HHS Public Access

Author manuscript

Ann Thorac Surg. Author manuscript; available in PMC 2022 January 01.

Published in final edited form as:

Ann Thorac Surg. 2021 January ; 111(1): 206–213. doi:10.1016/j.athoracsur.2020.06.056.

Antibiotic resistance is associated with morbidity and mortality after decortication for empyema

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Abstract

Background: Previous studies of decortication for empyema have demonstrated that patient characteristics are associated with mortality, but the relationship of infectious pathogen to outcome has not been described. Our objective was to analyze the association of microbiology and antibiotic resistance with post-operative mortality following decortication for empyema. We hypothesized that bacterial pathogens, antibiotic resistance and patient characteristics would all contribute to perioperative morbidity and mortality.

Methods: Patients undergoing pulmonary decortication for empyema from 1/1/2010–10/1/2017 were reviewed retrospectively. Cases were matched to microbiology cultures. The outcomes of interest was a composite of death, tracheostomy, initial ventilator support > 48 hours or unexpected ICU readmission. Antibiotic resistance was categorized as present or absent, and the number of antibiotics with resistance was counted for each patient. We describe the relationship of patient characteristics, antibiotic resistance, and microbiology to mortality.

Results: During the study period, 185 patients underwent decortication, 118 (63.8%) of which had a diagnosis of primary empyema. Positive culture results were present in 79/185 patients (43%). The most common isolate was Streptococcus, present in 29/79 (37%), followed by Staphylococcus in 19/79 (24%). 11/79 patients (13.9%) had fungal infections. 16/79 (20%) patients had polymicrobial empyema. 30/185 (16.2%) patients experienced the composite adverse outcome. In multivariable regression, the composite adverse outcome was associated with emphysema, candida in pleural culture, and antibiotic resistance count.

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Conclusions: Perioperative mortality and morbidity following decortication for empyema is significant. In this cohort, infections with increasing antibiotic resistance are associated with morbidity and mortality among patients with empyema.

Although a rare condition, empyema is associated with an in-hospital death rate in excess of 3% and estimated yearly healthcare expenditure over 1.2 billion dollars in the United States (1). Empyema is frequently treated with surgical decortication, which involves pleural debridement and evacuation of purulence. Data from the Society of Thoracic Surgeons' General Thoracic Surgery Database (STS-GTSD) suggests that decortication is associated with perioperative mortality of 3.1%,(2) but older studies suggest mortality rates of up to 9%.(3–5) In addition, 39% of patients experience a post-operative complication and 26% are discharged to a location other than home.(2) While patient factors are associated with poor outcomes, few studies have examined the relationship of infectious pathogen to outcomes.

The seminal study of empyema microbiology comes from 197 patients with positive cultures from 1973 to 1985.(6) That study established the importance of polymicrobial infections (23%) and β-lactamase type antibiotic resistance (38%). A 2004 study highlighted the importance of anaerobic bacteria in outcome, but found no association of bacteria to morbidity.(7) A 2006 study of 434 pleural infections from the British Thoracic Society included a microbiology analysis, which showed that mortality was associated with infections from gram-negative, Staphylococcus aureus and mixed aerobic infections, but did not report an association of antibiotics resistance and surgical outcome.(8) Finally, a study of 171 patients with empyema reported a high number of infections due to Klebsiella, and associated mortality with aerobic Gram-negative bacilli (22%).(9) A modern analysis of the relationship between surgery and empyema pathogens and resistance patterns is needed.

We performed an analysis of a single institution's surgical decortications for empyema to assess clinical outcomes of patients who underwent surgical decortication for empyema. Our objective was to analyze the association of microbiology and antibiotic resistance with post-operative adverse outcomes following decortication for empyema. We hypothesized that bacterial pathogens, antibiotic resistance, and patient characteristics would all contribute to perioperative morbidity and mortality.

