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Original Article

One Hundred and One Open Abdominal Aortic Aneurysm Repairs: 5 Years' Experience at Lampang Regional Hospital, Thailand

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Abstract

Objective: **To delineate the natural presentation of abdominal aortic aneurysm (AAA) patients in Lampang Regional hospital and audit the results of open AAA repair performed by one surgeon over a 5-year period.**

Methods: **A survey of 101 consecutive AAA patients during August 2005 and August 2010 was performed. Outcomes included hospital death, major complication, co-morbidity and causes of death after AAA repair.**

Results: **Among the 101 AAA patients, 66 (65%) underwent elective repair. Nine (9%) cases had ruptured AAA (1 case of free rupture, 8 cases of contained rupture). Twenty-six (26%) patients underwent urgent repair for the symptomatic AAA, including 7 (27%) with distal embolization causing limb and toe gangrene that required further amputation, 5 (19%) with aortoenteric fistula, 1 (3%) with thrombosed AAA, 6 (23%) with inflammatory AAA, 5 (19%) with infected AAA, 2 (7%) with infected previous aortic graft, and 3 (11.5%) with painful AAA of unknown cause. The 30-day hospital deaths included 2 patients (3%) in the elective group, 1 (100%) with free rupture, 2 (25%) with contained rupture and 3 (12%) in the urgent group. Major causes of death in 8 patients included 4 (50%) from ischemic heart disease, 2 (25%) from acute renal failure and 2 (25%) from respiratory failure due to chronic obstructive pulmonary disease (COPD).**

Conclusions: **The most significant comorbidity and cause of death of patients after AAA repair included ischemic heart diseases, renal failure and COPD.**

Keywords: **Abdominal aortic aneurysm; open abdominal aortic aneurysm repair**

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INTRODUCTION

Abdominal Aortic Aneurysms (AAAs) can be categorized according to the etiology: degenerative[1], inflammatory[2], post-dissection, traumatic, infectious and developmental anomalies. The majority of AAA occurs at the infrarenal level and remains asymptomatic until its size reaches 5.5 cm, at which time, according to the American College of Cardiology/American Heart Association (ACC/AHA) guidelines, the patient should undergo repair to eliminate the risk of rupture[3,4]. Emergency surgical repair of ruptured AAAs has an overall mortality of 90%, and urgent repair for symptomatic AAAs still has a mortality of at least 10%. However, elective surgical repair has less than 5% mortality, hence it should be offered to AAA patients before symptoms develop[5]. There have been many studies comparing open versus endovascular aneurysm repair (EVAR) of AAA in specialized medical centers, the prior assumption being that open repair produces superior durability, and EVAR requires more re-interventions. In the present study we review the results of open surgical repair of all AAAs (Lampang Regional Hospital does not currently offer EVAR) performed by one surgeon[6,7,8] during a 5-year period, describing the diagnosis, treatment, complications and mortality of AAAs, and compare this to results reported in the current literature.

PATIENTS AND METHODS

Patients with AAAs treated between August 2005 and August 2010 were identified in the hospital records, and operative notes, discharge summaries and out patients department (OPD) cards in follow up cases were reviewed. Patients were followed to determine the general condition, symptoms, physical examination and reevaluation with bedside duplex ultrasound examination one month after discharge from the hospital, then for the next three to six months for one year, and then annually. The study was conducted with approval of the Lampang Regional Hospital Research Ethics Committee. Data collected for each AAA patient included symptoms leading to the hospital, diagnosis, treatment, medical co-morbidity and complications. Elective surgical repair was defined as a planned repair in asymptomatic patients. Urgent repair was defined as a repair in symptomatic patients without rupture. Emergency repair was defined as a repair in ruptured AAAs, which included both free rupture into peritoneal cavity and retroperitoneal leakage. Hospital mortality was defined as death within one month after operation. All patients in the present study were operated on by one surgeon. Aortic repair was done via the transperitoneal approach (including minimal invasive aortic surgery for asthenic patients). Generally the operative steps were as follows: After entering abdominal cavity, the viscera were inspected for associated pathology. The small intestines were eviscerated to the right and placed within a sterile plastic bag to reduce fluid and prevent heat loss. The ligament of Treitz was exposed for further proximal aortic neck dissection and identification of the left renal vein to place the vertical aortic clamp against the vertebra just beneath the left renal vein. We do not encircle the proximal aortic neck with a vascular loop to avoid lumbar artery injury and disruption of lymphatic ducts. Both common iliac arteries were controlled in the same manner, to decrease the risk of inadvertent injury to both common iliac veins during circumferential dissection. Aneurysm sac was open using standard technique and vascular continuity was restored with inlay tubular or bifurcate Dacron graft. All anastomoses were done with 4/0 prolenevisiblack^{R}. Finally, we completely wrapped the repair with the native aortic wall, closed with 3/0 prolene, to protect the adjacent organs from the aortic graft.

The baseline data and outcomes were summarized as either mean and/or median and range, or counts and percentage. This was a descriptive study and no statistical hypothesis testing was performed.

RESULTS

Overall, 101 patients underwent AAA repair during August 2005 and August 2010 at Lampang Regional Hospital. Demographic data for these patients are presented in Table 1. Elective surgery was done in 66 patients (65%, with one non-surgical patient), 26 (26%) underwent urgent surgery, and 9 (9%) underwent emergency operation. The age and AAA size of all patients are shown in Table 2. All patients were examined with duplex ultrasound and/or CT angiography.

Table 3 shows that there were 85 (84%) patients with atherosclerotic AAAs. Six had bilateral common iliac aneurysm (CIA) in conjunction with AAA. Ten

Table 1 Demographic data for patients with AAA (August 2005 - August 2010), Lampang Regional Hospital

	Elective N = 66	Ruptured N = 9	Urgent N = 26
Gender: number (%)			
Male	37 (56)	4 (44)	9 (35)
Female	29 (44)	5 (56)	17 (65)
Risk factors: number (%)			
HT	22 (33)	4 (44)	3 (12)
IHD[a]	11 (17)	2 (22)	2 (8)
CRF[b]	5 (8)	1 (11)	1 (4)
PAD	1 (2)	0	0
Stroke[c]	1 (2)	0	0
COPD	3 (4)	1 (11)	1 (4)

[a]IHD = ischemic heart diseases: all documented and treated with aspirin, [b]CRF = chronic renal failure: Cr>2.0 mg%, [c]performance status = 1, HT = hypertension, PAD = peripheral arterial disease, COPD = chronic obstructive pulmonary disease

Table 2 Type of operation in relation to size and age in patients with AAA

	Type of Operation	Age (year) Median (range)	AAA size (cm.) Median (range)
Elective operation	Aortic graft	65 (50-81)	6.5 (4.8 - 8.2)
	Extra-anatomical bypass	75 (73-77)	5.4 (4.7 - 6.0)
Urgent operation	Aortic graft	80 (70-92)	5.5 (3.68 - 7.4)
	Extra-anatomical bypass	80 (77-82)	6.9 (6.5 - 7.4)
Emergency operation	Aortic graft	72 (64-81)	7.0 (6.0 - 8.0)
	Extra-anatomical bypass	77 (75-80)	8.1 (6.5 - 10.5)

AAA = Abdominal Aortic Aneurysm

Table 3 Demographic data for patients with atherosclerotic and non-atherosclerotic AAA, type of operation and operative mortality

	Aortic Graft	Extra-anatomical Bypass	Operative Mortality
Atherosclerotic			
Isolated infrarenal AAA	53	-	1
AAA with CIA aneurysm	16	-	1
AAA (Incidental finding)	4	-	-
AAA with TAA (< 5 cm.)	2	-	-
AAA with PAD	2	3	2
AEF (Aorto-enteric fistula)	5	-	-
Non atherosclerotic			
Mycotic AAA	1	3	1
Inflammatory AAA	6	-	-
Saccular AAA	5	-	1
Post pythiosisAAAa	-	-	1

[a]Two years after bilateral below knee amputation, AAA = Abdominal Aortic Aneurysm, TAA = Thoracic Aortic Aneurysm, PAD = peripheral arterial disease, CIA = common iliac artery, CFA = common femoral artery, SFA = superficial femoral artery

Table 4 Presenting symptoms or diagnosis which required urgent AAA repair

Distal embolization	
Toe gangrene	6
Limb gangrene	1
Aorto-enteric fistula	
Duodenum	4
Sigmoid colon	1
Thrombosed AAA with ALI	1
Pain (at site of AAA)	3
Mycotic AAA	
Salmonella	2
No growth	7
Inflammatory AAA	6

AAA = Abdominal Aortic Aneurysm; some patients have more than 1 symptom or diagnosis

had unilateral CIA, two had cholecystitis with AAA as an incidental finding, one also had gallstone with common bile duct stone, one had pancreatic cancer as well, two had a combination of descending thoracic aortic aneurysm (diameter < 5.0 cm) and AAA, and five patients had associated peripheral arterial diseases.

Table 3 also shows that aortic graft was used in 94 patients (93%) and extra-anatomical bypass in 6 (6%), while one patient with pythiosis did not undergo surgery to treat the aneurysm. There were 16 patients (16%) with nonatherosclerotic AAA, including 4 with mycotic AAA, 6 with inflammatory AAA, and 5 with saccular AAA. Two patients underwent reoperations for rebleeding due to anastomotic disruption, and one had acute right lower limb ischemia from suspected plaque disruption at the right CIA which required femoro-femoral bypass five hours after the AAA repair. In one patient, after the treatment for pythiosis of the peripheral vessels with bilateral below knee amputation for two years, a pulsatile abdominal mass with severe persistent abdominal pain developed. CT angiography demonstrated thick walled AAA 4.8 cm in size. Biopsy of the periaortic tissues revealed pythiosis of adjacent periaortic vessels.

Seven patients had severe co-morbid conditions, and were unfit for general anesthesia. All had difficult iliac runoff, which required extra anatomical bypass procedures, including four aorto-bifemoral bypass, one axillo-bifemoral bypass, and one aortoiliac with femoro-femoral bypass.

