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Antibiotic irrigation during pancreatoduodenectomy to prevent infection and pancreatic fistula: A randomized controlled clinical trial

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ABSTRACT

Background: Surgical site infection affects 25% of patients undergoing pancreatoduodenectomy. This double-blind, randomized controlled trial tested the efficacy of intraperitoneal antibiotic irrigation in decreasing infection and pancreatic fistula after pancreatoduodenectomy.
Methods: Patients undergoing pancreatoduodenectomy were randomized (1:1 ratio) to intraperitoneal antibiotic (polymyxin B, 500,000 units/L) irrigation or 0.9% NaCl irrigation. All patients received 1 dose of standard parenteral antibiotics within 1 hour of incision. The trial was powered to detect a 15% difference in any surgical site infection (primary endpoint) within 30 days after pancreatoduodenectomy.
Results: One hundred ninety patients undergoing pancreatoduodenectomy were randomized: 95 to antibiotic irrigation and 95 to saline irrigation. Groups were well matched regarding demographics, diagnosis, preoperative biliary stenting, bactibilia, texture of the pancreatic parenchyma, pancreatic and bile duct size, portal vein resection, and anastomotic technique. Overall, 30-day surgical site infection was observed in 24 (13%) patients: antibiotic irrigation in 10 (11%) versus saline in 14 (15%) ($P = .62$). Superficial (n = 9, 5%) and organ-space (n = 15, 8%) surgical site infection rates were 3% and 7% (antibiotic) and 6% and 8% (saline), respectively ($P > .31$). Clinically relevant postoperative pancreatic fistula occurred in 11 (12%) patients in the antibiotic arm and 10 (11%) in saline controls ($P > .95$).
Conclusion: The addition of antibiotic solution to intraperitoneal irrigation does not decrease the incidence of postoperative infectious complications or pancreatic fistula after pancreatoduodenectomy.

Introduction

Pancreatoduodenectomy (PD) is a complex procedure performed for patients with both benign and malignant diseases of the periampullary region. Although mortality from the procedure is reported to be less than 5% in high-volume centers, morbidity rates are much greater with reports indicating rates around 40%.[1,2] Two of the most common complications contributing to this high morbidity rate include surgical site infection (SSI) and postoperative pancreatic fistula (POPF). Studies have demonstrated that such complications are associated with increased mortality rates in patients undergoing pancreatic surgery.[3]

Many patients require preoperative biliary stenting to relieve obstructive jaundice before undergoing PD. Although stenting of the extrahepatic biliary tree affords biliary decompression, patients almost universally develop biliary colonization with enteric flora from the gastrointestinal tract. Thus, patients with preoperative biliary stents tend to have greater rates of wound infection and bacteremia after PD.[4,5] Resection of the extrahepatic bile duct during PD results in the spillage of contaminated bile into the operative field. Bacterial contamination of the peritoneum may not be treated adequately with only prophylactic intravenous antibiotics and may contribute to local complications, such as surgical site infections and anastomotic failures.

Dilutional irrigation of the peritoneal cavity with 0.9% NaCl or antibiotic solution is used commonly for abdominal operations that involve microbial contamination. Peritoneal lavage is intended to

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decrease bacterial load and decrease the risk of infection.[6] Although peritoneal irrigation typically consists of 0.9% NaCl , several antibiotic solutions have shown intended benefits. A recent randomized controlled study in colorectal surgery demonstrated the benefits of intraoperative antibiotic irrigation of the peritoneum. Rates of wound complications decreased from 14% to less than 5% and intra-abdominal abscesses from 6% to 0% for patients receiving antibiotic compared with saline irrigation.[7]

The benefits of intraoperative peritoneal irrigation during pancreatoduodenectomy have not been established. This randomized controlled trial evaluates the efficacy of antibiotic irrigation in decreasing the rate of SSIs and POPF among patients undergoing pancreatoduodenectomy.

Materials and Methods

This prospective, double-blind, single-institution, randomized controlled trial evaluated the benefits of peritoneal irrigation with antibiotic solution in patients undergoing PD. Approval for this study was gained through the Indiana University institutional review board, and the study was compliant with the Health Insurance Portability and Accountability Act.

