Optimal duration of antibiotics therapy after Video-assisted thoracoscopic surgery in thoracic empyema and complicated parapneumonic effusion

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Abstract

Background

There is no evidential report about the optimal duration of antibiotics use following Video-assisted thoracoscopic surgery debridement (VATS-D) in thoracic empyema (TE) or complicated parapneumonic effusion (PPE). The purpose of this study was to determine the optimal duration of antibiotics therapy after VATS-D for TE /PPE.

Methods

Between January 2011 and December 2019, total thirty-three patients (28 men, 5 women; median age 63 years) corresponding to ACCP category 3 or 4 recieving VATS-D were included in the study. Time until the body temperature (BT) confirmed to be less than 37.5 ºC and 37.0ºC, WBC to be less than10,000/μl, segmented neutrophil (seg) to be less than 80% were retrospectively analyzed.

Results

Median time from the onset of TE/PPE to operation was 13 days. Pre and postoperative antibiotics use were 5 and 7 days in median value. There was no hospital death within 30 days from the operation. Major complication occurred in 4 cases (3 respiratory failures and one cerebral infarction). Median postoperative hospital stay was 14 days. Success rate in TE/PPE treatment was 88%. The median number of days until the conditions met were BT > 37.5 ºC for 3 days, BT > 37.0 ºC for 6 days, WBC < 10,000 for 4 and seg < 80% for 7 days.

Conclusion

Optimal antibiotics duration of antibiotics use after VATS-D for TE/PPE is about 5 days. Urgent VATS-D will shorten the total antibiotics duration.

Introduction

The antibiotics treatment for thoracic empyema (TE) or complicated parapneumonic effusion (PPE) is always empiric. Usually, antibiotics treatment starts when drainage or surgical intervention are planned. The target bacteria are often unknown when the antibiotics is chosen. Bacterial cultures tend to prove negative so antibiotics treatment often have to be continued empirically.

Recommendation in the choice of antibiotics are described in guidelines such as Sanford Guide [1], British Thoracic Society (BTS) pleural disease guideline [2] or Japanese Association for infectious Disease/Japanese Society of Chemotherapy (JAID/JSC) guideline. According to the patient's risk and

community or hospital-acquired, the regimens are suggested in these guidelines but there is no evidential description about the optimal duration of antibiotics therapy.

Video-assisted thoracoscopic surgery debridement (VATS-D) is a common and evidential treatment for TE/ complicated PPE [3]. It shortens drainage duration or hospital stay [4]. However, the appropriate duration of antibiotics therapy following surgical intervention is unclear. Though it is said from a few to several weeks of antibiotics administration is required, we thoracic surgeons may not have an image that such long-term antibiotic administration is required after VATS-D in acute TE or complicated PPE.

The purpose of this study was to determine the optimal duration of antimicrobial therapy after VATS-D in TE /PPE from the point of view of the physical findings and laboratory data.

Material And Methods

Data were retrospectively collected from the registry of Ehime Medical Center. Cases receiving VATS-D for TE/PPE at Ehime Medical Center in the period from 2010 to 2019 were identified. Patient fulfilled Category 3 or 4 of the *American College of Chest Physicians (ACCP) Categorizing Risk for Poor Outcome in Patients with PPE* [5] after a thoracentesis, simple drainage or intraoperative collection of pleural effusion were identified and included to this study. Chronic empyema or empyema with bronchopleural fistula were excluded.

VATS-D procedures were performed under general anesthesia and one lung ventilation for all cases. Two or three trocars were placed for a thoracoscope or other instruments. The pleural cavity was debrided, loculated cavity was disrupted and fibrous adhesions were removed to make it into one cavity and re-expand the lung.

