Intrathoracic vacuum therapy in patients with thoracic empyema

by

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Glossary of abbreviations

ANOVA: analyzed using analysis of variance

ATS: American Thoracic Society

BPF: bronchopleural fistula

CT-guided: computer tomography-guided

EMM: estimated marginal means

ESBL: extended-spectrum beta-lactamases

HIV: human Immunodeficiency Virus

LOS: length of stay in hospital

Mini-VAC: minimally invasive vacuum-assisted closure

Mini-VAC-Instill: Minimally invasive vacuum-assisted closure with instillation

MRSA: methicillin-resistant Staphylococcus aureus

NPWT: Negative-pressure wound therapy

NSCLC: Non-small-cell lung cancer

OWT: Open window thoracostomy

OWT-VAC: Open window thoracostomy with Vacuum-assisted closure

VAC: Vacuum-assisted closure

VRSA: Vancomycin-Resistant Staphylococcus aureus

1. Introduction

Nowadays mainstream thoracic surgery has its main focus on lung cancer, while other topics, like procedures for inflammatory conditions are out of central scope of active research. As no new antibiotics have been developed since the 1980s and the patient's pool of potential candidates for pleural empyema is expanding, the question of optimising and further developing of the present protocols and techniques requires a closer look.

The number of therapy-resistant thoracic empyema cases (MRSA, VRSA, ESBL etc…) due to antibiotic abuse is on a sharp increase with a dark promise of the antibiotic apocalypse [1-2]. Extended surgeries and combined anticancer treatment modalities (neoadjuvant and adjuvant therapy) within and beyond the scope of thoracic surgery are contributing to the potential pool of postoperative empyemas [3]. The lung cancer procedures are performed in an ageing population: another cofactor

for inflammatory complications, due to comorbidities [4]. In addition, pleural sepsis in immunocompromised patients (transplantation, HIV, etc.) has become a frequent phenomenon [5]. Nevertheless, migration into Europe is leading to renaissance of pulmonary tuberculosis, non-tuberculous mycobacteriosis and other complex inflammations, formerly thought to nearly extinct in the Old Continent [6]. Furthermore, classic methods of wound therapy in debilitated patient are relatively expensive, so that one cm^2 wound treatment costs more than thousand U.S. dollars [7]. Another aspect is the price of surgery, which can be as high as 150 USD/operational minute in theater.

Different types of pleural empyemas (chronic and recurrent empyema, sepsis, high risk patients with multiple co-morbidities or immunosuppression) are commanding a need to optimise existing treatment modalities and to look for new approaches to treat that complex phenomenon. Contemporaneously, the introduction of vacuum-assisted closure therapy

in the general surgery provided new and more importantly faster and safer treatment options for a range of sources of infection [8-9].

Therefore a project was initiated with a focus on the pleural empyema and ways of development of the established modern methods and application of VAC in the chest were explored. Five years of active research, development and clinical testing on pleural empyema is summarised on the following pages.

2. Defined aims of the Thesis

2.1. Are there alternative modalities to standard Open Window Thoracostomy with equivalent success rates but less inconvenience and/or shorter treatment time?

2.2. Chest VAC is an in hospital method at the time being. What are the possibilities of continuation of the vacuum therapy in an outpatient setting?

2.3. In case of postresectional thoracic empyema what is the efficacy/applicability of intrapleural VAC when expandable lung as biological prosthesis is missing or diminished in volume/extent?

2.4. How to reduce interventional agressivity in thoracic empyema without compromising efficacy of VAC method?

2.5. What is the place of minimally invasive intrapleural VAC and how to develop further the method in complex situations caused by highly agressive bacteria and/or reduced immunity patients?

2.6. Which technique (OWT-VAC vs. Mini-VAC vs. Mini-VAC-Instill) is superior in the management of primary and postoperativ empyema in debilitated patients?

2.7. What are the limits of VAC therapy in the context of present paradigm of thoracic empyema and related intraparenchymal scenarios?

2.8. Is it possible to extent intrapleural VAC therapy applications to combined intraparenchymal /intrapleural - lung abscess cum pleural empyema scenarios - pathologies?

2.9. What are the indications summarized of intrathoracic VAC therapy up to day?

3. Focused Topics

Three main modalities i.e. OWT-VAC, MINI-VAC and MINI-VAC-Instill were investigated separately in order to evaluate the the effectiveness of intrathoracic negative pressure therapy for empyema thoracis and to compare the short-term and long-term outcomes of three different intrapleural vacuum-assisted closure techniques.

Internationally pioneering studies and their observations cover the topic and multi-peer reviewed reported results are forming the pillars of this clinically focused project.

