ORIGINAL ARTICLE

Postoperative Antibacterial Prophylaxis for the Prevention of Infectious Complications Associated With Tube Thoracostomy in Patients Undergoing Elective General Thoracic Surgery

A Double-blind, Placebo-Controlled, Randomized Trial

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Objective: To determine whether extended postoperative antibacterial prophylaxis for patients undergoing elective thoracic surgery with tube thoracostomy reduces the risk of infectious complications compared with preoperative prophylaxis only.

Design: Prospective, randomized, double-blind, placebo-controlled trial.

Setting: Brigham and Women's Hospital, an 800-bed tertiary care teaching hospital in Boston, Massachusetts.

Participants: A total of 251 adult patients undergoing elective thoracic surgery requiring tube thoracostomy between April 2008 and April 2011.

Interventions: Patients received preoperative antibacterial prophylaxis with cefazolin sodium (or other drug if the patient was allergic to cefazolin). Postoperatively, patients were randomly assigned (at a 1:1 ratio) using a computer-generated randomization sequence to receive extended antibacterial prophylaxis (n=125) or placebo (n=126) for 48 hours or until all thoracostomy tubes were removed, whichever came first.

Main Outcome Measures: The combined occurrence of surgical site infection, empyema, pneumonia, and *Clostridium difficile* colitis by postoperative day 28.

Results: A total of 245 patients were included in the modified intention-to-treat analysis (121 in the intervention group and 124 in the placebo group). Thirteen patients (10.7%) in the intervention group and 8 patients (6.5%) in the placebo group had a primary end point (risk difference, −4.3% [95% CI, −11.3% to 2.7%]; *P*=.26). Six patients (5.0%) in the intervention group and 5 patients (4.0%) in the placebo group developed surgical site infections (risk difference, −0.93% [95% CI, −6.1% to 4.3%]; *P*=.77). Seven patients (5.8%) in the intervention group and 3 patients (2.4%) in the placebo group developed pneumonia (risk difference, −3.4% [95% CI, −8.3% to 1.6%]; *P*=.21). One patient in the intervention group developed empyema. No patients experienced *C difficile* colitis.

Conclusions: Extended postoperative antibacterial prophylaxis for patients undergoing elective thoracic surgery requiring tube thoracostomy did not reduce the number of infectious complications compared with preoperative prophylaxis only.

Trial Registration: clinicaltrials.gov Identifier: NCT00818766

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THERE IS CURRENTLY NO CLEAR standard for the duration of use of prophylactic antibacterials in patients undergoing elective thoracic surgery requiring a tube thoracostomy (chest tube) placement. Currently, the approach to postoperative antibacterial prophylaxis for these patients varies widely among clinicians.[1,2] Postoperative prophylactic antibacterials are routinely given for 24 or 48 hours after the placement of the chest tube and often for even longer.[3-5] Reducing postsurgical infectious complications is an important goal,[6] but the unnecessary use of an-

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tibacterials is costly, may be associated with increased antimicrobial resistance and toxicity, and could be complicated by drug-resistant bacterial infections including *Clostridium difficile* colitis, which could be deadly.[7,8] Preoperative surgical prophylaxis using first-generation cephalosporins administered within 30 minutes before the incision time is currently recommended to prevent surgical site infections in clean or clean-contaminated operations.[6] Additional intraoperative antibacterials could also be administered for lengthy surgical procedures.[9] To assess whether additional antibacterials administered postoperatively to patients undergoing elective thoracic surgery with thoracostomy tube placement leads to a reduced rate of infectious complications, we compared 2 approaches for the prevention of surgical site infections. The first approach consists of administering standard preoperative antibacterial prophylaxis only, with no additional antibacterial therapy given postoperatively. The second approach also uses standard preoperative antibacterial prophylaxis, but with additional antibacterial therapy given for 48 hours postoperatively or until all thoracostomy tubes are removed, whichever comes first.

METHODS

STUDY DESIGN AND PARTICIPANTS

We conducted this randomized, double-blind, placebo-controlled study at Brigham and Women's Hospital, an 800-bed tertiary care teaching hospital in Boston, Massachusetts. Our study was approved by the hospital's institutional review board. Patients 18 years or older presenting for elective lung surgery who were expected to require tube thoracostomy were approached for participation in our study at the time of preoperative evaluation. Patients gave informed written consent prior to enrollment. Patients were ineligible to participate if any of the following procedures were planned: pneumonectomy, decortication, pleurodesis or pleurectomy, lung volume reduction, esophagectomy, or lung transplantation. Patients with known active infections prior to surgery, with cystic fibrosis, or with a history of antimicrobial use within 1 week of the surgery were excluded. Patients with an estimated glomerular filtration rate of less than 60 mL/min or with an allergic reaction to both β-lactam antibiotics and vancomycin hydrochloride were also excluded.