The following parameters were evaluated (1) Preoperative characteristics; age, sex, comorbidities, white blood cell count (WBC), percentage of segmented neutrophil, serum C-reactive protein level (CRP), antibiotics administration status, time from the onset of the disease to VATS-D, bacterial culture. (2) Postoperative characteristics; hospital stay, chest tube duration, major postoperative complications corresponding to Clavien-Dindo Classification grade or higher, re-hospitalization due to recurrence within 1 year, antibiotics administration status, period until the body temperature confirmed to be less than 37.5 ºC and 37.0ºC, WBC to be less than10,000/μl, segmented neutrophil to be less than 80%.

Results

In the period studied, 33 patients received VATS-D for TE /PPE (Table 1). Twenty-six cases (79%) was ACCP category 3 and 7cases were 4 (21%). Thirty cases (91%) were primary TE/PPEs and 3 (9%) were secondary. Among primary cases, chest computed tomography demonstrated pneumonia in 25 case and lung abscess in one case. They were considered to be the cause of TE/PPE. In rest 5 cases (15%), the cause was unknown. Three secondary cases followed lobectomy for lung cancer, percutaneous transhepatic gallbladder drainage for acute cholecystitis and traumatic hemopneumothorax.

Time from the onset or the diagnosis of TE/PPE to VATS-D was about two weeks (Table 2). Six mental disorder cases (5 schizophrenia and 1 severe depression) was included in this study (Table 1). Though, it is difficult to determine the onset of TE/PPE in these patients, the day complaint of fever, chest pain or dyspnea was noticed by the patient or a caregiver was set as the onset. Preoperative period in these cases tended to be longer than other cases mean 25 vs 14, median 30 vs 13 day, respectively.

The median Postoperative hospital stay was 14 days. Postoperative drainage duration was about a week. Major postoperative complication corresponding to Clavien-Dindo Classification grade or higher occurred in 4 cases (Table 2). Postoperative acute respiratory failure requiring ventilator management in 3, cerebral infarction in one case. No death in hospital was observed within 30 days after surgery. Recurrence and progression to chronic empyema were seen in 3 cases and 1 case, respectively. The recurrent cases were treated by simple drainage and chronic empyema was treated by omentoplasty.

Bacterial culture from pleural effusion was positive in 12 cases (36%). Streptococcus in 7, anaerobic bacteria 3, staphylococcus, neisseria, prevotella in 1 case, respectively were identified. Fluoroquinolone resistance was observed in 2 cases of anaerobic bacteria, and CLDM resistance was observed in 1 case, but no problematic resistant bacteria were observed.

Preoperative and post-operative antibiotics choice are shown in Table 3. Carbapenem or tazobactam/piperacillin (TAZ/PIPC) was selected in more than 60% of cases as an initial agent. Of these cases, 8 had postoperative conversion into fluoroquinolone or cephalosporin. On the other hand, switching to carbapenem or TAZ/PIPC from another agent was performed in 5 cases. During the post-operated course, 3 cases had converted the antibiotics (from cephalosporin to fluoroquinolone or sulbactum/ampicilin). In four cases, oral administration of levofloxacin (LVFX) was added before discharge.

Postoperative inflammatory parameters required 7 days to return to the normal values (Table 4). Body temperature was measured at least 3 times per day. Laboratory examination was performed routinely on the day after surgery and added when deemed necessary. Mean 5, median 4 times of laboratory examination were performed post-operatively before discharge.

Table 1. Characteristics of the patients			
	n(%)	**mean ± SD**	**median (range)**
Epidemiological data			
Gender			
male	28(85)		
female	5(15)		
age (years)		62 ± 11	63 (28–88)
Comorbidity	21 (64)		
diabetes	9 (27)		
cardiovascular	7 (21)		
cerebrovascular	3 (9)		
mental disorder	6 (18)		
cancer bearing	1 (3)		
use of steroids	1 (3)		
Ecog Performance Status			
0–1	30 (91)		
2	0		
3	3 (9)		
Laboratory examination			
WBC (/μl)		16800 ± 9,300	13200 (4800-50,000)
seg (%)		83.1 ± 5.9	83.5 (70.4–94.4)
CRP (mg/dl)		20.4 ± 9.8	18.8 (3.4–42.4)

