
Aorto-bifemoral graft removal	1
Intra-abdominal bleeding	1
Bowel ischaemia	5
Pseudo-obstruction	1
Colo-vesical fistula	1
Abdominal aortic aneurysm repair	1

example bacteria from colonic perforation or chemical from pancreatic enzyme leakage, is documented to have a significant morbidity and mortality studies show there is a direct link between the age of the patient and the risk of severe sepsis^[13-16]. We show that mortality is 53% in secondary peritonitis, which is not significantly higher than in obstructive indications for laparotomy. There is no significant difference in mortality if the location of the perforation is in the upper or lower GI tract.

Postoperative mortality in our study can be seen to occur most commonly within the first 2 wk and during the initial surgical admission. Death later following discharge is from unrelated causes such as acute MI or dementia, and therefore the immediate postoperative care of these patients is of high importance, as most patients who are discharged from hospital recuperate and there is a relatively low mortality following successful discharge.

A high preoperative ASA grade (3-5) of patients, suggesting significant medical co-morbidity preoperatively, was unsurprisingly seen to be associated with increased operative complications and a higher risk of perioperative death. Tan *et al*^[17] demonstrated a similar conclusion in trauma patients from the Auckland registry, by showing that key comorbidities taken from the APACHE 2 score which include cirrhosis, severe heart failure (NYHA IV), severe COPD, dialysis patients and the immunosuppressed have an increased mortality regardless of age. In our cohort these patients are represented by those with ASA 5 (life threatening illness) and all of these patients died, regardless of their age. However survival and mortality rates were of a similar proportion of those of ASA grades 3 and 4, which still represent severe comorbidity, and the mean ages of those who survived and died were equal. This suggests comorbidity rather than age is important in predicting mortality and is in agreement with the findings in the aforementioned study.

The high incidence of sepsis postoperatively may demonstrate that elderly patients are at increased risk of infection due to an aging immune system, reduced physiological reserve, and high incidence of polypharmacy. Sepsis in our patients had either a urinary or respiratory source; which may reflect poor respiratory function postoperatively from an aging respiratory tract, poor analgesia and the increased use of catheters and urinary incontinence in this age group. It may also suggest poor

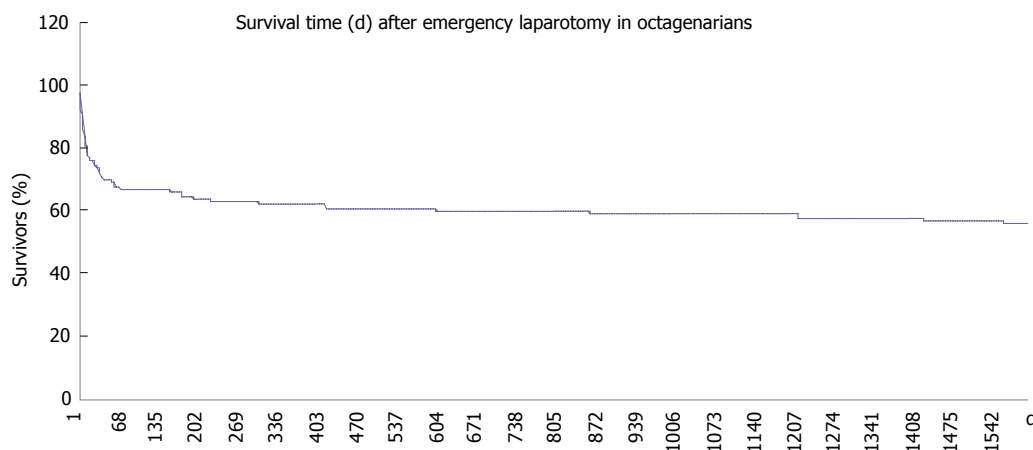


Figure 4 Survival post emergency laparotomy.

hydration and nutrition in these frail patients, although this should be correlated with the admission and post-operative malnutrition universal screening tool scores, a tool developed by the British Association of Parenteral and Enteral Nutrition in order to assess patients nutritional status^[18]. An objective study to determine quantitatively the effect of malnutrition on octogenarians undergoing emergency abdominal surgery may be an area for further study development.

Given the high risk nature of this group of patients, a multidisciplinary approach to care may be most appropriate in order to optimize patient care. This may involve elderly care physician input, dieticians, physiotherapists and occupational therapists alongside the general surgical team. This would allow optimisation of co-morbid conditions, optimize postoperative functioning and nutrition and allow prompt and safe discharge to an appropriate environment. This arrangement has already been established in orthopaedics in the care of elderly patients with femoral neck fractures and is well documented by the national hip fracture database^[19]. These orthopaedic patients are essentially in a similar position to the patients in our study; they are elderly patients with acute surgical problems.

In a conclusion, emergency laparotomy is a procedure which is well recognized to carry significant intra- and postoperative risk; and one which is not undertaken lightly by surgeons. The decision to operate in octogenarian patients is difficult and requires careful consideration of the patient's pre-morbid condition and counselling of both patients and relatives; thus highlighting the importance of patient selection^[20]. It has been shown that the seniority of both the anaesthetist and operating surgeon influences mortality, hence elderly patients should receive consultant led anaesthetic and surgical care on an appropriate emergency list at a reasonable time of day^[3]. Guidelines for the care of the elderly postoperative patient following extensive surgery are currently not routinely used and may be of significant use to medical and nursing staff untrained in elderly care, and therefore we recommend that these be put in place.

COMMENTS

Background

Ageing is associated with increases in operative and anaesthetic risk during emergency laparotomy. Literature concerning the outcomes following emergency laparotomy in the elderly is limited.