RANDOMIZATION AND MASKING

Eligible patients were randomly assigned (at a 1:1 ratio) to receive either normal saline (placebo arm) or additional antibacterial treatment (cefazolin or vancomycin for cephalosporin-allergic patients) immediately following surgery. These patients were randomly assigned in blocks of 4 via a randomization table that was prepared for our study, and patients were assigned to study arms sequentially by the members of the hospital's Investigational Drug Service, who were unaware of patient characteristics. Study drug doses were prepared by the Investigational Drug Service and administered in intravenous bags identical in appearance to those used in clinical practice. Nurses, clinicians, study investigators, and patients were masked to assigned study group throughout the study and were unaware of the block randomization strategy.

STUDY PROCEDURES AND OUTCOMES

All of the patients who enrolled in our study received the standard skin preparation (povidone-iodine) and the standard recommended doses of preoperative antibacterial therapy to prevent surgical site infection according to institutional guidelines. The patients with a prolonged operative time received additional antibacterial doses intraoperatively. Immediately after surgery, patients were randomly assigned to either additional postoperative antibacterials (intervention group) or placebo. Postoperatively, patients received either additional antibacterials or placebo for 48 hours or until all chest tubes were removed, whichever occurred first. Patients with no history of an allergic reaction to cephalosporins received cefazolin (1 g for patients weighing ≤80 kg and 2 g for patients weighing >80 kg) or placebo every 8 hours. Patients with a history of an allergic reaction to β-lactams received 1 g of vancomycin or placebo every 12 hours. Chest tube management was done by the surgical team as per routine postprocedure care.

The primary study end point was the combined incidence of the following postoperative infectious complications: surgical site infection, empyema, pneumonia, and the occurrence of *C difficile* colitis within 28 days of surgery. Definitions of the infectious end points are based on criteria from the Centers for Disease Control and Prevention and are listed in **Table 1**. The protocol's prespecified secondary end points were the length of hospital stay, the time to removal of the chest tubes, the need for a reoperation, the administration of additional antibacterials for any reason within 28 days after surgery, any allergic reactions, and 28-day all-cause mortality. Surveillance for study end points was performed daily while the patient was hospitalized, at the patient's 2-week postoperative clinic appointment (at which time all patients received routine chest radiography and evaluation by their surgeon), and by a telephone call at the end of 28 days.

Each potential infectious complication was adjudicated by 2 study investigators. If there was disagreement between the 2 study investigators on the outcome classification, a third investigator decided the final outcome after reviewing the data and following the preset end-point definitions. All end points and postrandomization data were verified and adjudicated before unblinding.

STATISTICAL ANALYSIS

The reported occurrences of surgical site infection, empyema, and postprocedure pneumonia following elective thoracic surgery range from 7% to 14%.[3,4,12-25] We estimated that we would need to enroll 352 patients with a power of 80% and a 1-sided α level of .05 to exclude more than 3% absolute difference between the treatment groups. The projected accrual period was 3 years, and no interim analysis was planned. The study accrual was stopped at 3 years owing in part to planned changes in preoperative methicillin-resistant *Staphylococcus aureus* screening and owing to funding constraints. Data were analyzed using SAS 9.2 software (SAS Institute). The Fisher exact test and the Wilcoxon rank sum test were used to compare binary variables and continuous variables, respectively. Logistic regression analysis was used to adjust for potential confounding factors.

RESULTS

Between April 4, 2008, and April 4, 2011, a total of 292 patients consented to participate in our study and were assessed for eligibility. Forty-one patients were ex-

