GETTING BETTER

nurse practitioner's research for quality improvement in cardiac surgery

RICHARD
VAN VALEN

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COLOFON

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01

GENERAL INTRODUCTION

GENERAL INTRODUCTION

The title of this document is *Getting better: nurse practitioner research into quality improvement in cardiac surgery*. The main title, *Getting better*, refers to the anxiety, hope and expectations of every patient undergoing cardiac surgery.(1) The title also refers to the efforts of all healthcare workers to constantly improve outcomes. Outcomes for individual patients, but also for patient groups and the healthcare system that treats them. Cardiothoracic surgeons and all others involved in the process of cardiothoracic surgery strive to minimise the risk of mortality and morbidity during and after cardiac surgery.(2) Reducing the already low rates of complications and mortality even further has a high priority, giving the patient an optimal chance of getting better.

The research in this thesis was primarily executed by a nurse practitioner. Nurse practitioners (NP) are nurses who have been trained at a Master of Science (MSc) level. They bridge the gap between the nursing and medical professions.(3) Within the Department of Cardiothoracic Surgery at Erasmus MC, Rotterdam, the Netherlands, NPs have been a part of multidisciplinary teams since 2001. Ever since, NPs have been working towards value-added care as an integrated part of the team.(4) For instance, NPs have suggested research hypotheses and have taken part in research. Previous research into the role of NPs has shown that they have an added role within multidisciplinary teams: not only do they help patients get better, they do the same for organisations.[5, 6] The specific NP perspective on patient care, combined with years of experience, has created a broad array of research questions that are clinically relevant and add to the body of knowledge in both nursing and medical science.

AIMS OF THIS THESIS

This thesis describes the efforts to reduce complications during and after cardiac surgery and to enhance the quality of patient care during the in-hospital stay after surgery. Several important topics for daily patient care will be addressed. In light of this goal, the scope and aims of the research described in this thesis are:

To improve patient outcomes after cardiac surgery by researching the following early peri-operative and long-term postoperative issues.

1) The effects of a protocol on cessation of anticoagulants and platelet-inhibiting medication on perioperative blood loss.

2) The effect of a novel approach to preventing postoperative wound infections: applying negative topical pressure on a closed wound.

3) Improving pain management after cardiac surgery with a nurse-driven pain protocol.

4) Improving knowledge about the management of rare complications after cardiac surgery by investigating and describing the diagnosis and management of atrio-esophageal fistula after the totally thoracoscopic maze procedure and of prosthetic valve endocarditis with *Propionibacterium acnes* (*P. acnes*).

To achieve these aims, several studies were done that will be introduced in this chapter. The thesis ends with a discussion about the various aims in relation to the findings of our studies.

OUTLINE OF THE THESIS

Blood loss due to anticoagulant usage

Depending on which type of heart disease patients have, they may need anticoagulants or platelet inhibitors. The need for these medications can also be influenced by co-morbidities such as pulmonary embolisms. Anticoagulants affect the formation of blood clots. As such, their administration is stopped before surgery to reduce blood loss during and after surgery and to reduce the need for a surgical re-exploration in case of excessive bleeding. However, stopping these medications too early can lead to thromboembolic complications.(5) National and international guidelines are available on timing the cessation of these medications correctly and determining when medication should not be stopped.(6) We conducted a study to determine whether using these guidelines as part of a protocol indeed leads to less blood loss, fewer surgical re-explorations and lower mortality after cardiac surgery (Chapter 2). We also investigated the effect of protocol non-compliance on postoperative blood loss and on costs, by comparing usage of blood products in groups of patients with and without protocol non-compliance.

Surgical site infections

Surgical site infections (SSIs) are serious complications after cardiothoracic surgery, contributing to postoperative morbidity, mortality and healthcare costs.(7) Studies have reported that up to 15% of patients develop a wound infection after cardiac surgery.(8, 9) Host factors contributing to the risk of SSIs after cardiothoracic surgery have been well described in the literature and include obesity, renal insufficiency, diabetes mellitus, advanced age, sex, chronic obstructive pulmonary disease, smoking, steroid use and length of hospitalisation before surgery (more than five days).(10, 11) Surgical risk factors include the use of one or two internal mammary artery (IMA) grafts, especially bilaterally, duration of surgery and perfusion time, prolonged mechanical ventilation, use of an intra-aortic balloon pump, postoperative bleeding, reoperation, sternal rewiring, extensive electro-cautery, shaving with razors, and use of bone wax.(11, 12) We propose that further reduction of SSIs can be accomplished by applying the principle of negative-pressure wound therapy (NPWT) on closed incisions (closed-incision negative-pressure wound therapy or ciNPWT). In theory, this would help to hold the incision edges together, reduce lateral tension and oedema, stimulate perfusion, enhance the development of granulation tissue and help reduce the chance of bacterial colonisation.(13-16) Chapter 3 of this thesis presents the theoretical background, which has been published in a book on wound management after

surgery. The next two chapters contain an overview of the literature (Chapter 4) and a consensus document by experts in the field (Chapter 5). Chapter 6 presents a case study in which the concept of ciNPWT is applied in a specific patient subgroup.

Pain after cardiac surgery

Pain after cardiac surgery is often described as severe during the first days post-surgery.(17) The causative agent is the sternotomy that is performed in the vast majority of patients undergoing cardiac surgery. The sternotomy and the consequent enlarging of the surgical field cause pain in the parasternal area, between the shoulder blades, and a general feeling of muscle ache in the days and weeks after surgery.(18-20)

During surgery and in the ICU, pain management can be aggressive and very effective. Patients are monitored continuously, and supportive measurements are used or easily available. However, pain management after the intensive care period can be more cumbersome. Patients are expected to mobilise and will experience discomfort during daily activities and actions such as coughing or laughing. Research into pain management has been primarily aimed at the intensive care unit and less at the nursing ward.(17, 18, 20) Currently, two types of pain management are used on the nursing ward: a patient-controlled analgesia regime, in which patients can auto-administer pain medication using a device with a safety lock-out to prevent overdosing, and a physician-prescribed regime of either subcutaneous analgesia or oral analgesia. (21)

A previous study has shown that the development of chronic pain can be initiated by intense pain in the acute postoperative phase (day one after surgery).(22) To combat this, we developed a novel approach, a nurse-driven protocol. This protocol enables nurses to administer analgesic medication without consulting a physician or nurse practitioner.(21) Our first study investigated the safety of the protocol (Chapter 7). Our second study investigated protocol effectiveness during a 6-year period (Chapter 8). This study revealed that average pain scores remained low, but protocol adherence was a problem. The two studies into postoperative pain revealed a problem associated with postoperative pain: a poor quality of sleep.

Sleep problems are among the issues most frequently mentioned by patients after cardiothoracic surgery. These problems can have an adverse effect on the duration of the hospital stay and on recovery.(23) We performed a study to assess the quality of sleep after cardiothoracic surgery (Chapter 9). The primary objective was to investigate the effect of cardiothoracic surgery on the quality of sleep. The secondary objective was to investigate the effects of sleep medication on the quality of sleep. We also investigated correlations with perioperative factors and related issues such as the type of surgery and medication administered.

Atrio-esophageal fistula

Atrio-esophageal fistula after totally thoracoscopic ablation (TTMAZE) of lone atrial fibrillation (AF) is a rare complication with high mortality and morbidity.(24, 25) AF is a common supraventricular arrhythmia that is characterised by chaotic contraction of the atrium.(26) AF

results in a significant healthcare burden and an increased risk of stroke and heart failure.(27) Patients with AF report a decrease in quality of life, mainly due to reduced exercise capacity and morbidity leading to increased hospitalisation.(28, 29) A specific group of patients present with lone AF, where no underlying structural heart disease is present. The term has primarily been applied to patients ≤60 years of age and identifies a group of individuals at lowest risk of complications associated with AF, including embolisation. However, these patients, too, report a poor quality of life due to the development of symptoms. (30) For subgroups who have therapy-resistant AF, intolerance for medication, or recurrent AF after an endovascular catheter-based intervention, a minimally invasive video-assisted thoracoscopic (VATS) approach has been developed.(31) This approach includes an epicardial ablation on the beating heart. The technique has been proven to be effective in the FAST study, a randomised controlled trial that showed greater efficiency in recovering and maintaining sinus rhythm compared to the catheter intervention group. However, more complications were seen in the surgical group.(32) After the introduction of this technique in our hospital, three patients presented with an atrio-esophageal fistula during a three-year period. This is a fistula that connects the esophagus and the left atrium of the heart and leads to air embolisation. Atrio-esophageal fistula first emerged in the field of electrophysiology as a complication of catheter-based ablations.(33) This condition is correlated with a high mortality rate, approximately 80%. Survivors of this condition often have significant neurologic deficits, which was also observed in these cases. Chapter 10 describes the clinical presentation of patients with atrio-esophageal fistula and the surgical technique for correcting this rare complication. Two letters to the editor were received, following this publication, and our response to these letters is also included in Chapter 10.

Propionibacterium acnes endocarditis

In this study, a specific type of endocarditis was investigated. Endocarditis is an infection of one or more heart valves and has an incidence of 30 to 100 episodes per million patient-years. (34-36) While endocarditis may be infrequent, the risk of an adverse outcome is high. The in-hospital mortality is around 20%, and more than one-third of patients die within the first year after diagnosis.(37-42)

Patients who are especially at risk for developing endocarditis are those who have undergone previous implantation of a prosthetic valve, device or lead. For this reason, prosthetic cardiac valves have been labelled as a predisposing cardiac condition for infectious endocarditis in the key guidelines.(43, 44)

Prosthetic valve endocarditis (PVE) is a complication with an even higher rate of mortality and morbidity than endocarditis in the absence of prosthetic material. In the literature, it is described as a relatively uncommon clinical entity. The reported incidence of PVE is between 0.3 and 1.2 cases per patient-year. It will affect 1% to 6% of patients with a cardiac valve prosthesis.(43, 45-48) The mortality ranges between 21% and 74%. (43, 46, 47, 49-51)

Our study focussed on *Propionibacterium acnes* (*P. acnes*) as the agent responsible for prosthetic valve endocarditis. In cardiac surgery, these bacteria are an uncommon substrate for primary valve, prosthetic valve or conduit infection, with a description of around 70 cases in English cardiac surgery literature to date.(52) Among these papers are several case reports and case series reporting on this bacterium in relation to endocarditis. *P. acnes* seems to have a preference for prosthetic valves. (53)

Chapter 11 describes 13 patients with a proven *P. acnes* prosthetic valve infective endocarditis that were followed for a 13-year period. The goal of the study was to give insight into the presentation, diagnosis, treatment and outcome for patients with this PVE. Questions concerning our work are answered in Chapter 11 in the form of a reply to a letter to the editor.

Chapter 12 elaborates on the difficulty of diagnosis and the therapeutic consequences for patients with *P. acnes* prosthetic valve infective endocarditis. This was done by describing a clinical case of proven *P. acnes* endocarditis.

DISCUSSION

Chapter 13 discusses the most significant findings of these studies and their implications for daily care. In addition to the discussion about the results of this thesis and the consequences for daily practice, the role and place of the nurse practitioner are addressed. Does the NP provide added value? And how can the NP optimise his or her role within the multidisciplinary team that helps patients get better after cardiac surgery?

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02

EFFECTIVENESS OF ADHERENCE TO A PREOPERATIVE ANTI-PLATELET AND ANTICOAGULATION CESSATION PROTOCOL IN CARDIAC SURGERY

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Submitted

ABSTRACT

Background: Reduction of blood loss after cardiac surgery remains challenging. The effectiveness of adherence to a protocol on cessation of anticoagulants and platelet inhibiting medications was investigated together with the influence of protocol violations on blood loss after surgery, use of blood products, the number of surgical re-explorations and 30-day mortality.

Methods: Between 2009 and 2013, data were collected prospectively for all elective procedures in adult patients undergoing cardiac surgery (N = 1637). Two groups were distinguished: group 1: the protocol for cessation or continuation of medication was followed (N = 1287 procedures, 78.6%), group 2: procedures in which protocol was violated (N = 350, 21.4%).

Results: Median blood loss in the complete cohort was 300ml per procedure (Interquartile range (IQR): 175-500ml). In 80 procedures (4.9%) re-exploration due to blood loss was performed. 30-day mortality was 1.6% (N= 27). Protocol violation was associated with increased blood loss (350ml (250-612) versus 275 ml (175-475), p=<0.001). Protocol violation was also associated with increased average use of Fresh Frozen Plasma (226ml vs 139ml, p<0.001), red blood cell transfusion (115 ml vs 87 ml, p=0.08) and thrombocyte transfusions (52 ml vs 37 ml, p=0.008). The risk of re-exploration between the groups did not differ (3.5% versus 5.5%, p = 0.39), nor did mortality risk (1.4% versus 1.7%, p=0.72).

Conclusions: This study illustrates that balancing the benefit of continuing platelet inhibitors or anticoagulants versus cessation before surgery remains challenging. If there is need to continue medication, blood loss will be higher compared with stopped medication according to protocol. This will result in a higher consumption of blood products although the decision to go for re-exploration and 30-day mortality do not seem to be impacted.