Patients and Methods

Patient Population

The study population consisted of all patients receiving decortication for empyema at a single academic medical center from 1/1/2010–10/1/2017. Empyema was defined as presence of pus, or purulent-appearing fluid, in the pleural space, and was not further characterized by "class".(10) For patients with multiple procedures, only the first procedure was evaluated. Operative approach was defined as thoracoscopic (VATS) if the procedure was exclusively thoracoscopic. Patients were characterized as primary or secondary empyema.(11) Primary empyema was empyema due to likely parapneumonic pleuropulmonary inflammation, while secondary was due to post-operative complications, trauma, esophageal perforation, or extension of a suppurative infection from the neck or abdomen. Patients' microbiology records were also collected and analyzed.

Outcome Measures

The study endpoints were death and post-operative complications. Patients were defined as having a complication if the complication occurred during the hospital admission or in the 30-days after a procedure. Complications were categorized according to established definitions(12), and the severity of each complication was not collected. Pneumonia was excluded as a complication due to possible interrelation with a diagnosis of empyema. Death was defined as in-hospital or 90-day mortality from the procedure. The primary study endpoint was a composite outcome of 90-day mortality, tracheostomy, post-operative ventilator use >48h, or unexpected ICU admission. Post-operative length of stay was defined as the number of days from initial operative intervention to discharge. Readmission was defined as readmission to any hospital within 30 days from surgery.

Patients were categorized as “culture positive” if any pleural culture was positive during their hospitalization, including cultures obtained from preoperative thoracentesis. Empyema was considered polymicrobial if multiple organism types were cultured during their hospitalization, not necessarily from a single culture result. Organisms were categorized as having antibiotic resistance if any antibiotic tested was categorized as resistant. A resistance count was calculated, which is the total number of antibiotics a given patients bacterial isolate (or isolates) were resistant to. For polymicrobial infections, the resistance count represented the total number of antibiotics with resistance (ie if two bacteria were resistant to the same single antibiotic, the resistance count would be 1). Serum albumin was collected from the electronic medical record if a result was available within 30 days prior to decortication. Cause of death was abstracted from patient discharge summary, death certificate, or both.

Statistical Methods

Continuous variables are summarized as median and interquartile range. Frequencies and percentages are presented for categorical variables. The differences across groups were assessed using Kruskal Wallis test and Chi-square. Multivariable models used logistic regression. Candidate variables were identified using selection from the univariate analyses ($p \leq 0.3$). Stepwise backward selection was performed on the multivariable regression using the candidate variables identified from the univariable analysis with significance for removal set at $p \geq 0.2$. For models which include bacteria type and antibiotic resistance, the denominator for analyses is all patients, not just patients with positive cultures.

Probability values of less than 0.05 were considered statistically significant, and there was no adjustment made for multiplicity of comparisons. All statistical calculations were performed using STATA/MP software Version 16.1. [StataCorp. College Station, TX: StataCorp LP.] This research was approved by the University Hospitals Institutional Review Board as exempt of informed consent given the retrospective nature of the study (UH 05-16-11)

Results

During the study period, 185 patients received decortication for empyema, 118 (63.8%) for primary empyema and 67 (36.2%) for secondary empyema. The characteristics of the study cohort are shown in Table 1. Notably, 157 (84.9%) patients received a VATS procedure, 14 (7.6%) of cases were converted from VATS to open, and 14 (7.6%) received open procedures.

Of the 185 decortications, 103 organisms were cultured in 79 (42.7%) patients. Gram positive organisms were most common (60/79, 75.6%) and were more common among primary empyema than secondary (40/45 (88.9%) vs 20/34 (58.8%), p=0.002). Polymicrobial infections occurred in 17 patients (21.5%) and were more common among secondary empyema (11/34 (32.4%) vs 6/45 (13.3%), p=0.042). The most common bacterial organisms were Streptococcus species (29/79, 36.7%), Staphylococcus aureus (19/79, 24.1%), and Pseudomonas species (6/79, 7.6%). Fungi were identified in 11/79 patients (13.9%), the most common of which were candida species (9/11, 81.8% – 8/9 candida albicans). Antibiotic resistance was categorized for 73 patients with positive cultures, and among them, 39/73 (53.4%) demonstrated resistance to at least one antibiotic.