There were 8 hospital deaths: 2 (3%) after elective repair, 3 (33%) after emergency operations for ruptured AAA, and 3 (11%) after urgent surgery. Cardiac (4/8, 50%), renal (2/8, 25%) and pulmonary failures (2/8, 25%) were the leading causes of death. Operative death occurred in six of these patients.

DISCUSSION

Successful open AAA repair is based on a thorough understanding of anatomical details of the aneurysm of each patient, such as the proximal extension to the renal artery, concomitant common iliac artery aneurysm with or without hypogastric artery aneurysm, or other severely occluded diseased arterial braches. Visceral collateral circulation, such as those surrounding the inferior mesenteric artery, should be identified. Preoperative imaging with CT angiography can help define the many anatomical variations,which the duplex ultrasound cannot demonstrate. Careful preoperative assessment with history taking, physical examination, especially peripheral pulse (carotid bruit, DeBakey's test for estimated extension of the proximal aortic neck), chest radiographs, electrocardiography, and serum electrolytes measurements must be done to identify any major surgical risks.

From the demographic data presented, all patients in this study were elderly with associated comorbidities, such as ischemic heart disease, renal failure, cerebrovascular disease, peripheral arterial disease, and chronic lung disease. Hypertension and ischemic heart disease were the dominant comorbid diseases for all three treatment groups in the present study. Presenting symptoms of AAA which required urgent repair are shown in Table 4. Interestingly, there were six patients with inflammatory AAA. All six had only the inner lumen to use for anastomosis, bypass procedures, and to help achieve hemostasis. Nonetheless, the results of the repair were good, as demonstrated by follow up CT scan and the resolution of symptoms.

Three patients in the study needed a second operation. Two patients in the ruptured AAA group had intra-abdominal bleeding, which required reoperation, and one patient in the urgent repair group had acute limb ischemia and a further bypass procedure was done.

The overall mortality was 3% for elective group, 33% for ruptured group and 11% for the urgent

group. The most common postoperative complications and causes of death were cardiac, pulmonary and renal failure[9,10]. The author would like to stress the technique of not encircling the proximal aortic neck, and especially not encircling both common iliac run-offs, so as to avoid inadvertent injury to the lymphatic structures, retro-aortic lumbar artery and the common iliac vein. This requires the shortening of the aortic cross-cramp time, and entails minimal blood loss.

In the era of EVAR, studies have demonstrated that all-cause mortality was similar between EVAR and open repair, both in the mid-term and the long-term. In centers where EVAR is not available, open AAA repair remains the best treatment option. Acceptable peri-operative morbidity and mortality, especially for elective AAA repair[11], could be achieved, consistent with the current literature. The author encourages all general surgeons in provincial hospitals who have a special interest in vascular surgery to do AAA repair in selected cases, especially for patients less than 80 years of age and who have minimal co-morbidity[12]. Open AAA repair in experienced hands may yet produce superior durability and freedom from graft related re-intervention than EVAR.

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Original Article

An Anatomical Study for Selective Neurectomy of the Calf Muscles

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Abstract

Background: **Calf hypertrophy is an aesthetic concern for women. Many methods such as liposuction, botulinum toxin type A injection and muscle resection have been used to reduce the calf size with reasonable results. A technique of selective neurectomy of the medial gastrocnemius and soleus muscles is used to improve the result of calf muscle reduction. There are few reports of selective neurectomy for calf hypertrophy in clinical cases and of anatomical study of nerves to gastrocnemius and soleus muscle.**

Objective: **To demonstrate the anatomical variation of nerves to gastrocnemius and soleusmuscles.**

Methods: **Thirty five cadaveric legs (22 males and 13 females) with an average age of 43.7 years were dissected to determine the location of nerves to the gastrocnemius and soleus muscles. Number, direction and location of these nerves were recorded.**

Results: **The nerve to the soleus muscle had 2 branches: medial and lateral. The nerve to medial gastrocnemius had 1 branch in 31 (89%) and 2 branches in 4 (11%) of the legs examined. The nerve to the lateral gastrocnemius had only 1 branch in all legs. Eighteen male legs (82%) had 1 branch of nerve to the medial gastrocnemius and 4 male legs (18%) had 2 branches. All female legs had 1 branch of nerve to the medial gastrocnemius.**

Conclusion: **The nerves to medial and lateral soleus muscles have a constant number of branches, but the nerve to the medial gastrocnemius has variable number of branches.**

Keywords: **Selective neurectomy, calf muscle reduction, anatomical study**

Introduction

Calf hypertrophy is an aesthetic concern for women, especially in Asians. The causes of the enlarged calves are either an excess of subcutaneous fat or calf muscle hypertrophy, or both[1]. There are many methods for reducing the calf circumference, depending on the cause, such as liposuction in patients with excessive subcutaneous fat, and muscle resection, botulinum toxin injection and radiofrequency treatment for muscle hypertrophy[2-7]. The effect of Botulinum toxin injection is only temporary, and needs to be repeated every four to six months[7,8]. The resection of

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gastrocnemius muscle is time consuming and has risks such as hematoma formation and contour irregularity[9]. Also, the recovery period is long. Selective neurectomy of the nerve to gastrocnemius and soleus muscles can reduce the size of the muscles permanently, with a short recovery period. This procedure requires knowledge of the precise anatomy and variation of these nerves[5-8]. Few anatomical studies can be found in the literature[5,6]. The aim of the present study was to determine the number of muscular branches of the tibial nerve to the gastrocnemius and soleus muscles. The results should be helpful for selective neurectomy for calf reduction.

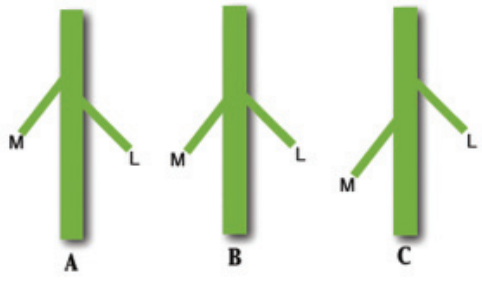

Figure 1 The relation of nerves to gastrocnemius muscles. (A) Diverging point of the nerve to medialgastrocnemius is superior to that of the nerve to lateral gastrocnemius (54%). (B) Diverging points of nerves are the same (29%). (C) Diverging point of the nerve to medial gastrocnemius is inferior to that of the nerve to lateral gastrocnemius (17%)

Material and methods

Thirty five cadaveric legs (22 males and 13 females) with an average age of 43.7 years were dissected to study the course of nerves to gastrocnemius and soleus muscles. This study was approved by the research ethics committee of the Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand. The cadavers were prepared by the usual methods. Each cadaver was placed prone with hip in neutral position and the knee extended. The popliteal region was exposed and the location of all branches of the popliteal nerve was recorded. Four bony landmarks were used as reference points: medial and lateral epicondyles of the femur and medial and lateral malleoli. Two heads of the gastrocnemius were retracted apart to trace the entrance of nerve branches into the muscles. Demographic data, number and position of the branches of the nerves to gastrocnemius and soleus muscles were recorded.

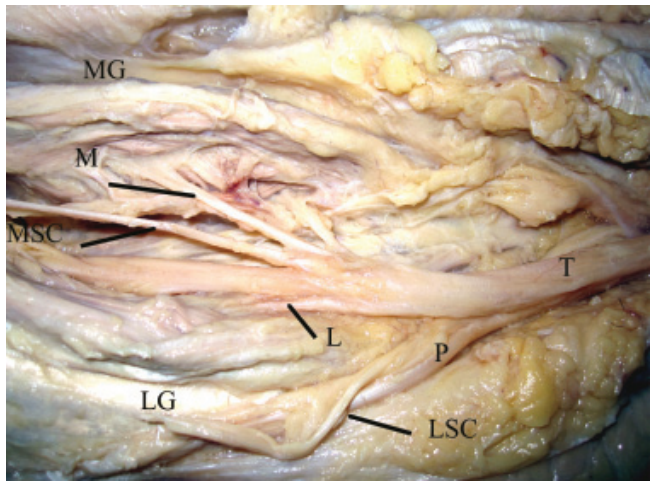

Figure 2 Demonstration of the medial (M) and lateral (L) branches of the nerve to gastrocnemius muscle. T, tibial nerve; P,peroneal nerve; MSC, medial sural cutaneous nerve; LSC, lateralsural cutaneous nerve

Results

The nerve to the gastrocnemius muscle arose from the tibial nerve in three different ways: 1) the nerve to the medial gastrocnemius muscle diverged superiorly to that of the lateral gastrocnemius muscle in 19 specimens (54%); 2) in 10 specimens (29%), the nerves to the medial and lateral gastrocnemius muscles diverged at the same level; 3) the nerve to the medial gastrocnemius muscle diverged inferiorly to that of the lateral gastrocnemius muscle in 6 specimens (17%) (Figure 1). Thirty one specimens were found to have one branch of nerve to the medial gastrocnemius (89%) and 4 specimens had 2 branches (11%). Eighteen of 22 males had 1 branch of nerve to the medial gastrocnemius (82%) and 4 males had 2 branches (18%). All 13 females had 1 branch of nerve to the medial gastrocnemius. The nerve to the lateral gastrocnemius muscle originated from the tibial nerve with one branch in all specimens (Figure 2). The nerve to the soleus muscle originated from tibial nerve in all specimens. The diverging site was at the same level as the nerve to gastrocnemius in 6 of 35 specimens (17%) and lower in 29 specimens (83%). Each specimen had only one branch each of medial and lateral sural nerve.