Research frontiers

Many scoring systems exist to aid the surgeon and anaesthetist in determining preoperative risk, such as the American Society of Anesthesiologists (ASA) score, POSSUM and APACHE scores but these are of limited use in older patients or in the emergency setting. The decision to manage operatively or conservatively is very important and poses many difficult ethical and moral problems. Future quality and quantity of life in patients, whether undergoing surgery or not, is subjective and unpredictable therefore preoperative counselling of patients and relatives is highly important

Innovations and breakthroughs

Emergency laparotomy is a topic of major concern to both surgeons and managers alike. The high complication risk may lead to longer hospital stays and prove a costly procedure for trusts. Current literature concerning patients over 80 years old and the outcomes following their surgery is lacking and therefore we undertook this project in order to fully evaluate this potentially dangerous subgroup of patients, and add to the current literature to guide clinical decision making.

Applications

Current literature is lacking for octogenarian patients, therefore this study was undertaken in order to guide healthcare professionals in the decision making process and management of elderly patients with acute abdominal surgical problems.

Peer Review

The topic was reviewed as being clinically relevant, and was comparative with previous literature as described in trauma patients.

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P- Reviewer Mittal AS- Editor Wen LL L- Editor A
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An 81-year-old gentleman with symptomatic Bochdalek hernia

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Abstract

An 81-year-old gentleman with congenital polycystic kidney disease presented to his primary care physician with dysphagia, gastroesophageal reflux refractory to medical management, and 11.25 kg weight loss in a 6 mo-period. A barium swallow misdiagnosed a paraesophageal hernia for a Bochdalek hernia. Herein, we highlight how a Bochdalek hernia may be disregarded in the differential diagnosis and how providers can resort to a more common diagnosis, a paraesophageal hernia, which is more frequently encountered in old age and whose radiologic appearance might mimic a Bochdalek hernia.

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Key words: Polycystic kidney disease; Paraesophageal hernia; Bochdalek hernia; Diaphragmatic hernia; Diaphragmatic hernia repair

Core tip: Bochdalek hernias are seldom encountered in elderly patients. Hence, our goal is to briefly shed light on this less common hernia of the diaphragm and highlight its diagnosis and current treatment options, which are very different from that of a paraesophageal hernia, a common misdiagnosis.

Rajput MZ, Fisichella PM. An 81-year-old gentleman with symptomatic Bochdalek hernia. *World J Gastrointest Surg* 2013; 5(7): 222-223 Available from: URL: <http://www.wjgnet.com/1948-9366/full/v5/i7/222.htm> DOI: <http://dx.doi.org/10.4240/wjgs.v5.i7.222>

INTRODUCTION

Congenital diaphragmatic defect, a hernia of Bochdalek, is a rare defect resulting from the failure of the postero-lateral diaphragmatic folds to fuse *in utero*^[1]. While often devastating in neonates who present with life-threatening respiratory distress, these hernias may occasionally remain asymptomatic, and the defect will not be recognized until later in life. Typical symptoms of a Bochdalek hernia include abdominal pain, dyspnea, gastroesophageal reflux, nausea, and vomiting^[1,2]. On physical exam, patients may exhibit diminished breath sounds and presence of bowel sounds in the chest^[3]. However, many patients remain asymptomatic, and the diagnosis is made only incidentally through routine imaging for other reasons. Moreover, polycystic kidney disease may be considered as indicator of a soft tissue disease with enhanced risk for hernias. The incidence of late-onset Bochdalek hernias has not been clearly determined, although reported rates range from 0.17% to as high as 12.7%^[4,5]. Symptomatic patients are typically males with left-sided defects^[3].

Frontal and lateral radiographs of the chest may demonstrate loops of bowel with air fluid levels in the chest with concomitant elevation of the hemidiaphragm; however, it may be difficult to appreciate the presence of a hernia on plain films, especially with coexisting thoracic pathology, such as atelectasis, consolidation, or an anterior mediastinal mass^[6]. Moreover, chest radiographs may reveal no abnormalities despite the presence of the defect, particularly if the herniation is intermittent and the patient is asymptomatic. As a result, chest computed tomography (CT) scan is considered the test of choice to confirm the diagnosis^[7]. A barium swallow can also be an



Figure 1 Barium swallow showing a left sided Bochdalek hernia with herniated gastric fundus.

adequate diagnostic test, as in the case herein presented, which was initially incorrectly diagnosed in another hospital as a paraesophageal hernia.

CASE REPORT

An 81-year-old gentleman with congenital polycystic kidney disease presented to his primary care physician with dysphagia, gastroesophageal reflux refractory to medical management, and 11.25 kg weight loss in a 6 mo-period. After an upper endoscopy ruled out any organic abnormalities, he underwent a barium swallow, which is shown in Figure 1. Subsequently the patient was referred to our center for treatment of a paraesophageal hernia, although the barium swallow clearly demonstrates a Bochdalek hernia. As Bochdalek hernia is seldom encountered in patients in their 80s, the health care providers disregarded this eventuality in his differential diagnosis and resorted to a more common diagnosis, a paraesophageal hernia, which is more frequently encountered in old age and whose radiologic appearance might mimic a Bochdalek hernia. Hence, our letter has the goal to briefly shed light on this less common hernia of the diaphragm and highlight its diagnosis and current treatment options, which are very different from that of a paraesophageal hernia.

DISCUSSION

Although there are no well-established indications for surgery, given the risk of incarceration and strangulation, repair of the hernia is advised regardless of symptomatology^[3]. Traditionally, surgery has been performed either via laparotomy, particularly in the emergency setting, or thoracotomy, which is often the approach of choice

in chronic hernias due to the dense adhesions of the herniated stomach in the chest^[1]. Minimally-invasive techniques, particularly thoracoscopy, may also be utilized; thoracoscopy provides the surgeon excellent visualization of the herniated viscera and eases the difficulty in lysing adhesions to the thoracic cavity^[1,7,8]. Interrupted, nonabsorbable sutures are typically used in the repair with mesh placement in larger defects^[1,3]. Both open and minimally invasive approaches have yielded excellent results with no reported recurrences found among the literature^[3]. Our patient underwent a left thoracotomy with lysis of dense adhesions along the fundus of the stomach and reduction of the herniated viscus back into the abdomen. The diaphragmatic defect was repaired with an oval-shaped Gore-Tex, DualMesh patch. The patient was discharged home on post-operative day 5 with complete resolution of his symptoms and no recurrence on follow-up imaging. At one year, he is doing well.