Antibiotics susceptibilities are shown in Table 2. Methicillin resistant Staphylococcus aureus (MRSA) was identified in 8/73 patients (42.1% of S. aureus, 10.9% of patients with sensitivity categorized). Among patients with ESKAPE pathogens, resistance to parental aminopenicillin with β-lactamase inhibitor (eg amoxicillin-clavulanic acid, piperacillin-tazobactam) was identified in 12/73 patients (37.5% of ESKAPE cultures, 16.4% of patients with sensitivity categorized). Among patients with antibiotic resistance categorized, the median resistance count was 1 (IQR 0–5).

Although patients with primary and secondary empyema were similar by demographic characteristics, their culture results differed in several ways. [Table 3] Gram-negative organisms (13/34 (38.2%) vs 5/45 (11.1%), p=0.004) and polymicrobial infections (11/34 (32.4%) vs 6/45 (13.3%), p=0.042) were more common in secondary empyema. Antimicrobial resistance was more common in secondary empyema (23/34 (76.7%) vs. 16/45 (37.2%), p=0.001), also reflected in higher resistance count among secondary empyema (2 (0–8) vs 0 (0–2), p=0.009).

Outcomes of decortication are shown in Table 4. Death (90-day) occurred in 14/185 patients (7.6%). Cause of death was available in 10/14 patients, and most commonly cardiac arrest (8/10, 80%). A summary of cause of death and contributing factors is shown in supplemental table 1. The primary outcome of interest was a composite of death, tracheostomy, post-operative ventilator use >48h, or unexpected ICU admission, and occurred in 30 patients (16.2%). Factors associated with this composite adverse outcome are shown in Table 5. Preoperative steroid use (0/155 (0%) vs 3/30 (10.0%), p<0.001), lower serum albumin (median 2.2 (1.9–2.7 vs 1.8 (1.5–2.3), p=0.006) and longer times from admission to surgery (3 days (1–6) vs 5.5 days (3–8), p=0.038), were associated with the composite adverse outcome. Among 79 patients who were culture “positive”, there was a trend towards worse outcome associated with candida organisms (5/63 (7.9%) vs 4/16(25.0%), p=0.055).

Although the presence of any antibiotic resistance was not associated with the composite adverse outcome (29/59 (49.2%) vs. 10/14 (71.4%), p=0.133), there was a trend towards higher resistance count and adverse outcome (median 0 (0–4) vs 1.5 (0–11.5), p=0.056).

Stepwise backwards multivariable logistic regression was performed among all patients with those patients who were culture negative categorized as not having specific organisms or antibiotic resistance. In this analysis, emphysema, candida in pleural culture, and antibiotic resistance count were independently associated with the composite adverse outcome [Table 6]. The analysis was repeated among only “culture positive” patients, which showed age, secondary empyema, candida in pleural culture, and antibiotic resistance count were associated with the adverse outcome [Table 7].

Comment

The relationship of infectious organism and outcomes is poorly defined in thoracic empyema. Recent analysis of the STS-GTSD studies has identified patient factors associated with poor outcomes but was unable to evaluate the effect of infectious organisms.(2) Herein, we show that antibiotic resistance is associated with adverse outcomes after decortication. Although empyema is rare (4.7/100,000 in 2014), empyema is associated with significant morbidity and mortality, estimated at 3.4% nationally.(13, 14) Nationally, empyema is associated with hospitalizations over 10 days and cost over $105,000 per admission, for an estimated aggregate cost of $1.2 Billion yearly in the US.(14) Empyema, however, has become an “orphan” condition in that there is little research in this area with only 337 articles published in 2018 with the subject “empyema” relative to over 3,000 for “esophageal cancer”, a condition with similar prevalence (4.3/100,000).(14, 15) A 2017 consensus guideline from the American Association for Thoracic Surgery made several recommendation regarding the management of patients with empyema(16), and suggests “parenteral second- or third- generation cephalosporin … with metronidazole or parental aminopenicillin with β-lactamase inhibitor” for community acquired empyema. For seconadary empyema, the recommendation is to “include antibiotics active against methicillin-resistant Staphylococcus aureus and pseudomonas.”(16) No recommendations were made regarding antifungal agents.(16)