Discussion

Bulky calf is considered to be aesthetically unpleasing especially in Asian women with short stature[1]. Liposuction is the treatment of choice when excessive subcutaneous fat is the cause. Prolonged edema, irregularity of skin, and fibrosis are the common complications[4]. Botulinum toxin type A injection can reduce the calf circumference by partial denervation of the gastrocnemius muscle by blocking the release of acetylcholine. In animal studies, muscle fibers injected with the toxin showed atrophy histologically within 10 to 14 days after injection. But the effect of the toxin lasts only four to six months. Repeated injections are required, and because the paralysis is often unpredictable, occasional asymmetries and unaesthetic outcomes occur[7]. Radio-frequency cauterization can reduce the volume of the gastrocnemius by releasing energy to the muscle causing focal coagulation necrosis[10]. There have been reports of extensive fibrosis of the calf muscle and plantar flexion contracture caused by this device[11].

Surgical operations intended to reduce the muscle volume can be classified into direct (muscle resection) and indirect (selective neurectomy) methods. Combined resection of gastrocnemius and part of soleus muscle is the most effective procedure for reduction of the calf circumference, but it has many drawbacks such as technical difficulty, significant post-operative pain, prolonged recovery, significant scarring, and calf irregularity. Endoscopic-assisted muscle resection can be done with a small incision, under direct vision, and can minimize the risk of bleeding and neurovascular injury, but requires much experience and special instruments[12]. Selective neurectomy of gastrocnemius and soleus muscles is a simple procedure with minimal morbidity and a reliable outcome. The advantages include a short incision, short operative time and recovery time, but the improvement in calf circumference may be mild and a flat calf appearance may occur with this method.

Tsai et al. reported incomplete denervation of the gastrocnemius after neurectomy[5]. This finding emphasizes the importance of the anatomic study of the nerves to gastrocnemius and soleus muscles. In the present study, we found that the nerve to the medial gastrocnemius divides into 2 branches in 11% of the specimens. All nerves to the soleus muscle diverged from tibial nerve in the present study. But Hwang et al. found that 70% of branches to the soleus muscle diverged from tibial nerve and 30% from the nerve to lateral gastrocnemius[6]. Thus, there are variations in the anatomy of the nerves to gastrocnemius and soleus muscles. Surgeons who wish to do selective neurectomy should be aware of these variations, and use a nerve stimulator during the procedure and perform meticulous dissection. This should improve the results of neurectomy.

Conclusion

There were variations in the anatomy of the nerves to gastrocnemius and soleus muscles. The surgeon should be aware of these variations if he or she wishes to obtain good results from selective neurectomy for calf reduction.

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Original Article

Clinical Outcomes of Patients with Symptomatic Malrotation of the Intestine: A 25-year Experience

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Abstract

Objective: **The aim of this study was to review results of the treatment of patients with symptomatic malrotation within a 25-year period at a single tertiary institute in Thailand.**

Material and Method: **A retrospective study of patients with malrotation of the intestine who were treated at Queen Sirikit National Institute of Child Health between 1985 and 2009 was undertaken. Special attention was paid to clinical presentations, radiologic findings and results of treatment. Patients who were found to have malrotation as an incidental finding at laparotomy for other diseases were excluded from the study.**

Results: **A total of 153 patients underwent laparotomy for correction of symptomatic malrotation. Most of the patients developed symptoms, mostly bilious vomiting, within 30 days after birth. Upper gastrointestinal series were performed in 112 patients and revealed high gut obstruction, abnormal position of the duodenojejunal junction and corkscrew sign in 97 (87%), 74 (60%), and 38 (34%) patients, respectively. Patients were divided into three groups based on operative findings. Group A represented 58 patients, of whom 80% were neonates, who had only duodenal obstruction due to Ladd's band compression. Only one patient died postoperatively because of congestive heart failure from congenital heart disease. Group B included 75 patients who had midgut volvulus without intestinal necrosis. Approximately 70% of group B were neonates, and 3 died from complications of tetralogy of Fallot, severe pneumonia and gastric perforation, respectively. Group C included the 20 remaining patients who developed midgut volvulus with intestinal necrosis (involving 20% to 100% of the small intestine). Of these 20 patients, 17 (85%) were neonates and 8 (40%) died from extensive (> 70%) bowel gangrene. Patients who survived extensive bowel resection had the total length of viable small bowel over 30 cm. The mortality rate for all 153 patients was 7.8%.**

Conclusion: **Patients with malrotation developed symptoms within the neonatal period in approximately 80% of the cases. About two-thirds of intestinal malrotations presented with midgut volvulus and 20% of these had bowel gangrene. Necrosis over 70% of the small intestine was a significant risk factor for mortality in patients with midgut volvulus.**

Keywords: **Malrotation, midgut volvulus, intestinal necrosis**

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INTRODUCTION

Malrotation of the intestine usually presents with symptoms of intestinal obstruction in infancy and childhood, commonly caused by Ladd's band compression and midgut volvulus[1-4]. If symptoms first develop in older children, these may present with intermittent abdominal pain and vomiting and frequent repeated hospital admissions in some cases[5-7]. Intestinal necrosis secondary to midgut volvulus is the most serious complication of this abnormality[5]. Malrotation is sometimes found incidentally during surgical correction of abdominal wall defects, congenial diaphragmatic hernia and intestinal atresias. The authors undertook this retrospective review to determine the incidence of, and assess the impact of age at operation and eventual outcome in, patients with symptomatic malrotation of the intestine treated at a single tertiary institute over a 25-year period.

MATERIALS AND METHODS

After the study proposal (EC 142/2553) was approved by the Institutional Review Board, a retrospective review was performed of all patients with intestinal malrotation treated between January 1985 and December 2009. Information including clinical presentations, radiological findings, treatment and results were evaluated. Patients who were found to have malrotation as an incidental finding at laparotomy for other diseases such as omphalocele, gastroschisis, congenital diaphragmatic hernia, intrinsic duodenal obstruction, and other intestinal atresia or stenosis were excluded from the study. The data were analyzed by the Chi-square, Fisher's exact test, *t*-test, and Mann-Whitney U test as appropriate, with a p-value less than 0.05 considered significant.

Table 1 Clinical presentations in 153 patients

Symptoms / Signs	No. of patients	Percentage (%)
Bilious vomiting	119	78
Non - bilious vomiting	32	21
Abdominal pain	27	18
Abdominal distension	35	23
Hyperbilirubinemia	24	16
Bloody stool	16	11

RESULTS

During the 25-year period, 153 patients (111 males, 42 females) were operated on for symptomatic malrotation of the intestine at Queen Sirikit National Institute of Child Health. Eighteen of the 153 patients were born at Rajavithi Hospital, while the remaining were born at other hospitals. As the total number of neonates born at Rajavithi Hospital from 1985 to 2009 was 318,524, the crude incidence of symptomatic malrotation at Rajavithi Hospital was approximately 1 per 18,000 live births. The age of the patients ranged from one day to nine years. Approximately 80% (123 cases) were under one month old. Bilious vomiting was the most common presenting symptom, seen in 78% of patients (Table 1). Intermittent abdominal pain commonly developed in 27 older children (18%) and bloody stool was noted in 16 patients (11%).

Plain films of the abdomen revealed various

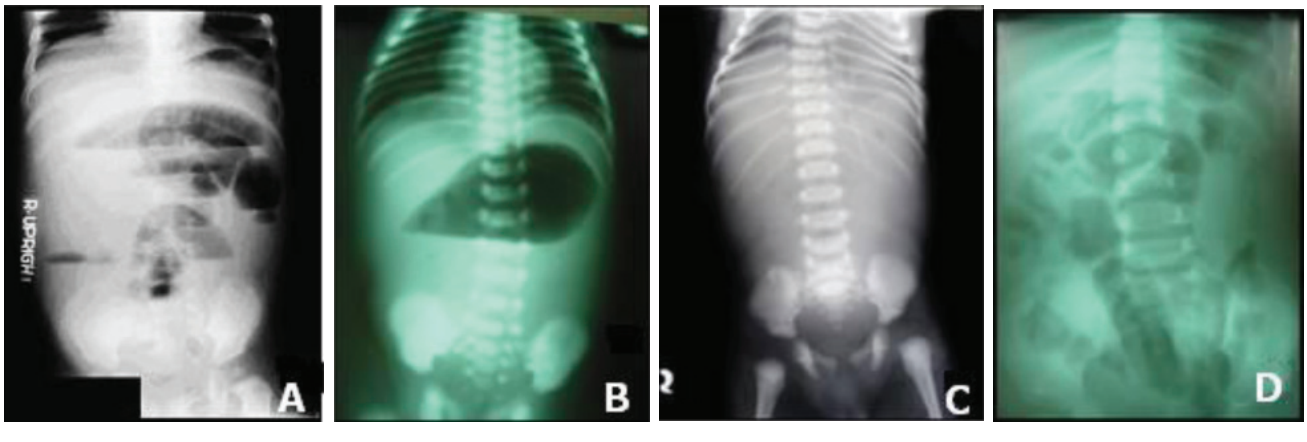

Figure 1 Plain films of abdomen in malrotation A. Complete small bowel obstruction B. High gut obstruction (only one gas bubble in the stomach) C. Gasless abdomen D. Normal finding