In summary, although rare, a hernia of Bochdalek may need to be considered in the differential diagnosis for patients in the old age who have foregut symptoms. A careful and unbiased interpretation of radiologic tests is essential to recognize the disease and perform the correct operation.

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P- Reviewer Klinge US- Editor Zhai HH L- Editor A
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Reconstruction of the hepatic artery with the middle colic artery is feasible in distal pancreatectomy with celiac axis resection: A case report

Hideki Suzuki, Yasuo Hosouchi, Shigeru Sasaki, Kenichiro Araki, Norio Kubo, Akira Watanabe, Hiroyuki Kuwano

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Abstract

Despite the advance of diagnostic modalities, carcinoma in the body and tail of the pancreas are commonly presented at a late stage. With unresectable lesions, long-term survival is extremely rare, and surgery remains the only curative option for pancreatic cancer. An aggressive approach by applying extended distal pancreatectomy with the resection of the celiac axis may increase the resectability and analgesic effect but great care must be taken with the arterial blood supply to the liver and stomach. Sometimes, accidental injury to the pancreaticoduodenal artery compromises collateral blood flow and leads to fatal complications. Therefore, knowledge of any alternative restoration of the compromised collateral flow before surgery is essential. The present case report shows a patient with a pancreatic body cancer in whom the splenic, celiac, and common hepatic arteries were involved with the tumor, which extended almost to the root of the gastroduodenal ar-

tery. We modified the procedure by reanastomosis between the proper hepatic artery and middle colic artery without vascular graft. The postoperative course was uneventful, and the patient was discharged on postoperative day 19. The patient was immediately free of epigastric and back pain.

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Key words: Pancreatic body-tail cancer; Celiac artery resection; Arterial reconstruction

Core tip: The present case report shows a patient with a pancreatic body cancer in whom the splenic, celiac, and common hepatic arteries were involved with the tumor, which extended almost to the root of the gastroduodenal artery. We modified the procedure by reanastomosis between the proper hepatic artery and middle colic artery without vascular graft.

Suzuki H, Hosouchi Y, Sasaki S, Araki K, Kubo N, Watanabe A, Kuwano H. Reconstruction of the hepatic artery with the middle colic artery is feasible in distal pancreatectomy with celiac axis resection: A case report. *World J Gastrointest Surg* 2013; 5(7): 224-228 Available from: URL: <http://www.wjgnet.com/1948-9366/full/v5/i7/224.htm> DOI: <http://dx.doi.org/10.4240/wjgs.v5.i7.224>

INTRODUCTION

Carcinoma of the body of the pancreas is often discovered at an advanced stage by reason of lack of symptoms. Because the only long-term survivors of cancer of the pancreatic body have been those who have undergone resection, complete surgical resection is the only treatment that may lead to a prolonged survival^[1]. However, the

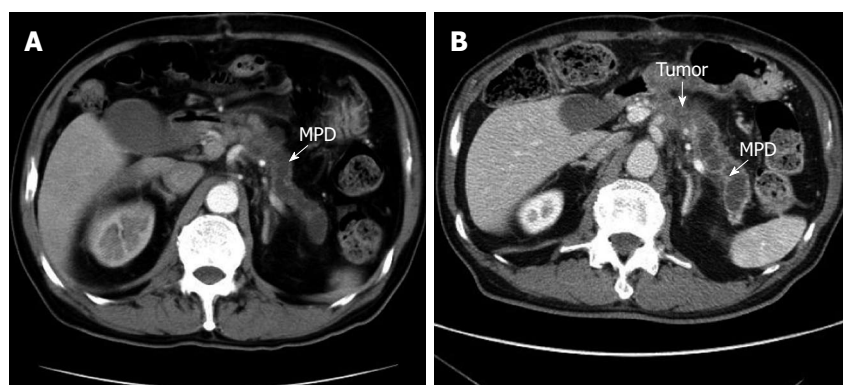


Figure 1 Computed tomography scan demonstrating the dilatation of the main pancreatic duct (A) and a tumor of the pancreatic body which invaded the celiac artery after the abdominal aortic aneurysm operation (B). MPD: Main pancreatic duct.

resection rate is low, and chances for resection are often lost to distant metastasis, regional invasion into adjacent organs, or the involvement of major vessels. Tumor involvement of the common hepatic artery (CHA) and/or celiac axis (CA) is a primary reason for this. Several high-volume pancreatic centers have reported that advanced pancreatic body/tail carcinoma can be safely treated by left-sided pancreatectomy with en bloc resection of infiltrated major vascular structures^[2]. These methods were supported by the reported prognosis of the patients, which seems to be similar to that in patients without resection of major vascular structures^[3].

Hirano *et al.*^[4] reported that, in patients who underwent distal pancreatectomy with en bloc celiac axis resection (DP-CAR), the surgical margins were histologically clear in 95% of patients and the postoperative mortality rate was 0%, despite a high morbidity rate (48%). The estimated overall 1- and 5-year survival rates were 72% and 17%, respectively, and the median survival was 21 mo. Moreover, radical distal pancreatectomy with en bloc resection of the celiac artery, celiac plexus, and celiac ganglions is reported to provide patients with locally advanced cancer of the pancreatic body with complete and enduring pain relief^[5]. Therefore, radical surgery is justifiable in patients with advanced cancer of the pancreatic body, even when it has invaded adjacent major vessels, such as the celiac artery and/or the portal vein. When performing DP-CAR surgery, it is essential to preserve the arterial blood supply to the stomach and liver. The arterial blood supply during this procedure is maintained by the collateral pathways *via* the pancreatoduodenal arcades from the superior mesenteric artery to the gastroduodenal and hepatic arteries, which develop immediately after ligation of the celiac artery^[6]. However, there are some cases in which the gastroduodenal artery arises from the area close to the CA. In such a situation, it would be difficult to preserve the gastroduodenal artery during DP-CAR surgery. In addition, the effort to preserve the gastroduodenal artery during surgery introduces risk of injury. In this case, we performed DP-CAR with reconstruction of the common hepatic artery by use of the middle colic artery in the patient with gastroduodenal artery (GDA) arising from the area close to the CA. We here report a technique used for reconstruction that was feasible in the case of shutoff of the arterial blood sup-

ply to the liver in DP-CAR.