INTRODUCTION

Blood loss after cardiac surgery is a burden for patients and institutions and increases health care costs. Excessive blood loss most often results in prolonged intensive care stay and increased use of blood products.(1) Documented side effects of blood transfusions are the transmission of pathogens, immunological response and metabolic disorders.(2) Research into the prevalence, treatment and prevention of (excessive) blood loss has a long history in cardiac surgery. Despite continued research and improvements of protocols and peri-operative care, the number of re-explorations for blood loss remains a concern.(3-5)

Modifiable factors to reduce blood loss can be sorted into process-related, procedure-related and patient-related categories.(6) Currently, guidelines recommend a systematic multimodality and multidisciplinary approach to reduce blood loss and the number of re-explorations that are needed in patients undergoing cardiac surgery.(7) The objective of this study is to explore the effectiveness of implementing a protocol for the management of anticoagulants prior to cardiac surgery. Specifically, the association between adherence to a preoperative anticoagulation/ antiplatelet therapy cessation protocol and the following outcomes was studied: (1) blood loss in the first 12 hours after elective cardiac surgery, (2) the amount of blood products used (red blood cells (RBC), Fresh Frozen Plasma (FFP), and thrombocytes), (3) number of re-explorations for bleeding and (4) mortality.

METHODS

Initial protocol

An initial protocol aimed to reduce postoperative blood loss after cardiac surgery was introduced in clinical practice in January 2008 and was based on literature and guidelines at that time. It contained only those measures that were supported by the multidisciplinary team.[8-10] This protocol was presented to all medical professionals –nurses, perfusionists, anaesthetists, intensivists, residents and surgeons – in our centre, who were responsible for cardiac surgery patients. In addition, referring centres were notified of changes in the preoperative workup. The complete protocol is presented in *Appendix 1*.

The current study

This study was conducted in a university teaching hospital in the Netherlands and was approved by the institutional review board (MEC 2008-162). The need for informed consent was waived as the protocol we used was the standard of care for our patients.

The main goal of this study was to investigate one particular aspect of the implemented protocol: *effectiveness of protocol implementation for the management of anticoagulant therapy prior to cardiac surgery (preoperative section, Appendix 1)*. The ward nurse confirmed preoperatively whether the anticoagulant medication was stopped on time by asking the patient.

Study cohort

Between 2009 and 2013, data were collected prospectively for all elective adult cardiac surgical procedures, including procedural information, process characteristics and protocol adherence. During this period, the intention was to treat all included patients according to the protocol. Data collection started at the moment that a patient was accepted for surgery and continued up to 30 days after surgery. Emergency procedures, heart transplantation or implantation of cardiac support devices (e.g. left ventricular assist device) were excluded from the study. In addition, if a patient required a second cardiac surgical procedure during the admission (except a re-exploration for bleeding), the second procedure was excluded from the study. For each procedure, data were gathered about the amount of blood loss, need for reintervention due to blood loss, use of blood products, mortality and preoperative trombo-embolic events.

The following two study groups were defined:

- **Protocol adherence** (= group 1) consisting of the following subgroups:
  - *Group 1a*: no use of anticoagulation/antiplatelet medication. *This group contained 447 procedures.*
  - *Group 1b*: anticoagulation/antiplatelet medication was stopped timely prior to surgery. *This group contained 745 procedures.*
  - *Group 1c*: anticoagulation/antiplatelet therapy was continued until the surgical procedure (according to protocol). *This group contained 76 procedures.*
  - *Group 1d*: anticoagulation/antiplatelet therapy was stopped partly (e.g. coumarins were stopped, but acetylsalicylic acid (ASA) was used until the day of the surgery) according to the protocol. *This group contained 19 procedures.*

- **Protocol violation** (= group 2): procedures where the protocol was violated with regard to timely cessation of anticoagulation/antiplatelet medication prior to surgery. *This group contained 350 procedures.*

Protocol adherence and use of blood products

The usage of different blood products was compared between group 1 and group 2. Data was gathered on the usage of Fresh Frozen Plasma (FFP), Trombocytes and Red Blood Cells (RBC). Per study group the percentage of procedures where blood products were used was also investigated. The cost for extra use of blood products was calculated by taking the mean usage of blood products per procedure (total use of blood products divided by the number of procedures in the particular group). The mean difference between the groups was subsequently used for calculating the costs due to extra use of blood products

Subgroup analyses and risk factor selection

Outcomes were measured for all procedures and subgroup analysis was performed for the following types of surgery: coronary artery bypass grafting (CABG), valve surgery, concomitant CABG and valve surgery, and other types of cardiac surgery.

The variables that were considered as potential risk factors for the outcomes are shown in Appendix 2. These were the logistic EuroSCORE 1® variables and variables thought to be of clinical importance. In addition to these variables, the individual surgeon was also examined as independent variable.

Statistical methods

Unpaired T-tests were used for continuous data (range, median and standard deviation). Non-normally distributed data (Kolmogorov-Smirnov test) were compared using the Mann-Whitney U-test. Categorical data were presented as frequencies and compared using the Chi-Square test or the Fisher Exact test where appropriate. All tests were 2-sided, with an alpha level of 0.05. In addition to doing comparative statistics, we identified independent predictors for all end points. Multicollinearity of the considered potential risk factors was checked: there were no factors with significant collinearity (variance inflation factor <3). Linear regression analysis was used to identify predictors for continuous endpoints (blood loss and used blood products). Logistic regression analysis was used to identify predictors for binary endpoints (re-explorations and thirty-day mortality). This was done by performing univariate analyses for all potential predictors and entering them into multivariate analyses if $p<0.10$. All analyses were performed with SPSS statistical software, version 24.0, release 2016 (IBM, Armonk, NY).

RESULTS

During the study period, 1617 patients underwent 1637 unique surgical procedures. Fourteen patients (0.9%) underwent 3 surgical procedures during the study period and 6 (0.4%) patients underwent 2 surgical procedures. Of the 1637 surgical procedures, in 1287 (78.6%) there was adherence to protocol (group 1) and in 350 (21.4%) the protocol was violated (group 2). The characteristics of both groups are presented in Table 1. The group of protocol violations presented significantly more often with a history of previous cardiac surgery or unstable angina and underwent more often urgent surgery.

Use of anticoagulation/antiplatelet medication

In 1190 of the 1637 procedures (72.7%), either platelet-inhibiting medication or coumarins (= groups 1b + 1c + 1d + 2) were used. Detailed information on the type of anticoagulation/antiplatelet medication for both group 1 and 2 is shown in Table 1. Of these 1190 procedures with use of anticoagulation/antiplatelet therapy, in 840 (70.5%) procedures the protocol was followed (group 1). Within this group of 840 procedures, in 745 procedures (88.7%) anticoagulation/antiplatelet medication was stopped timely before surgery (group 1b) and in 95 procedures (11.3%) anticoagulation/antiplatelet medication was continued according to the protocol (group 1c and group 1d). Furthermore, in 350 (29.5%) procedures the protocol was violated with regard to anticoagulation/antiplatelet medication (group 2).

TABLE 1. Baseline comparison of the study groups

	Group 1: Protocol adherence (N =1287)	Group 2: Protocol violation (N = 350)	P-value
Female sex	425 (33%)	69 (19.7%)	<0.001
Urgent surgery	17 (1.3%)	23 (6.6%)	<0.001
COPD	159 (12.4%)	41 (11.8%)	0.8
PVD	117 (9.1%)	65 (18.7%)	<0.001
Previous cardiac surgery	144 (11.3%)	7 (2.0%)	<0.001
Active endocarditis	23 (1.8%)	3 (0.9%)	0.2
Critical preoperative condition	44 (3.4%)	36 (10.4%)	<0.001
Unstable angina pectoris	36 (3%)	46 (13.3%)	<0.001
Recent myocardial infarction	97 (7.6%)	109 (31.4%)	<0.001
Diabetes mellitus	249 (19.5%)	93 (26.9%)	0.003
CVA history	38 (3%)	19 (5.5%)	0.02
History of endocarditis	14 (1.1%)	0 (0%)	0.05
Age: median (IQR)	65.0 (56-73)	66.0 (60-73)	0.04
Creatinin: median (IQR)	83.0 (72-98)	85.0 (74-99)	0.11
Logistic Euroscore ® : median (IQR)	4.0 (2.1-7.7)	3.3 (1.7-6.9)	0.01
ASA use in group	639	341	<0.001
ASA continued	*94 (14.7%)*	*331 (97.1%)*	*<0.001*
ASA violation	*0 (0%)*	*324 (97.9%)*	*<0.001*
ASA timely stopped	545 (85.3%)	10 (2.9%)	<0.001
Clopidogrel use in group	141	155	<0.001
Clopidogrel continued	*40 (28.4%)*	*111 (71.6%)*	*<0.001*
Clopidogrel violation	*0 (0%)*	*108 (97.3%)*	*<0.001*
Clopidogrel timely stopped	*101 (71.6)*	*44 (28.4%)*	*<0.001*
Coumarin group use in group	220	26	<0.001
Coumarin continued	*0 (0%)*	*5 (19.2%)*	*<0.001*
Coumarin violation	*0 (0%)*	*5 (100%)*	*<0.001*
Coumarin timely stopped	*220 (100%)*	*21 (80.8%)*	*<0.001*
DAPT use in group	162	184	<0.001
DAPT Continued	*0 (0%)*	*85 (46.2%)*	*<0.001*
DAPT violation	*0 (0%)*	*85 (100%)*	*<0.001*
DAPT timely stopped	*162 (100%)*	*99 (53.8%)*	*<0.001*
Use of any anticoagulation/ antiplatelet medication	840 (65.3%)	350 (100%)	<0.001

Abbreviations: ASA: Acetylsalicylic acid COPD: Chronic Obstructive Pulmonary Disease PVD: Peripheral Vascular Disease CVA Cerebro-Vascular Accident CABG: Coronary Artery Bypass Grafting DAPT: Double Antiplatelet Therapy,IQR: Interquartile range (25th and 75th percentile).

Protocol violation was present in all types of surgery, with the highest percentage of violation in CABG procedures (38.1% N=289). Protocol adherence was highest in the group of patients using coumarins (N=241 (97.7%)) (Appendix 2).

Mortality, blood loss and re-explorations

Overall 30-day mortality in the complete group of 1637 procedures was 1.6% (N=27). This was 1.7% (N=22) in group 1 (protocol adherence) and 1.4% (N=5) in group 2 (protocol violation). Data regarding blood loss in the different types of procedures is shown in Table 2.

No significant association was found between the individual surgeon and the amount of blood loss or the risk of re-exploration (Appendix 3).

Protocol adherence, blood loss and use of blood products

Compared to the group of protocol adherence (group 1), there was more blood loss in procedures where protocol was violated (group 2)(median 350ml (IQR 250-612) versus 275ml (IQR 175-475), $p<0.001$). Table 3 shows the differences in use of blood products between group 1 and group 2. In procedures where the protocol was violated, there is a trend for higher use of RBC ($p=0.08$) and, in addition, significantly more use of thrombocytes and FFP ($p=0.008$ and $p<0.0001$, respectively).

Table 3 shows that the average difference in red blood cell transfusion between protocol adherence and protocol violation is 28 ml per procedure. Based on 1000 elective cardiac surgery procedures per year, the potential savings could be 30.000 euros per year. This is based on an average cost of 282 euros per unit of RBC (265ml), as charged by Sanquin, the national blood bank of the Netherlands, in 2016.

Independent predictors for blood loss

Urgent surgery and surgery on the thoracic aorta were associated with increased blood loss. The use of clopidogrel and DAPT was also associated with increased risk of blood loss, even if it was stopped according to protocol prior to surgery (group 1b). A comparable result was observed in group 1c. In group 2 more blood loss was observed in procedures where ASA, clopidogrel and DAPT were continued. Table 4 shows a detailed summery of independent predictors for blood loss.

Trombo-embolic events

During this study, no preoperative trombo-embolic events were registered in our study groups.

TABLE 2. Blood loss per type of cardiac surgery

	Total group	CABG	Valve surgery	CABG and valve surgery	Other
	Mean and median in ml (IQR)	Mean and median in ml (IQR)	Mean and median in ml (IQR)	Mean and median in ml (IQR)	Mean and median in ml (IQR)
Blood loss	414, 300 (175-500)	411, 325 (225-500)	371, 225 (150-425)	590, 425 (275-700)	325, 200 (125-362)
Red blood cell use	93, 0 (0-0)	76, 0 (0-0)	89, 0 (0-0)	181, 0 (0-275)	73, 0 (0-0)
Fresh Frozen Plasma use	157, 0 (0-0)	115, 0 (0-0)	171, 0 (0-0)	295, 0 (0-325)	118, 0 (0-0)
Thrombocyte use	40, 0 (0-0)	35, 0 (0-0)	40, 0 (0-0)	69, 0 (0-0)	27, 0 (0-0)
	N (%)	N (%)	N (%)	N (%)	N (%)
Re-exploration	80 (4.9%)	17 (2.2%)	42 (7.1%)	14 (7%)	7 (7.7%)
30-day mortality	27 (1.6%)	9 (1.2%)	10 (1.7%)	5 (2.5%)	3 (3.3%)

Abbreviations: CABG: Coronary Artery Bypass Grafting Other: congenital surgery, aortic surgery, aortic valve and aortic surgery, IQR: Interquartile range (25th and 75th percentile).