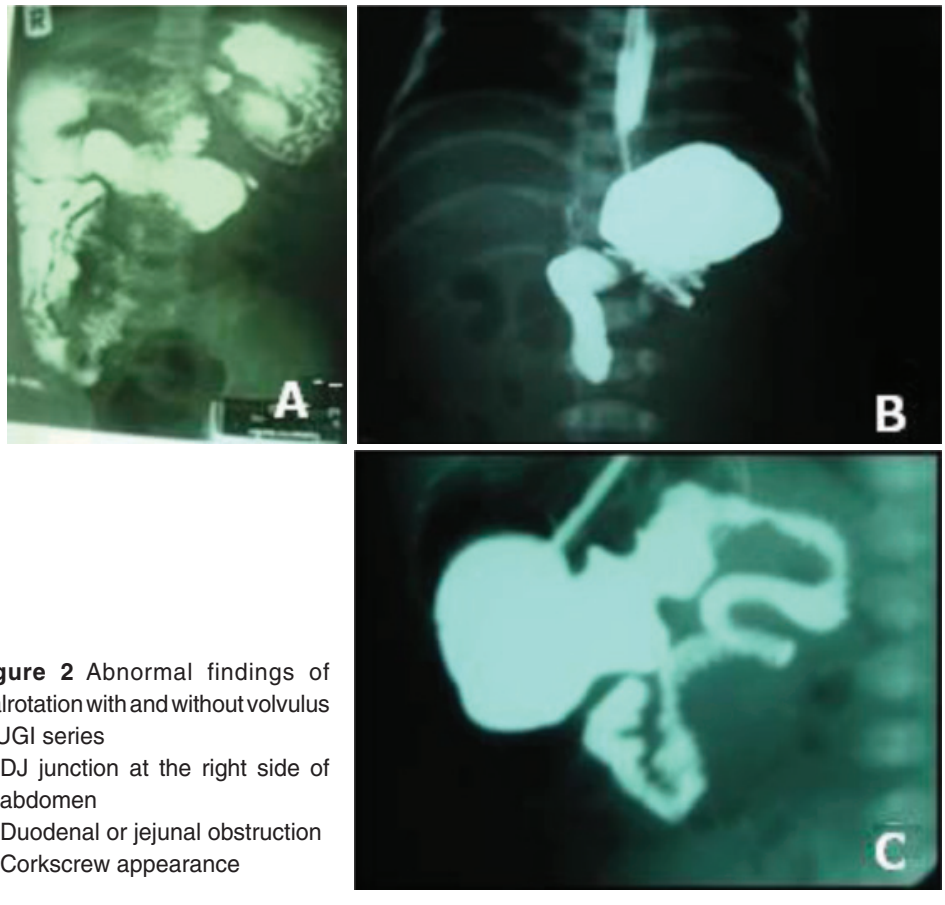

Figure 2 Abnormal findings of malrotation with and without volvulus in UGI series
A. DJ junction at the right side of abdomen
B. Duodenal or jejunal obstruction
C. Corkscrew appearance

patterns including small bowel obstruction, gas only in the stomach, gasless abdomen, and normal radiological finding in 115 (75%), 18 (12%), 15 (10%) and 5 (3%) patients, respectively (Figure 1). Upper gastrointestinal (UGI) series were done in 112 patients. Radiologic abnormalities included abnormal position of the duodenojejunal (DJ) junction, duodenal or jejunal obstruction and corkscrew appearance in 97 (87%), 74 (60%) and 38 (34%) patients, respectively (Figure 2). Barium enema (BE) was performed in only three cases and revealed abnormal position of the cecum in the right upper quadrant of abdomen (Figure 3).

All patients underwent laparotomy and were divided into three groups based on the operative findings. Duodenal obstruction, mostly at the second part, due to Ladd's band compression (group A) was noted in 58 patients (38%). The remaining 95 patients (62%) had malrotation with clockwise midgut volvulus (Figure 4). Seventy five of the 95 patients (79%) were found to have midgut volvulus with viable intestine after counterclockwise derotation of the volvulus (group B), whereas 20 patients (21%) with midgut

Figure 3 Abnormal position of the cecum at the right upper quadrant in a patient with malrotation

volvulus had intestinal necrosis (group C). Patients were operated on within the first month of life in approximately 80% of cases in group A, 70% in group B and 85% in group C; the median ages at operation were 10.5, 14, and 3 days, respectively. The average/

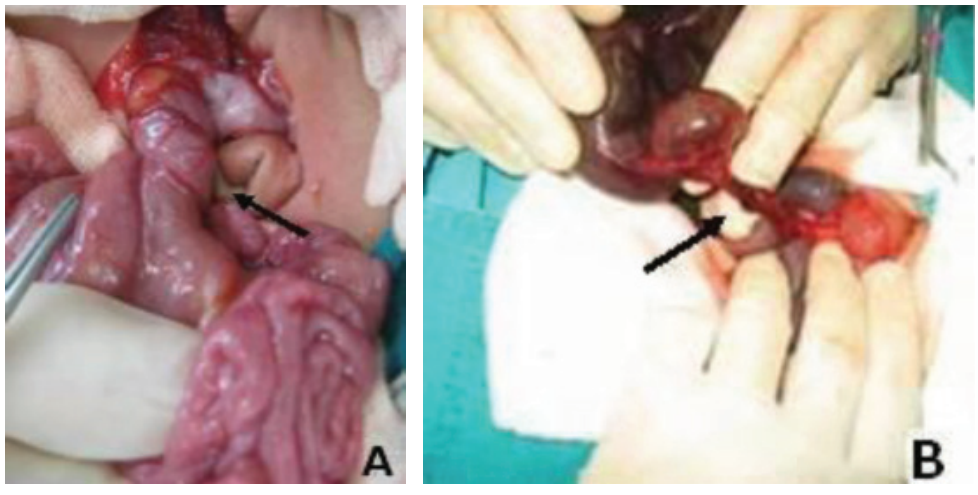

Figure 4 Presence of clockwise rotation in midgut volvulus
A. In a 25-day neonate without bowel necrosis
B. In a 8-day old neonate with extensive bowel necrosis

Table 2 Comparison of age operation and time interval from symptoms to operation between each group

Demographic data	Group A	Group B	Group C	p-value
Age at operation (days)				
Range	1-3285	3-3315	1-2035	A vs. B = 0.734
Mean	242.6±667.3	206.9±539.8	125.7±404.2	A vs. C = 0.464
Median	10.5	14	3	B vs. C = 0.532
Time interval from symptoms to operation				
Range	1-180	1-30	1-9	A vs. B = 0.100
Mean	13.7±28.7	7.9±8.0	2.7±2.3	A vs. C = 0.092
Median	4	5	2	B vs. C = 0.005

Table 3 Comparison of age at operation and mortality between each group

Age at operation	Group A		Group B		Group C	
	No.	Death	No.	Death	No.	Death
0 - 1 month	46	1	53	3	17	6
1 - 3 month	6	0	7	0	1	1
3 - 12 month	1	0	5	0	0	0
Over 1 year	5	0	10	0	2	1
Total	58	1 (1.7%)	75	3 (3.4%)	20	8 (40%)

Comparison between groups: group A vs. group B (1.7% vs. 3.4%, p = 0.631)
group A vs. group C (1.7% vs. 40%, p < 0.001)
group B vs. group C (3.4% vs. 40%, p < 0.001)

median age at operation of the patients in each group was not significantly different (Table 2). The average time interval from symptoms to operation in group A and group B was not significantly different (Table 2) but these were significantly or marginally higher than that of group C.

Regarding hospital mortality, 12 patients died (7.8%) and 10 of these (80%) were in neonatal period during presentation of symptoms and operations. Patients in group C had the highest mortality rate of 40%, whereas the mortality rates in group B and group A were 3.4% and 1.7%, respectively (Table 3). There was no recurrent midgut volvulus in the survivors. However, postoperative small bowel obstruction due to adhesions occurred in 5 of the 141 survivors (3.5%), 1 case in group A, 2 cases in group B and 2 cases in

Table 4 Associated congenital anomalies

Associated anomalies	No.	Associated anomalies	No.
Group A (27 cases)		**Group B (5 cases)**	
Congenital heart diseases	12	Anorectal malformations	2
Down's syndrome	5	Tetralogy of Fallot	1
Meckel's diverticulum	4	Situs inversus	1
Anorectal malformation	3	Dysplastic kidney	1
Situs inversus	2	Vesicoureteral reflux	1
Laryngomalacia	2	Mesenteric cyst	1
Omphalomesenteric duct	2		
Duplication of the duodenum	1	**Group C (2 cases)**	
Hiatal hernia	1	Anorectal malformation	1
Vertebral anomalies	1	Duplication of the jejunum	1
Other	3		

Some patients have more than one anomaly.

Table 5 Detailed description of the 20 patients in group C (midgut volvulus with bowel necrosis)

No	Age at operation (days)	Time from onset to operation (days)	Percentage of bowel necrosis (%)	Length of viable bowel (cm)	No. of operation	Major complications	Results
1	13	9	90	10	2	SBS[a], sepsis	dead
2	2	2	70	35	2	SBS[a]	survived
3	1	1	70	40	2	sepsis	dead
4	2	1	40	60	1	-	survived
5	8	2	40	60	1	-	survived
6	375	2	90	10	3	SBS[a], sepsis	dead
7	45	1	100[b]	0	2	sepsis	dead
8	2	1	80	25	2	anastomotic leak, sepsis	dead
9	2035	1	70	30	3	SBS[a]	survived
10	3	3	40	60	1	-	survived
11	5	5	40	65	1	-	survived
12	2	2	70	30	2	SBS[a]	survived
13	1	1	90	10	2	anastomotic leak, sepsis	dead
14	6	4	80	15	2	SBS[a], sepsis	dead
15	10	3	70	30	2	SBS[a]	survived
16	2	2	20	80	1	-	survived
17	3	2	90[c]	10	3	SBS[a], sepsis, gut obstruction	survived
18	2	1	100[b]	0	3	sepsis	dead
19	16	8	20	80	1	-	survived
20	3	2	60	40	2	SBS[a], sepsis, gut obstruction	survived

[a]SBS = short bowel syndrome; [b]No resection of necrotic bowel and no drainage; [c]Only Penrose drain placement, no resection of necrotic bowel

group C. Associated congenital anomalies were more common in patients in group A than those of other groups (Table 4). One patient in group A succumbed after Ladd's procedure and appendectomy due to severe congenital heart disease with congestive heart failure (CHF). Three patients in group B died postoperatively due to CHF from tetralogy of Fallot (1 case), severe pneumonia (1 case) and sepsis from preoperatively ruptured stomach (1 case).