Table 2. Post operative course			
	n(%)	**mean ± SD**	**median (range)**
major complication	**4 (12%)**		
respiratory failure	3 (9%)		
cerebral infarction	1 (3%)		
hospital stay (day)		**16.3 ± 9.1**	**14 (7–51)**
drainage duration (day)		**7.4 ± 7.2**	**6 (2–43)**
antibiotics duration (day)		**7.2 ± 4.9**	**7 (1–18)**
Failure of TE/PPE treatment	**4 (12%)**		
recurrence	3 (9%)		
progression to chronic empyema	1 (3%)		

Table 3. Pre/Post -operative antibiotics		
	pre-operative	post-operative
	n (%)	n (%)
Carbapenem	**18 (55)**	**15 (45)**
MEPN	15	12
IPM/CS	1	1
DRPM	2	2
Penicillin	**12 (36)**	**6 (18)**
TAZ/PIPC	3	3
SBT/ABPC	9	3
Fluoloquinolon	**2 (6)**	**9 (27)**
PZFS	2	3
CPFX	-	2
LVFX p.o.	-	4
Cepharosporin	**1 (3)**	**10 (30)**
CFPM	1	1
CMZ	-	2
CEZ	-	5
CTRX	-	2
Lincomycin	**7 (21)**	**3 (9)**
CLDM	7	3
MEPN meropenem, IPM/CS imipenem/cilastatin, DRPM doripenem, TAZ/PIPC tazobactam/piperacilin, SBT/ABPC sulbactam/ampicillin, PZFS pazofloxacin, CPFX ciprofloxacin, LVFX p.o. Levofloxacin per os CFPM cefepime, CMZ cefmetazole, CEZ cefazolin, CTRX ceftoriaxone CLDM clindamycin		

Table 4. Post-operative inflammatory parameters

	mean ± SD	median (range)
Body temperature		
<37.5ºC	4.5 ± 4.4	3 (0–18)
<37.0ºC	7.4 ± 7.5	6 (0–18)
White blood Cell		
<10,000/μl	6.1 ± 5.5	4 (1–22)
seg < 80%	7.1 ± 3.9	7 (0–17)

Discussion

In TE/PPE therapy, the choice of antibiotics is always empiric. In the present study, broad spectrum agents such as carbapenem or broad-spectrum penicillin are used in almost all cases as an initial antibiotics. The choice depends on the patient's risk status or whether the empyema is community-acquired or nosocomial. In selecting the initial antibiotics, the target bacteria are often unknown so patients are treated empirically without culture data. The microbiological diagnosis is said to achieved only in just over 50% [6] and it takes about a week to recognize the microbial etiologies. This means culture data often do not reflect the full disease process and the treatment is not always based on the culture data. Only Gram stain from the pleural effusions and peripheral blood or properties of the pleural effusions are the tips of the target bacteria. Thus, choosing broad spectrum agents are unavoidable in the induction of TE/PPE treatment.

When switching the antibiotics from broad to narrow spectrum agent pre and postoperatively the decision should made empirically because the target often remains invisible. The reasons for switching into narrow agents, in our study, were the pre-operative fever reduction or intraoperative finding showing only serous effusion in all loculated cavities. On the other hand, when converting the antibiotics into broad agent, the decision is often made based on prolonged fever elevation or remaining of the high level of WBC count. These decisions are not based on the result of bacterial culture so it does not correspond to so-called de-escalation or escalation of antibiotics. The ACCP category of the pleural effusion was 3 in 26 cases (79%). Preoperatively, pleural effuison was always obtained from one of the loculated cavities. Disrupting the loculated cavity in VATS-D, even in the case preoperative diagnosed was category 3, often proves the contents of cavities to be homogenous and some cavity contains pus. Therefore, the differential diagnosis of category 3 and 4 or PPE and TE was often unclear. Thus, PPE and TE were examined without distinction in this study.