Table 1. Definitions of Infectious End Points

Infectious End Point
Surgical site infections
Superficial surgical site infection involves only skin or subcutaneous tissue around incision and has at least 1 of the following criteria:
Purulent drainage
Organisms isolated from aseptically obtained culture
Pain or tenderness, localized swelling, redness or heat, and the incision is deliberately opened by surgeon.
Diagnosis of a superficial wound infection by surgeon
Deep surgical site infection involves deep soft tissues, such as fascia or muscle, and has at least 1 of the following:
Purulent drainage from the incision but not from the organ/space of the surgical site
Deep incision spontaneously dehisces or is deliberately opened by surgeon when the patient has at least 1 of the following signs or symptoms: fever (>38°C), localized pain, or tenderness.
An abscess or other evidence of infection involving the incision is found on direct examination (ie, histopathologic or radiographic examination).
Diagnosis of a deep wound infection by surgeon
Empyema
Positive pleural culture result or purulence within the thoracic space and leukocytosis or fever (>38°C)
Pneumonia
A new infiltrate on chest radiograph associated with at least 3 of the following:
Fever (>38°C)
Purulent sputum
Leukopenia (WBC count of <4000/μL) or leukocytosis (WBC count of >11 000/μL)
Sputum culture with pathogenic bacteria
Increased oxygen requirements
Clostridium difficile colitis
Positive for *C difficile* toxin assay results and any 1 of the following:
New diarrhea
Ileus or toxic megacolon
Leukopenia (WBC count of <4000/μL) or leukocytosis (WBC count of >11 000/μL)
Findings from sigmoidoscopy, colonoscopy, or histopathologic examination consistent with *C difficile* infection

Abbreviation: WBC, white blood cell.
SI conversion factor: To convert WBC count to $\times 10^9$ per liter, multiply by 0.001.
[a] Definitions obtained from Garner et al[10] and Gerding et al.[11]

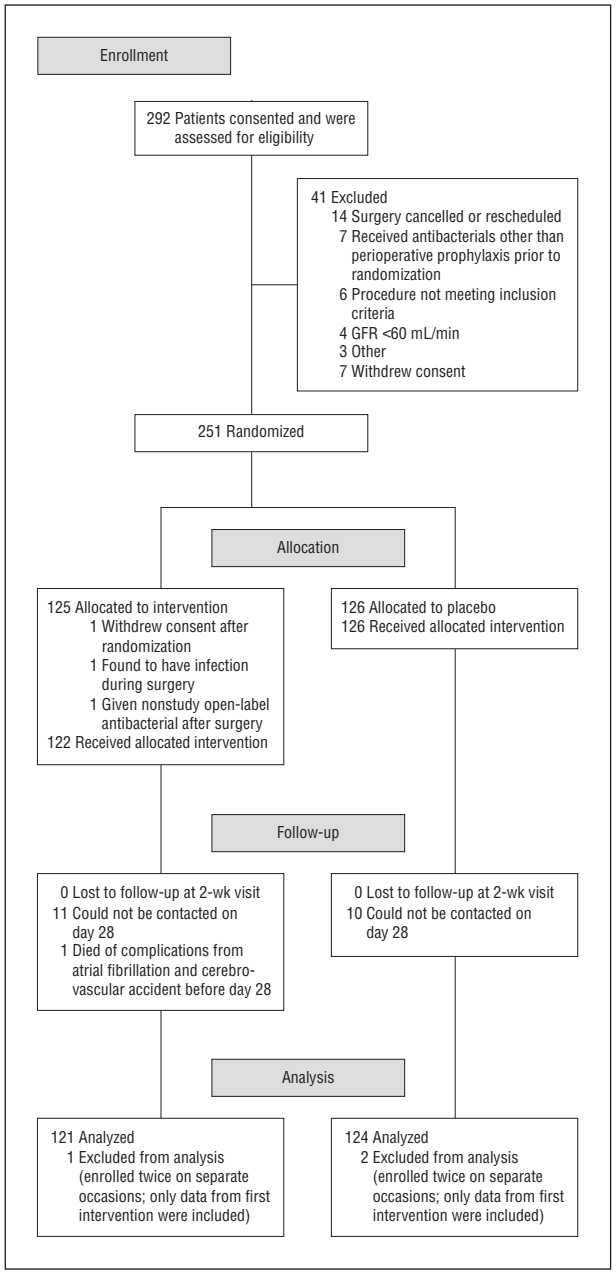

Figure. Patient flowchart showing the enrollment and randomization of 292 patients for a prospective, randomized, double-blind, placebo-controlled trial to determine whether extended postoperative antibacterial prophylaxis for patients undergoing elective thoracic surgery with tube thoracostomy reduces the risk of infectious complications compared with preoperative prophylaxis only. GFR indicates glomerular filtration rate.

cluded (**Figure**). Of those who were excluded, the most common reasons for exclusion were cancellation of surgery (14 patients [34.1%]), receipt of antibacterials other than preoperative prophylactic antibiotics (7 patients [17.1%]), and a procedure not meeting inclusion criteria (6 patients [15.0%]).