The 20 patients in group C had midgut volvulus

with intestinal necrosis. Average ± SD and median percentage of small bowel necrosis was 66.5% ± 32.8% and 70%, respectively (ranged from 20% to 100%). All 20 patients underwent laparotomy with counter clockwise derotation of the volvulus and Ladd's procedure. A second look operation was noted in 10 cases (50%) and 4 cases (20%) required a third operation for definitive bowel resection. Only 6 patients (30%) had a segmental resection of necrotic bowel with appendectomy at the first laparotomy (Table 4). Eight patients (40%) succumbed from short bowel syndrome and septicemia. Of the 12 survivors 11 had small bowel necrosis ranging from 20% to 70% and the remaining viable small bowel length was at least 30 cm. They required extended treatment for short bowel syndrome. One exceptional case (No. 17) had small intestinal necrosis of approximately 90%, with remaining 10 cm of viable small intestine. The necrotic bowel was never resected. He developed many complications including enterocutancous fistula, septicemia, adhesive small bowel obstruction and prolonged paralytic ileus. He required four episodes of reoperation in a long hospital stay of over one year. He ultimately survived and was doing well in the last three years of follow-up.

DISCUSSION

The true incidence of intestinal malrotation is unknown because some cases are asymptomatic and remain undiagnosed. Bryne[8] reported an incidence of 1 per 6000 live births for symptomatic malrotation, compared with 1 per 18,000 live births in the present study. Estrada[9] estimated an incidence of 1 per 200 autopsies, and a clinical incidence of 1 per 25,000 admissions. Kantor[10] reported an incidental finding of malrotation in 0.2% of contrast studies of the gastrointestinal tract at any age. Many previous studies reported that 60% of the patients with malrotion developed clinical presentations within one month of age[1-3,11,12]. Our study revealed that approximately 80% of patients were under one month of age at surgery. Acute onset of bile-stained vomiting in neonates and infants with previously normal oral intake is the most common symptom of malrotation. Other manifestations included irritability or drowsiness and the passing of bloody stool. Chronic intermittent or vague abdominal pain with or without vomiting is commonly found in older children[5-7,11,12]. Passing of bloody stool was observed in 11% of our patients overall, but this presentation was noted in 80% of patients with midgut volvulus and intestinal necrosis (group C). Stewart[2] suggested that most neonates with obstruction from malrotation had association with midgut volvulus.

Plain abdominal radiographs revealed various findings such as small bowel obstruction, complete duodenal obstruction, only gas in the stomach, gasless abdomen or even normal intestinal gas distribution[11-14]. At our institute, UGI study is the investigation of choice for the diagnosis of malrotation with or without midgut volvulus. Classic radiological sign of malrotation is the malposition of the DJ junction at the right side of vertebral spine. A spiral or corkscrew appearance is the typical sign of midgut volvulus[3,11-14]. BE was historically recommended and is still used in some centers[14]. The advantage of BE is its relative safety in malrotation with midgut volvulus, but radiological findings may be difficult to interpret. BE may show abnormal position of the cecum, mostly in the right upper quadrant of abdomen. This finding may be found in some normal infants with incomplete fixation of the cecum at the right lower quadrant without malrotation. More recently color Doppler ultrasonography has been used to demonstrate the whirlpool sign for the diagnosis of midgut volvulus[15,16]. In addition, abdominal computerized tomographic (CT) scan can be also used to demonstrate superior mesenteric vein thrombosis in malrotation with chronic midgut volvulus[14].

Surgical correction by Ladd's procedure and appendectomy is the treatment of choice for intestinal malrotation. The entire bowel is mobilized from the peritoneal cavity to outside of the abdomen. Andrassy and Mahour[3] suggested that failure to extract the entire bowel outside the abdomen could lead to misdiagnosis or incomplete dissections of the bands. In patients with midgut volvulus, detorsion by counterclockwise rotation must be performed and the bowels should be covered with warm sponges to promote vascular recovery. If extensive intestinal necrosis is highly suspected, the abdomen should be closed and a second-look operation planned within 24-48 hours. We would like to suggest suturing only the skin or using of silastic sheath or other synthetic material to temporarily cover the abdominal wound in

order to prevent abdominal compartment syndrome during the wait for a second-look operation.

Many investigators have studied various factors which might influence hospital mortality, including age of patients[2,18,19] and delayed diagnosis[9,20]. The present study supported the association between mortality and younger age (Table 3). However, time interval between onset of symptoms and operation was not associated with an increase in mortality, especially if the obstruction or midgut volvulus was not tight. Messineo et al[21] studied clinical factors affecting mortality in children with malrotation of the intestine and found that significant risk factors included presenting symptoms in neonatal period, presence of serious abnormalities, and presence of necrotic bowel over 75%. These were similar to the findings of present study (Tables 3 to 5). Severe associated anomalies and preoperative complications were the major causes of death in patients with malrotation and midgut volvulus without bowel gangrene. Our study suggested that mortality was higher when the necrotic bowel was over 70%. Percentage of bowel necrosis did not correlate with degree of midgut volvulus and time interval from onset to operation. Extent of bowel necrosis was related rather to tight compression from clockwise volvulus of the midgut.

The incidence of postoperative adhesive small bowel obstruction was reported to vary widely from 3% to 24%[22,23]. This complication occurred in 5 of the 141 survivors (3.5%) in the present study. Murphy and Sparnon[24] emphasized long-term follow-up to parents regarding the risk and symptoms of postoperative small bowel obstruction in order to decrease the morbidity of this complication.

CONCLUSION

The present study demonstrated that clinical presentation of malrotation can occur at any age but approximately 80% occur within the neonatal period. Sudden bilious vomiting was the typical symptom in neonates and infants, whereas abdominal pain with or without vomiting was more common in older children. Two thirds of intestinal malrotation developed midgut volvulus and 20% of these had intestinal necrosis. Major causes of death in malrotion without intestinal necrosis included severe congenital anomalies and serious preoperative complications. For midgut volvulus with bowel gangrene, necrosis of over 70% of the intestine was an important risk for mortality. Patients who survived extensive bowel resection had viable small bowel of at least 30 cm.

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Original Article

Selective Curative Approaches for Thoracic Esophageal Cancer

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Abstract

Objective: **To determine the survival probability of patients with carcinoma of the esophagus who underwent en bloc esophagectomy and to compare two en-bloc surgical approaches.**

Materials and Methods: **Between October 2005 and September 2008, 81 patients with the diagnosis of esophageal carcinoma were treated at Suratthani Hospital. Esophagectomy was performed on 64 (79%) of these patients, 18 of whom had upper or mid esophageal carcinoma and underwent three-phase esophagectomy, while 46 had low esophageal carcinoma and underwent the Ivor Lewis operation. We analyzed the location and histology of the tumor, the number and level of lymph nodes, operative morbidity and mortality, and their influence on survival probabilities.**

Result: **The overall survival probability at 5 years was 19 %. The 5-year survival probabilities for the three-phase esophagectomy (upper and mid esophageal cancer) and the Ivor Lewis operation (low esophageal cancer) were 4 % and 25%, respectively, which were significantly different. There was no left cervical lymph node metastasis in patients who underwent the Ivor Lewis operation. The most common complication was wound infection. Most patients died from sepsis or myocardial infarction. The overall operative (hospital) mortality rate was 8 %.**

Conclusion: **Location of the tumor should strongly influence the type of surgery performed for esophageal carcinoma, and seemed to significantly affect the survival probabilities in the present study.**

Keywords: **Esophageal carcinoma, three-phase esophagectomy, Ivor Lewis operation**

Introduction

Patients with thoracic esophageal carcinoma usually present late in the course of their disease. By the time symptoms develop, such as dysphagia, the tumor has spread beyond the esophagus in most cases. Many patients have major adjacent organ involvement, mainly the aorta, trachea and bronchus, precluding surgical resection. The result of treatment for thoracic esophageal cancer is therefore poor.

For patients with resectable disease and those with cancer confined within the chest, surgery remains the basic method of management for this malignancy. The en-bloc operation, which includes not only a complete removal of the tumor but also an extended dissection of the lymph nodes in the mediastinum and abdomen, is one mainstay of treatment for this malignancy for the past 20 years. The location of the malignancy usually determines the approach of en-

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bloc surgery.

The aim of this prospective non-randomized study was to evaluate the outcomes of a series of patients with intrathoracic esophageal cancer, who underwent either three-phase esophagectomy with lymph node dissection or Ivor Lewis esophagectomy with extended lymph node dissection by using tumor location to select the type of surgery.

Patients and Methods

Between October 2005 and September 2008, patients at Suratthani Hospital with histologically proven thoracic esophageal cancer were recruited into the study. Patients with multiple distant metastasis or in advanced, inoperable, stages by clinical and endoscopic evidence or radiologic investigations were excluded from the study. Thus patients in the study underwent potentially curative esophagectomy. Data extracted for analysis included the location and histology of the tumor, the number and level of lymph nodes removed, operative time, hospital stay, operative morbidity, hospital mortality and survival time.

Before surgery all patients underwent barium swallowing, esophagogastroscopy with biopsy, plain chest radiography, computed tomography of the chest and abdomen and echocardiography. Bronchoscopy was performed in patients with tumors at the level of 20 to 25 cm from upper incisor teeth. Patients included in the study were divided into two groups. The first group consisted of patients with malignancy located between 20 and 25 cm from the incisor teeth. Three-phase esophagectomy was performed in these patients. The first phase or step of the operation was via right thoracotomy using the posterolateral incision at the fourth intercostal space. An en-bloc resection of the tumor was done along with additional mediastinal, paraesophageal, paratracheal, para-aortic and subcarinal lymph node dissection. The second step was the intraabdominal part via a midline incision. The stomach was mobilized by dividing the left gastric and left gastroepiploic arteries. The celiac nodes were dissected, and a feeding jejunostomy tube was placed. The last step was via a left cervical incision. The stomach was pulled up to the neck and anastomosed to the cervical esophagus by hand after left cervical lymph node dissection.