TABLE 3: Impact of protocol violations on blood loss

	Group 1 (protocol adherence)	Group 2 (protocol violation)	P-value
	Mean and median in ml (IQR)	Mean and median in ml (IQR)	
Blood loss	436, 275 (175-475)	485, 350 (250-612)	<0.001
Red blood cell use	87, 0 (0-0)	115, 0 (0-0)	0.08
Fresh Frozen Plasma use	139, 0 (0)	226, 0 (0-325)	<0.001
Thrombocyte use	37, 0 (0-0)	52, 0 (0-0)	0.008
	N (%)	N (%)	
Re-exploration	66 (5.5%)	14 (3.5%)	0.39
30-day mortality	22 (1.7%)	5 (1.4%)	0.72
Percentage of procedures with usage of blood products			
	N (%)	N (%)	
Red blood cell	262 (20.4%)	84 (24%)	0.14
Fresh Frozen Plasma	240 (18.6)	101 (28.9%)	<0.001
Trombocytes	168 (13.1%)	65 (18.6%)	0.009

Abbreviations: IQR: Interquartile Range (25th and 75th percentile).

TABLE 4: The result of continuation of different types of anticoagulant medication on increased blood loss, increased use of RBC, thrombocytes, Fresh Frozen Plasma and increased risk of re-exploration

	Multivariate analysis									
	Blood loss		Use RBC		Use Trombo		Use FFP		Re-exploration	
	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value
ASA use	0.108	<0.001	NS	NS	0.125	<0.001	NS	NS	NS	NS
ASA continued	0.066	0.03	0.056	0.046	NS	NS	0.078	0.004	NS	NS
Clopidogrel continued	0.058	0.03	0.113	<0.001	0.216	<0.001	NS	NS	NS	NS
Clopidogrel violation	NS	NS	NS	NS	NS	NS	0.113	<0.001	NS	NS
Coumarin use	0.108	<0.001	0.071	0.004	NS	NS	0.096	<0.001	NS	NS
Type of surgery	NS	NS	0.125	<0.001	NS	NS	0.104	<0.001	NS	NS
Aortic surgery	0.106	<0.001	NS	NS	NS	NS	0.110	<0.001	2.03	<0.001
Surgery other CABG	NS	NS	NS	NS	0.157	<0.001	NS	NS	0.84	0.02
Urgent surgery	NS	NS	0.093	<0.001	NS	NS	0.056	0.02	1.29	0.03
Critical preoperative condition	NS	NS	NS	NS	0.065	0.01	NS	NS	NS	NS
Age	NS	NS	0.085	0.001	NS	NS	0.070	0.006	NS	NS
Active endocarditis	NS	NS	0.099	<0.001	NS	NS	NS	NS	NS	NS

Abbreviations: ASA: Acetylsalicylic acid, RBC: Red Blood Cell, FFP: Fresh Frozen Plasma, CABG: Coronary Artery Bypass Grafting.

DISCUSSION

This study shows that adherence to the preoperative part of our institutional blood loss reduction protocol is associated with a significant decrease in blood loss. This study also pinpoints that violations of the protocol are predominantly seen in the group of CABG procedures, a group in which preoperative anticoagulation management can be challenging. These patients often require urgent or emergent surgery or have undergone recent implantation of drug-eluting stents which require continuation of platelet inhibitors. Furthermore, this study shows that although blood loss was higher in procedures where the protocol was violated, this did not affect 30-day mortality or the number of re-explorations needed due to blood loss.

It has been well established that stopping anticoagulant/antiplatelet therapy leads to less blood loss during and after surgery.(8-11) For this reason, preoperative cessation of antiplatelet and/or anticoagulation therapy is included in current hospital protocols. Most of the studies concerning this topic focus on mortality and re-explorations.(10, 12-14). The value of the current study is that it focusses on the daily clinical practice of working with such a protocol, in which protocol violations will occur. Cessation of anticoagulants carries the risk of thrombo-embolic complications.(9, 15) During the investigated period, none of these complications were seen. This suggests that applying this protocol is safe and does not lead to a higher rate of thrombo-embolic complications. This knowledge, combined with the increased amount of blood loss and use of blood products in procedures where the protocol was violated, suggests that applying and strictly enforcing the protocol is worthwhile.

Impact of new anticoagulant medication

In the investigated time-frame, the protocol we used prescribed temporarily ceasing the use of clopidogrel as single agent or as part of dual antiplatelet therapy 5 to 7 days before surgery (with an expected and accepted risk of 1% increase in myocardial infarction).(9) Our current practice, which arose after the time-frame of this study, is using new platelet inhibitors (P2Y12 inhibitors) such as ticagrelor. Our new protocol states that while most surgical procedures can be performed safely on DAPT or at least on acetylsalicylic acid (ASA) alone with acceptable rates of bleeding, ceasing P2Y12 inhibitors is not recommended in high-risk cohorts (high-risk anatomy or on-going ischaemia).(7) This more liberal protocol supposedly results in less ischaemia or infarction but is likely to lead to more postoperative blood loss. Hansson *et al* showed that continuation of ticagrelor led to markedly more blood loss and more blood transfusions than continuation of clopidogrel.(3) This makes it reasonable to state that our findings will be even more outspoken if extrapolated to current guidelines on myocardial revascularisation.(7)

The role of the surgeon

Of all precautions and instructions incorporated in the introduced protocol, surgical aspects are almost absent. In general, surgeons are considered to already be doing everything they can to limit blood loss during surgery. It is self-explanatory that it is impossible to form consensus on each possible surgical technique and include it in a blood reduction protocol. To rule out that

the surgeon is an independent predictor of blood loss, we performed multivariate analysis with all the surgeons as a predictor. Results showed that individual surgeons are not a predictor of more blood loss or more re-explorations. The role of the anaesthesiologist and perfusionist were not examined in this study.

Anticoagulant/antiplatelet therapy and blood loss

Although the use of ASA, clopidogrel and DAPT leads to more blood loss, it does not result in an increased number of re-explorations. For DAPT, this was a surprising finding. The use of DAPT has been described to result in increased blood loss, usage of FFP and blood transfusion in other studies.(16) We were not able to confirm any increased blood loss from continued use of DAPT in this study. There is, however, an increased use of blood products as reported in other studies. The finding that more blood loss is not associated with more re-explorations (involved treatment team decision) seems in contradiction and is also not in line with other studies.(13, 14, 17) A possible explanation could be that more blood loss is expected and accepted by both surgeons and intensivists in these groups. The decision to perform a re-exploration is probably postponed in these cases, which is reasonable since coagulation pathways are disrupted by protocol violations. Pharmacological optimisation of coagulation is vital before deciding to perform surgical re-exploration. Point-of-care testing (bedside tests that give an accurate and swift result on, for example, platelet function) provides an important tool in the management of this kind of blood loss and should be an integral part of peri- and postoperative care, especially in those with continued use of platelet inhibitors.(4)

Costs related to protocol violations

In light of increasing healthcare costs, cost-effectiveness is becoming an important aspect of healthcare. Patients undergoing cardiac surgery are at a higher risk of receiving blood products.(18) In the group of protocol violation the amount of blood loss was higher as was the use of blood products. Reducing the amount of blood loss in these patients will not only result in a cost reduction for the hospital but will also reduce the risk of potentially harmful blood transfusions.

Strengths and limitations

The major strength of this study is that it shows how challenging it can be to implement and use a guideline-based protocol in daily clinical practice. Another strength is the relatively large number of procedures included in this study. Furthermore, this study provides an insight into healthcare costs related to excessive blood loss.

However, this study also has several limitations. It is a retrospective study based on procedure data from a single-centre tertiary-care university hospital. Furthermore, no data are available about measures taken in addition to the protocol to reduce blood loss preoperatively. In addition, the reasons for protocol violations are unknown, so they cannot potentially contribute to a more effective protocol.

CONCLUSIONS

Balancing the benefit of continuing platelet inhibitors or anticoagulants versus cessation before surgery remains challenging. Current guidelines advise to continue medication in the high-risk cohorts, such as those with left main lesion or ongoing ischemia. This study shows that if there is need to continue medication, blood loss will be higher compared to the group that stopped medication according to protocol. This will result in a higher consumption of blood products although the decision to go for re-exploration and 30-day mortality do not seem to be impacted.

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APPENDIX 1. Clinical protocol for cessation of anticoagulants and platelet-inhibiting medications

Preoperative section

The surgeon assesses haemoglobin (Hb), haematocrit (Ht) and platelet count when accepting the patient and treats underlying disease.
Prior to admission, the secretary or referring hospital instructs elective patients to discontinue:

- Clopidogrel 4 days prior to surgery;
  - unless a drug-eluting coronary stent was implanted recently (within 6 months);
- Aspirin 3 days prior to surgery;
  - unless a coronary stent was implanted (bare metal and drug eluting);
- Coumarin derivatives 2 days prior to surgery.

During admission, the ward nurse checks if these drugs were discontinued properly. Heparin is started (20,000 IE/24h) for patients who normally use coumarin derivatives if:

- international normalised ratio (INR) < 3.0 and mitral valve replacement in history;
- INR < 2.0 and atrial fibrillation in history;
- INR < 2.5 for all other indications.

Perioperative section

The tranexamic acid dose used during the entire procedure is 50-100 mg/kg.
A baseline thromboelastogram (TEG) is made prior to initiating cardiopulmonary bypass.
Autologous blood is taken if the patient has a good left ventricular function and Hb is above 8.5 mmol/L.
Red cell saving devices are used during each procedure.
A follow up TEG is made after ending cardiopulmonary bypass.
If a hyperdynamic hemodilution approach is used, Ht levels are kept 0.20 L/L or higher.
The patient is re-warmed to at least 35.5 degrees Celcius (rectal or bladder temperature) at the end of the procedure.
Hemofiltration is performed if Ht is below 0.20 L/L and an adequate volume is available.
The patient is weaned from cardiopulmonary bypass only if Hb is above 4.5 mmol/L and Ht is above 0.20 L/L.

Postoperative section

Ringer's lactate can be administered to a maximum of 2 L per 24 hours.
The patient is actively rewarmed further with an air warming blanket.

Transfusion algorithm

Blood loss > 200 mL/h without known TEG or lab results and no clot formation in the drains

- 2,500 IE protamine is administered.

No or moderate blood loss (< 100 mL/h), but with abnormal lab results

- if fibrinogen < 1.5 g/L => 5 mL/kg Fresh Frozen Plasma (FFP);
- if platelet count < 50,000 => 1 unit platelet transfusion;
- if activated partial thromboplastin time (aPTT) > 50s, but < 65s => 2,500 IE protamine;
- if aPTT > 65s => 5,000 IE protamine.

Blood loss > 100 mL/h

- if $R/R_{heparinase}$ in TEG > 50% prolonged => 2,500 IE protamine;
- if $R/R_{heparinase}$ in TEG > 100% prolonged => 5,000 IE protamine;

APPENDIX 1. (continued)

Postoperative section

- if aPTT > 40s, but < 50s => 1,000-2,500 IE protamine;
- if aPTT > 50s => 5000 IE protamine;
- if prothrombin time (PT-INR) > 18s (50% prolonged) or R in TEG> 10 min => 5 mL/kg FFP;
- if PT-INR > 22s (80% prolonged) or R in TEG > 14 min => 10 mL/kg FFP;
- if mean amplitude (MA) in TEG < 45 or platelet count < 100,000 => 1 unit platelet transfusion;
- if MA in TEG < 45 and platelet count > 100,000 => 0.4 mcg/kg desmopressin acetate (DDAVP);
- if platelet count < 100.000 and recent aspirin or clopidogrel => 1 unit platelet transfusion followed by 0.4 mcg/kg DDAVP;
- if fibrinogen < 1.5 g/L => 10 mL/kg FFP;
- if Ht < 0.25 L/L => erythrocyte transfusion until Ht is 0.26-0.28 L/L;
- if LY30 in TEG >7.5% => 2 g tranexamic acid.

Blood loss > 200 mL/h

As with 'blood loss > 100 mL/h' plus:

- use blood products only instead of plasma expanders if filling is required based upon hemodynamics;
- alternating transfusion of 2 platelet units and 1 FFP unit;
- after every second FFP unit (=every 6th unit) => 0.5 g CaCl2 slow IV;

Blood loss > 300 mL/h or persisting blood loss

- if blood loss is more than 200 mL/h for 2 hours or more the surgeon is notified;
- if blood loss is more than 400 mL/h, more than 300 mL/h for 2 hours, or more than 200 mL/h for 3 hours and lab and TEG values are normal and no clots formation in the drains:
- 2 g tranexamic acid;
- treat hypertension if existent;
- the surgeon decides if a re-exploration is indicated

APPENDIX 2. Baseline characteristics and type of anticoagulation medication for the subgroups

	Total group N= 1637	CABG N = 758	Valve surgery N = 589	CABG and valve surgery N = 199	Other N =91
Age: median (IQR)	66 (57-73)	67 (60-74)	63 (51-72)	70 (64-75)	49 (32-65.3)
Female sex	494 (30.2%)	145 (19.1%)	242 (41.1%)	61 (30.7%)	46 (50.5%)
Serum creatinin level: median (IQR)	84 (72-98)	85 (74-98)	81 (70-95)	89 (75-106)	75 (62-88)
Logistic EuroSCORE I: median (IQR)	4.0 (2.1-7.5)	2.4 (1.5-4.9)	4.6 (2.4-8.9)	6.6 (4.0-11.7)	5.5 (2.1-11.7)
Previous CVA	57 (3.5%)	30 (4%)	17 (2.9%)	8 (4.1%)	2 (2.2%)
COPD	200 (12.3%)	91 (12%)	66 (11.3%)	33 (16.7%)	10 (11.1%)
Previous cardiac surgery	151 (9.3%)	124 (16.4%)	101 (17.2%)	8 (4%)	26 (28.9%)
Critical preoperative state	80 (4.9%)	47 (6.2%)	18 (3.1%)	14 (7.1%)	0 (0%)
Active endocarditis	26 (1.6%)	0 (0%)	21 (3.6%)	5 (2.5%)	0 (0%)
Urgent procedure	528 (32.5%)	358 (47.5%)	92 (15.7%)	70 (35.3%)	8 (8.9%)
Surgery thoracic aorta	183 (11.2%)	2 (0.3%)	121 (20.6%)	16 (8.1%)	44 (48.9%)
ASA use	980	662	160	141	17
ASA continued	425 (43.4%)	341 (51.5%)	29 (18.1%)	51 (36.2%)	4 (23.5%)
ASA violation	324 (33.1%)	267 (40.3%)	13 (8.1%)	43 (30.5%)	1 (5.9%)
Clopidogrel use	374	247	19	27	3
Clopidogrel continued	151 (40.4%)	129 (52.2%)	7 (36.8%)	13 (48.1%)	2 (66.7%)
Clopidogrel violation	108 (28.9%)	96 (38.9%)	1 (5.3%)	11 (40.7%)	0 (0%)
DAPT use	346	293	20	31	2
DAPT continued	133 (38.4%)	115 (39.2%)	5 (25%)	11 (35.5%)	2 (100%)
DAPT violation	85 (24.6%)	76 (25.9%)	0 (0%)	9 (29%)	0 (0%)
Coumarin use	246	56	133	41	16
Coumarin continued	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Coumarin violation	10 (4.0%)	8 (14.2%)	2 (1.6%)	0% (0%)	0 (0%)
Any violation	350 (21.4%)	289 (38.1%)	15 (2.5%)	45 (22.6%)	1 (1.1%)

Abbreviations: ASA: Acetylsalicylic acid, CABG: Coronary Artery Bypass Grafting, Other: congenital surgery, aortic surgery, aortic valve and aortic surgery, CVA: Cerebro-Vascular Accident, COPD: Chronic Obstructive Pulmonary disease, DAPT: Double Antiplatelet Therapy, IQR: Interquartile Range (25th and 75th percentile).