A total of 251 patients were randomly assigned postoperatively to receive either extended antimicrobial prophylaxis (intervention group; n = 125) or no additional antibacterial prophylaxis (placebo group; n = 126). Of the 125 patients allocated to receive extended prophylaxis, 3 did not receive the allocated intervention: one withdrew consent, one was found to have an infection during surgery, and one erroneously received a nonstudy open-label antibacterial after surgery. All patients allocated to receive placebo received the allocated intervention. Three patients (1 in the intervention group and 2 in the placebo group) were enrolled twice in our study at separate occasions. Only data from their first enrollment in our study were analyzed. All patients completed the 2-week visit. We were unable to contact 21 patients (11 in the intervention group and 10 in the placebo group) for the day 28 follow-up telephone call. One patient in the intervention group died of complications of atrial fibrillation and cerebrovascular accident before day 28.

A total of 245 patients were included in the final analysis (121 in the intervention group and 124 in the placebo group). Sixteen patients had protocol violations after being randomly assigned (7 in the intervention group and 9 in the placebo group): 6 patients received addi-

Table 2. Baseline Characteristics of Intention-to-Treat Population

Characteristic	Patients, No. (%)		*P* Value
	Intervention Arm (n = 121)	Placebo Arm (n = 124)	
Age, median (range), y	63 (24-85)	62 (26-84)	.48
Female sex	69 (57.0)	70 (56.5)	.99
BMI, median (range)	26.6 (15.2-39.8)	27.7 (16.0-51.4)	.35
Race			
White	112 (92.6)	113 (91.1)	.76
Other	9 (7.4)	11 (8.9)	
Surgical approach			
VATS	66 (54.6)	66 (53.2)	.89
Thoracotomy	55 (45.4)	58 (46.8)	
Procedure type			
Wedge resection	78 (64.5)	68 (54.8)	.52
Lobectomy	33 (27.3)	43 (34.7)	
Segmentectomy	7 (5.8)	7 (5.7)	
Pleural biopsy	1 (0.8)	3 (2.4)	
Exploration	2 (1.7)	3 (2.4)	
Duration of operation, median (range), h	3.2 (1.1-8.4)	3.4 (1.3-8.0)	.40
Antibacterial prophylaxis used			
Cefazolin sodium	111 (91.7)	116 (93.6)[a]	.63
Vancomycin hydrochloride	3 (2.5)	4 (3.2)	.99
Other	7 (5.8)[b]	4 (3.2)[c]	.23
Time to antibacterial administration prior to incision,[d] median (range), min	31.0 (−206 to 80)	34.5 (−76 to 120)	.10
Administration after incision	5 (4.4)	2 (1.6)	.27
Administration time not documented	7 (5.8)	2 (1.6)	.56
Additional intraoperative doses of antibacterial administered	4 (3.3)	9 (7.3)	.25

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); VATS, video-assisted thoracoscopic surgery.
[a] One patient received levofloxacin and metronidazole hydrochloride in addition to cefazolin.
[b] Six patients received clindamycin, and 1 patient received levofloxacin.
[c] Three patients received clindamycin, and 1 patient received levofloxacin and metronidazole.
[d] Incision time was not recorded for 9 patients (ie, 114 in the intervention arm and 122 in the placebo arm).

tional doses of the study drug after removal of the chest tube (3 in each arm), 4 patients missed 1 study drug dose (3 in placebo group and 1 in intervention group), 3 patients had a study drug dose delayed by 2 hours or more (2 in the placebo group and 1 in the intervention group), 2 patients inadvertently received 1 dose of wrongly assigned study drug (1 in each arm), and 1 patient in the intervention group received 1 lower dose of cefazolin.

The patients' baseline characteristics are summarized in **Table 2**. The median age and body mass index and the proportions of patients with regard to sex and race were similar in both arms. The median duration of operation, the type of surgery, the type of antibacterial prophylaxis used, the median time to antibacterial administration prior to incision, and the number of additional intraoperative doses of antibacterials administered were all similar in both groups. The type of surgical approach (video-assisted thoracoscopic surgery [VATS] vs open thoracotomy) was similar in both groups. Wedge resection was the most commonly performed surgical intervention (146 of 245 patients [60.0%]), followed by lobectomy (76 of 245 patients [31.0%]). Cefazolin was used for preoperative prophylaxis in 227 of the 245 patients (93.0%).