The second group consisted of patients with tumors below 25 cm from the incisor. The procedure used was the Ivor Lewis operation, performed as follows: Through an abdominal incision, a stomach tube was created, and a feeding jejunostomy tube placed. The thoracic esophagus was resected via a right thoracotomy incision. Lymphatic dissection was the same as for the three-phase esophagectomy, including a left cervical lymph node dissection (done as a part of the present study). The stomach tube was anastomosed to the proximal esophagus by hand using synthetic absorbable sutures via the thoracotomy incision. However, if the estimated free proximal margin was less than 5 cm, the procedure was converted to the three phase operation to maintain at least 5-cm margins. We did not perform a pyloroplasty or any drainage procedures after gastric pull up.

All patients underwent contrast-enhanced radiologic study for the assessment of the integrity of the esophagogastric anastomosis, 7 days after the operation. Operative mortality was defined as hospital death within the first 30 days after operation. All tumors were staged by the TNM classification system (7th ed). Survival time was defined as the duration between the year of the index operation till the year of death before September 2011, otherwise survival was censored at that time.

Continuous variables were summarized as mean and standard deviation or median and range as appropriate. Categorical variables were summarized as counts and percentages. Survival probabilities were calculated using a spline-based smoothed estimation method for interval-censored data. Statistical analysis was performed using Stata 9 software (Stata Corp, College Station, TX, USA).

Results

There were 81 patients with histologically proven esophageal cancer during the recruitment period. Seventeen patients were excluded because of metastasis and advanced disease, leaving a total of 64 patients in the study. There were 44 men and 20 women. The median age was 61 years, with a range between 38 and 74 years. There were 18 patients in the three-phase esophagectomy group, and 46 patients in the Ivor Lewis group. Clinical characteristics of patients in the

Table 1 Clinical Characteristics

	Three-phase esophagectomy N =18	Ivor Lewis esophagectomy N =46
Age (years): median (range)	60 (40 to 73)	61 (38 to 74)
Sex: M/F (%)	11/7 (61/39)	33/13 (72/28)
Grade of dysphagia: number (%)		
Grade 1	0	0
Grade 2	0	0
Grade 3	4 (22)	3 (7)
Grade 4	10 (56)	31 (67)
Grade 5	4 (22)	12 (26)
Grade 6	0	0

No statistically significant differences between groups for all characteristics (at 5% level)

two groups are presented in Table 1. Pathological findings are presented in Table 2. The outcomes of the operations are presented in Table 3.

The median ages of patients in the three-phase esophagectomy and Ivor lewis groups were 60 years (range, 40 to73 years) and 61 years (range, 38 to 74 years) respectively. Most patients were presented with grade 4 to 5 dysphagia. There were higher proportions of men in both the three-phase esophagectomy (61%) and Ivor Lewis groups (72%). All these characteristics were not significantly different between the two groups at the 5% level (Table 1).

All patients in the three-phase esophagectomy group had squamous cell carcinoma of the esophagus, while 72% (33/46) of patients in the Ivor Lewis group had squamous cell carcinoma ($p = 0.013$ by Fisher's exact test) (the remaining had adenocarcinoma). The majority of patients in both groups had poorly differentiated cancer. The majority had TNM stage III disease. Regional node metastasis was almost the same for both groups, but patients in the Ivor Lewis group had no left cervical lymph node metastasis, which was the only statistically significant finding ($p < 0.001$ by Fisher's exact test; Table 2).

The operative time was similar for both groups of patients, as was the length of hospital stay. Similar types of complications occurred in both groups of patients. There was a tendency for more pneumonia to occur in patients undergoing the Ivor Lewis operation.

Table 2 Pathological findings

Pathological findings	Three-phase esophagectomy N = 18	Ivor Lewis esophagectomy N =46
Squamous cell carcinoma: number (%)		
Well-differentiated	6 (33)	7 (15)
Moderated -differentiated	3 (17)	3 (7)
Poorly - differentiated	9 (50)	23 (50)
Adenocarcinoma: number (%)		
Well-differentiated	0	3 (7)
Moderated -differentiated	0	0
Poorly - differentiated	0	10 (22)
Lymph node involvement: number (%)		
Celiac node	4 (22)	16 (35)
Subcarinal node	15 (83)	36 (78)
Paratracheal node	14 (78)	37 (80)
Mediastinal node	10 (56)	28 (61)
Para esophageal node	12 (67)	30 (65)
Left cervical lymph node	6 (34)	0
Staging: number (%)		
I	0	0
IIa	0	2 (4)
IIb	3 (17)	2 (4)
III	15 (83)	42 (92)
IV	0	0

No statistically significant differences between groups for almost all findings (at 5% level), except the presence of adenocarcinoma (Fisher's exact test $p = 0.013$), and left cervical node metastasis (Fisher's exact test $p < 0.001$)

Table 3 Outcomes of esophagectomy

Operative outcomes	**Three-phase esophagectomy N = 18**	**Ivor Lewis esophagectomy N = 46**
Complications and death: number (%)		
Pneumonia	1 (6)	6 (13)
Anastomosis leakage	1 (6)	2 (4)
Wound infection	2 (11)	4 (9)
Myocardial contusion	1 (6)	1 (2)
Death	1 (6)	4 (9)
Duration of operation (hours): median (range)	4.3 (3.5 to 5.1)	4.2 (3.5 to 4.6)
Hospital stay (days): median (range)	20 (11 to 30)	21 (13 to 45)
Follow-up time (years): median (range)	2.5 (1 to 5)	4 (1 to 7)

No statistically significant differences between groups for almost all findings (at 5% level), except follow-up time (rank test p = 0.022)

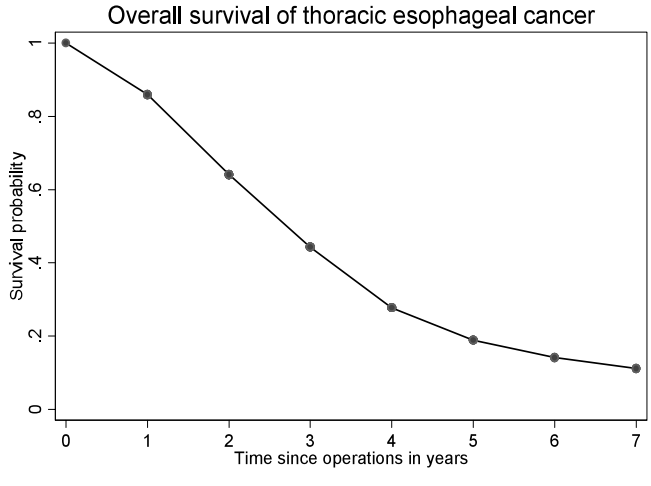

Figure 1 Smoothed overall survival probability of thoracic esophageal cancer patients who underwent en-bloc esophagectomy

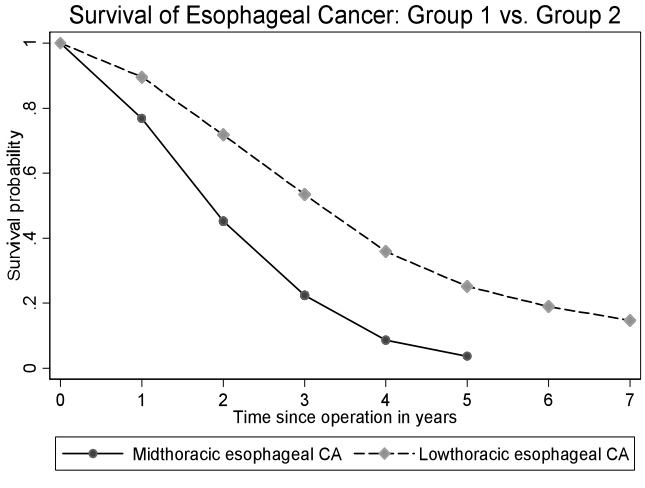

Figure 2 Comparing the smoothed survival probability of groups 1 (three-phase esophagectomy) and 2 (Ivor lewis esophagectomy) patients

The hospital mortality rate was 8 % (5 in 64 patients). All hospital mortality was due to either sepsis or myocardial infarction. Patients in the Ivor Lewis group were followed for a significantly longer time (p = 0.022 by rank test; Table 3).

The overall survival probabilities at 1 year, 3 years and 5 years after operation were 82% (95% CI: 75% to 92%), 44% (95% CI: 32% to 56%) and 19% (95% CI: 11% to 29%), respectively. The smoothed overall survival curve is presented in Figure 1. The survival probabilities for the three-field esophagectomy group at 1 year, 3 years and 5 years were 77% (95% CI: 58% to 88%), 22% (95% CI: 9% to 40%) and 4% (95% CI: 0 to 14%), respectively. The survival probabilities for the Ivor Lewis esophagectomy group at 1 year, 3 years and 5 years were 90% (95% CI: 80% to 95%), 53% (95% CI: 39% to 66%) and 25% (95% CI: 14% to 38%), respectively. The survival probabilities of the two groups, shown in Figure 2, were statistically different by the log-rank test (p = 0.006).

Discussion

Although esophagectomy remain the standard surgical treatment for patients with operable esophageal cancer, the result of treatment remains poor. The 5-year survival rates in most series (Table 4) rarely exceed 30% even for those in whom potentially

Table 4 Results of esophagectomy for esophageal cancer from previous reports

Author	Year	N	Operation	Death Rate (%)	Complications (%)	Adeno/ Squamous	5-yr survival (%)
Karl[8]	2000	143	TT	2.1	29	82/18	29 (3-yr)
Orringer[2]	1999	800	TH	4.5	NS	69/28	23
Vigneswarren[6]	1997	132	TH	2.3	72	77/23	21
Ellis[1]	1997	454	TH/TT	3.7	30	67/33	30
Lieberman[4]	1995	258	TT	5	NS	52/48	27
Putnam[3]	1994	221	TT/TH	6.8	75	66/33	19
Gertsch[5]	1993	100	TH	3	68	57/43	23
Golminc[9]	1993	67	TH/TT	7.4	51	all squamous	NS
Gelfand[7]	1992	160	TH	2.5	NS	75/25	23

NS, not stated; TH: transhiatal, TT: transthoracic

curative resection is performed (R0 resection). Many centers believe that en bloc esophagectomy is a reasonable treatment for esophageal cancer because of the poor prognosis[1-9]. The long term survival of patients with esophageal cancer is poor due to extensive tumor invasion through the muscular layer and lymphatics, as well as late presentation. Therefore, esophagectomy with complete removal of metastatic regional lymph nodes is considered by some as essential for a curative resection of esophageal carcinoma.