APPENDIX 3. Univariate analysis risk factors blood loss in total cohort of patients

	Univariate analysis							
	Blood loss		Use RBC		Use trombocytes		Use FFP	
	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value
Total group N=1637								
Urgent surgery	0.023	0.35	0.101	<0.001	0.006	0.8	0.067	0.01
Age	0.785	0.06	0.079	0.003	0.040	0.1	0.049	0.05
Type of surgery	0.035	0.16	0.083	0.001	0.053	0.03	0.093	<0.001
COPD	-0.036	0.15	0.006	0.8	-0.032	0.2	-0.023	0.4
Neurological dysfunction	-0.018	0.46	0.051	0.04	0.047	0.06	-0.019	0.5
Creatinine	0.033	0.18	0.066	0.01	0.002	0.9	0.058	0.02
Active endocarditis	0.013	0.59	0.1	<0.001	-0.037	0.1	0.026	0.3
Critical preop condition	0.049	0.05	0.081	0.001	0.077	0.002	0.054	0.03
Unstable angina pectoris	-0.018	0.47	0.004	0.9	0.003	0.9	0.004	0.9
Pulmonary hypertension	0.0	0.1	0.003	0.9	-0.024	0.3	0.036	0.1
Emergent surgery	-0.051	0.04	-0.121	<0.001	-0.043	0.08	-0.026	0.3
Non-CABG cardiac surgery	0.011	0.65	0.070	0.01	0.059	0.02	0.092	<0.001
Aortic surgery	0.070	0.01	0.043	0.08	0.036	0.1	0.110	<0.001
LV function	-0.043	0.08		NS		NS		NS
Surgeon	0.006	0.81		NS		NS		NS
EuroSCORE 1®	0.046	0.07		SIGN		SIGN		SIGN
ASA use	0.087	<0.001	0.043	0.08	0.071	0.004	0.01	NS.
Clopidogrel use	0.074	0.003	0.073	0.003	0.083	0.001	0.054	0.03
Coumarin use	0.063	0.01	0.091	<0.001	0.006	NS	0.108	<0.001
DAPT use	0.076	0.002	0.052	0.04	0.080	0.001	0.02	NS
ASA continued	0.109	<0.001	0.070	0.01	0.084	0.001	0.065	0.01
Clopidogrel continued	0.094	<0.001	0.109	<0.001	0.137	<0.001	0.096	<0.001
Coumarin continued	0.0	NS	0.044	0.08	0.0	NS.	0.04	0.09
ASA violated	0.077	0.002	0.026	NS	0.035	NS	0.072	0.003
Clopidogrel violated	0.057	0.02	0.074	0.003	0.096	<0.001	0.111	<0.001
Coumarin violated	0.0	NS	0.044	0.08	0.0	NS	0.04	0.09
DAPT violated	0.039	NS	0.040	NS	0.059	0.02	0.086	0.001

Abbreviations: ASA: Acetylsalicylic acid, DAPT: Dual Antiplatelet Therapy, RBC: Red Blood Cells, FFP: Fresh Frozen Plasma, COPD: Chronic Obstructive Pulmonary Disease, LV function: Left Ventricular function.

03

NEGATIVE PRESSURE WOUND THERAPY AS PREVENTION MEASURE AFTER CARDIAC SURGERY: PRINCIPALS AND TECHNIQUES

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ABSTRACT

Reduction of surgical site infections (SSI) rates after (cardiac) surgery remains an important topic for all involved in the surgical domain. These infections lead to a higher risk for mortality and an increased morbidity in the individual patient. Despite many advances in perioperative care, however, the percentage of SSI has not declined. On a macro level, the costs associated with SSI are enormous, and all possible interventions to reduce SSI should be investigated.

A possible new intervention is negative topical pressure therapy on clean, closed surgical wounds. In this chapter the theory behind this technique is explored, advice on patient selection is given, and treatment duration is discussed.

INTRODUCTION

About 250 million major surgical procedures are performed worldwide each year.[1] The surgical wound, however, can be at risk for complications. These include infection, seroma, hematoma, local skin ischemia, necrosis and dehiscence as well as delayed healing in the short term and poor healing or abnormal scarring in the long term. Surgical site infections (SSI) have been the focus of surveillance programmes and prevention initiatives worldwide, not only to reduce the incidence of wound infection and improve the outcomes for individual patients but also to reduce the associated costs for healthcare systems.

An emerging trend in preventative therapies is to reduce surgical sites complications. Negative pressure wound therapy (NPWT) is one of the interventions that can be used in patients at risk for a wound infection after surgery. In this chapter NPWT as a prevention measure is discussed by summarising the principles, current techniques, most used devices, clinical application, findings from recent studies and cost-effectiveness.

Normal wound healing

To understand the mechanism through which NPWT works on a clean, closed, surgical wound, understanding normal wound healing is important. Briefly summarised, the phases of wound healing consist of haemostasis, inflammation, proliferation and remodelling.[2] For surgical wounds, the basic principles are the same. Haemostasis is characterised by vascular constriction, combined with platelet aggregation and fibrin formation. During the inflammation period, the wound is infiltrated with neutrophils, monocytes (which differentiate into macrophages) and lymphocytes. This is essentially the body's response to injury. During proliferation, new blood vessels are formed, collagen is synthesised, and the extracellular matrix takes shape. The final phase involves remodelling of the structures, both by remodelling of the collagen and maturation of the blood vessels and later regression. These phases can be disrupted by patient factors as well as environmental factors.

Factors affecting wound healing

The factors that impact wound healing can be placed into two categories: local and systemic factors.[3] The local factors that influence wound healing are multifactorial but can be divided into either a perfusion deficit or accumulation of fluids. Perfusion is defined as blood flow in the affected area. Poor blood flow leads to low oxygen tension which can result in ischemia and even necrosis in wounds. The other important negative factor is accumulation of fluid in or near the wound. This can be oedema but also blood or other fluids, which also leads to impaired perfusion of the inflicted area. Fluid in the wound area can also facilitate growth of micro-organisms, leading to infections.

Systemic factors have been well established in research. The more important factors are diabetes, obesity, age, use of specific types of medication and malnutrition.

Diabetes can have a detrimental effect on wound healing.[4] On a molecular level the decreased angiogenic response, collagen accumulation and the quantity of granulation tissue are the most important factors that cause this detrimental effect.

Obesity is a precursor for several important inhibitors in wound healing. The risk of surgery in obese patients is higher, not only for wound infections but also for cardiovascular complications. This applies mostly to patients with morbid obesity (Body Mass Index of 40 kg/m^2 or greater). Three factors contribute to this increased risk. The first is the avascularity of the adipose tissue, which leads to poorer oxygenation and limited infiltration of leucocytes, neutrophils and macrocytes. The second is related to the habitus of these patients, which leads to higher demands on personal hygiene.[5] The third is the effect of lateral forces on wound edges. Large amounts of tissue can increase lateral tension, leading to decreased perfusion and thus decreased oxygen saturation of the wound and contributing to wound dehiscence and infections. Obesity and wound healing risk is discussed in more detail later on in this chapter.

Age and the associated frailty that is often seen with increasing age can contribute to higher rates of wound complications. Wound healing is negatively affected by age. The stages of normal wound healing, as described earlier, are less efficient or slower. The inflammatory response is delayed and can also be decreased compared to younger adults. Remodelling is still present but is less effective. The important phase of collagen formation is qualitatively different (and has a poorer quality) and also leads to poorer wound healing. Diseases that affect wound healing are more prevalent in the elderly and have a greater adverse effect on healing than in young adults. Elderly patients have co-morbidities and often use medication that can impair wound healing. [6]

Medication use and nicotine usage

Medications that are strongly associated with an increased risk for surgical site infections (SSI) usually have a negative effect on the immune. For example, bleomycin (chemotherapeutic agent) decreases blood vessel formation in a wound.[7] In daily practice patients using steroids require more attention. Steroid medication has several negative effects, for example on the tensile strength of tissues and the resulting impaired wound contraction. Most importantly, steroid medication leads to delayed healing due to its anti-inflammatory and immunosuppressant effects.[5]

For smokers, the dangers of nicotine have been well established. In cardiac surgery smokers have been shown to have higher rates of SSI.[8] The mechanism is based on the vasoconstrictive quality of nicotine. Leading to poorer circulation (and microcirculation) and healing.

Malnutrition

Malnutrition is primarily seen in patient groups who are already at risk for impaired wound healing: elderly patients, patients with chronic health problems and patients with a very limited (one-sided) diet (this can also apply to morbidly obese patients).

The most important factor is the lack of protein in the diet of these patients. Decreased protein intake leads to impaired wound healing due to decreased production of collagen, fibroblast proliferation and poorer angiogenesis.[9]

Radiation therapy

Radiation therapy can impair wound healing, even many decades after treatment. Immediately after radiotherapy, the inflammatory and proliferative phases are disrupted the most. More importantly, especially after a prolonged period, fibrosis and poor tissue quality can cause wound problems. For this reason, radiation of the surgical area is a major risk factor for SSI.[10]

Wound healing and cardiac surgery

SSIs remain a problem after cardiac surgery. Research shows a rate of 1% to 3% of deep sternal wound infections (DSWI) and a rate of 2% to 6% for superficial wound infections.[11] These complications can be very serious and they contribute significantly to postoperative morbidity, mortality, and healthcare costs.[12] The wounds from cardiac surgery occur at three locations: the sternotomy, the lateral thoracotomy and donor sites for graft material (e.g. the venectomy wound after harvesting of the vena saphena magna). Each location offers its own challenges in wound healing.

Host factors contributing to the risk of SSI after cardiac surgery have been well described in the literature and include previously discussed topics such as obesity, diabetes mellitus, advanced age, sex, smoking and steroid use, along with length of hospitalisation before surgery (more than 5 days).[13, 14] Surgical risk factors include the use of 1 or 2 internal mammary artery (IMA) grafts (especially bilaterally), duration of surgery and perfusion time, prolonged mechanical ventilation, use of an intra-aortic balloon pump, postoperative bleeding, re-operation, sternal rewiring, extensive electro-cautery, shaving with razors, and use of bone wax.[14, 15]

The median sternotomy wound is traditionally closed with surgical steel wires. Thereafter the suprasternal tissues are closed. The skin can be closed by either intracutaneous sutures or skin staples. After this a wound dressing is applied. Depending on the surgeon's preference, the dressing is removed after 24 hours or 48 hours. Note that the wounds discussed in this chapter are "clean wounds". The definition for a clean wound is a non-infective operative wound in which no inflammation is encountered, and no colonised cavity is entered during the surgical procedure. In addition, these cases are elective or semi-elective, primarily closed, and drained with a closed drainage system (if required).

History of preventive measures

In recent decades enormous progress has been made in the absolute reduction of SSI after cardiac surgery. However, high-risk patients still have an SSI rate of up to 15% after cardiac surgery.[16] Further reduction of these rates has been difficult, primarily due to the increasing number of

co-morbidities in cardiothoracic surgery patients and secondly due to the improvement in peri- and postoperative care, which enables sicker patients to survive but with more postoperative complications such as SSI.

Research into prevention of complications ranges from the best way to harvest internal mammary arteries (pedicled of skeletonised) to the usage and duration of antibiotic prophylaxis. Previous studies have proposed many interventions to lower the risk of wound infection after surgery. However, the evidence is not always sufficient. Another important aspect is the continuing need to identify patients who are at risk for wound infections.

Negative pressure wound therapy (NPWT) is one of the interventions that can be used in patients at risk for a wound infection after surgery. NPWT is a wound care system consisting of a foam or dressing that is covered with an airtight adhesive film. Tubing connects the foam to an electronic pump that regulates and delivers an adjustable negative pressure.[17] Initially, the treatment was used for acute and chronic open wounds.