CASE REPORT

A 78-year-old male was referred to the emergency ward of the Gunma Prefectural Cardiovascular Center with acute onset abdominal pain. A computed tomography (CT) scan of the thorax and abdomen confirmed an infrarenal abdominal aortic aneurysm (AAA) and evidence of a contained acute rupture to the left retroperitoneum. Therefore, emergency surgery for AAA was performed. A follow-up CT revealed dilatation of the main pancreatic duct from the body to the tail. However, a tumor at the body of the pancreas was not identified (Figure 1A). Four months after the operation, the patient had severe epigastric and back pain, and his serum level of carbohydrate antigen 19-9 (CA19-9) was elevated to 652 U/mL. Therefore, he was referred to the Department of General Surgical Science, Graduate School of Medicine, Gunma University 6 mo after the AAA surgery. Dilatation of the main pancreatic duct was evident in CT, and the tumor, identified at the body of the pancreas, had invaded the CA and CHA (Figure 1B). Endoscopic retrograde cholangiopancreatography (ERCP) demonstrated a stricture of the main pancreatic duct in the body of the pancreas (Figure 2). Abdominal angiography showed that the CA and splenic artery (SA) were involved with a tumor of the pancreatic body (Figure 3). These findings were consistent with a diagnosis of locally advanced cancer of the body of the pancreas that invaded the CA and SA. Preoperative evaluation of angiography showed that the GDA arose near the CA (Figure 3).

The patient then underwent a DP-CAR. An extended Kocher maneuver was performed. Because of the previous surgery, there was severe adhesion at the retroperitoneum. The origin of the superior mesenteric artery (SMA) and CA was palpated and confirmed to be uninvolved. The greater sac was then entered adjacent to the colon, and the splenocolic ligament was divided, allowing the inferior border of the body and the tail of the pancreas to be incised. The tumor originated from the body of the pancreas, and the celiac and common hepatic arteries were involved. Following the common hepatic artery, it was found to be densely encased by a tumor extending almost to the root of GDA. The GDA was exposed and



Figure 2 Endoscopic retrograde cholangiopancreatography showing a stricture of the main pancreatic duct in the body of the pancreas. MPD: Main pancreatic duct.

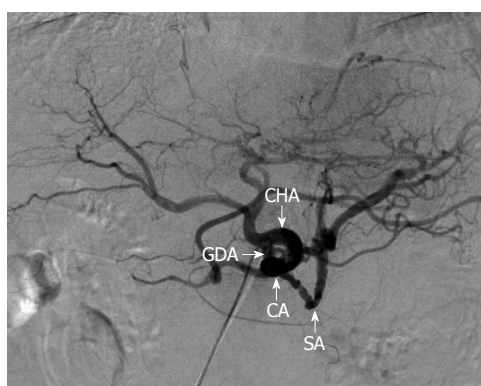


Figure 3 Abdominal angiography showing splenic and celiac arteries involved with a solid tumor in the pancreatic body and the gastroduodenal artery arising from the area close to the celiac. SA: Splenic CA: Celiac axis; CHA: Common hepatic artery; GDA: Gastroduodenal artery.

encircled with a proximal vessel loop. By dissecting the right celiac ganglion and celiac nerve plexus, the origin of the CA was exposed. The body and the tail of the pancreas were freed from the posterior abdomen in this inflamed adhesion retroperitoneal plane. The dissection was continued from the hilum of the spleen to the superior mesenteric vein. The spleen was released from its attachment to the diaphragm, allowing it to be lifted and retracted medially. A portion of Gerota's fascia was lifted with the specimen to expose the left kidney and renal vessels. Gerota's fascia was then excised in continuity. The inferior mesenteric vein was ligated inferiorly. At that time, we completely excised the GDA, which was involved with the tumor under the pancreas. Despite the presence of tumor involvement at the GDA, curative pancreatic resection with arterial resection was considered to be possible. Therefore, the GDA was ligated and divided proximal to the artery. After cutting the proper hepatic artery at the root of the GDA, the stump of the proper hepatic artery (PHA) and the middle colic artery (MCA) were anastomosed using an end-to-end technique with 7-0 prolene interrupted sutures and surgical loupes at $\times 2.5$ magnification (Figure 4). The pulsation of the

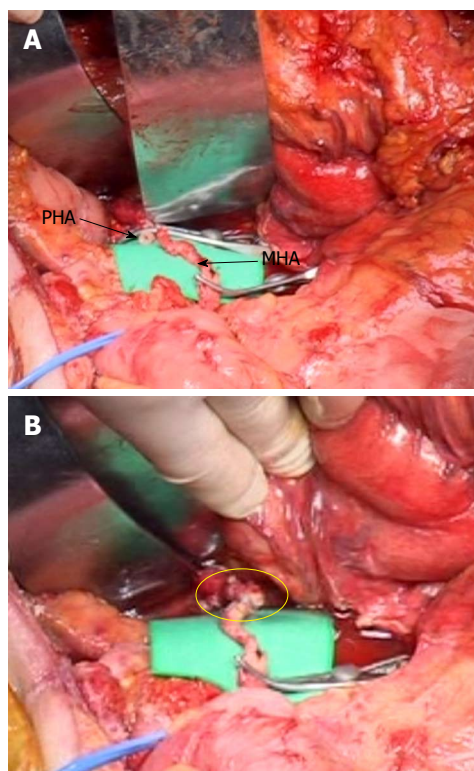


Figure 4 Operative photograph showing that reconstruction was completed. End-to-end anastomosis was performed between the proper hepatic artery (PHA) and the middle colic artery (MCA) (yellow circle). A: Before anastomosis; B: After anastomosis.