This en-bloc resection, however, has not been clearly shown to improve long term survival over other types of resection. Additionally, the en bloc surgical approach of choice, i.e. either the three phase or the Ivor Lewis approach, remains controversial[10-13]. In the present study, we reviewed the long term outcomes of our series of operable esophageal cancer patients who underwent potentially curative en-bloc esophagectomy, and compared the three-phase and Ivor Lewis approaches. Although the present study cannot directly answer the question of long term benefits or the superiority of either operation, we hope our data can contribute something to the discussion.

We chose the three-phase esophagectomy and the Ivor Lewis operation for patients with esophageal cancer over other non-en bloc operations, such as transhiatal esophagectomy, for several reasons. En-bloc approaches enabled the complete visualization and resection of all abdominal and thoracic esophagus along with the mediastinal lymph tissue. The gastroesophageal anastomosis either at the apex of right chest in the Ivor Lewis operation, and at the left neck in the three-phase esophagectomy, can be done with minimal tension. The proximal margin of resection can be examined and made grossly tumor-free with ease. Left cervical lymph node dissection can be performed routinely.

Patients in the present series were assigned to each operative approach based on tumor location. We can tailor the lymph node dissection based on tumor location. For example, in a nationwide Japanese study[14], correlations between regional node involvement and tumor location were found. In patients with upper thoracic cancer, the rate of cervical node metastasis was 42.3%, that for mediastinal nodes was 63.1%, and for abdominal nodes 19%. Metastatic rates for middle thoracic esophageal cancer were 27.5% for cervical nodes, 55.8% for mediastinal nodes and 41% for abdominal nodes. For lower thoracic esophagus, metastasis was seen in 10.9% of cervical nodes, 43.5% of mediastinal nodes, and 67.4% of abdominal nodes[14]. We chose to perform three-phase esophagectomy for thoracic esophageal cancer, and Ivor Lewis operation for lower esophageal cancer because of these lymph node metastasis-tumor location correlations.

In the present study patients in group 1 with mid thoracic esophageal cancer who underwent three-phase esophagectomy had 34% cervical node metastasis rate, 56 to 83% mediastinal group node metastasis rate mainly in subcarinal nodes and 22 % abdominal node metastasis rate (Table 2). Patients in group 2 with low esophageal cancer who underwent Ivor Lewis operation had no cervical lymph node metastasis, but had metastasis to the mediastinal nodes in 61 to 80 % of patients mainly in the paratracheal nodes, and 35 % metastasis to the abdominal lymph nodes. These findings are in accord with the Japanese study[14], and show a biological behavior consistent with the fact that

the esophageal submucosa is rich in lymphatics that extend longitudinally as well as laterally. The longitudinal network of lymphatics implies frequent cancer spread to nodes in neck, the thorax, and the abdomen despite tumor location. Once a tumor has breached the muscular layers, the incidence of positive regional nodes exceeds 75%[15].

The overall survival of resectable, nonmetastatic thoracic esophageal cancer in the present study was 19% at 5 years. Few patients with mid-thoracic esophageal cancer who underwent three-phase esophagectomy survived up to 5 years, with an estimated 4% 5-year survival based on a statistical model. However, patients with low thoracic esophageal cancer had a 25% 5-year survival rate after Ivor Lewis esophagectomy. These survivals were significantly different. Our operative mortality was 6 to 9%, with very few anastomotic leakages (4 to 6%). There was a 6 to 13% rate of postoperative pneumonia. These outcomes were similar to other studies[16].

Results of the present study compared favorably with those previously published. Skinner et al have shown that both the number of metastatic lymph node and depth of tumor invasion had adverse effects on survival[10]. Therefore, en-bloc esophagectomy with complete removal of metastatic lymph nodes and resection of the digestive tract for at least 10 cm on either side of the tumor and complete excision of adjacent involved tissues should be expected to improve long term survival[11-13]. The number of positive nodes was another important determinant of survival as reported by Akiyama et al[17], which predicted worse prognosis in patients with seven or more positive nodes. Baba et al[18] reported that injection of technetium labeled rhenium colloid into the esophageal wall can help identify lymphatic structures that may contain metastatic cancer.

In the present study, location of the tumor was significantly related to the survival probabilities. Higher thoracic esophageal cancers were probably more aggressive biologically even after adjustment for tumor stage, with the presence of cervical node metastasis a marker of aggressiveness. The different en-bloc operative approaches probably had no significant effect on survival. Nonetheless, different en-bloc operations are still recommended for tumors at different locations, because rates of cervical lymph node metastasis differ, such that these nodes may not need to be removed in low esophageal cancer, and the esophagogastric anastomosis site can differ as well.

Finally, squamous cell carcinoma was the most common type of esophageal cancer in the present study. Despite a rising incidence of adenocarcinoma of the esophagus, especially in Western clinics[19,20], squamous cell carcinoma of esophagus remains the dominant type in Thailand.

Conclusion

The author believes that en bloc esophagectomy should be the standard of care for esophageal carcinoma, and the result of the present study may encourage other medical centers to improve on the technique and to select cases for this operative approach based on the location of the cancer. However, the procedures are technically demanding and time consuming. Postoperative care requires careful attention, especially for pulmonary complications and detection of anastomosis leakage and wound infection. From the above evidence, it can be concluded that this aggressive surgical approach is at least competitive with other standards of treatment for thoracic esophageal cancer.

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Original Article

Efficacy and Safety of Intravenous Single-agent Antibiotics - Cefoperazone/Sulbactam in Non-critically Ill Surgical Patients with Intra-abdominal and Soft Tissue Bacterial Infection

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Abstract

Purpose: **To evaluate the efficacy and safety of intravenous single-agent antibiotic Cefoperazone/Sulbactam for the treatment of bacterial infection among surgical patients.**

Methods: **This prospective opened non-comparative clinical trial was conducted in the Department of Surgery, Faculty of Medicine Siriraj Hospital, Bangkok, Thailand from 1October 2008 to 30 September 2009. Therapeutic Cefoperazone/Sulbactam (Sulcef®) at the dose of 1.5 grams was given intravenously every 12 hours to patients with bacterial infection who needed emergency or elective surgical interventions, and the APACHE II score was equal or less than 15. All patients were scheduled for follow-up visits at 7, 14 and 30 days after the first dose of intravenous Cefoperazone/Sulbactam for monitoring the clinical outcomes.**

Results: **Thirty-five patients were enrolled and 31 patients had completed the follow up. There were 17 males and 14 females with the mean age of 53 years (range 20-85 years). The clinical efficacy of Cefoperazone/Sulbactam to improve or cure patients was 87%, whereas the bacterial eradication rate was 84%. Neither drug-related serious adverse reaction nor drug allergy was observed.**

Conclusions: **Cefoperazone/Sulbactam demonstrated broad-spectrum antibacterial coverage in patients infected with gram-positive, gram-negative and anaerobic bacteria. Intravenous Cefoperazone/Sulbactam is safe and effective for empirical treatment of bacterial infection among surgical patients.**

Keywords: **Antibiotics, monotherapy, surgical infection, intra-abdominal infection, skin and soft tissue infection**

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Introduction

Surgical infection (SI), such as skin and soft tissue infection and intra-abdominal infection, is a common problem in surgical practice. It is significantly associated with high morbidity and mortality. Empirically antimicrobial therapy in conjunction with appropriate surgery is considered the principle of management of SI[1].

Effective empiric antibiotics should have broad-spectrum antibacterial activity against common pathogens specific to each organ. Inappropriate treatment of bacterial infection may lead to high costs and even death. Antimicrobial resistance has been dramatically increasing, especially among gram-negative bacteria, which is commonly resistant to beta-lactam antibiotics.

Briefly, the mechanism of beta-lactam antibiotic resistance could occur through the bacterial production of beta-lactamases that lead to amide bond destruction. Thus, the beta-lactam ring is disrupted and unable to bind with penicillin-binding proteins. This process leads to neutralization of bactericidal effects. To overcome this problem, the beta-lactamase inhibitors are added into beta-lactam antibiotics. The beta-lactamase inhibitors permanently bind to the beta-lactamase at the active site of serine hydroxyl group[1-2].

The combination of beta-lactam antibiotics and beta-lactamase inhibitors, also called beta-lactam/beta-lactamase inhibitors (BLBI) have been used as a single agent or monotherapy for both prophylactic and therapeutic purposes[3-4]. Well-known examples of such agents include amoxicillin/clavulanate and cefoperazone/sulbactam. These combinations also enhance the bactericidal activity against both gram-positive and gram-negative bacteria.

The spectrum of BLBIs may cover gram-positive bacteria such as *Staphylococcus aureus, Staphylococcus epidermidis* and *Staphylococcus pyogenes*, and may cover gram-negative bacteria such as *Haemophilus influenza*, *Escherichia coli*, *Proteus* spp., *Citrobacter* spp., Serratia spp., *Enterobacter* spp., *Neisseria gonorrhoeae*, *Neisseria meningitidis* and *Acinetobacter* spp. In addition, BLBIs also cover anaerobic bacteria such as *Bacteroides fragilis*, *Fusobacterium* spp. and *Eubacterium* spp.[3-8]

BLBIs commonly have a half-life of 1-2 hours on average. They effectively distribute into various organs and body fluids, including the gallbladder, bile, skin, uterus and ovary[9-10].