Research into the mechanism of this therapy has shown that NPWT helps to enhance the development of granulation tissue, stimulate perfusion, reduce colonisation by bacteria, reduce lateral tension and oedema and protect the wound from external sources of infection.[18]

In the preventative domain, it has been used to improve outcomes after skin and biomatrix grafts, where it stabilises the graft to prevent shearing and removal.[19] It also aids in removal of exudate, which leads to less seroma formation.

Prevention and NPWT

The currently used terminology for technique is closed incision NPWT (ciNPWT). The most important mechanisms of NPWT in acute or chronic wounds that can be applied to clean surgical wounds are the following:

Reduction of lateral forces

The function of sutures or other surgical closure methods is to bring the wound edges together and to reduce lateral tension. Lateral wound tension may result in dehiscence of the wound, resulting in local granulation tissue formation and hypertrophic scarring in the healed incision. It also puts the wound at risk for poorer perfusion, with lower oxygenation status of tissue and increased risk of impaired wound healing. Figure 1a and 1b show the difference in perfusion of the area (by reduction of lateral tension). The greener section in the figure shows improved perfusion, which reduces the chance of wound complications.

Reduction of oedema, haematoma and seroma

Proponents of NPWT claim that it increases the activity of lymphatic drainage in the deep tissue. A second important precursor of infection is the collection of blood and serum. These fluids in sub-incisional tissues create dead spaces. This also increases the risk of infection.[20]

Infection prevention from exogenous sources

The wound is covered by the foam during the last phase of the surgery in a sterile environment. This coverage by the foam and device is continued during 5 to 7 days, making exposure to and infection from exogenous sources less likely. One of the products (the Prevena®) contains a small percentage of ionic silver (0.019%). According to the manufacturer, the ionic silver in the fabric reduces colonisation by bacteria such as *Staphylococcus epidermidis* and *Staphylococcus aureus* and by fungi. These mechanisms affect the various risk factors differently (Table 1). This table is a summary of various studies and guidelines.[20-24]

FIGURE 1A. Incision without ciNPWT

FIGURE 1B. incision with ciNPWT

TABLE 1. Effect of NPWT on risk factors for wound complications

	Reduction lateral forces	Increase perfusion pressure	Reduction oedema	Protection exogenous sources	Enhance granulation tissue
Obesity	++	++	++	++	+
Diabetes mellitus	-	++	-	++	+
Steroid usage	-	++	-	++	+
Malnutrition	-	+	++	+	+
Post-radiation therapy	-	++	+	+	++

NPWT ON CLOSED WOUNDS

Device options

A vacuum-assisted closure system, which can be used for open as well as closed incisions (VAC® KCI, San Antonio, Texas), has been used the longest. This system consists of separate elements which have to be brought together by the operator. A single layer of non-adhesive gauze should be placed over the closed incision to avoid skin maceration, followed by a thin strip (1.0–1.5cm) of foam (V.A.C. GRANUFOAM ® DRESSING, KCI, San Antonio, TX, USA). The foam is a hydrophobic

material with large pores that help to drain fluids and reach the negative pressure. An occlusive transparent dressing is placed over the foam, and negative pressure is applied to the foam through an incision in the drape via a pressure-sensing pad with tubing connected to the therapy unit, thereby creating the environment for NPWT. This device delivers a negative pressure of –125mmHg (adjustable 50 - 125mmHg). Silver-impregnated foam is also commercially available. An advantage of this device is that the foam can be cut and shaped to fit the wound edges exactly, for example for non-linear incisions (Figure 2).

ciNPWT systems have evolved substantially in recent years and are now available as single-use devices designed specifically for the management of closed incisions. Two simplified NPWT devices became commercially available in 2010 (PREVENA® KCI, San Antonio, USA) and 2011 (PICO®; Smith & Nephew, Hull, UK). These NPWT devices consist of a single-use battery-powered negative-pressure therapy device, an easy-to-place dressing (simple peel-and-place process) and either a very small or easily portable system, facilitating its use in the outpatient setting. The PREVENA® system has a skin interface layer containing 0.019% ionic silver and a canister for collecting incision exudate. It delivers negative pressure of –125mmHg (Figure 3). The PICO® system has no canister at all; the liquid is removed by evaporation through a semipermeable dressing. It delivers a negative pressure of – 80mmHg (Figure 4). Both systems incorporate all the functional elements of standard incisional NPWT, but in a simplified manner. The major difference between the products is the effect on lateral tension. Ex vivo experiments have shown a significantly higher reduction of incision width in favour of the Prevena® system.

The three devices discussed above are currently the most frequently used systems on the market. No clinical studies of self-fabricated NPWT devices or studies comparing the efficiency of two different NPWT devices were found in the literature.

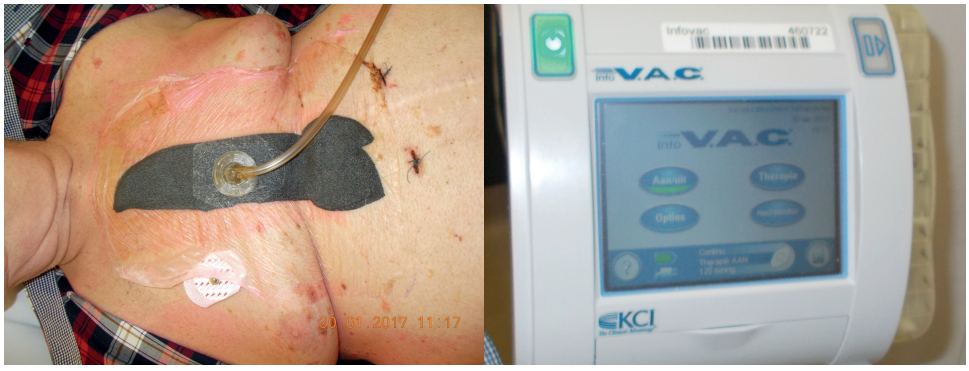

FIGURE 2. Self- constructed NPWT prevention system, consisting of VAC INFO® by KCI

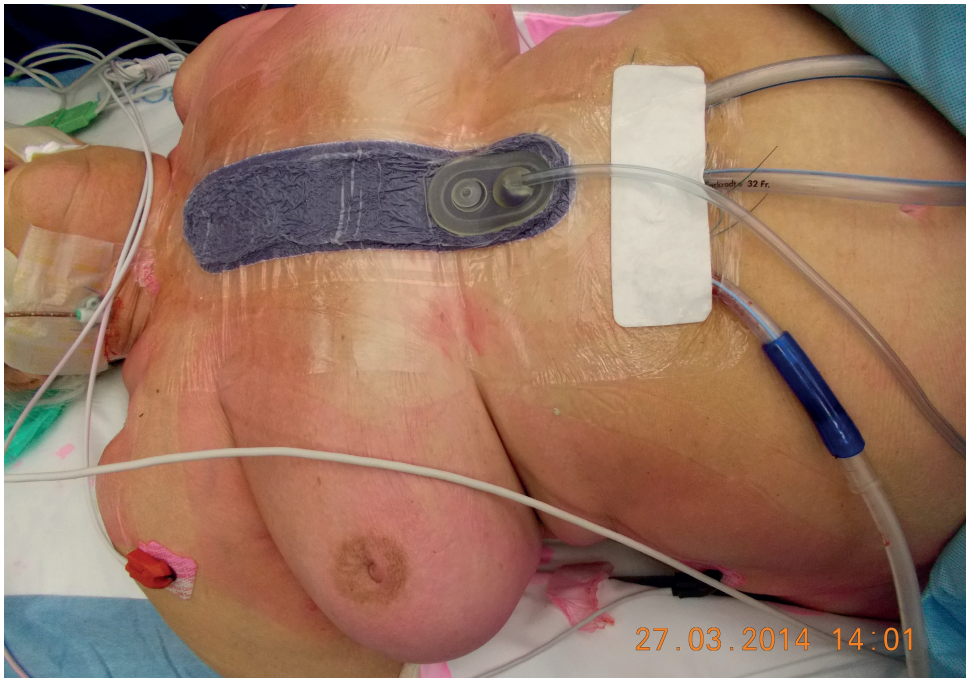

FIGURE 3. Placement of Prevena® in theatre following closure of the sternotomy wound

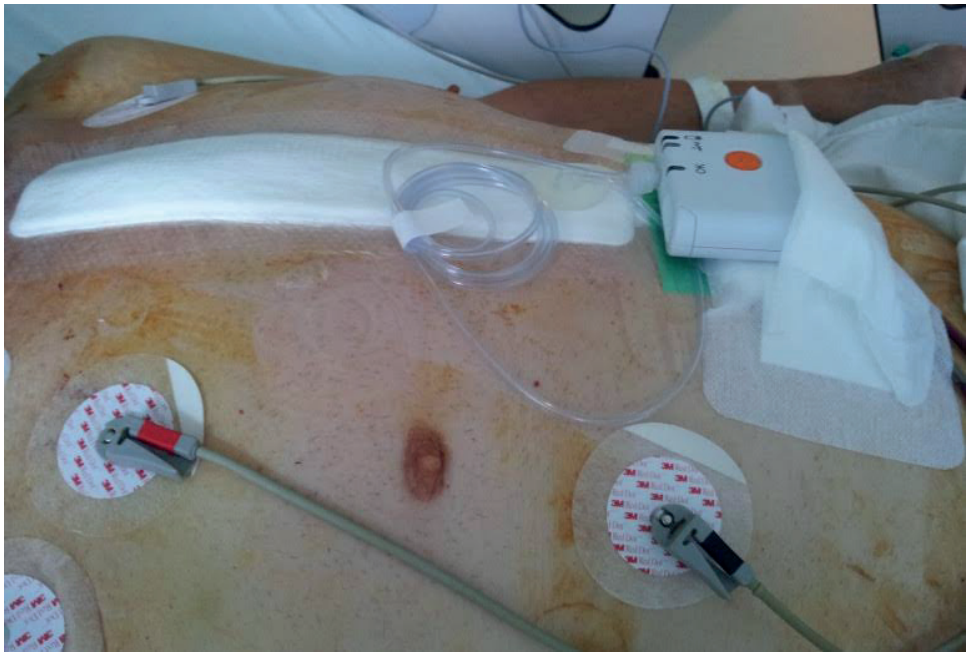

FIGURE4. PICO(r)® device

Technical application

Chlorhexidine, iodine or alcohol should be used for skin preparation, with careful drying to prevent foil blistering. NPWT must be applied immediately after surgery to clean, surgically closed incisions in a sterile field (while the patient is still in the operating room and before the sterile drapes have been removed).

When a conventional or self-fabricated NPWT (i.e. V.A.C. GRANUFOAM ® or a reticulated open-cell foam) dressing is used, a non-adherent layer should be placed between the foam dressing and the skin; placing the foam dressing directly against the skin can lead to maceration. The dressings designed specifically for closed incisions (i.e. the PREVENA® or PICO® systems) can be applied directly to the skin due to their skin-friendly surface.

The optimum area of tissue that should be subjected to NPWT is still a point of contention. Ideally, the NPWT should cover all incision edges to ensure reduction of lateral forces and suction of fluids. In any case, the wound should be covered entirely. Incomplete coverage of the wound leads to a higher risk of exogenous contamination and fluid accumulation in the untreated area.

To ensure an adequate seal, chest tubes should be placed lower. Placing drains and pacing wires away from wound edges help in achieving an air-tight seal. Before transferring a patient to ICU or the ward, check of the air-tight seal is essential. Areas that demand special are below the breasts and the most distal part of the wound. After applying the dressing, the therapy should be started by following the instructions on the product label.

Level of negative pressure

Despite the relatively good understanding of the mechanisms through which incisional NPWT might have an effect, surprisingly little information is available on the optimum negative pressure for clinical use. A major review of 33 recent studies on this topic, including study reports from orthopaedic surgery, cardiothoracic surgery, abdominal, plastic and vascular disciplines, showed that a range of pressure levels have been used with NPWT devices (with -75mmHg and -125mmHg being the most frequently used) without any obvious benefits or detriments in clinical efficacy.[25] No clinical studies have been published on the effects of various levels of negative pressure on desirable endpoints such as reduced haematoma or seroma, reduced oedema, increased wound strength or fewer complications. The emergence of single-use devices with a fixed pressure setting could reduce the likelihood that such studies being performed.[4,5] A study in pigs used gauze pads at -125mmHg and showed reduction in haematoma, improved wound strength and improved visual appearance.[6] Negative pressure between -50mmHg to -150mmHg applied to the zone of tissue surrounding the incision appears to be the principle cause of the effect, although much scope remains for investigation. Higher levels of negative pressure therapy (surpassing -150mmHg) can damage cardiac structures.

duration

Discontinuation criteria of NPWT for closed incisions have not been clearly defined. Variability in treatment duration may depend on procedure, type and localisation of incision and patient factors.

Opinions differ on the optimal timing for discontinuation of NPWT for closed incisions. Some advocate continuing therapy until no oedema fluid is evident in the canister for 12 hours, usually 24-72 hours after surgery.[21] The expert consensus is that minimal drainage is important.[22] However, that study was initiated prior to the availability of home NPWT and small portable units. Participants only used the NPWT for an average of 2-5 days because they were ready for discharge.