PHA recovered after completion of the anastomosis and was also identified by Doppler ultrasonography. The neck of the pancreas was transected over the right side of the portal vein (PV). The left side of the SMA was dissected with the surrounding lymph node. Care was taken to preserve the inferior pancreaticoduodenal artery (IPDA) arising from the SMA or the first jejunal artery. The left gastric artery was then divided, and, thereafter, the short gastric vessels along the greater curvature were ligated. Finally, the celiac trunk was divided at its origin with a transfixing suture, and the specimen was removed.

Histopathological examination of surgical specimens revealed mucinous carcinoma of the pancreas. There was prominent formation of mucinous nodules and a mucinous carcinoma including a large quantity of mucus (Figure 5). The peak aspartate/alanine aminotransferase (AST/ALT) was 1844/1265 U/L on the first postoperative day and gradually returned to a normal level over two weeks. The postoperative course was uneventful, and the patient was discharged on postoperative day 19. Postoperative 3D-CT angiography revealed that patency was maintained in the anastomosis between the GDA and the MCA (Figure 6). The patient was free from epigastric and back pain immediately and doing well after the operation. Five months after the operation, metastatic lesions were noted in the hilar of the liver by CT scan but without local recurrence. The patient was diagnosed with cholangitis and died of hepatic failure about 6 mo after the surgery.

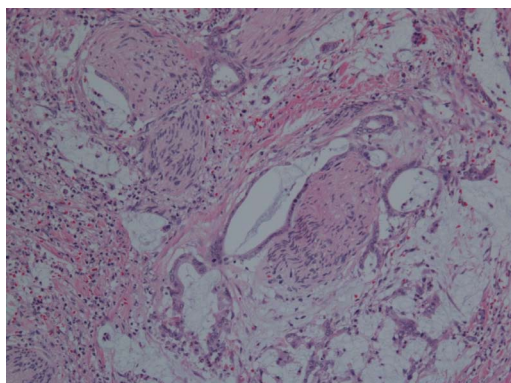


Figure 5 In the pathological findings, there was a prominent formation of mucinous nodules and mucinous carcinoma including large quantities of mucus. Final histopathological diagnosis of the resected specimen shows mucinous carcinoma (with an intraductal papillary-mucinous tumor, Hematoxylin eosin staining, $\times 100$).

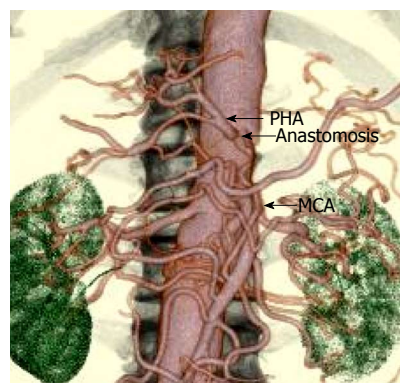


Figure 6 Postoperative evaluation of the proper hepatic artery by 3D-computer tomography angiography. The arrows indicate the anastomosis between the proper hepatic artery (PHA) and the middle colic artery (MCA).

DISCUSSION

Adenocarcinoma of the body and tail of the pancreas often presents in the advanced stage and is considered unresectable in the majority of patients. The traditional determinants of unresectability with such cancers are the presence of hepatic metastases, peritoneal dissemination of the tumor, and local invasion of major vascular structures, even in the absence of distant disease. With unresectable lesions, long-term survival is extremely rare. Surgery is the only curative option for pancreatic cancer^[1]. Improved operative techniques have led to improved results and long-term survival outcomes for patients with pancreatic cancer following surgery^[7]. Through cumulated experience in the operative and perioperative management of patients undergoing pancreatic surgery, the criteria for resectability have gradually expanded.

Hirano *et al.*^[4] reported that they performed DP-CAR on 37 patients to treat locally advanced cancer of the pancreatic body involving the common hepatic artery and/or celiac axis. The estimated 1- and 5-year survival rates were 72% and 17%, respectively, and the median survival was 21 mo. Moreover, radical distal pancreatectomy with en bloc resection of the celiac artery, celiac plexus, and celiac ganglions is reported to provide patients with locally advanced cancer of the pancreatic body with complete and enduring pain relief^[5]. Since the perineural and neural invasion of the nerve plexus is one reason for the high recurrence rate of pancreatic cancer, dissection of the surrounding neural plexus is necessary in curative surgery. Concomitant resection of the celiac artery with a distal pancreatectomy facilitates lymph node and neural plexus dissection around the celiac artery.

Great care was taken to maintain the arterial blood supply to the liver and stomach during the surgery before the transection of the CA. It is essential to protect the blood flow from the SMA *via* the pancreaticoduodenal arcades to the GDA. Arterial blood flow through the GDA can nourish the liver and stomach *via* the PHA, right

gastric artery, and right gastroepiploic arteries (GEA). However, vascular anomalies in the peripancreatic region, including the hepatic artery and SMA as well as the CA, have been reported elsewhere^[8]. Because collateral circulation is significantly important in DP-CAR, a careful preoperative work-up is necessary. Even with vascular anomalies, it is justifiable to perform extended surgery with arterial resection for pancreatic cancer, given that surgery is the only curative option. Sometimes the dorsal pancreatic artery, which arises from the SMA, leads to the GDA. At times, an SMA dorsal artery plays an important role in the collateral circulation in patients with celiac axis stenosis^[9]. In such cases, considerable attention must be paid when dissecting around the GDA. However, definitive assessment or recognition of the risk of ischemia of the liver and the stomach can only be made intraoperatively. In our case, the GDA was intact in the preoperative examination but arose from the area close to the CA and was involved with a tumor under the pancreas. In that situation, it is difficult to preserve the GDA for curative surgery. We decided to anastomose the PHA with the MCA during the curative operation. A specimen of the pancreas revealed that microscopic curative resection was possible. In addition, there were no serious complications following surgery. Therefore we believe that the techniques used for this reconstruction, which was a feasible and safe procedure, required shutoff of the arterial blood supply to the liver in DP-CAR.