This study is a contemporary evaluation of the microbiology of empyema and demonstrates differences in infectious organism rates by empyema type. Compared to earlier studies,(6, 11) this study showed a higher rate of sterile culture with only 79/185 (42.7%) having “positive” cultures compared to 76% among 179 patients studied from 1973 to 1997. The rate of “unspecified empyema” appears to be increasing in the pediatric population as well.(17, 18) Despite lower number of cultured organisms, we show high rate of gram negative bacteria, fungi and ESKAPE pathogens. Although gram negative empyema has previously been associated with poor prognosis,(9) gram negative bacteria were not associated with poor outcomes in this analysis. We identified fungi in 11 patients (5.9% of all patients, 13.9% of culture positive patients). Candida infection was associated with the composite adverse outcome among all patients (OR 6.2, P=0.016). Regarding treatment with antifungal agents, in the absence of specific guidelines, we recommend treatment with antifungals in a similar manner to intra-abdominal infections, where anti-fungal agents should be considered

in empiric therapy of “severely ill patients at risk for infection with Candida species” “(Grade1-B)” or “less severely ill patients at risk for infection with Candida Species” “(Grade 2-B)”, such as those with “yeast on gram stain of infected…fluid”.(19) ESKAPE organisms were seen in 32 of the patients in this study (17.3% of all patients, 44.3% of “culture positive” patients). ESKAPE organisms also demonstrated resistance to AATS recommended antibiotics, with 37.5% of ESKAPE cultures resistant to parental aminopenicillin with β-lactamase inhibitor. We believe that the high rate of ESKAPE organisms is empyema cultures is concerning and highlights the role for antibiotic stewardship in empyema.

Few studies have evaluated antibiotic resistance in empyema. Brook reported β-lactamase-producing organisms in 38% of positive cultures (6), whereas we found that antibiotic resistance occurred in 53% of positive cultures with resistance categorized, and that resistance was especially prevalent among secondary empyema (76.7%). Oxacillin resistance was identified in 42.1% of Staphylococcus aureus isolates, which is similar to previous studies of MRSA in empyema, occurring in 14% of empyema isolates.(20) Another finding of this analysis was that the “resistance count” was independently associated with the composite adverse outcome. The resistance count is a surrogate, in our opinion, for the burden of antibiotic resistance, and demonstrates how bacteria with increasing antibacterial resistance can be difficult to treat. The resistant count may also be a surrogate for other virulent features of bacterial infection or even a measure of the host’s exposure to health care systems. The association of antimicrobial resistance to morbidity highlights not only the importance of appropriate antibiotic administration to target resistant organisms, but also the need for antibiotic stewardship. Ongoing efforts to reduce inappropriate antibiotic administration are appropriate to suppress antibiotic resistant organisms.

This study has several limitations. As a retrospective study at a single academic center, the results may not be generalizable to other settings. Although we believe that all patients had “complicated” empyema,(10) we have not analyzed patients by empyema stage, and this may have biased the results. Furthermore, the cohort is only patients receiving decortication, which may be associated with specific infectious agents. Nonetheless, we believe that these findings are similar to other reports(20), and therefore likely represent the current landscape of bacterial pathogens in academic medical centers. Community hospitals may have fewer complex cases and therefore lower rates of organisms such as fungal infections, which are associated with immunosuppression and/or repeated antibiotic exposure.(19) Another limitation of the data is that we do not account for previous antibiotic treatment. Antibiotics treatment prior to pleural fluid sampling may have altered the microbiome of empyema patients and altered the findings of this analysis. For example, outpatient treatment with oral antibiotics may have “selected for” antibiotic resistant organisms in this cohort of patients receiving decortication. Furthermore, there was no standardized protocol for handling the surgical fluid samples, thereby introducing variability in sample handling and limiting accuracy. Differences in culture technique may have varied over time and affected the findings of this analysis. For example, genomic analyses were not used, which may have led to limitations in sensitivity and specificity. Lastly, the number of antibiotics tested was different for each bacterial isolate and also varied over time. This may have led to “missed” antibiotic resistance, which may in turn have altered the analysis of antibiotic count. Lastly,

we have analyzed a composite outcome of death, tracheostomy, post-operative ventilator use >48h, or unexpected ICU admission in this analysis, which may have biased the results from other factors related to adverse outcomes. Certainly other patient-centered outcomes (hospital disposition, need for tracheostomy, etc) are critical to follow in these patients, and we strongly advocate for further research in this area.