Later studies have reported slightly longer duration of incisional NPWT, likely due to increasing use of home NPWT devices. A study of the current literature reported a large variation in duration of treatment before first change of dressing, ranging from 2 days to 7 days (median 5) in the group treated with NPWT.[23]

Complications

NPWT should be removed immediately if the skin is exposed to the foam (i.e. if the non-adhesive layer between the skin and the foam of a conventional NPWT is incomplete or forgotten). Otherwise, the skin can be seriously damaged. If the operated area is no longer sterile, the NPWT should not be applied again.

If patients present clear signs of wound infection, the NPWT should be discontinued immediately.

Contraindications

There are no specific contraindications to NPWT use on closed incisions. NPWT dressings containing silver should not be used in patients with sensitivity to silver. Use caution if patients have blistering around the wound or inflammation, cellulitis or erysipelas surrounding the incision. The therapy should only be applied on clean surgical wounds.

Removal

After switching off the negative pressure, the NPWT dressing should be carefully removed. The absence of signs of inflammation such as oedema and erythema and adequate closure of the wound edges suggest that the wound has healed adequately.

DISCUSSION

NPWT has become a frequently used modality in the treatment of a large variety of dehiscent wounds and infected wounds. The capabilities of this modality to reduce wound dimensions, to enhance angiogenesis in the wound and to reduce oedema are important factors contributing to the success of NPWT.

Another important factor is reducing lateral tension on the wound. Excessive lateral tension diminishes perfusion and can contribute to poor wound healing. This is not only a problem in infected wounds; excessive lateral tension can also increase the risk of wound complications after cardiac surgery, especially in the morbidly obese or females with large mammae.

Three options are currently available for practitioners to use NPWT on a closed wound after "clean" surgery. Two are commercially available: 1) a wound incision management system which delivers a negative pressure of -125mmHg and has a canister for collecting drained fluids; 2) a system that delivers lower negative pressure levels (-80mmHg). It has no canister and uses an evaporation-based method to prevent maceration of the skin or build-up of fluids. The third option is to custom build the granufoam.

NPWT should be applied only under sterile conditions, if possible immediately following skin closure. Ideally, the system should be left undisturbed for at least five days, unless the patient develops clear signs of wound infection, such as pain. If re-exploration is needed, a new sterile set should be applied. Re-exploration is an important risk factor for developing wound complications after surgery.

Regarding cost effectiveness, the current systems should only be used for patients with a high likelihood of wound complications after surgery. No validated models are currently available for identifying patients at risk for wound infections. However, morbidly obese patients and those with a poorly regulated diabetes mellitus are clearly at high risk. Furthermore, patients with large mammae and the previously discussed risk factors should be considered for this therapy.

Conclusive scientific evidence on the efficacy of NPWT is not yet available. Although this therapy has been used successfully in large case series, large randomised clinical trials with convincing results are lacking. According to current guidelines, NPWT can be considered for patients at risk. [24]

Increasing evidence indicates that NPWT can be used in various types of surgery. Recent studies on NPWT in plastic surgery, orthopaedics and trauma surgery have shown promising results. However, randomized clinical trials to further build the evidence for this treatment modality are lacking.

In the future, risk models should be developed to identify patients at risk. Recent studies have shown that obesity, large mammae, poorly managed diabetes mellitus and immune suppressive medication are the most important risk factors for SSI. The risk model should take these factors into account. The clinician should use these models to make a decision on which patient to apply NPWT. The costs of these devices (both commercially available and self-built) demand that clinicians balance the costs of the device and the benefits for individual patient. The costs of these devices will remain a discussion point as long as these devices are used in patients with only a slightly elevated change for wound complications.

Equally important is that clinicians not only use NPWT as preventative measure but also strive to optimise the condition of the patient. While it may be advisable to use NPWT for a malnourished patient, it is even more important for a dietician to be involved to improve the condition of the patient.

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TIPS FOR USE

Preoperative phase

- Select patients that are at risk, for example the morbidly obese, poorly regulated diabetics and patients after radiotherapy.
- Discuss NPWT with patient as a preventative measure.

Operative phase

- Intraoperative phase
- Consider type of incision and approach (if possible)
- Consider placement of the incision to accommodate the NPWT dressing
- Consider placement of the port, tubing or wires, by leaving sufficient distance between them and the wound edges to secure the seal
- Consider the size and the shape of the incision wedges and select an appropriate NPWT dressing. Try to cover the wound completely
- Prepare the patient's skin with an antiseptic solution (chlorhexidine, iodine, or alcohol). The skin must be hair free and dry to ensure dressing adhesion and formation of a seal.
- Take extra care in areas within which an air-tight seal can be difficult (for example below the breasts). Gel strips may be useful to aid adhesion in areas that are difficult to seal
- Apply the dressing only under aseptic conditions (immediately after surgery, in the operating theatre and before the sterile drapes have been removed) and according to the manufacturer's instructions
- When using a conventional or home-made NPWT, always place a non-adherent layer between the foam dressing and the skin to avoid skin maceration of the healthy skin.
- After applying the dressing, start therapy by following the instructions on the product label. It is easily seen if the vacuum has been successful achieved

Postoperative phase

- Inspect the dressing, canister (if present), and power unit regularly
- If the dressing needs to be changed, use an aseptic technique. We do not recommend changing of dressing after cardiothoracic surgery to avoid the risk of contamination, which could lead to mediastinitis.
- In the case of reoperation, we strongly suggest placing a new NPWT unit, as reoperation is a risk factor on its own for wound infections.
- Leave the dressing in place for up to 5-7 days, according to manufacturer's instructions and availability of outpatient clinic access for removal, unless there are concerns about the incision or dressing change is required
- When the dressing is removed, if the incision is closed, dry and without signs of infection, the NPWT may be discontinued and there is no need to reapply NPWT or a conventional dressing

- Provide patients who are discharged from hospital with written information about how to care for the NPWT system, and when and how to contact a healthcare professional
- If signs of SSI occur, discontinue NPWT immediately and treat the patient according to standards of care

04

USE OF INCISIONAL NEGATIVE PRESSURE WOUND THERAPY ON CLOSED MEDIAN STERNAL INCISIONS AFTER CARDIOTHORACIC SURGERY: CLINICAL EVIDENCE AND CONSENSUS RECOMMENDATIONS

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ABSTRACT

Negative pressure wound therapy is a concept introduced initially to assist in the treatment of chronic open wounds. Recently, there has been growing interest in using the technique on closed incisions after surgery to prevent potentially severe surgical site infections and other wound complications in high-risk patients. Negative pressure wound therapy uses a negative pressure unit and specific dressings that help to hold the incision edges together, redistribute lateral tension, reduce oedema, stimulate perfusion, and protect the surgical site from external infectious sources. Randomised, controlled studies of negative pressure wound therapy on closed incisions in orthopaedic settings have shown the technology to reduce the risk of wound infection, wound dehiscence, and seroma, and there is accumulating evidence that it also improves wound outcomes after cardiothoracic surgery. Identifying at-risk individuals for whom prophylactic use of negative pressure wound therapy would be most cost-effective remains a challenge; however, several risk-stratification systems have been proposed and should be evaluated more fully. The recent availability of a single-use, closed incision management system offers surgeons a convenient and practical means of delivering negative pressure wound therapy to their high-risk patients, with excellent wound outcomes reported to date. Although larger, randomised, controlled studies will help to clarify the precise role and benefits of such a system in cardiothoracic surgery, initial evidence from clinical studies and from the authors' own experiences appears promising. In light of the growing interest in this technology amongst cardiothoracic surgeons, a consensus meeting, which was attended by a group of international experts, was held to review existing evidence for negative pressure wound therapy in the prevention of wound complications after surgery and provide recommendations on the optimal use of negative pressure wound therapy on closed median sternal incisions after cardiothoracic surgery.

INTRODUCTION

Surgical site infections (SSIs) are serious complications after cardiothoracic surgery and contribute significantly to postoperative morbidity, mortality, and healthcare costs.[1–3]Studies have reported that up to 15% of patients develop a wound infection after cardiac surgery;[4–7]with rates of SSIs ranging from 0.5 to 22.2%.[8–14]Incidence rates for deep sternal wound infection (DSWI) have ranged from 0.4 to 2.6%,with mortality rates of between 7 and 35% reported with conventional therapies such as surgical revision with open packing dressing, rewiring over a surgical drain(s), or reconstruction with vascularised soft tissue flaps compared with only 2.7–7.1% in uninfected controls.[2,6,11,15–23] Mortality rates were particularly high (up to 74%) in patients with DSWI due to methicillin-resistant Staphylococcus aureus (MRSA).[24,25] Host factors contributing to the risk of SSIs after cardiothoracic surgery have been well described in the literature and include obesity, renal insufficiency, diabetes mellitus, advanced age, sex, chronic obstructive pulmonary disease, smoking, steroid use and length of hospitalisation (>5 days).[1,19,22,23,26] Surgical risk factors include the use of one or two internal mammary artery (IMA) grafts (especially bilaterally and when using the pedicle IMA), duration of surgery and perfusion time, prolonged mechanical ventilation, use of an intra-aortic balloon pump, postoperative bleeding, re-operation, sternal rewiring, extensive electro-cautery, shaving with razors, and use of bone wax.[1,23] Surgical incisional wounds have traditionally been closed by primary intention using sutures, staples, or a combination of these methods. After closure of clean surgical incisions, wound care may include the use of traditional gauze dressings, and more advanced therapies such as hydrocolloids, growth factors, cultured skin, low energy ultrasound, and negative pressure wound therapy (NPWT) (V.A.C.® Therapy, Kinetic Concepts, Inc., San Antonio, TX, USA). NPWT is a treatment concept introduced initially to assist in the treatment of chronic open wounds.[27] NPWT uses a negative-pressure device and specific dressings to create a negative-pressure environment at the wound site. This helps to hold the incision edges together,[28] reduces lateral tension and oedema,[29,30] stimulates perfusion,[27,31–35] enhances the development of granulation tissue,[27,36,37]reduces bacterial colonisation of wound tissues,[27,38] and protects the surgical site from external infectious sources.[39] NPWT has also become a well-established method for improving outcomes after skin grafting, where the technique is used to prepare the wound surface for graft acceptance and to stabilise the graft to prevent shearing and removal.[40,41] In this clinical setting, removal of exudate reduces the risk of haematoma and seroma formation and helps to prevent contamination.[42] Increased granulation facilitates revascularisation and attachment of the graft to the wound bed.[43] Numerous clinical studies have shown the successful use of NPWT in the management of both skin and biomatrix grafts (reviewed by Gupta in 2012).[43] Recently, there has been growing interest in using the technique on closed incisions to prevent potentially severe SSIs and other wound complications in high-risk individuals. This paper aims to review existing evidence for NPWT in the prevention of wound complications after surgery and to provide consensus recommendations on optimising the use of NPWT after cardiothoracic procedures. The paper has been developed from a consensus meeting held in Amsterdam in November 2011.

NPWT for prevention of wound complications: clinical evidence

Randomised controlled trials (RCTs), retrospective studies, and case series provide a substantial body of evidence that the use of either NPWT or closed incision management (CIM; Prevena™ Therapy [Kinetic Concepts, Inc., San Antonio, TX, USA]) (Figure 1) may reduce the incidence of wound infections and other wound complications in a variety of post-surgical wound types (Table 1).[28,41–51]

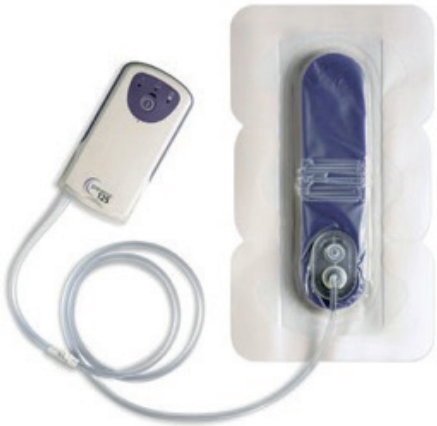


FIGURE 1. Closed incision management system to deliver negative pressure wound therapy. (Prevena^{tm} Incision Management System, Kinectic Concepts, Inc., San Antionia, TX, USA)

Stannard et al. (2012)[51] examined the use of NPWT to prevent wound dehiscence and infection following high-risk lower extremity fractures.[51] This multicentre, prospective, randomised, controlled study included 249 patients with 263 fractures. Patients were randomised to receive standard postoperative dressings (control group; *n*=122 fractures) or NPWT (*n*=141 fractures) over the surgical incision after open reduction and internal fixation of the fractures.[51] A total of 14 infections (9.7% of fractures) were reported in the NPWT group compared with 23 infections (19% of fractures) in the control group (p=0.049) (Figure 2). The relative risk of developing an infection was 1.9 times higher in control patients than in those treated with NPWT (95% confidence interval 1.03–3.55). A significant reduction in the risk of wound dehiscence after discharge was also observed in the NPWT group (8.6% of fractures) versus the control group (16.5% of fractures) (p<0.044). NPWT was applied for a mean of 2.5 days (range<1–9.0 days) in this study; and these patients were ready for hospital discharge half a day earlier than patients in the control group (not statistically significant), which more than offset the cost of the NPWT. The investigators concluded that, based on the results of this study, prophylactic application of NPWT to high-risk wounds before their failure appeared to be an efficacious treatment strategy. These findings confirm earlier reports or two small, randomised controlled trials of NPWT in trauma patients, in which NPWT was associated with not only decreased draining from surgical incisions but also improved wound healing.[50]

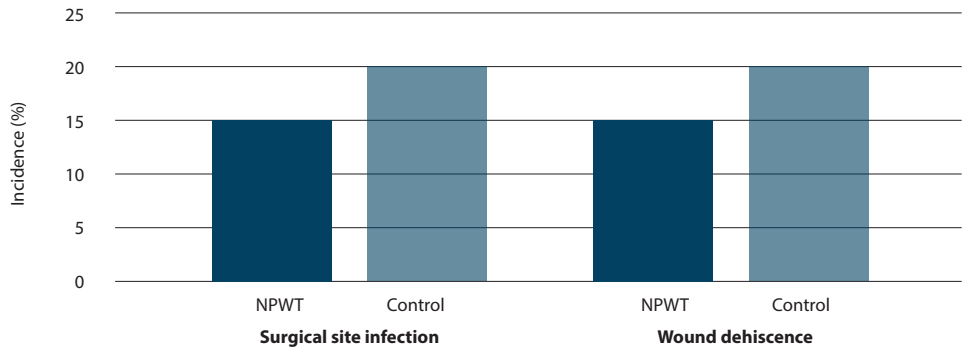


FIGURE 2. Incidence of surgical site infection and wound dehiscence in a randomised controlled study of negative pressure wound therapy (NPWT) versus standard dressing over surgical incisions after open reduction and internal fixation of 263 fractures in 249 patients[50].