3.1. OWT-VAC [10]

Objective: For patients with postoperative pleural empyema, OWT is often necessary to prevent sepsis. VAC is a well-known therapeutic option in wound treatment. The efficacy and safety of intrathoracal VAC therapy, especially in patients with pleural empyema with bronchial stump insufficiency or remain lung, has not yet been investigated. *Methods:* Between October 2009 and July 2010, eight consecutive patients (mean age of 66.1 years) with multimorbidity received an OWT with VAC for the treatment of postoperative or recurrent pleural empyema. Two of them had a bronchial stump insufficiency. *Results:* VAC therapy ensured local control of the empyema and control of sepsis. The continuous suction up to 125 mm Hg

cleaned the wound and thoracic cavity and supported the rapid healing. Additionally, installation of a stable vacuum was possible in the two patients with BPF. The smaller bronchus stump fistula closed spontaneously due to the VAC therapy, but the larger remained open. The direct contact of the VAC sponge did not create any air leak or bleeding from the lung or the mediastinal structures. The VAC therapy allowed a better re-expansion of remaining lung. One patient died in the late postoperative period (day 47 p.o.) of multiorgan failure. In three cases, VAC therapy was continued in an outpatient service, and in four patients, the OWT was treated with conventional wound care. After a mean time of three months, the chest wall was closed in five of seven cases. However, two patients rejected the closure of the OWT. After a follow-up at 7.7 months, neither recurrent pleural empyema nor BPF was observed. *Conclusions:* Patients with complicated empyema were successfully treated with OWT and VAC therapy, so the use of this procedure should be considered

early. The most important advantages of the OWT with VAC were fast-tract treatment of sepsis and local control of the pleural cavity. Suction therapy could also improve pulmonary function (re-expansion). The presence of bronchial stump fistulas or residual lung tissue is not a contraindication for vacuum-assisted closure. Furthermore, the length of hospitalization seems to be shortened, based on comparasion with historical data and common experience. Immediate OWT and VAC-therapy installation is advantageous. Outpatient treatment with VAC-therapy is feasible.

3.2. Mini-VAC [11]

Objective: Until 2011 more and more reports have demonstrated the advantages of VAC therapy in patients with Stage II and III empyema thoracis. However the initiation of this approach and the procedure used to change the VAC sponge require an OWT, with resection of the ribs and a secondary surgical procedure for closure. Having obtained

experience and positive tests the feasibility of the minimally invasive insertion of the VAC system without OWT were proven. A consecutive case series project of pleural empyema managed by Mini-VAC therapy without classical OWT was performed. *Methods:* Six consecutive patients with multimorbidity (Karnofsky index ≤50%) treated for a primary or secondary pleural empyema between January 2011 and February 2012. *Results:* Local control of the infection and control of sepsis were satisfactory in all 6 of the patients treated by Mini-VAC therapy. The suction used did not create any air leaks or bleeding from the lung or mediastinal structures. Mini-VAC therapy allowed a reduction of the empyema cavity and improved the re-expansion of the residual lung. Mini-VAC therapy resulted in a rapid eradication of the empyema. The chest wall was closed in all patients during the first hospital stay. All patients left the hospital in good health (Karnofsky index >70%) and with a non-infected pleural cavity at a mean of 22 ± 11 days after Mini-VAC installation. Pleural empyema was not

detected in any of the 6 patients at the 3-month follow-up appointment. *Conclusions*: The Mini-VAC procedure with the abdication of an OWT offers a rapid treatment for complex pleural empyema with minimal surgical effort and the opportunity for a primary closure of the empyema cavity.

3.3. Mini-VAC-Instill [12]

Objective: Open questions for the Mini-VAC treatment were in 2014 whether this new technique is applicable in patients with bronchopleural fistula, and whether simultaneous antibiotic/antiseptic flushing during VAC therapy is possible (VAC Instill). As the feasibility study of Mini-VAC-Instill [66] showed promising results, a prospective study was initiated. *Methods:* From December 2012 to November 2014, 15 critically ill patients with empyema thoracis (primary and secondary) were scheduled for Mini-VAC-Instill therapy. The data had been collected prospectively. Inclusion criteria were as follows: poor general condition (Karnofsky

index ≤50%) and multimorbidity (≥3 organ diseases) or immunosuppression. The patients received treatment without classical thoracic fenestration by using intrapleural vacuum-assisted/instillation therapy dressing for severe (ATS Stage IIb–III) pleural empyema. *Results:* Fifteen patients (13 males, median age: 71 years) underwent intrathoracic Mini-VAC-Instill dressings for the management of pleural empyema without bronchopleural fistula. The median length of vacuum therapy was 9 days (5–25 days) and the median number of VAC changes per patient was 1 (1–5). In-hospital mortality was 6.7% (n = 1) and was not related to Mini-VAC-Instill therapy or intrathoracic infection. Control of intrathoracic infection and closure of the chest cavity was achieved in 85.7% of surviving patients (12 of 14). After the follow-up at an average of 13.2 months (range, 3–25 months), we observed recurrence once, 21 days after discharge. Two patients died in the late postoperative period (Day 43 and Day 100 after discharge) of fulminant urosepsis and