Postoperatively, the most common pathologic finding was malignancy (76.0%) (86 in the intervention group vs 100 in the placebo group). The number of postoperative chest tubes placed and the median time to removal of all chest tubes were similar in both arms (**Table 3**). The number of postoperative doses of study drug administered was similar in both arms (median, 5 doses [range, 0-6 doses]; $P = .70$).

Thirteen patients had at least 1 or more events as part of the primary study end point in the intervention group compared with 8 patients in the placebo group (risk difference [RD], −4.3% [95% CI, −11.3% to 2.7%]; $P = .26$) (**Table 4**). Six patients had surgical site infections in the intervention group compared with 5 patients in the placebo group (RD, −0.9% [95% CI, −6.1% to 4.3%]; $P = .77$). Seven patients were diagnosed with pneumonia in the intervention group compared with 3 patients in the placebo group (RD, −3.4% [95% CI, −8.3% to 1.6%]; $P = .21$). One patient in the intervention group had an empyema. This patient also had a surgical site infection. No patient in either group developed *C difficile* colitis or an allergic reaction to a drug.

Of the 245 patients included in the final analysis, 63 (26.0%) received additional antibacterials postoperatively during the study period (32 in the intervention group compared with 31 in the placebo group). Of these 63 patients, 21 (33.3%) received additional antimicrobials because they had one of the study outcomes (surgical site infection, pneumonia, or empyema). The most common indications for additional antimicrobials during the study period, excluding patients with study end points, were urinary tract infection (15 patients [6.1%]), upper respiratory tract infection (13 patients [5.3%]), and additional surgical interventions (9 patients [3.7%]) (Table 3). The median time to use of additional antibac-

Table 3. Postrandomization Findings in Intention-to-Treat Population

Finding	Patients, No. (%)		*P* Value
	Intervention Arm (n = 121)	Placebo Arm (n = 124)	
Pathologic results from surgery			
Malignancy	86 (71.1)	100 (80.6)	.07
Benign pathology	32 (26.4)	24 (19.4)	
Other	3 (2.5)[a]	0 (0)	
No. of postoperative chest tubes			
1	92 (76.0)	89 (71.8)	.73
2	28 (23.1)	34 (27.4)	
3	1 (0.8)	1 (0.8)	
Time to removal of all chest tubes, d			
Median	2	2	.76
Range	0-32	0-33	
IQR	1-3	1-3	
Length of hospital stay, d			
Median	3	3	.72
Range	1-35	0-31	
IQR	2-5	2-5	
Additional antibacterials <28 d after randomization	32 (26.4)	31 (25.0)	.88
Indication for additional antibacterials during follow-up			
Study end point	13 (10.7)	8 (6.5)	.25
Urinary tract infection	7 (5.8)	8 (6.5)	
Upper respiratory tract infection	4 (3.3)	9 (7.3)	
Additional surgical interventions	3 (2.5)	6 (4.8)	
Biopsy findings	2 (1.7)	0 (0)	
PCP prophylaxis	2 (1.7)	0 (0)	
Unknown	1 (0.8)	0 (0)	
Time to additional antibacterials after surgery for patients without study end point, median (range), d	12 (1-28)	5 (1-30)	.31
Reoperation during study follow-up	5 (4.1)	10 (8.1)	.29

Abbreviations: IQR, interquartile range; PCP, *Pneumocystis jiroveci* pneumonia.
[a] One patient had tuberculosis, 1 had aspergillosis, and 1 had histoplasmosis.

Table 4. Primary Study End Point Results

End Point	Patients, No. (%)		Risk Difference (95% CI)	*P* Value
	Intervention Arm (n = 121)	Placebo Arm (n = 124)		
Composite end point	13 (10.7)[a]	8 (6.5)	−4.3 (−11.3 to 2.7)	.26
Surgical site infection	6 (5.0)	5 (4.0)	−0.93 (−6.1 to 4.3)	.77
Pneumonia	7 (5.8)	3 (2.4)	−3.4 (−8.3 to 1.6)	.21
Empyema	1 (0.8)	0 (0)		.49
Clostridium difficile colitis	0 (0)	0 (0)		

[a] One patient in the intervention arm had both a deep surgical site infection and an empyema.