Pachowsky et al. (2012) conducted a prospective, randomised evaluation of NPWT using CIM after total hip arthroplasty.[47] In this study, 19 patients were randomised to receive either standard dry wound dressings (control group; *n*=10) or CIM (*n*=9) over the sutured wound area. All patients received two Redon drains, one in the deep areas of the wound close to the prosthesis and one above the closed fascia. Ultrasound examination on Day 10 post-surgery revealed that 90% of patients in the control group and 44% of the patients in the NPWT group had developed a seroma. The average seroma volume was 5.08 ± 5.11ml in the control group compared with only 1.97 ± 3.21ml in the NPWT group (p=0.021). The control group received antibiotics for a mean of 11.8 ± 2.8 days compared with 8.4 ± 2.2 days in the NPWT group (p=0.005). Retrospective studies[48,49] and case series[46] suggest similar benefits of NPWT in terms of a low incidence of infections and other complications after orthopaedic surgery. Evidence for the benefits of NPWT in preventing wound complications after cardiothoracic surgery has accumulated through published retrospective chart review studies[44,52] and case studies.[28,45] Atkins et al. (2009) reported on 57 adult cardiac surgery patients who had received NPWT over a clean, closed median sternotomy incision because they were considered to be at increased risk of sternal wound infection(SWI) and other wound healing complications.[44] At the completion of the cardiac surgical procedure, the sternotomy incision was closed as per routine practice.

TABLE 1. Summary of studies using negative pressure wound therapy on closed, clean surgical incisions

Reference	Study type	Patients	Results/Conclusions
49	2 RCTs of NPWT vs. standard postoperative dressings (control)	44 patients with high-energy trauma wounds with draining hematomas (*n*=31 control; *n*=13 NPWT) 44 patients with high-risk fractures (*n*=24 control; *n*=20 NPWT)	High-energy trauma wounds: Control group drained a mean of 3.1 days vs. 1.6 days for NPWT (p=0.03) High-risk fractures: Control group drained a mean of 4.8 days vs. 1.8 days for NPWT (p=0.02)
50	RCT of NPWT vs. standard postoperative dressings (control)	249 patients with 263 high-risk lower extremity fractures requiring stabilisation (*n*=122 control; *n*=141 NPWT)	Significant decrease in infections with NPWT: 14 infections; 9.7% of fractures (NPWT) vs. 23 infections; 19% of fractures (controls) (p= 0.049) Relative risk of developing an infection was 1.9 times greater in control group than in NPWT group (95% CI 1.03–3.55) Significant decrease in risk of wound dehiscence after discharge with NPWT: 12 dehiscences; 8.6% of fractures (NPWT) vs. 20 dehiscences; 16.5% of fractures (control) (p=0.044)
46	RCT of NPWT vs. standard dry wound dressings (control)	19 patients following total hip arthroplasty (*n*=10 control; *n*=9 NPWT)	Incidence of seroma at 10 days: 44% of patients (NPWT) vs. 90% of patients (control) Significant reduction in average seroma volume with NPWT: 1.97 ± 3.21 mL (NPWT) vs. 5.08 ± 5.11 mL (control) (p = 0.021)
44	Prospective cohort of patients receiving NPWT	10 high-risk patients following CABG	All wounds healed completely; no complications reported No statistical information provided
43	Retrospective chart review of patients receiving NPWT	57 adults with sternal wounds at high risk of infection	Based on risk assessment, at least three sternal wound infections were anticipated, but none were reported NPWT was easily applied and well tolerated No statistical information provided
47	Retrospective chart review of patients receiving NPWT	19 morbidly obese patients (BMI > 40) with acetabular fractures	No reported complications No statistical information provided

TABLE 1. (continued)

Reference	Study type	Patients	Results/Conclusions
48	Retrospective chart review: NPWT vs. standard postoperative dressings (control)	301 patients with acetabular fractures (*n*=66 control; *n*=235 NPWT)	Incidence of deep wound infections: 6.15% (4/66) of patients (control) vs. 1.27% (3/235) (NPWT) (*p*=0.0414) Incidence of dehiscence: 3.03% (2/66) (control) vs. 0.04% (NPWT)
45	Case series of patients receiving NPWT	35 patients with foot and ankle trauma, revision hip arthroplasty, proximal femoral and tibial fracture fixation	Average time of NPWT use just over 3 days, which saved an average of 4 conventional dressing changes No statistical information was provided in the publication No infections had occurred in high-risk patients receiving NPWT at 3 months postoperatively No statistical information provided
28	Case series of patients receiving NPWT	4 high-risk patients following CABG using internal mammary arteries (*n*=1), transmetatarsal amputation (*n*=1) or abdominal hysterectomy (*n*=2)	All wounds healed well; no complications reported No statistical information provided

BMI = body mass index; CABG = coronary artery bypass graft; CI = confidence interval; DSWI = deep sternal wound infection; NPWT = negative pressure wound therapy; RCT = randomised controlled trial.

A single layer of non-adhesive gauze was placed over the clean, closed incision followed by a thin strip (1.0–1.5cm) of silver-impregnated foam (V.A.C. GRANUFOAM SILVER® DRESSING, Kinetic Concepts, Inc., San Antonio, TX, USA). An occlusive transparent dressing was placed over the foam, and negative pressure was applied to the foam through an incision in the drape via a pressure-sensing pad (T.R.A.C.™ Pad, Kinetic Concepts, Inc., San Antonio, TX, USA) with tubing connected to the therapy unit (V.A.C.® Therapy, Kinetic Concepts, Inc., San Antonio, TX, USA), thereby creating the environment for NPWT. Therapy was continued for 4 days postoperatively. Of the 57 NPWT-treated patients, 77.2% were obese, 54.4% were diabetic, and 50.9% were obese and diabetic. Overall, 50.9% of the NPWT-treated patients underwent coronary artery bypass graft (CABG) with one internal mammary artery, nearly 20% underwent concomitant CABG and other cardiac procedures such as valvular heart surgery or atrial maze procedure, and 14% underwent CABG with bilateral mammary artery use. NPWT was well tolerated by all patients until completion, and no recordable amount of exudate wound fluid was reported in any patient. In this study, the estimated risk for postoperative DSWI was based on risk scores developed by Fowler et al. in 2005.[13] This scoring system assigns points for individual preoperative and intra-

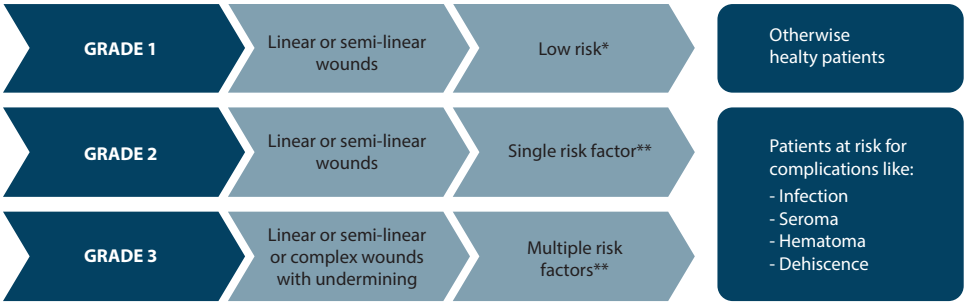
operative risk factors for major postoperative infection, enabling a probability of infection (%) to be estimated.[13] Based on this system, the estimated average risk for developing per DSWI in this group of high-risk surgical patients was 6.1 ± 4.0%; therefore, at least three cases of DSWI were anticipated in this series of 57 patients. Ten patients (17.5%) required readmission within the first 30 days after discharge; however, no admissions were due to sternal wound complications (Table 2).[43]

TABLE 2. Postoperative details of 57 high-risk adult cardiac surgery patients who received negative pressure wound therapy on the clean, closed sternotomy incision immediately after surgery and for 4 days postoperatively[40]

Variable	
Hospital length of stay (mean ± SD, days)	9.8 ± 10
Median length of hospital stay (days)	7.0*
Number of patients readmitted† (%)	10 (17.5%)
Heart failure	7
Pleural/pericardial effusion	3
Number of sternal wound infections predicted/observed	3/0
Mortality, *n* (%)	1 (1.8%)

*Range for hospital stay not provided.
†Within the first 30 days post initial hospital discharge.

In this population of high-risk patients treated with NPWT, there were no reports of DSWI or superficial SWI, leading the authors to recommend that NPWT should be strongly considered for patients with increased risk of SWI. No data relating to a 1-year follow-up of these patients were reported in this paper. More recent evidence comes from Colli, who used CIM over the surgical incisions of a small prospective cohort study of 10 patients at high risk for SWI (Fowler risk score 8–30)following CABG surgery.[45] All 10 patients received CIM for 5 continuous days immediately following standard wound closure. Wounds and surrounding skin were inspected following removal of the CIM dressing and at day 30 after surgery. The system was well tolerated, and all patients experienced complete wound healing with no evidence of early or late wound infections. These preliminary findings demonstrate the favourable efficacy and safety of CIM in preventing wound complications after cardiac surgery; however, larger, randomised, controlled trials are warranted to more clearly define the patient population and wound types that would benefit most from this type of therapy. Whether CIM will be able to prevent sternal dehiscence or DSWI with sternal involvement remains a key issue, but according to current clinical evidence, the benefits of the system in terms of promoting skin healing may help to impede dehiscence and/or the development of DSWI. Indeed, most recent findings from a prospective study indicate that NPWT may prevent postoperative wound infections.[53]



* No pre-existing medical conditions
** Known risk factors: diabetes, obesity, smoker, hypertension, steroid use, radiation, etc

FIGURE 3. Patient grading system adapted from Stannerd et al[28] for determination of which closed surgical incisions are best suited for incisional negative pressure wound therapy

Consensus statement

- Based on current published evidence, NPWT appears to effectively prevent wound complications when used over clean, closed surgical incisions, including median sternal incisions.

Modern approaches to applying NPWT/CIM

NPWT systems have evolved substantially in recent years and are now available as single-use devices designed specifically for the management of closed incisions in patients at risk of postoperative wound complications. The CIM device used in the studies by Colli (2011)[45] and Pachowsky et al. (2012)[47] consists of a single-use (i.e. completely disposable) NPWT unit, canister, and dressing that are designed for application over clean, closed, sutured or stapled incisions in a simple peel-and-place process. The dressing is comprised of a polyurethane film with an acrylic adhesive that provides adhesion of the dressing to the skin surrounding the incision and a polyurethane shell that encapsulates the foam bolster and interface layer, providing a closed system. The dressing has a built-in pressure indicator and a skin interface layer containing 0.019% ionic silver, which wicks fluid from the skin surface and reduces bacterial colonisation within the fabric. The single-use, battery-powered therapy unit delivers negative pressure in the system between −75 and −125mmHg. The system also contains a sterile 45ml canister for collection of incision exudate and additional drape patch strips that may be used to help seal leaks around the dressing.

Consensus recommendation

- Single-use devices such as CIM are recommended for the management of closed incisions in patients at high risk of postoperative wound complications.