DP-CAR surgery may facilitate resection in patients with tumors that are classified as T4 and require total clearance of the pancreatic and celiac lymph nodes^[2-4]. The clinical benefit of extended pancreatic resections must, however, be balanced with the risk of the procedure. Therefore, knowledge of the reconstruction artery during DP-CAR surgery is essential. Konishi *et al.*^[10] reported that they reconstructed the hepatic artery using a graft of the splenic artery from the resected specimen because of weak pulsation of the proper hepatic artery after occlusion of the celiac axis. No complications related to hepatic ischemia were observed. Kondo *et al.*^[11] reported that, in compromised collateral flow *via* the pancreatodu-

denal arcades, the MCA and GEA bypass is one of the procedures of choice to reestablish collateral flow.

Immediately after the AAA operation, dilatation of the main pancreatic duct from the body to the tail of the pancreas is the most likely indicator of a main duct type intraductal papillary mucinous tumor (IPMN). However, in this case the tumor grew rapidly after the AAA operation. The final pathological diagnosis showed mucinous carcinoma. Mucinous carcinoma of the pancreas is a rare type of tumor that is sometimes difficult to diagnose. Sakamoto *et al.*^[12] reported that endoscopic ultrasonography (EUS) and contrast-enhanced harmonic EUS are useful for the correct diagnosis of small pancreatic tumors, including synchronous and metachronous occurrence of IPMN and ductal adenocarcinoma. If EUS is performed at the earliest possible time, an accurate differential diagnosis between main pancreatic duct type IPMN and mucinous carcinoma can be made.

In the case reported here, the results remain unsatisfactory, although the patient is doing well and the resection resulted in the elimination of epigastric and back pain immediately after surgery. To improve the possibility of survival, a search for effective systemic chemotherapeutic agents and their testing in trials with neoadjuvant and/or adjuvant therapy with radiotherapy is essential to complement the oncologic benefit achieved after a complete surgical resection.

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Hepatic paraganglioma and multifocal gastrointestinal stromal tumor in a female: Incomplete Carney triad

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Core tip: The Carney triad (CT) describes the coexistence of multiple neoplasms including gastrointestinal stromal tumors (GISTs), extra-adrenal paraganglioma and pulmonary chondroma. We report a case of an incomplete CT. CT is a very rare syndrome but Carney et al thoroughly documented its clinical manifestations. The presence of pulmonary chondroma and paraganglioma should be verified, especially in young women with multifocal GISTs to rule out CT.

Hong SW, Lee WY, Lee HK. Hepatic paraganglioma and multifocal gastrointestinal stromal tumor in a female: Incomplete Carney triad. *World J Gastrointest Surg* 2013; 5(7): 229-232 Available from: URL: <http://www.wjgnet.com/1948-9366/full/v5/i7/229.htm> DOI: <http://dx.doi.org/10.4240/wjgs.v5.i7.229>

Abstract

The Carney triad (CT) describes the coexistence of multiple neoplasms including gastrointestinal stromal tumors (GISTs), extra-adrenal paraganglioma and pulmonary chondroma. At least two neoplastic tumors are required for diagnosis. In most cases, however, CT is incomplete. We report a case of an incomplete CT in a 34-year-old woman with a multifocal GIST and non-functional paraganglioma of the liver. Preoperative evaluation with a gastrofiberscope and abdominal computed tomography revealed multiple gastric tumors resembling GISTs and a single liver lesion which was assumed to have metastasized from the gastric tumors. The patient underwent total gastrectomy and partial hepatectomy. Histologic findings confirmed multiple gastric GISTs and paraganglioma of the liver. We report a case of a patient with incomplete expression of CT.

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Key words: Carney triad; Gastrointestinal stromal tumor; Paraganglioma

INTRODUCTION

The Carney triad (CT) initially described the triad of gastric leiomyosarcoma, functioning extra-adrenal paraganglioma, and pulmonary chondroma^[1]. Later, gastric leiomyosarcoma was replaced with gastric gastrointestinal stromal tumors (GISTs) and several cases of paragangliomas were known to be non-functioning^[2]. GISTs in childhood or adolescence can occur as sporadic diseases unrelated to a syndrome, and can present as either a familial disorder [Carney-Stratakis syndrome (CSS)] or part of non-hereditary CT^[3]. The differential diagnosis of CT from sporadic gastric GISTs is crucial because CT differ considerably from sporadic gastric GISTs in clinical both course and prognosis^[2]. Here, we report a CT case with multiple gastric GISTs and paraganglioma of the liver.

CASE REPORT

An otherwise healthy 34-year-old woman visited our hospital after being diagnosed with gastric tumors *via* gastro-

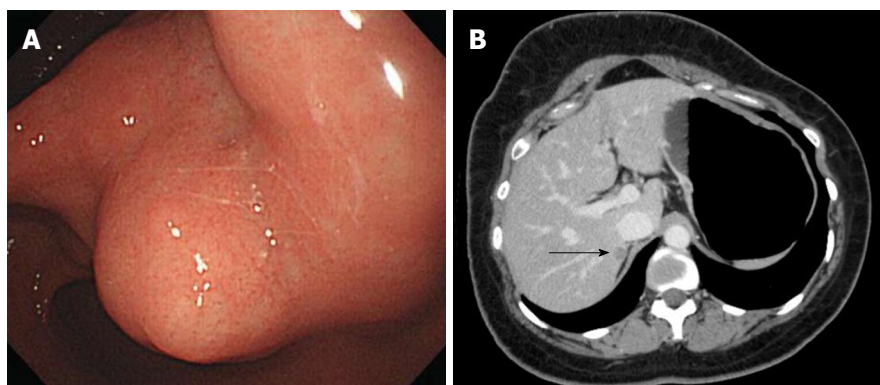


Figure 1 Esophagogastroduodenoscopy. A: Gastroendoscopy revealed an antral submucosal tumor without ulceration and hemorrhage; B: Computed tomography revealed a hypoattenuating nodule in segment VII of the liver, with peripheral weak enhancement in the portal phase (arrow).