Inclusion criteria included patients 18 years of age or older who were scheduled for nonemergent open pancreatoduodenectomy for any disease diagnosis. Exclusion criteria included patients who were pregnant, imprisoned, or undergoing concomitant colectomy or hepatectomy; with any established allergy to study medications; with a preoperative serum creatinine >2.0 mg/dL; and unable to provide informed consent.

Once enrolled, consented patients were randomized in a 1:1 ratio to treatment with either antibiotic or placebo (0.9% NaCl) irrigation under a blocked randomization scheme without stratification criteria. The patient, treating surgeon, and research nurse coordinator were all blinded to the assigned treatment during the study.

All patients underwent an informed consent process during the preoperative clinic visit that included a thorough description of the study and discussion with the treating surgeon and a dedicated research nurse. After completion of the consent process for study enrollment, each patient was assigned a study number by the study coordinator. The Department of Biostatistics provided randomization lists for enrolled patients. On the day of operation, an investigational pharmacist cross-referenced the patient study number with the randomization list and prepared and delivered the study irrigant to the operating room in a uniform container.

Intervention, study drugs, and protocol

All patients received 1 dose of parenteral antibiotics within 60 minutes of the initial skin incision. Perioperative parenteral antibiotics consisted of 2 grams of intravenous ceftriaxone and 1 gram of intravenous metronidazole in all patients. Redosing of antibiotics was not required in any case. The use of prophylactic antibiotics postoperatively was not performed routinely. Intraoperative bile cultures were used to guide antibiotic decision-making regarding organisms and resistance patterns in the event of an infectious complication.

Randomized patients received either the study drug or the placebo during the reconstructive phase of the operation. The selection of polymyxin B as the study drug was based on the favorable risk profile, cost-effectiveness, and activity against resistant, gram-negative organisms.[8,9] The study drug consisted of polymyxin B (500,000 U) in 1 L of 0.9% NaCl. The placebo drug consisted of 1 L of 0.9% NaCl with no antibiotic. Two liters of study drug or placebo solution were irrigated in each case. One liter of irrigation was instilled at the site of the pancreaticojejunostomy immediately after completion of the anastomosis. One liter of irrigation solution was applied to the site of the choledochojejunostomy or hepaticojejunostomy immediately after completion. Each liter of solution was removed from the operative field by direct suctioning after 1 to 5 minutes of gentle manual lavage.

The standard institutional protocol for the prevention of SSIs was used in all patients. Preoperative measures include intranasal mupirocin and chlorhexidine gluconate bathing. Perioperative measures include hair removal with clippers, operative site and hand preparation with an alcohol-based antiseptic solutions, hyperoxia, normothermia, intensive glucose control, use of an incisional wound barrier device, and exchange of the surgical gloves before closure of the fascia and skin closure with clean instruments (clean-closure). Skin closure was performed with staples or subcuticular suture combined with surgical glue. Incisional negative pressure wound therapy was not used in this study. Patients were discharged home with a gauze dressing or no dressing; deviation was only in the event of a superficial SSI in which management was deferred to the treating surgeon.

Definitions and outcomes

The primary outcome of this study was a superficial or organ-space SSI. Secondary outcomes included POPF, postoperative duration of stay, and overall morbidity and mortality. Outcomes were monitored and recorded prospectively by a dedicated research study nurse.

Superficial (incisional) and organ-space SSIs were reported according to widely accepted definitions.[10] Superficial or deep SSIs were defined as an infection that occurred within 30 days of the index operation and involved either skin or subcutaneous tissue or the fascial or muscle layer of the incision, respectively. At least 1 of the following criteria was necessary for superficial or deep SSI: (1) purulent incisional drainage but not from the organ-space component of the surgical site; (2) organisms isolated from an aseptic culture of fluid or tissue from the superficial incision; (3) 1 or more signs or symptoms of infection (pain or tenderness, localized swelling, redness, and heat) and a superficial incision deliberately opened by a surgeon, either found to be culture-positive or not cultured (a culture-negative finding did not meet this criterion); (4) deep incision that spontaneously dehisced or was deliberately opened by a surgeon and found to be culture-positive or not cultured (a culture-negative finding did not meet this criterion) with at least 1 of the signs or symptoms of fever (>38°C), localized pain, or tenderness; and (5) an abscess or other evidence of infection involving the deep incision found on direct examination, during reoperation, or by histopathologic or radiologic examinations.