terials after surgery for patients without a study end point were 12 days (range, 1-28 days) in the intervention group and 5 days (range, 1-30 days) in the placebo group ($P = .31$). Fifteen patients (6.1%) required a reoperation: 5 in the intervention group and 10 in the placebo group ($P = .29$). Among the 15 patients who required a reoperation, only 1 procedure (decortication) was performed for a patient in the intervention group who had empyema. The other 14 reoperations were performed for the following reasons: vocal cord paralysis (n = 3), percutaneous gastric tube placement (n = 2), air leak (n = 2), tracheostomy (n = 1), hemothorax (n = 1), chest wall hematoma (n = 1), chest wall necrosis without infection (n = 1), adhesiolysis (n = 1), nasal septal deviation (n = 1), and skin lesion excision (n = 1). The median length of stay (3 days) was no different between the 2 arms. Nine patients (7.3%) in the placebo arm had upper respiratory tract infection compared with 4 patients (3.3%) in the intervention arm. Although these patients did not meet definition criteria for pneumonia, we explored the effect of additional postoperative antimicrobial treatment on an expanded composite end point that included any respiratory tract infection for which patients received additional antibacterial treatment. When any respiratory tract infection for which additional antibacterials were prescribed were included in the composite outcome, there were no differences in the number of outcomes in either group (17 events in each arm; RD, −0.34% [95% CI,

−9.0% to 8.3%]; $P = .99$). The number of events was similar in both groups (6 in the intervention group and 5 in the placebo group) when pneumonia was excluded from the composite end point (RD, −0.93% [95% CI, −6.12% to 4.26%]; $P = .77$).

COMMENT

To establish evidence-based standards for surgical prophylaxis for patients undergoing elective general thoracic surgical procedures requiring the placement of a chest tube, we examined whether additional postsurgical antibacterial prophylaxis for 48 hours or until all chest tubes were removed, whichever occurred first, decreased further the rate of infectious complications compared with standard preoperative prophylaxis only. We also examined the possible deleterious effects that could potentially be associated with the use of extended antibacterial prophylaxis (ie, allergic reaction and *C difficile* colitis).

The major finding in our study is that extended postsurgical prophylaxis did not offer any additional benefits in terms of reducing the overall rate of postoperative infectious complications when compared with placebo. In fact, more composite end points occurred in the intervention arm compared with the placebo arm (10.7% vs 6.5%; $P = .26$).

We explored several important variables that could have skewed the results of our study. All variables were evenly distributed in both arms of the study. The baseline characteristics in the intervention arm and the placebo arm were all well balanced, including age, weight, body mass index, procedure type, and duration of surgery. The majority of patients received their preoperative prophylactic antimicrobials within 60 minutes of the incision time (Table 2), as recommended by the Centers for Disease Control and Prevention and the Society of Thoracic Surgeons practice guidelines.[6,26]

The estimated occurrence of surgical site infection, empyema, and postoperative pneumonia in patients undergoing elective thoracic surgery varies widely among studies depending on the criteria employed to define infectious end points, the type of surgery performed (VATS vs open thoracotomy), and the preoperative antimicrobial prophylactic regimen used. In most studies,[3,4,12-17,19-25] the estimated occurrences of surgical site infection, pneumonia, and empyema after elective thoracic surgical procedures range from 7% to 14%.

In our study, the overall rate of infectious complications and the rates of surgical site infection, pneumonia, and empyema were all within those observed in similar studies involving elective thoracic surgery (8.6%). Of the 245 patients, 132 (54.0%) underwent a VATS; this procedure has a relatively lower rate of perioperative complications compared with an open thoracotomy.[16,18,19,25,27-31] In our study, the number of patients who underwent an open thoracotomy and the number of patients who underwent a VATS were similar in both arms of our study ($P = .89$) (Table 2). More infectious outcomes were noted in the open thoracotomy group (11.5%) compared with the VATS group (6.1%), which is consistent with previously published studies.[16,18,19,25,27,28,30,31]

Several studies[32,33] have documented that an important proportion of postoperative infectious complications develop after the patient has been discharged from the hospital. This makes it challenging to correctly classify and capture study end points after hospital discharge. In our study, the compliance rate of patients at 2 weeks after surgery was 100%. Patients were physically seen and examined by the operating surgeon, underwent chest radiography, and were assessed for the occurrence of any of the study end point. In addition, we were able to contact the majority of patients at postoperative day 28. We were unable to reach 22 patients (9%) by phone at day 28; however, we were able to assess for occurrence of any study end point by reviewing the documented follow-up visits for all patients.