At present, various regimens of monotherapy and combined therapy of antibiotics have been used as empiric treatment of SI. Combined therapy such as Ceftriaxone and Metronidazole has been commonly used as the first line empiric agents for mixed aerobic and anaerobic bacterial infection. However, in a setting where lack of nursing staff and huge ward workload is a major issue, monotherapy may be more favorable than a combined regimen.

One of the most widely used monotherapy regimen for the treatment of SI includes BLBI such as Cefoperazone/Sulbactam. Excellent efficacy and safety of intravenous Cefoperazone/Sulbactam for the treatment of SI has been reported in the literature[11-12]. However, these studies were mainly conducted in the western population, whose pharmacokinetics and pharmacodynamics could be different from those of Thai patients. Also, bacterial susceptibility to various antibiotics could be different in different settings as well. The aim of the present study was to evaluate the efficacy and safety of intravenous Cefoperazone/Sulbactam for the treatment of SI in Thai patients.

Material and Methods

After obtaining ethical approval from the Institutional Review Board, a prospective opened non-comparative clinical trail was conducted in the Department of Surgery, Faculty of Medicine Siriraj Hospital, Bangkok, Thailand from 1 October 2008 to 30 September 2009. Patients were enrolled with the following inclusion criteria: age over 18 years, having intra-abdominal infection or skin and soft tissue infection which required intravenous antibiotics with or without surgical interventions, and the APACHE II score was at most 15. Patients were excluded by any one of the following criteria: previous history of hypersensitivity or allergy to penicillin, cephalosporins or their derivatives; pregnancy; lactation; renal insufficiency; hepatic impairment; and refusal to participate.

All patients received empiric intravenous Cefoperazone/Sulbactam (Sulcef®, Siam Pharmaceutical, Thailand) at the dose of 1.5 grams administered every 12 hours for at least 5 days with therapeutic intention. Collection of blood, pus, discharge and

Table 1 Demographic data, diagnosis, and treatment

Data	Number (%); n = 31
Sex	
Male	17 (54.8)
Female	14 (45.2)
Age (mean ± SD)	52.9 ± 19.1
APACHE II Score (mean ± SD)	6.3 ± 3.9
Co-morbidity	17 (54.8)
Diabetes mellitus	8(25.8)
Hypertension	10 (32.3)
Dyslipidemia	2 (6.5)
Gouty arthritis	1 (3.2)
Hepatitis	1 (3.2)
Parkinsonism	1 (3.2)
Cerebrovascular disease	1 (3.2)
Ischemic heart disease	1 (3.2)
Diagnosis	
Skin and soft tissue infection	6 (19.4)
Necrotizing fasciitis	4 (12.9)
Ischiorectal abscess	2 (6.5)
Intra-abdominal infection	25 (80.6)
Bowel gangrene or perforation	9 (29.0)
Ruptured appendicitis and appendiceal abscess	6 (19.4)
Acute cholangitis	4 (12.9)
Acute colonic diverticulitis	3 (9.7)
Others	3 (9.7)
Treatment modalities	
Operations	26 (83.9)
Celiotomy and bowel resection	7 (22.6)
Appendectomy	4 (12.9)
Percutaneous drainage	4 (12.9)
Soft tissue debridement	3 (9.7)
Biliary drainage / ERCP	3 (9.7)
Colectomy	2 (6.5)
Cholecystectomy	1 (3.2)
Ileostomy	1 (3.2)
No operation	5 (16.1)

SD: standard deviation; ERCP: endoscopic retrograde cholangiopancreatography

necrotic tissue were carried out for bacterial culture and susceptibility test as needed. Patients underwent surgical intervention such as incision and drainage or intra-abdominal operations as appropriate. The choice of operative procedures depended on the diagnosis and intraoperative findings. Additional oral antibiotics such as oral BLBIs or oral cephalosporin plus metronidazole were prescribed to patients as switched therapy if indicated. Patients were discharged from the hospital if they had no fever, normal bowel function, good ambulation and no signs of infection. All patients were scheduled for follow-up examinations at 7, 14 and 30 days postoperatively for monitoring the outcomes.

Results

This prospective opened non-comparative clinical study was conducted on a series of 35 patients with American Society of Anesthesiology (ASA) status I-III. Of the 35 patients, 31 completed the study. Four patients were excluded from the study by the exclusion criteria. There were 17 males (55%) and 14 females (45%) aged between 20 to 85 years (mean 52.9 years,

Table 2 Outcomes

Data	Number (%) ; n = 31
Clinical improvement	
Cure/Improvement	27 (87.1)
Failure	4 (12.9)
Adverse reactions	11 (35.5)
Anorexia	8 (25.8)
Nausea	8 (25.8)
Vomiting	7 (22.6)
Diarrhea	3 (9.7)
Constipation	3 (9.7)

Table 3 Microbiology

Data	Number (%); n = 31
Microbiology	
Positive culture by site	17 (54.8)
Blood	4 (12.9)
Abdominal pus/ discharge	9 (29)
Skin and soft tissue	2 (6.5)
Central line	1 (3.2)
Intra-articular fluid	1 (3.2)
Positive culture by species	22 (71)
Enterabacter cloacae	1/22 (4.5)
Group C *streptococci*	1/22 (4.5)
Alpha-hemolytic *streptococci*	2/22 (9)
Methicillin-susceptible *S. aureus*	3/22 (13.6)
E. coli ESBL negative	6/22 (27.3)
E. coli ESBL positive	4/22 (18.2)
Salmonella sp.	1/22 (4.5)
Enterococcus faecalis	1/22 (4.5)
Klebsiella pneunoniae	3/22 (13.6)

ESBL: extended spectrum beta-lactamase

standard deviation (sd), 19.1 years). Seventeen patients (54.8%) had any of the following underlying diseases: diabetes mellitus, hypertension, dyslipidemia, gouty arthritis, hepatitis, Parkinsonism, cerebrovascular disease and ischemic heart disease. The mean APACHE II score was 6.3 (sd 3.9). Diagnosis, treatment, and surgical procedures in these patients are shown in Table 1. The clinical efficacy of Cefoperazone/Sulbactam to improve or cure patients was 87% (27/31), whereas bacterial eradication rate was 84% (26/31). All four patients who failed to be treated by Cefoperazone/Sulbactam had at least one of the comorbidities. No specific disease, surgical intervention, or type of bacteria was clearly responsible for treatment failure. The majority of positive bacterial culture was found from abdominal pus or discharge (9/31, 29%). *Escherichia coli* was the predominant bacteria among positive cultures (10/22, 45.5%). Interestingly, Escherichia coli with positive extended spectrum beta-lactamase (ESBL) was found in 18.2% (4/22) of specimens. Neither drug-related serious adverse reaction nor drug allergy was observed.

Discussion

Li Jia-tai et al. (1997) has studied the efficacy and safety of Cefoperazone/Sulbactam in the treatment of bacterial infection in 235 patients compared with cefotaxime[13]. The efficacy rate of Cefoperazone/Sulbactam was 95% compared with 90% of cefotaxime ($p = 0.186$). The bacterial eradication rate of Cefoperazone/Sulbactam and cefotaxime was 85% and 81% respectively ($p = 0.467$). Both regimens showed no significant difference in terms of adverse events (7.8% vs 8.7%, $p = 0.813$). These adverse reactions included skin rash, nausea, vomiting, thrombophlebitis, rising liver enzymes including alanine aminotransferase, alkaline phosphatase and aspartate aminotransferase. Engin and colleagues (1991) also demonstrated the efficacy and safety of cefoperzone/sulbactam in surgical infection and found the clinical cure rate to be 91% even though they reported a case of drug intolerance with rising glutamic oxaloacetic transaminase, glutamic pyruvic transa-minase, alkaline phosphatase, as well as prolonged bleeding time[14]. Jauregui and colleagues (1990) reported the efficacy of Cefoperazone/Sulbactam compared with that of gentamicin plus clindamycin in 152 patients with intra-abdominal infection[15]. Cefoperazone/Sulbactam had 86.8% cure rate whereas gentamicin plus clindamycin had only 61.8% cure rate ($p < 0.006$). This study, therefore, confirmed the better efficacy of Cefoperazone/Sulbactam in the treatment of intra-abdominal infection.

In the present study, the bacterial eradication rate of 84%, with clinical efficacy of 87% supported the effectiveness of this antimicrobial regimen. This result seemed to be comparable to those of previous studies. In the present study, a high incidence of postoperative anorexia, nausea and vomiting was found (25.8%, 25.8% and 22.6% respectively) within the first 24 hours. These events could have been side effects of general anesthesia as well as those of narcotics used for postoperative pain control. However, these events

were only temporary, and were dramatically improved after 24 hours. Symptomatic treatment using antiemetic agents such as intravenous metoclopramide or ondansetron was sufficient for most patients. Diarrhea and constipation both occurred in 14.3% of patients within the first 48 hours, and could be either true adverse drug reactions or normal early postoperative events. They also disappeared after 72 hours. No drug-induced hypersensitivity syndrome or serious adverse reaction was seen in the present study.

Intravenous Cefoperazone/Sulbactam as a single antimicrobial agent is more convenient to use compared to the commonly used combination of ceftriaxone and metronidazole. However, the surgeon should be aware of adverse drug reactions. Careful medical history should be taken to determine if the patient has had any previous allergy symptoms such as urticaria, pruritus, angioedema, bronchospasm, hypotension or arrhythmia, especially previous serious adverse drug reaction (e.g., drug-induced hypersensitivity syndrome, drug fever, or toxic epidermal necrolysis)[8].

Conclusion

The present study demonstrated the broad-spectrum antibacterial coverage of Cefoperazone/Sulbactam in Thai patients infected with gram-positive, gram-negative and anaerobic bacteria. Parenteral Cefoperazone/Sulbactam is a safe and effective single agent antibiotic for the treatment surgical infection in Thai patients.

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