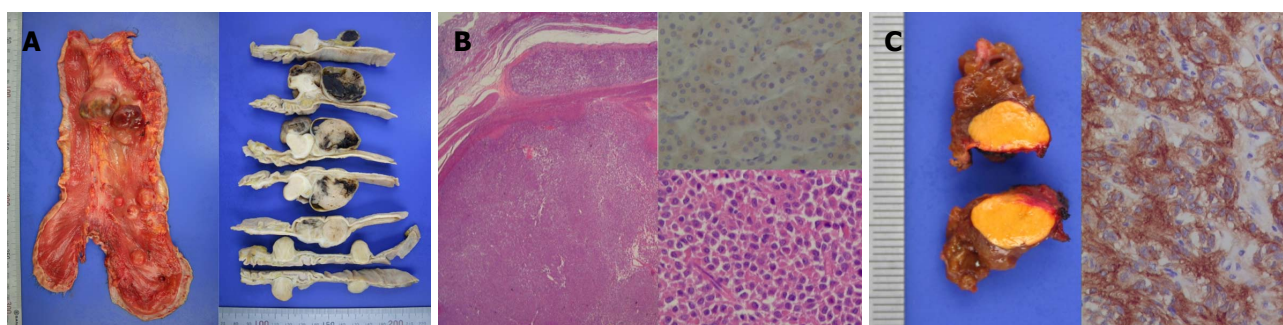


Figure 2 The patient underwent total gastrectomy, regional lymphadenectomy, and partial hepatectomy of segment VII. A: Macroscopically, gastric tumors were located in the submucosal layer, were round to oval and, relatively well demarcated, and exhibited multiple nodules ($n = 8$); B: Gastric tumor demonstrated cellular epithelioid gastrointestinal stromal tumors with discohesive pattern of growth (HE, $\times 40$) and mild nuclear atypia (hematoxylin and eosin, $\times 200$) (lower right), exhibiting diffuse cytoplasmic membranous immunoreactivity for CD117 (immunohistochemical stain, $\times 200$) (upper right); C: Hepatic partial resection revealed an oval, well circumscribed, orange yellow, soft, solid tumor, 12 mm \times 7 mm (left) and microscopically, synaptophysin-positive, hepatic tumor cells were arranged in nests (so called 'zellballen') (right), surrounded by S100 protein-positive, sustentacular cells (immunohistochemical stain, $\times 400$).

fiberscopic screening at a community hospital. She had no specific symptoms or signs related to gastric tumors. She had no specific past medical history involving hypertension. There was no abnormality of her past or familial history related to endocrine disease or gastrointestinal malignancies. An initial physical examination showed no significant abnormalities. Laboratory findings were also unremarkable. Tumor markers, such as carcinoembryonic antigen and carbohydrate antigen 19-9, were within normal limits.

Esophagogastroduodenoscopy revealed a multifocal gastric tumor, suspicious for a GIST, in the whole stomach. The tumors were multiple small exophytic polypoid lesions in the whole stomach from fundus to antrum. The largest tumor was approximately 4 cm, was located in the antrum and was not ulcerated (Figure 1A). Abdominal computed tomography revealed pathologic lesions in the proximal antrum, enlarged perigastric lymph nodes, and a lesion in segment VII of the liver. This hepatic lesion was assumed to have metastasized from the gastric tumors (Figure 1B). Chest radiography revealed no evidence of lung metastasis. Positron emission tomography revealed hyper-dense areas in the antrum and perigastric lymph nodes in areas other than the liver.

The patient underwent total gastrectomy, regional lymphadenectomy, and partial hepatectomy of segment VII. Based on macroscopic examination, the sporadic

gastric stromal tumorlets were multifocal subserosal exophytic polypoid nodules ($n = 8$). The tumors ranged from 7 mm \times 5 mm to 40 mm \times 35 mm (Figure 2A). The largest tumor was located at the lesser curvature of the antrum. The gastric mucosa was grossly unremarkable, without ulceration or tumefaction. All eight tumors were diffusely immunoreactive with CD 117 (KIT) and CD34 antibodies, confirming the diagnosis of GISTs (Figure 2B). The average mitotic count was 6/50 high power fields suggesting an intermediate risk of malignancy (prognostic group 2C). The resection margins and lymph nodes were free of neoplasia. The hepatic tumor was 12 mm \times 7 mm in diameter, with a bright orange yellowish color and a relatively well-defined tumorous nodule. Microscopically, the tumor cells were arranged in small nests (so called "zellballen", which are distinctive cell balls), set in a vascularly rich stroma. Immunohistochemical stains disclosed synaptophysin-positive tumor cell nests surrounded by S100 protein-positive sustentacular cells (Figure 2C). These findings were consistent with benign primary paraganglioma. A 24 h urine study assaying for metanephrine, epinephrine, and norepinephrine was performed 10 d after the operation and revealed no abnormalities.

The postoperative course was uneventful, and the patient was discharged from the hospital in good condition. No adjuvant chemotherapy was administered, and no evi-

dence of recurrence was detected at the 1-year follow-up.

DISCUSSION

Multifocal hyperplasia of the interstitial cells of Cajal is a precursor of hereditary GIST in patients with germline mutations of c-KIT or alpha platelet-derived growth factor receptor (PDGFRA), but precursor lesions of sporadic GISTs have not yet been defined^[4]. Carney *et al.*^[1] first described the association of gastric epithelioid leiomyosarcoma with pulmonary chondroma and functioning extra-adrenal paraganglioma of unknown origin, which today is known as CT. CT is defined by the coexistence of the following three tumors: extra-adrenal paraganglioma: only functioning extra-adrenal paragangliomas were initially included and non-functioning extra-adrenal paragangliomas were added later; gastric GISTs, previously known as gastric epithelioid leiomyosarcoma; and pulmonary chondroma (hamartoma)^[2]. For the diagnosis of CT, at least two of the these major components are necessary. Recently, CSS was reported. This syndrome is a dyad of paraganglioma and gastric stromal sarcoma. CSS is inheritable in an autosomal dominant pattern, affects both males and females, and does not present pulmonary chondroma^[5]. We considered our case as CT because the patient had no family history of related tumors.