Although a rare surgical infection, empyema is associated with significant morbidity and mortality. Despite variation in the spectrum of infectious organisms by empyema type, antibiotic resistance is common. The association of the antibiotic resistance count with adverse outcome highlights the importance of appropriate antibiotics choice and antibiotic stewardship. We believe that there is controversy regarding ideal antimicrobial treatment and duration of treatment in empyema, and believe that ongoing studies in this area are appropriate.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1:

Description of cohort: 185 patients receiving decortication for empyema at a single institution 1/2010–10/2017. Data presented as Median (IQR) or n (%).

Factors		Total cohort
Age (years)		58.4 (47.2–70.6)
Sex	Male	125 (67.6%)
Race	Caucasian	140 (76.1%)
BMI		26.0 (22.0–31.4)
BMI > 35		29 (15.7%)
Hypertension		92 (49.7%)
Steroid Use		3 (1.6%)
COPD		34 (18.4%)
Congestive Heart Failure		18 (9.7%)
Coronary Artery Disease		23 (12.4%)
Peripheral Vascular Disease		9 (4.9%)
Diabetes		25 (13.5%)
ASA class	1	0
	2	11 (5.9%)
	3	137 (74.1%)
	4	37 (20.0%)
Operative Approach	VATS	157 (84.9%)
	VATS → Open	14 (7.6%)
	Open	14 (7.6%)
Time from Admit to Surgery	Days	3 (1–6)
Empyema Type	Primary	118 (63.8%)
	Secondary	67 (36.2%)

Table 2:

Bacteria types, antibiotic sensitivity among 79 patients with culture “positive” empyema.

Bacteria type	Number (%) n=79	Amoxicillin Clav.	Azithromycin	Aztreonam	Ceftriaxone	Clindamycin	Cefoxitin	Cefazolin	Colistin	Ciprofloxacin	Cefepime	Cefuroxime	Cefotetan	Daptomycin	Doripenem	Erythromycin	Ertapenem	Gentamicin	Imipenem	Levofloxacin	Linezolid	Meropenem	Oxacillin	Penicillin	Pip. Tazobactam	Rifampin	Trimeth-Sulfa	Tigecycline	Vancomycin
Streptococcus Species	29 (36.7%)				14/15 (93.3%)	0/2 (0%)								1/1 (100%)		2/2 (100%)				3/3 (100%)	3/3 (100%)		1/1 (100%)	27/28 (96.4%)			1/1 (100%)	1/1 (100%)	28/28 (100%)
Enterococcus Species	4 (5.1%)									2/3 (66.7%)				3/3 (100%)		1/3 (33.3%)				2/3 (66.7%)	4/4 (100%)			2/2 (50%)		0/4 (0%)			2/2 (50%)
Staphylococcus Aureus	19 (24.1%)	10/18 (55.6%)			11/19 (57.9%)	14/19 (73.7%)		1/8 (12.5%)		14/19 (73.7%)	0/7 (0%)	0/7 (0%)		19/19 (100%)		7/19 (63.2%)	0/7 (0%)	19/19 (100%)	0/7 (0%)	14/19 (73.7%)	19/19 (100%)	0/7 (0%)	11/19 (57.9%)	2/19 (10.5%)		19/19 (100%)	18/19 (94.7%)	1/1 (100%)	19/19 (100%)
Klebsiella Species	4 (5.6%)	3/4 (75%)	0/1 (0%)	1/3 (33.3%)	1/3 (33.3%)		1/3 (33.3%)	2/4 (50%)	1/1 (100%)	3/4 (75%)	1/3 (33.3%)	1/3 (33.3%)	1/3 (33.3%)		0/3 (0%)		2/3 (66.7%)	2/4 (50%)	2/3 (66.7%)	3/4 (75.0%)		2/3 (66.7%)			3/4 (75.0%)		2/4 (50%)	0/1 (0%)	
Pseudomonas Species	6 (7.6%)			3/6 (50%)	1/2 (50%)				1/2 (50%)	5/6 (83.3%)	5/6 (83.3%)							5/6 (83.3%)	4/6 (66.7%)	5/6 (83.3%)		4/6 (66.7%)			5/6 (83.3%)				
Enterobacter Species	2 (2.5%)	0/2 (0%)		1/2 (50%)	2/2 (100%)		0/2 (0%)	0/2 (0%)		1/2 (50%)	2/2 (100%)	1/2 (50%)	1/1 (100%)				2/2 (100%)	2/2 (100%)	2/2 (100%)			2/2 (100%)			2/2 (100%)		2/2 (100%)	1/1 (100%)	