carcinoma-related multiorgan failure, respectively. Analysis of the follow-up interviews in the outpatient clinic showed a good quality of life and a subjectively good long-term aesthetic result. *Conclusions:* Mini-VAC-Instill therapy allows automatic local instillation of antiseptic fluids in the infected cavity, following continuous drainage and suction for the purpose of cleaning and healing empyema. For debilitated empyema patients with poor general condition and sepsis, standard videothoracoscopic or open surgical methods are often too invasive. Mini-VAC-Instill procedure in these high-risk patients is less demanding, therefore recommendable. This technique is safe and highly compatible with high-risk patients. Contraindications of the therapy are coagulopathy, permanent pain and allergic reaction to the materials. Accumulated evidence in this issue topic, although limited, suggests that the Mini-VAC can potentially alleviate morbidity and decrease the length of the hospital stay in selected patients with empyema. These

results have yet to be proven by larger studies and clinical trials.

3.4. Lung Abscess and VAC [13]

Background: Despite significant advances in the treatment of thoracic infections, complex lung abscess remains a problem in modern thoracic surgery. We describe the novel application of vacuum-assisted closure for the treatment of a lung abscess. The technical details and preliminary results are reported. *Methods:* After the initial failed conservative treatment of an abscess, minimally invasive surgical intervention was performed with vacuum-assisted closure. The vacuum sponges were inserted in the abscess cavity at the most proximal point to the pleural surface. The intercostal space of the chest wall above the entering place was secured by a soft tissue retractor. The level of suction was initially set to 100 mm Hg, with a maximum suction of 125 mm Hg. The sponge was changed once on the 3rd postoperative day.

Results: The abscess cavity was rapidly cleaned and decreased in size. The mini-thoracotomy could be closed on the 9th postoperative day. Closure of the cavity was simple, without any short- or long-term treatment failure. This technique reduced the trauma associated with the procedure. The patient was discharged on the 11th postoperative day. *Conclusions:* Vacuum-assisted closure systems should be considered for widespread use as an alternative option for the treatment of complicated pulmonary abscess in elderly, debilitated, immunocompromised patients after failed conservative treatment.

4. Original Observations

Internationally pioneering observations in the topic and multi-peer reviewed results are forming the pillars of this clinically focused project. The data and their conclusions are presently transforming the state of art treatment protocols of Thoracic Empyema.

4.1. The results presented and their documented international acceptance prove, that the “a priori” intrathoracic vacuum therapy is a safe and simple alternative to OWT alone in the management of medical unstable patients with pleural empyema.
The most important advantages of the OWT with VAC were fast detoxication of sepsis and local control of the pleural cavity. Furthermore, the length of hospitalization was shorter in patients with immediate OWT and VAC-therapy installation.

4.2. OWT-VAC therapy on thoracic empyema was proven as a safe and efficient method as outpatient treatment, reducing costs and hospital load alike. Nevertheless, the Mini-VAC-(Instill) dressings should be routinely changed every 3–4 days, in the OT, to allow precise and continued monitoring of infection and to keep the wound for rapid secondary closure.

4.3. Intrapleural VAC therapy was proven to have a beneficial effect on the re-expansion of the

remaining lung tissue following previous resection. No patient had a local complication due to local suction.

4.4. Initiation of a priori intrathoracic VAC therapy of the empyema without classical OWT was introduced and further developed by Mini-VAC-Instill technique. Using this method OWT was omitted, enabling a safe and short treatment with subsequent early chest wall closure.

4.5. An upgrade of Mini-VAC was developed with added instillation of antiseptics in invasive aggressive empyema thoracis – i.e. high agressivity bacteria and/or reduced immunity patients. This technique is safe and highly compatible with high-risk patients.

4.6. Comparing the methods applied and analysed, OWT-VAC has equivalent efficacy to Mini-VAC-(Instill) at managing both primary and secondary (postoperative) thoracic empyema. Mini-VAC-Instill

vs. OWT-VAC/Mini-VAC provide the fastest empyema clearance and healing.

4.7. It was proven by clinical series and by a clinical case report, that against the received wisdom, presence of lung tissue, bronchopleural fistula, smaller bronchial stump insufficiency, local malignancy and the lung abscess cum pleural empyema scenario is amenable for intrathoracic VAC application.

4.8. Standard pleural VAC therapy offers rapid treatment for pleural empyema combined with intraparenchymal abscess formation. The method is superior to the historically established Monaldi drainage and its derivates.

4.9. The existing internationally accepted flow-chart was revised incorporating all the present modalities in thoracic empyema treatment including VAC therapy.