CT predominately affects females (over 80% of cases) in their 2nd and 3rd decades and often presents with unpredictable outcomes^[6]. The first tumor identified is usually a gastric GIST. The most common initial clinical manifestation is a GIST with bleeding. Associated symptoms and signs are anemia, hematemesis, and melena. Gastric GISTs in CT are usually multifocal and, antral based. These tumors are wild-type for common mutations in the receptor tyrosine kinase gene KIT and for the homologous oncogene PDGFRA in contrast to most sporadic GISTs in adults^[7,8]. Gastric GISTs in CT frequently metastasize to regional lymph nodes, thus contrasting with common GISTs. The reason for this high rate of lymph node metastasis is not known^[9]. Surgical resection is the only curative therapy for gastric GISTs with CT. Although partial resection is initially performed, further resection or total gastrectomy is required when multiple tumors reside in the entire stomach or recur after tumor resection.

In our case, the preoperative detection of perigastric lymph nodes suggested metastasis. However, a pathologic assessment did not reveal metastasis. According to clinical practice guidelines for GISTs in Japan, for the treatment of a GIST that has already metastasized to other organs but is considered to be resectable, surgery is the preferred treatment modality^[10]. In this case, percutaneous biopsy of the liver lesion had a substantial risk of tumor cell spillage through the needle track. Moreover the tumor was located immediately adjacent to the inferior vena cava, so percutaneous biopsy was considered to be difficult and risky for this patient. Therefore, we

performed a total gastrectomy and resection of the liver tumor simultaneously, without preoperative pathologic confirmation of the liver lesion.

Other CT neoplasms are usually found when the lesion is evaluated for gastric GISTs. These neoplasms are often misinterpreted as metastatic GISTs and are treated as such. Our patient was preoperatively diagnosed with a multifocal gastric GIST with hepatic metastasis. The incidence of hepatic metastasis from gastric GISTs in CT was reported to be 17.7%^[2]. Postoperative histologic findings were consistent with primary hepatic paraganglioma and we confirmed the diagnosis of CT.

The most common combination is the association of GISTs with pulmonary chondroma (75%)^[6]. Combinations of GIST and paraganglioma as observed in our case, account for 44% of CT cases^[6].

Frequent sites of paraganglioma in CT are the aortopulmonary body, sympathetic chain, retroperitoneum, and carotid body. Only two cases of hepatic paraganglioma similar to our case were reported among 79 patients with CT in Carney's series^[2]. Paragangliomas are rare neuroendocrine tumors arising from neural-crest-derived chromaffin cells. Although paragangliomas may present anywhere along the sympathetic paraganglia chains from the neck to the pelvis, most reside intra-abdominally, in the superior para-aortic area^[11].

Mortality from the triad depends on gastrointestinal hemorrhage, metastatic disease and hypertensive phenomena. Symptoms and signs of catecholamine excess were observed in 13 (35%) of 37 paraganglioma patients with CT^[2]. In our case, we could not confirm whether the hepatic paraganglioma was functioning because the preoperative diagnosis of the liver lesion was metastasis and because initial blood and urine chemistry evaluation for catecholamine could not be performed. Considering the lack of symptoms or signs, the paraganglioma was assumed to be non-functioning. When CT is suspected in patients with multiple gastric GISTs, a radiologic and chemical work-up should be undertaken to rule out paraganglioma.

Although most CD117-expressing GISTs are aggressive, these tumors respond to imatinib. Tumors in younger patients with CT are less aggressive and less responsive to imatinib but still metastasize^[12]. Most deaths of CT patients are due to malignant GISTs but several cases are due to paraganglioma (3/77, 3.8%)^[13]. At the onset of the syndrome, all three types of tumors are detected in very few cases (1%). The mean interval between the detection of the first and second tumors has been reported to be 8.4 years^[2]. Eventually, early surgery can reduce both short and long-term mortality from bleeding and metastasis, respectively.

In conclusion, CT is a very rare syndrome, but Carney and colleagues thoroughly documented its clinical manifestations. The presence of pulmonary chondroma and paraganglioma should be verified, especially in young women with multifocal GISTs, to rule out CT. A careful long-term follow-up is required to detect metachronous tumors.

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- 15 Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis serial online, 1995-01-03, cited 1996-06-05; 1(1): 24 screens. Available from: URL: <http://www.cdc.gov/ncidod/eid/index.htm>

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Units

Use SI units. For example: body mass, *m* (B) = 78 kg; blood pressure, *p* (B) = 16.2/12.3 kPa; incubation time, *t* (incubation) = 96 h, blood glucose concentration, *c* (glucose) 6.4 ± 2.1 mmol/L; blood CEA mass concentration, *p* (CEA) = 8.6 24.5 μ g/L; CO₂ volume fraction, 50 mL/L CO₂, not 5% CO₂; likewise for 40 g/L formaldehyde, not 10% formalin; and mass fraction, 8 ng/g, *etc.* Arabic numerals such as 23, 243, 641 should be read 23243641.

The format for how to accurately write common units and quantities can be found at: http://www.wjgnet.com/1948-9366/g_info_20100312191949.htm.

Abbreviations

Standard abbreviations should be defined in the abstract and on first mention in the text. In general, terms should not be abbreviated unless they are used repeatedly and the abbreviation is helpful to the reader. Permissible abbreviations are listed in Units, Symbols and Abbreviations: A Guide for Biological and Medical Editors and Authors (Ed. Baron DN, 1988) published by The Royal Society of Medicine, London. Certain commonly used abbreviations, such as DNA, RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA, mAb, can be used directly without further explanation.

Italics

Quantities: *t* time or temperature, *c* concentration, *A* area, *l* length, *m* mass, *V* volume.

Genotypes: *gylA*, *arg 1*, *c myc*, *c fos*, *etc.*

Restriction enzymes: *EcoRI*, *HindI*, *BamHI*, *Kbo I*, *Kpn I*, *etc.*

Biology: *H. pylori*, *E. coli*, *etc.*

Examples for paper writing

All types of articles' writing style and requirement will be found in the

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