Organ-space SSIs were defined as an infection that occurred within 30 days of the index operation that was related to the operation and involved any part of the body excluding the skin, fascia, or muscle layers, and met at least 1 of the following criteria: (1) purulent drainage from a drain that was placed through a stab wound into the organ or space; (2) organisms isolated from aseptic culture of fluid surrounding intra-abdominal organs and spaces; (3) an abscess or other evidence of infection involving the organ or space found on direct examination, during reoperation, or by histopathologic or radiologic examination; and (4) any intraperitoneal collection requiring percutaneous drainage.

Intraoperative drains placed near the pancreaticojejunostomy were monitored for daily output and analyzed daily for amylase levels on the first 3 days postoperatively. POPF were defined according to the International Study Group on Pancreatic Fistula

Table I
Comparison of demographics, primary diagnosis, preoperative intervention, and preoperative laboratory indices

	Antibiotic irrigation (n = 95)	Saline irrigation (n = 95)	*P* value
Demographics			
Age, mean (±SEM) years	63.7 (±1.3)	64.4 (±1.5)	.75
Hypertension, n (%)	58 (61)	57 (60)	1.0
Diabetes mellitus, n (%)	30 (32)	27 (28)	.75
History of acute pancreatitis, n (%)	23 (24)	24 (25)	1.0
Coronary artery disease, n (%)	13 (14)	14 (15)	1.0
COPD, n (%)	15 (16)	5 (5)	.03
Tobacco, n (%)	61 (64)	44 (46)	.02
Chronic pancreatitis, n (%)	12 (13)	10 (11)	.82
Indication for PD			
Periampullary cancer, n (%)	68 (72)	70 (73)	
IPMN, n (%)	8 (8)	5 (5)	
Chronic pancreatitis, n (%)	6 (6)	7 (7)	
PNET, n (%)	6 (6)	4 (4)	
Duodenal adenoma/adenocarcinoma, n (%)	3 (3)	4 (4)	
Metastatic disease, n	2	2	
Other, n	2	3	.83
Preoperative intervention and indices			
ERCP, n (%)	58 (61)	56 (59)	.88
Biliary stent, n (%)	56 (59)	53 (56)	.77
Stent exchange, n (%)	18 (19)	18 (19)	1.0
Neoadjuvant chemotherapy, n (%)	25 (26)	24 (25)	1.0
Albumin, mean g/dL (± SEM)	3.9 (±0.1)	3.8 (±0.1)	.82
Creatinine, mean mg/dL (± SEM)	1.0 (±0.1)	0.9 (±0.03)	.29
Total bilirubin, mean mg/dL (± SEM)	1.8 (±0.3)	1.6 (±0.2)	.68

ERCP, endoscopic retrograde cholangiopancreatography; *IPMN*, intraductal papillary mucinous neoplasm; *PNET*, pancreatic neuroendocrine tumor; *SEM*, standard error of mean.

(ISGPF).[11] The diagnosis of POPF required drain output of any measurable volume of fluid on or after postoperative day 3 with an amylase content greater than 3 times the upper limit of laboratory normal. POPF were further qualified as grade A, grade B, or grade C according to strict ISGPF definitions.[11] Clinically relevant postoperative pancreatic fistula (CR-POPF) is defined as a grade B or grade C POPF as defined by the ISGPF.[11]

Statistical analysis

Statistical analysis was performed using IBM SPSS statistics version 25.0 (IBM Corp, Armonk, NY) with independent biostatistical oversight from the Center for Outcomes Research Education in Surgery. Descriptive statistics for continuous data included median, mean, range, and standard error of mean depending on normality of the distribution of the variable. Categorical data were expressed as numbers and percentages. Where applicable, independent groups *t* tests and Pearson correlation or Fisher exact tests were performed for univariate subgroup analysis. Statistical significance was defined as $P < .05$.

Historic data demonstrate an infectious complication rate of 25% for major hepatopancreatobiliary operations involving 1 or more gastrointestinal anastomoses.[10,12,13] Predicting an absolute risk reduction of 15% for the primary study outcome within the treatment arm, the study was designed to detect such a difference with 80% power and 5% type I error rate. Using a 2-sided chi-square test, the study's power analysis calculated 82 patients in each arm. The power analysis was performed only for the primary endpoint of SSIs.