Although our study was closed to enrollment before reaching its target accrual, the findings demonstrate the lack of benefit of extended antibacterial prophylaxis for patients who undergo elective thoracic surgical procedures that require chest tube placement. More end points occurred in the intervention arm (10.7%) than in the placebo arm (6.5%) (RD, −4.3% [95% CI, −11.3% to 2.7%]). The 95% CI of the RD on the composite end point between treatment arms excluded our protocol's prespecified 3% RD in favor of extended antimicrobial prophylaxis. It is unlikely that increasing the number of patients enrolled would have resulted in a clinically meaningful difference that would make the findings in our study less applicable. In addition, the numbers of patients who received additional antimicrobials during the follow-up period were similar in both arms. When any respiratory tract infection for which additional antibacterials were prescribed were included in the composite outcome, there were no differences in the number of outcomes in either group (17 events in each arm; RD, −0.34% [95% CI, −9.0% to 8.3%]).

The findings in our study might not be applicable to all types of thoracic surgical procedures. Patients undergoing more complex procedures such as pneumonectomy, lung volume reduction, and esophagectomy were not eligible for enrollment in our study. Patients requiring these types of procedures often have coexisting morbidities that inherently carry an increased risk of infectious complications, including fistulization, dead space infection, and the prolonged placement of drains. Our findings, however, may be applicable to the vast majority of elective clean or clean-contaminated thoracic surgical procedures requiring tube thoracostomy placement. These findings could also be extrapolated to other types of surgery in which a tube or a drain is inserted in sterile fashion in a sterile compartment for a short period of time.

In summary, extending postoperative surgical prophylaxis for patients undergoing elective general thoracic surgery with chest tube placement does not seem to offer any additional benefits in terms of reducing infectious complications compared with standard preoperative surgical prophylaxis. Although not demonstrated in our study, extending nonbeneficial antibacterial prophylaxis to the postsurgery period could potentially be associated with adverse effects such as the selection of more drug-resistant organisms, allergic reactions, drug toxicities, *C difficile* colitis, and higher costs.