This study may be deviated from the international standards because metronidazole (MNZ) is not used and procalcitonin is not measured as an inflammatory marker. This is attributed to the special circumstances in Japan, intravenous MNZ and measuring procalcitonin were not commercially available or not covered by health insurance until late 2014 and early 2016. Nowadays, Japanese guideline

JAID/JSC recommends MNZ in combination with ABPC or 4th generation cephalosporin as second choice regimen in both multidrug resistance risk and risk-free cases. For the purpose of suppressing the use of carbapenem to avoid antimicrobial resistance, MNZ may be chosen much in the future. Serum procalcitonin level guided antibiotics use is reported to reduce antibiotics use [6]. Serum level of procalcitonin rise or fall rapidly in bacterial infection with high sensitivity and specificity. It may be a useful biomarker for diseases such as TE/PPE that require empiric discontinuation or change of antibiotics.

VATS-D is an evidential treatment for TE/PPE. It is said to shorten the chest tube duration and hospital stay [4], reduce hospital death or one year mortality compared with simple drainage or intrapleural fibrinolytic therapy [6, 8]. The reported success rate in VATS-D is about 90% [3, 6, 8]. Although description about the duration of antibiotics use are few. In our study duration of antibiotics use was 2 weeks. Though the duration of antibiotics was shorter than the description in guidelines, the success rate in our study was 88% and it was similar to previous reports. On the other hand, it took two weeks from the onset to the operation. Urgent VATS-D is required to shorten the total hospital stay and the duration of antibiotics use.

There is no evidential consensus on the optimal duration of antibiotics therapy after surgical intervention in TE/PPE. The Sanford Guide states 4–6 weeks [1]. In BTS guideline, it is stated about 3 weeks may be optimal [2]. These descriptions include both surgical and non-surgical cases. There seems to be no consensus on when to quit antibiotics therapy, especially after surgery. In present study, the fever exceeding 37.5ºC remained 3 days in median. WBC count and percentage of segmented neutrophil took from 4 to 7 days to return to the normal base value. Discontinuation of antibiotics was decided based on patient's physical or laboratory data. The post-operative duration of antibiotics use in this study was 7 days in mean and median value. Pre-operatively antibiotics were used about 5 days. Antibiotics treatment in their primary care doctors was not reflected in the data we used. However, since the time from the onset to surgery was about 2 weeks, the total pre-operative antibiotics is expected to be up to 2 weeks at the longest. As a result, total antibiotics duration including post and preoperation can be estimated 3 weeks in this study and post-operative antibiotics duration following VATS-D must be required about 5 days.

Conclusions

Parameters considered in the study suggested the routine antibiotics duration following VATS-D for TE/PPE is about 5 days. Empiric use of broad-spectrum antibiotics is unavoidable in many cases. Urgent VATS-D and close observation of the patient's physical or laboratory data must reduce the long-term administration of the broad-spectrum antibiotics.

Abbreviations

TE
thoracic empyema

PPE
parapneumonic effusion
BTS
British Thoracic Society
JAID/JSC
Japanese Association for infectious Disease/Japanese Society of Chemotherapy
VATS-D
Video-assisted thoracoscopic surgery debridement
ACCP
American College of Chest Physicians:WBC:white blood cell count
CRP
C-reactive protein level
CLDM
Clindamycin
TAZ/PIPC
Tazobactam/piperacillin
LVFX Levofloxacin
MNZ
Metronidazole.

Declarations

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Authors' contributions

SY, KI and YS were responsible for the conception and designs of the study. SY, HS and MM performed surgery. MA, MS, TY and SY performed perioperative management on the patients. YS, YM, NS and YS revised the manuscript. All authors read and approved the final manuscript.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The research was in compliance with the Declaration of Helsinki. This study was approved by the Ethical Commitee of National Hospital Organization Ehime Medical Center and the written informed consent was waived because our study was retrospective design.

Consent for publication

Not applicable

Competing interests

The authors declare no competing interests.

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