Results

A total of 190 patients met inclusion criteria and were enrolled in the study over a 24-month period from 2015 to 2017. Ninety-five patients were randomized to the treatment arm (antibiotic irrigation) and 95 patients to the control arm (saline irrigation). All patients enrolled in the study were followed to the 90-day endpoint.

Patient demographics are shown in Table I. Mean age and comorbidities were similar between groups; however, the antibiotic irrigation group had a greater percentage of patients with chronic obstructive pulmonary disease (COPD) and tobacco use. No difference in indication for PD existed between groups. No difference was observed between groups in rates of preoperative endoscopic retrograde cholangiopancreatography, biliary stenting, laboratory indices, or neoadjuvant chemotherapy.

POPF SSIs

The overall incidence of SSI, including superficial and organ-space infection as the primary endpoint, was 12.6% (n = 24). No difference in SSI rate was observed between the treatment and control groups (10% vs 15%; $P > .61$). The overall incidence of superficial SSI and organ-space SSI was 4.7% (n = 9) and 7.9% (n = 15), respectively. The diagnosis of superficial SSI was made by (n = 4) purulent discharge (criteria 1), (n = 4) symptoms of infection with surgical opening of the wound (criteria 3), and (n = 1) culture positivity (criteria 2). The diagnosis of organ-space SSI was made by culture positivity (criteria 2) in all cases. The rate of superficial SSI was 3% vs 6%, and the rate of organ space infection was 7% vs 8% ($P > .31$ each).

The overall incidence of POPF and CR-POPF was 28.4% (n = 54) and 11.1% (n = 21), respectively. No difference was observed in the rates of POPF (26% vs 29%) or CR-POPF (12% vs 11%) between the treatment and control groups ($P > .63$; Table II). All patients in this study underwent a duct to mucosa anastomotic technique for the pancreaticojejunostomy. No difference was observed in estimated blood loss, pancreatic duct size, gland texture, operative time, blood transfusion rates, or fistula risk score between the treatment and control groups.

Table II
Comparison of pancreatic fistula risk factors and POPF

Risk factors and outcome	Antibiotic irrigation (n = 95)	Saline irrigation (n = 95)	*P* value
Estimate blood loss, mean mL (± SEM)	477.5 (64)	550.7 (54)	.38
Pancreatic duct size, mean mm (± SEM)	3.8 (0.2)	3.5 (0.2)	.41
Gland texture, n (%)			
Soft	46 (48)	47 (50)	.97
Intermediate	11 (12)	10 (11)	
Firm	38 (40)	38 (40)	
Operative time, mean minutes (± SEM)	301 (11)	316 (10)	.34
Transfusion, n (%)	22 (23)	31 (33)	.20
Fistula Risk Score, mean (± SEM)	3.4 (0.3)	3.6 (0.2)	.50
Any POPF, n (%)	25 (26)	29 (31)	.63
Clinically relevant POPF, n (%)	11 (12)	10 (11)	1.0

SEM, standard error of mean.

Table III
Comparison of further postoperative outcomes

Postoperative outcome	Antibiotic irrigation (n = 95)	Saline irrigation (n = 95)	*P* value
Duration of stay, median days (range)	7 (4-32)	8 (4-25)	.69
Delayed gastric emptying, n (%)	4 (4)	6 (6.3)	.75
Bile leak, n (%)	4 (4)	4 (4)	1.0
Urinary tract infection, n (%)	3 (3)	1	.62
Venous thromboembolism, n (%)	0	3 (3.2)	.25
Organ failure, n	1	2	1.0
Sepsis, n	0	2	.50
Cholangitis, n	0	1	1.0
Myocardial infarction, n	1	0	1.0
Any postoperative complication, n (%)	26 (27.4)	30 (31.6)	.63
30-day mortality, n (%)	1	2	1.0
90-day mortality, n (%)	4 (4)	4 (4)	1.0

Morbidity and mortality

Postoperative outcomes within 90 days of operation are shown in Table III. The median postoperative duration of stay for the overall cohort was 8 days (range, 4–32 days). The overall incidence of postoperative organ failure and sepsis was 1.6% (n = 3) and 1.1% (n = 2), and the overall 30-day and 90-day mortality was 1.6% (n = 3) and 4.2% (n = 8), respectively. Delayed gastric emptying developed in 5.3% (n = 10), bile leak in 4.2% (n = 8), urinary tract infection in 2.1% (n = 4), venous thromboembolism in 1.6% (n = 3), cholangitis in 0.5% (n = 1), and myocardial infarction in 0.5% (n = 1). No differences in these general or pancreatectomy-specific complications were observed between the treatment and control groups.