Table 3:

Relationship of empyema classification to patient characteristics and culture results. Data reported at N(%) or Median (IQR). Comparison using chi-square, fisher's exact or Kruskal-Wallis test.

Characteristic	Primary Empyema (n=119)	Secondary Empyema (n=66)	P-Value
Age	57.1 (45.2–68.1)	60.1 (45.5–71.2)	0.080
Male	85 (72.0%)	40 (59.7%)	0.085
BMI > 35	21 (17.8%)	8 (11.9%)	0.292
Hypertension	52 (44.1%)	40 (59.7%)	0.041
Steroid Use	2 (1.7%)	1 (1.5%)	0.917
Congestive Heart Failure	13 (11.0%)	5 (7.5%)	0.433
Chronic obstructive pulmonary disease (COPD)	22 (18.6%)	12 (17.9%)	0.901
Coronary Artery Disease	13 (11.0%)	10 (14.9%)	0.439
Peripheral Vascular Disease	6 (5.1%)	3 (4.5%)	0.854
Diabetes	17 (14.4%)	8 (11.9%)	0.637
Time from Admit to Surgery	3 (1–6)	4 (1–7)	0.223
Culture "positive"	45 (38.1%)	34 (50.8%)	0.096
Gram Positive	40 (88.9%)	20 (58.8%)	0.002
Gram Negative	5 (11.1%)	13 (38.2%)	0.004
Fungus	4 (8.9%)	7 (20.6%)	0.137
Anaerobic	3 (6.7%)	3 (8.8%)	0.720
Polymicrobial	6 (13.3%)	11 (32.4%)	0.042
ESKAPE*	11 (24.4%)	21 (61.7%)	0.001
Any resistance	16 (37.2%)	23 (76.7%)	0.001
Resistance Count	0 (0–2)	2 (0–8)	0.009

ESKAPE= enterococcus, staph aureus, Klebsiella, Acinetobacter, Pseudomonas, Enterobactericeae

Table 4:

Outcomes of 185 patients receiving decortication. Data presented as Median (IQR) or n (%). Comparison using Chi square, fisher's exact* or Kruskal-Wallis test. The primary outcome of the study was a composite outcome† of death, tracheostomy, post-operative ventilator use >48h, or unexpected ICU admission.

Event	Median (IQR) or n (%)
Death (90-days)	14 (7.6%)
Any complication	66 (35.7%)
Composite outcome†	30 (16.2%)
Return to Operating Room	23 (12.4%)
Airleak >5 days	12 (6.4%)
Atelectasis requiring bronchoscopy	2 (1.1%)
Respiratory failure	59 (31.9%)
Tracheostomy	6 (3.2%)
Bronchopleural fistula	1 (0.5%)
Pulmonary embolism	0
Initial ventilator support > 48 hours	9 (4.9%)
Myocardial Infarction	0
Deep Venous Thrombosis	1 (0.5%)
Post-op pRBC transfusion	23 (12.4%)
Unexpected ICU admission	9 (4.9%)
Length of hospitalization (days)	12 (7–19)
Discharge to home	101 (44.8%)
Unplanned readmission	72 (38.9%)

pRBC: packed red blood cells, ICU: intensive care unit

Table 5:

Factors associated with the primary outcome of interest ([α]a composite of death, tracheostomy, post-operative ventilator use >48h, or unexpected ICU admission) among 185 patients receiving decortication for empyema (*among patients with positive cultures). Continuous data presented as median (IQR) and compared using Kruskal Wallis. Categorical data presented n (%) and compared using chi-square or Fischer's exact test†.