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REFERENCES

1. Allen MS. Perioperative antibiotics: when, why? *Thorac Surg Clin*. 2005;15(2):229-235, vi.
2. LoCicero J III. Prophylactic antibiotic usage in cardiothoracic surgery. *Chest*. 1990;98(3):719-723.
3. Bernard A, Pillet M, Goudet P, Viard H. Antibiotic prophylaxis in pulmonary surgery: a prospective randomized double-blind trial of flash cefuroxime versus forty-eight-hour cefuroxime. *J Thorac Cardiovasc Surg*. 1994;107(3):896-900.
4. Olak J, Jeyasingham K, Forrester-Wood C, Hutter J, al-Zeerah M, Brown E. Randomized trial of one-dose versus six-dose cefazolin prophylaxis in elective general thoracic surgery. *Ann Thorac Surg*. 1991;51(6):956-958.
5. Otani S, Endo S, Sato Y, Hasegawa T, Saito N, Sohara Y. Feasibility of short-term antibiotic prophylaxis after pulmonary resection [in Japanese]. *Kyobu Geka*. 2004;57(13):1171-1174, discussion 1175-1176.
6. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR; Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. Guideline for Prevention of Surgical Site Infection, 1999. *Am J Infect Control*. 1999;27(2):97-132, quiz 133-134, discussion 96.
7. Greenstein AJ, Byrn JC, Zhang LP, Swedish KA, Jahn AE, Divino CM. Risk factors for the development of fulminant *Clostridium difficile* colitis. *Surgery*. 2008;143(5):623-629.
8. Zerey M, Paton BL, Lincourt AE, Gersin KS, Kercher KW, Heniford BT. The burden of *Clostridium difficile* in surgical patients in the United States. *Surg Infect (Larchmt)*. 2007;8(6):557-566.
9. Hranjec T, Swenson BR, Sawyer RG. Surgical site infection prevention: how we do it. *Surg Infect (Larchmt)*. 2010;11(3):289-294.
10. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. *Am J Infect Control*. 1988;16(3):128-140.
11. Gerding DN, Johnson S, Peterson LR, Mulligan ME, Silva J Jr. *Clostridium difficile*-associated diarrhea and colitis. *Infect Control Hosp Epidemiol*. 1995;16(8):459-477.
12. Boldt J, Piper S, Uphus D, Füssle R, Hempelmann G. Preoperative microbiologic screening and antibiotic prophylaxis in pulmonary resection operations. *Ann Thorac Surg*. 1999;68(1):208-211.
13. Duque JL, Ramos G, Castrodeza J, et al; Grupo Cooperativo de Carcinoma Broncogénico de la Sociedad Española de Neumología y Cirugía Torácica. Early complications in surgical treatment of lung cancer: a prospective, multicenter study. *Ann Thorac Surg*. 1997;63(4):944-950.
14. Hazelrigg SR, Magee MJ, Cetindag IB. Video-assisted thoracic surgery for diagnosis of the solitary lung nodule. *Chest Surg Clin N Am*. 1998;8(4):763-774, vii.
15. Inderbitzi RG, Grillet MP. Risk and hazards of video-thoracoscopic surgery: a collective review. *Eur J Cardiothorac Surg*. 1996;10(7):483-489.
16. Jancovici R, Lang-Lazdunski L, Pons F, et al. Complications of video-assisted thoracic surgery: a five-year experience. *Ann Thorac Surg*. 1996;61(2):533-537.
17. Kaiser LR. Video-assisted thoracic surgery. Current state of the art. *Ann Surg*. 1994;220(6):720-734.
18. Kaiser LR, Bavaria JE. Complications of thoracoscopy. *Ann Thorac Surg*. 1993;56(3):796-798.
19. Krasna MJ, Deshmukh S, McLaughlin JS. Complications of thoracoscopy. *Ann Thorac Surg*. 1996;61(4):1066-1069.
20. Nan DN, Fernández-Ayala M, Fariñas-Alvarez C, et al. Nosocomial infection after lung surgery: incidence and risk factors. *Chest*. 2005;128(4):2647-2652.
21. Rovera F, Imperatori A, Militello P, et al. Infections in 346 consecutive video-assisted thoracoscopic procedures. *Surg Infect (Larchmt)*. 2003;4(1):45-51.
22. Stéphan F, Boucheseiche S, Hollande J, et al. Pulmonary complications following lung resection: a comprehensive analysis of incidence and possible risk factors. *Chest*. 2000;118(5):1263-1270.
23. Tarkka M, Pokela R, Lepojärvi M, Nissinen J, Kärkölä P. Infection prophylaxis in pulmonary surgery: a randomized prospective study. *Ann Thorac Surg*. 1987;44(5):508-513.
24. Turna A, Kutlu CA, Ozalp T, Karamustafaoglu A, Mulazimoğlu L, Bedirhan MA. Antibiotic prophylaxis in elective thoracic surgery: cefuroxime versus cefepime. *Thorac Cardiovasc Surg*. 2003;51(2):84-88.
25. Yim AP, Liu HP. Complications and failures of video-assisted thoracic surgery: experience from two centers in Asia. *Ann Thorac Surg*. 1996;61(2):538-541.
26. Engelman R, Shahian D, Shemin R, et al; Workforce on Evidence-Based Medicine, Society of Thoracic Surgeons. The Society of Thoracic Surgeons practice guideline series: antibiotic prophylaxis in cardiac surgery, part II: antibiotic choice. *Ann Thorac Surg*. 2007;83(4):1569-1576.
27. Downey RJ. Complications after video-assisted thoracic surgery. *Chest Surg Clin N Am*. 1998;8(4):907-917, x.
28. Craig SR, Hamzah M, Walker WS. Video-assisted thoracoscopic pneumonectomy for bronchial carcinoid tumor in a 14-year-old girl. *J Pediatr Surg*. 1996;31(12):1724-1726.
29. Walker WS, Craig SR. Video-assisted thoracoscopic pulmonary surgery—current status and potential evolution. *Eur J Cardiothorac Surg*. 1996;10(3):161-167.
30. Walker WS, Pugh GC, Craig SR, Carnochan FM. Continued experience with thoracoscopic major pulmonary resection. *Int Surg*. 1996;81(3):255-258.
31. Giudicelli R, Thomas P, Lonjon T, et al. Video-assisted minithoracotomy versus muscle-sparing thoracotomy for performing lobectomy. *Ann Thorac Surg*. 1994;58(3):712-717, discussion 717-718.
32. Reimer K, Gleed C, Nicolle LE. The impact of postdischarge infection on surgical wound infection rates. *Infect Control*. 1987;8(6):237-240.
33. Manian FA, Meyer L. Comprehensive surveillance of surgical wound infections in outpatient and inpatient surgery. *Infect Control Hosp Epidemiol*. 1990;11(10):515-520.