Bactibilia

Microbiology cultures of bile samples obtained intraoperatively were positive in 89 patients (46.8%)—44 patients in the antibiotic treatment irrigation group and 45 in the saline control irrigation group. Antibiotic irrigation did not decrease rates of superficial or organ space SSI, POPF, CR-POPF, or 30-day or 90-day mortality for the subgroup of patients with bactibilia (Table IV).

Discussion

Postoperative infectious complications and POPF are a substantial cause of morbidity after PD and result in increased treatment costs and postoperative durations of stay. The burden of treating infectious complications after PD is greater than $15,000 in direct costs per event.[14–17] SSIs, representing the most common and potentially preventable complication after PD, were selected as the primary study endpoint. This double-blind, randomized controlled trial evaluated the effectiveness of peritoneal antibiotic irrigation in decreasing superficial and organ-space SSIs after PD. The addition of polymyxin B to the saline irrigation after completion of the pancreatic and biliary anastomosis had no effect on the rates of superficial, deep, or organ-space SSIs. Furthermore, antibiotic irrigation had no effect on postoperative rates of POPF.

Recent studies have used antibiotic irrigation of the peritoneum as a method to decrease SSIs and wound drainage in a variety of specialized operative procedures.[7,18] The efficacy of peritoneal irrigation to decrease postoperative complications, however, has not been studied in hepatopancreatobiliary surgery. PD requires 3 anastomoses that potentially contribute to microbial contamination of the peritoneal cavity during operation. Polymyxin B is an antibiotic isolated from *Paenibacillus polymyxa* with a broad spectrum of activity against nearly all gram-negative bacteria, including organisms found commonly found in colonized bile, such as *Escherichia coli, Klebsiella pneumoniae,* and *Enterobacter* species.[4,8,9,19] Peritoneal irrigation with polymyxin B solution does not decrease postoperative superficial, deep, or organ-space SSIs when compared with saline irrigation alone.

POPF remains another cause of considerable morbidity after PD. Risk factors for POPF include soft gland texture, small diameter of the pancreatic duct, and substantial procedural blood loss.[11] Previous studies have not shown a correlation between preoperative biliary stenting or bactibilia with the development of POPF after PD.[20,21] Likewise, this prospective randomized trial demonstrated no difference in rates of POPF or CR-POPF between patients receiving antibiotic or saline irrigation. This finding supports the lack of any direct correlation among bactibilia, peritoneal bacterial contamination, and integrity of the pancreaticojejunostomy anastomosis.

Table IV
Comparison of postoperative outcomes among patients with bactibilia (n = 89)

Postoperative outcome	Antibiotic irrigation (n = 44)	Saline irrigation (n = 45)	*P* value
Any surgical site infection, n (%)	5 (11)	6 (13)	.78
Superficial, n (%)	2 (5)	3 (7)	1.00
Deep organ-space, n (%)	3 (7)	3 (7)	1.00
POPF, n (%)	12 (27)	13 (29)	1.00
CR-POPF, n (%)	4 (9)	3 (7)	.71
30-day mortality, n	0	0	1.00
90-day mortality, n	1	2	1.00

The incidence of bactibilia in patients undergoing PD is increased in undergoing preoperative biliary stenting. Bactibilia has been established as a putative risk factor for the development of superficial and organ-space infections after PD.[5,19,21] Although bactibilia was present in 46% of patients in this study, the incidence of postoperative superficial or organ-space SSIs did not differ in patients with bactibilia receiving antibiotic or saline irrigation. Concentrations of specific components of bile acids interfere with the efficacy of antibiotics.[22] This potential factor may have limited the ability of antibiotic solution irrigation to decrease superficial and organ-space SSIs in patients with bactibilia.