		No composite adverse event (n=155)	Composite adverse event [α] (n=30)	p-value
Age (years)		58.2 (46.7 – 69.7)	59.4 (51.8–74.3)	0.254
Body Mass Index (BMI)		25.7 (21.9–31.2)	28.1 (24.4–33.9)	0.120
Hypertension		74 (47.7%)	18 (60%)	0.219
Steroid Use		0	3 (10%)	<0.001
Congestive Heart Failure		13 (8.4%)	5 (16.7%)	0.161
Chronic obstructive pulmonary disease (COPD)		26 (16.7%)	8 (26.7%)	0.200
Coronary artery disease		17 (11.0%)	6 (20.0%)	0.170
Peripheral vascular disease		9 (5.8%)	0	0.176
Diabetes		20 (12.9%)	5 (16.7%)	0.581
ASA class > 2		144 (92.9%)	30 (100%)	0.132
Preoperative serum albumin (g/dL)		2.2 (1.9–2.7)	1.8 (1.5–2.3)	0.006
Thoracoscopic approach (vs open + conversion VATS to open)		132 (85.2%)	25 (83.3%)	0.798
Time from admit to surgery (days)		3 (1–6)	5.5 (3–8)	0.038
Empyema type	Primary	102 (65.8%)	16 (53.3%)	0.193
	Secondary	53 (34.2%)	14 (46.7%)	
Culture positive		63 (40.7%)	16 (53.3%)	0.198
	Polymicrobial*	13 (20.6%)	4 (25%)	0.704
	Candida*	5 (7.9%)	4 (25.0%)	0.055
	Anaerobe*	5 (7.9%)	1 (6.3%)	0.820
	ESKAPE organism*	23 (36.5%)	9 (56.3%)	0.151
	Gram-positive*	49 (77.8%)	11 (68.8%)	0.451
	Gram-negative*	14 (22.2%)	4 (25.0%)	0.813
	Fungus*	7 (11.1%)	4 (25.0%)	0.152
	Any antibiotic resistance (N=73)*	29 (49.2%)	10 (71.4%)	0.133
	Antibiotic resistance count (n=73)*	0 (0–0)	0 (0–2)	0.056

ASA: American Society of Anestheologists, VATS: video assisted thoracoscopic surgery, ESKAPE= enterococcus, staph aureus, Klebsiella, Acinetobacter, Pseudomonas, Enterobactericeae

Table 6:

Multivariable regression of factors associated with the composite adverse outcome (death, tracheostomy, post-operative ventilator use >48h, or unexpected ICU admission) among 185 patients undergoing decortication for empyema with patients who are culture negative treated as not having specific organisms and resistance count=0 (n=140). Cofactors for regression chosen using backwards selection from univariable modeling (α<0.3), and included age, body mass index, hypertension, steroid use, congestive heart failure, coronary artery disease, emphysema (COPD), peripheral vascular disease, ASA class (≤2 vs >2), time to surgery, whether the pleural fluid cultures were “positive”, secondary (vs primary) empyema, candida organism, ESKAPE organism, preoperative blood albumin level, and resistance count. Cofactors analyzed using stepwise backwards section with p-value to be removed from the model of ≥0.2.

Variable	Odds Ratio	95% CI	P-value
Emphysema (COPD)	2.944	0.974–8.900	0.056
Candida infection	6.228	1.411–27.485	0.016
Resistance Count	1.121	1.032–1.217	0.007

Table 7:

Multivariable regression of factors associated with the composite adverse outcome among only patients with positive cultures (n=64).

Variable	Odds Ratio	95% CI	P-value
Age (years)	1.042	0.999–1.087	0.062
Secondary empyema (vs primary)	4.345	0.943–20.011	0.059
Candida infection	4.225	0.770–23.159	0.097
Resistance Count	1.142	1.012–1.288	0.002