The double-blinded, randomized controlled design of this trial is a noteworthy strength of the study; however, this study has limitations. Potential adverse effects from polymyxin B irrigation of the peritoneum were not evaluated. The overall incidence of SSI was much less than the historic, short-term outcomes from this institutional database of PDs that directed the power calculation during the study design period.[13] Compared with outcome data captured in large retrospective studies focusing on infectious complications after PD, the rates of SSI for patients in this present study were remarkably low.[23,24] Although considered the control arm of this study, saline irrigation of the peritoneum by itself may provide benefit in decreasing infectious complications after PD. Further, the use of a wound barrier device combined with a clean-closure technique may be critical to improving SSI rates. Periampullary malignancy is the indication for most patients undergoing PD, thus a combination of factors including nutrition and immunologic and inflammatory responses may have influenced postoperative SSI rates. Despite randomization, more patients with chronic obstructive pulmonary disease and tobacco use were assigned to the antibiotic arm of this prospective study. The use of tobacco has been associated previously with increased infectious complications after operation.[25] The increased tobacco use in the intervention arm of the study may have prevented the detection of any clinically relevant decrease in postoperative infectious complications when compared with the control.

Infectious complications and POPF contribute to morbidity after PD and are justifiably a focus for future projects of improvement of operative outcomes. The addition of antibiotic solution to routine intraperitoneal irrigation did not decrease the incidence of SSIs or POPF after PD.

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Conflict of interest/Disclosure

The authors have indicated that they have no conflicts of interest regarding the content of this article.

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Discussion

Dr Robert C.G. Martin (Louisville, KY): Congratulations, Dr. Maatman. I also want to congratulate the senior author, Dr. House, for putting on a large-volume, efficient, prospective randomized control trial, which we sometimes don't see as often in surgical oncology.

I also want to congratulate you. You actually did get better. Even though the saline and polymixin didn't work, you had a significant Hawthorne effect. You went from a historical control of 24% down to 13%, so you already improved overall surgical quality just by looking at it. So I would say it's a "negative study," but it's clearly a positive study for your institution.

I have a couple of quick questions. First is a methodology. We talked about this before, and you provided me the manuscript, and I sent you some of these questions. How did you truly double-bind the operative surgeon as well as the surgical nurse who are charting fees in regards to who got polymixin? So I would just be curious if you can walk us through that methodology and how you got that buy-in, which I think is critical.

The second is obviously there has been a wealth of data coming out of the World Health Organization, specifically in response to CMS not paying for surgical site infections for colon and hysterectomy. In regards to other factors, in regards to hyperbaric oxygen, glycemic control, temperature management, chlorhexidine baths the day before, did you look at some of what have been established as the key 12 factors for level 2 and level 1 evidence, and whether that played a role, and were they already institutional based, or were there potentially differences within that?

Third is the presence of a surgical site infection. Your manuscript outlines how you would obviously define that, but how many of these were sort of that redness that you showed us on one of your slides? Or were some of them ones you had to unzip the whole patient and then had to do dressing changes and come back to your office every week, and then you have to put them on a vac, and a lot of times you are very worried about those patients because you are delaying their adjuvant chemotherapy, which is ultimately a big quality parameter, especially in your malignant patients.

Last, what was your microbiology, and more importantly, your antibiotic management? I know you looked at the infections within your biliary, but then how do you manage those patients if you have got a positive culture? It usually comes back day 2 postoperatively, and maybe that's when your 72-hour, 36-hour antibiotic has run off. Do you continue that antibiotic, or do you take it as, "Oh, yeah, their bile is infected; we'll kind of see what happens"?

Dr Thomas K. Maatman: To further discuss our consent randomization, all patients are seen preoperatively in clinic, and the study was discussed with them by the treating surgeon as well as our dedicated nurse coordinator. Once they were consented with the study, the nurse coordinator then assigns them a study number. We were provided a randomization list by our Department of Biostatistics, and our investigational pharmacist on the day of surgery would correlate the patient's study number with the randomization list, and then either provide the control or study drug, and deliver it to the operating room, so that way there's no one in the room including the surgeon who knew which irrigation was going to be used.

Regarding the World Health Organization's perioperative and postoperative recommendations for decreasing surgical site infections, to my knowledge, I can happily say we use most of them. The only one that I have to double-check is whether or not we consistently used hyperbaric oxygen during these cases. We also, in all of these cases, added a wound barrier device, changed surgical gloves prior to closure of fascia, and performed a clean closure in all cases. I think it would be interesting to look back before these were implicated and see if there is a difference, and if the difference was actually related to the implication of these techniques.

Our postoperative surgical site infection definitions mirrored the definitions from the CDC [Centers for Disease Control]. In the absence of positive culture, either from the wound or from the deep organ space, the diagnosis for superficial surgical site infections was based on physical exam findings of purulent discharge, edema, increased tenderness, or at the surgeon's discretion if he felt this was a surgical site infection.

For deep organ space infections, it was either purulent discharge from the deep organ-space drain or radiographic findings, or findings at the time of reoperation.

In our series of the 24 patients, the majority of those that were diagnosed with superficial surgical site infections were based on physical exam and not wound culture, but 100% of our deep organ space were based on culture from an aseptically obtained, percutaneous drain, or culture at the time of reoperation.

To answer your last question about what our practice is with bile cultures, all patients will get a bile culture at the time of operation. We only give the preoperative dose of antibiotics, and none of these patients received postoperative prophylactic antibiotics. The bile culture data are used strictly for if a patient were to go on to develop a surgical site infection or cholangitis, as it would help guide antibiotic decision making in regard to organisms and antibiotic resistance.

Dr Scott Gruber (Detroit, MI): There is no benefit, but is there any harm? In terms of increasing costs for those that do get an SSI infection, does it tend to be with organisms that are more resistant to antibiotics?

Is there an increase in *C diff*? In other words, is there any harm to adding this?

Dr Thomas K. Maatman: As far as the risk of doing this, I don't think there is any additional risk except potentially for cost, but it is a relatively cheap solution.

I think a large portion of the benefit came from a dedicated up to five minutes of irrigation after each anastomosis was completed.

We didn't have enough culture data to look at the organisms that grew from the surgical site infections, but I think that would be interesting to look at to see if there are any certain organisms that would grow more frequent after polymyxin. We did not see any difference in the *C diff* rates. They were both very low.

Dr Gerald Larson (Louisville, KY): Dr. Maatman, I congratulate you on a very nice presentation. Twenty years ago there was some

concern about the risk of biliary stents that were placed preoperatively causing or setting up postoperative infection. In your study, 57% and 56% of your patients in the 2 groups had a stent, but it did not seem to correlate with the postoperative problems that you measured in your study.

Would you comment on that, and also the role of stenting with regard to neoadjuvant therapy? Are more patients receiving neoadjuvant therapy where they need the stent to control the jaundice for 3 months before the definitive operation? How that might factor in?

If you had total control of a patient coming in, would you prefer or recommend a stent placement while you are preparing for the operation, or would you prefer no stent?

Dr Thomas K. Maatman: I will try to answer your questions the best I can. Regarding stent placement first, I think about half of our patients are getting neoadjuvant therapy, another half are getting stents for symptomatic jaundice, such as pruritus, malnutrition, or elevated INR [international normalized ratio].

When looking at those patients that received biliary stenting preoperatively, we did associate this with an increased risk of positive bile cultures, which has been shown in the literature previously. Additionally, we actually correlated specific organisms with certain types of postoperative complications, so it's not necessarily the presence of positive bile cultures that we found, but instead the specific organisms within the bile that drive certain postoperative complications.

If I had my choice of what to do, and I think if you asked all of our surgeons you might get a different answer on whether to operate up front or to do stenting and neoadjuvant therapy, but I think my preference would be to undergo stenting and neoadjuvant therapy.

Dr Margo Shoup (Danbury, CT): Have you all altered your antibiotic decision preoperatively when a patient has been stented versus those that have not? I think that goes along with Dr. Martin's question that it's been shown many years ago that stenting was possibly related to increased infections, but as a result of that, antibiotic of choice really should be targeted a little bit more with gram-negative based on patients with preoperative stent?

Dr Thomas K. Maatman: I'll kind of allude again to the other study we performed. We actually found in our series that the more common bacteria we are seeing during the time of this study is actually gram-positive, most commonly *Enterococcus*. We currently use ceftriaxone and metronidazole in all patients, but I think the addition of ampicillin is something to consider to cover *Enteroccocus*, which is poorly covered by ceftriaxone. We have not made any changes to date.