Using NPWT in cardiothoracic surgery: selecting appropriate patients

Prevention of surgical site infections remains of pressing concern to all healthcare professionals and relies on the use of strict pre-, intra- and postoperative infection control measures to optimise the patient condition and to minimise contamination risk.[54,55] Appropriate choice of incisional wound dressing and treatment, which are integral to most infection control guidelines, will depend on local preferences and availability, but should always be based on robust cost-effective evidence. NPWT is an advanced technology that, based on data from the Stannard et al. randomised controlled trial,[51] has been shown to be a cost-effective option when used for the prevention of wound infection and dehiscence in high-risk patients. However, questions remain over the best way to define high-risk patients in clinical practice. In the studies by Atkins et al. (2009)[44] and Colli (2011),[45] the risk of DSWI was assessed using the Fowler system.[13] According to this system, the use of both internal mammary arteries is assumed to double the risk of surgical wound infection, based on a previous evaluation of DSWI in this setting.[56]Additionally, a distinction is made between obese individuals with a body mass index (BMI) of 30–40 kg/m^2 and those with a BMI>40 kg/m^2, with increased risk of surgical wound infection assigned to the latter category. Stannard et al. (2009) proposed a simpler universal patient grading system to help determine which closed surgical incisions may be best suited for NPWT (Figure 3).[28] Under this system, Grade 1 patients have linear or semi-linear wounds and no pre-existing medical conditions and are considered at low or no risk of developing post-surgical wound complications such as infection, seroma, haematoma, or dehiscence. Grade 2 patients have linear or semi-linear wounds and at least one moderate- to high-risk factor (i.e. diabetes, obesity, smoking, hypertension, steroid use, radiation exposure), making them candidates for post-surgical NPWT. Grade 3 patients have linear, semi-linear, or complex wounds with undermining and one or more risk factors and may, therefore, benefit most from prophylactic use of incisional NPWT. We believe that risk factors for major infections after cardiothoracic surgery can be divided into three categories: major, intermediate, and minor (Table 3). Like Fowler et al. (2005),[13] we consider a BMI≥40 kg/m^2 and insulin-dependent diabetes to be major risk factors, but we also include a low BMI (<18 kg/m^2) and chronic kidney disease (GFR<30ml/min/1.73 m^2 for≥3 months) requiring dialysis in this category. Intermediate, but still important, risk factors include a BMI between 35 and 39kg/m^2, diabetes mellitus requiring oral hypoglycemic medications, chronic kidney disease not requiring dialysis, the use of both internal mammary arteries, and long-term immunosuppressive medication. Some of the minor risk factors include BMI 30–34 kg/m^2, female sex, and age>75 years.

Consensus recommendations

- CIM should be considered for use in all high- or at-risk patients, regardless of skin type, with the aim of *preventing* wound infection and dehiscence after surgery.
- Selection of high-risk patients for postoperative use of NPWT should be based on a careful assessment of preoperative risk factors.
- Patients with one or more major risk factors (e.g. BMI < 18 or ≥ 40 kg/m^2, insulin-dependent diabetes mellitus or dialysis treatment for chronic kidney disease) are strong candidates for prophylactic use of NPWT.
- Patients with two or more intermediate (or major) risk factors (e.g., use of bilateral mammary arteries, diabetes mellitus, chronic lung disease or receiving long-term immunosuppressive medication) may also benefit from postoperative NPWT.
- We strongly recommend using CIM in heart, lung, and heart/lung transplantation patients in view of the high degree of immunosuppression required; however, sternum stability is vital.

TABLE 3. Proposed classification of preoperative risk factors for major infections after cardiothoracic surgery

Major
• BMI < 18 or ≥ 40 kg/m^2
• Insulin-dependent diabetes mellitus
• Dialysis in patients with chronic kidney disease (GFR < 30 mL/min/1.73 m^2 for ≥ 3 months)
Intermediate
• BMI 35–39 kg/m^2
• Diabetes mellitus (type 1 or 2 receiving oral hypoglycemic medication or diet)
• Chronic kidney disease (GFR < 30 mL/min/1.73 m^2 for ≥ 3 months)
• Use of bilateral mammary arteries
• Long-term immunosuppressive medication
• Previous chest wall radiotherapy
• Chronic lung disease (GOLD class > II)
Minor
• BMI 30–34 kg/m^2
• Peripheral vascular disease
• Female gender
• Age > 75 years
• Cardiac reoperation for CABG procedure
• Left ventricular ejection fraction < 30%
• Acute myocardial infarction within 90 days prior to surgery
• Hospitalised at least 7 days before surgery

BMI = body mass index; CABG = coronary artery bypass graft; GFR = glomerular filtration rate; GOLD = Global initiative for chronic Obstructive Lung Disease.

Optimising the use of NPWT in cardiothoracic surgery

The authors of this consensus document have considerable experience in using the CIM for the prevention of wound complications after cardiothoracic surgery and have found the system to be easy to use and well tolerated by patients. The system should be applied immediately after surgery, in a sterile field (i.e. while the patient is still in the operating room and before the sterile drapes have been removed), to clean, closed incisions for a period of 5–7 days. When used preventively, the system should ideally be left undisturbed for at least 5 days, unless the patient develops clear signs of wound infection, such as pain. If the dressing is lifted to observe the incision, a new dressing should be applied.

If the wound extends beyond the length of the dressing, the dressing can be applied over part of the incision. It should not be placed over drains or wires, should not be used to treat open or dehisced surgical incisions, and should not be used in patients with sensitivity to silver. Skin preparation should include the use of chlorhexidine, iodine or alcohol with careful drying to prevent foil blistering. Drains should be placed in a lower position when planning to use CIM (see case studies). The system should be removed carefully with the vacuum turned off. Adequate closure of the wound, no redness at the incision site, and no evidence of oedema upon dressing removal would suggest that the wound has healed adequately. In our experience, concerns regarding the canister becoming too full of fluid are unfounded. A summary of consensus recommendations for optimising the use of CIM after cardiothoracic surgery is presented in Table 4.

TABLE 4. Consensus recommendations for optimising the use of closed incision management after cardiothoracic surgery

Goal of treatment	• Prevention of wound infection and dehiscence in all at-risk patients
Appropriate patients	• All heart, lung and heart/lung transplantation patients • All patients with major or multiple intermediate risk factors (see Table 3)
Length of treatment	• 5–7 days (aim for at least 5 days undisturbed)
Skin preparation	• Chlorhexidine, alcohol or iodine with careful drying
Placement	• Should not be placed over drains or wires • Position drains in a lower position when planning to use system postoperatively
Re-application frequency	• Single-use dressing only. If lifted to observe the incision, a new dressing must be applied
Treatment success criteria	• Adequate wound closure • No redness at the incision site • No evidence of oedema
Precautions	• Should not be used to treat open or dehisced surgical incisions or patients who have excessive amounts of exudate that may exceed 45 mL canister limit • Should be used with caution on patients with fragile skin surrounding the incision and patients who are at increased risk of bleeding
Contraindications	• Silver sensitivity

CASE STUDIES

The three case studies presented here show examples of the prophylactic use of NPWT over clean, closed surgical incisions after cardiothoracic surgery.

Case study 1: Urgent triple CABG and mitral valve replacement (MVR) via sternotomy

This 70-year-old male presented with a non-ST elevation myocardial infarction (Figure 4). His medical history included type 2 diabetes, peripheral vascular disease, renal insufficiency, hyperlipidaemia, and pulmonary hypertension. The patient was diagnosed with triple vessel coronary artery disease and severe mitral insufficiency. An urgent triple CABG and MVR were performed. Due to his elevated risk of postoperative incision complications, the CIM system was used, with the dressing applied along the incision (Figure 4A) with special care taken to leave sufficient distance between the inferior aspect of the incision and the chest tubes in order to secure an adequate seal (Figure 4B). On postoperative day 3, the patient experienced a cardiopulmonary arrest requiring immediate resuscitative chest compressions. However, the integrity of CIM dressing was maintained. On postoperative day 8, the CIM dressing was removed. The incision edges appeared well apposed and were healing appropriately (Figure 4C). In contrast, the chest tube sites, which were not treated with CIM, demonstrated some drainage. The patient was discharged home on postoperative day 18 with his incision continuing to heal well.

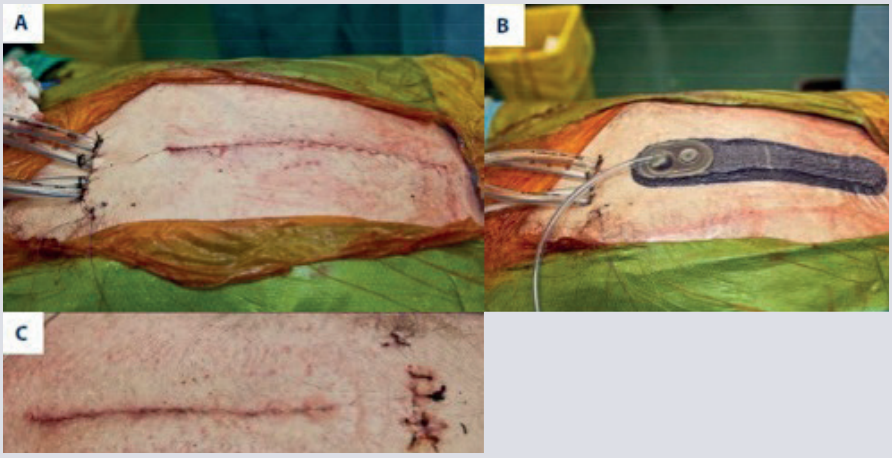


FIGURE 4. Closed incision management of a 70-year-old male following coronary artery bypass graft and mitral valve replacement via sternotomy. Images reproduced with the patient's permission. (Photo's courtesy of Dr Zane ATKINS)

Case study 2: CABG and MVR via sternotomy

This 65-year-old male presented with progressive angina and a positive exertional stress test (Figure 5). His medical history included diabetes mellitus, obesity (BMI 38 kg/m^2) and chronic obstructive pulmonary disease. Cardiac catheterization demonstrated severe, three-vessel coronary artery disease. Four-vessel CABG was performed utilising left IMA to left anterior descending coronary artery and reverse saphenous vein grafts to the right coronary artery, ramus intermedius artery, and first diagonal artery, separately. The standard median sternal incision was approximately 10 inches in length. Sternal re-approximation was performed with stainless steel cables and the skin was closed with subcuticular sutures. The CIM dressing was applied in the operating theatre and remained in place until it was removed on postoperative day 5.The patient was discharged on postoperative day 6.

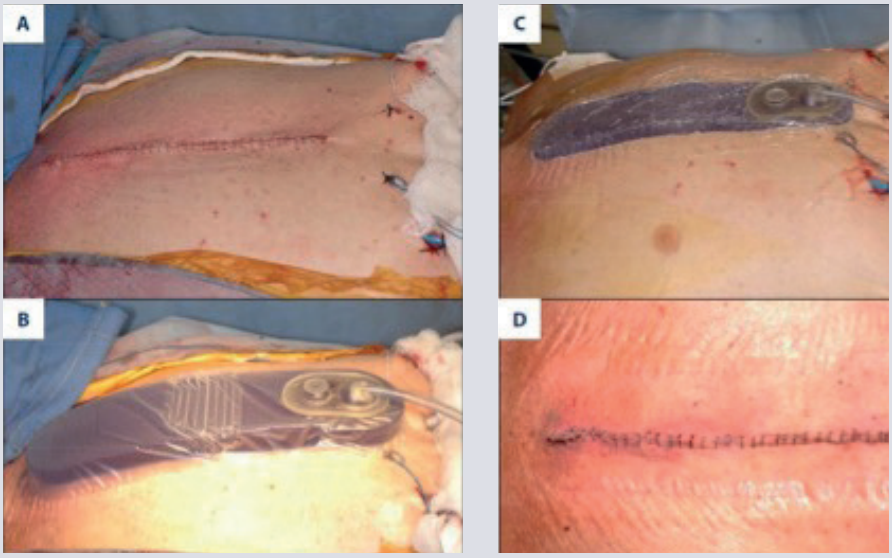


FIGURE 5. Closed incision management of a 65-year-old male following coronary artery bypass graft and mitral valve replacement via sternotomy. Images reproduced with patient's permission (Photo's courtesy of Dr Zane Atkins)

Case study 3: Elective CABG in a morbidly obese female

This 77-year-old morbidly obese female (BMI 57.5 kg/m^2) underwent an elective CABG due to angina functional class III/IV (Figure 6). She was at high risk of developing DSWI as a result of her obesity, insulin-dependent diabetes mellitus, and long-term use of systemic prednisolone for chronic obstructive pulmonary disease (Gold [Global initiative for chronic Obstructive Lung Disease] class II). Revascularization was achieved using bilateral internal mammary grafting, as neither the saphenous vein nor the radial artery was useable. Transdermal stitches were used to close the incision. The CIM system was selected prior to surgery, allowing the drains to be placed in a low position in order to accommodate both the dressing and the short stature of the patient. The CIM dressing was applied carefully, under sterile conditions, along the incision and left undisturbed for 5 days. The dressing was removed on postoperative day 6; there was no oedema or infection present, and the wound was healing well. The patient was discharged on postoperative day 10, with no surgical wound infection, even at the 30-day follow-up. To date, the CIM system has been used successfully on 32 of the contributing author's (AM) patients with no signs of surgical wound infection during hospitalisation or at the 30-day follow-up.

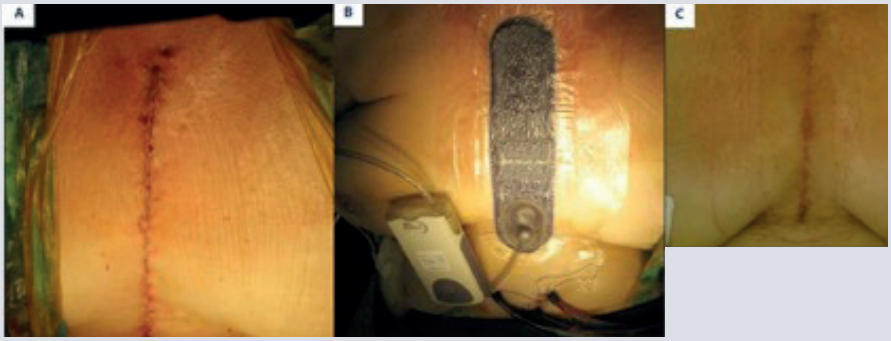


FIGURE 6. Closed incision management of a 77-year-old, morbidly obese female who underwent elective coronary artery bypass graft. Images reproduced with patient's permission. (A) Day 0: Clean closed surgical incision. (B) Day 0: Placement of CIM dressing. (C) Day 6: Surgical incision following removal of CIM system. (Photo's courtesy of Dr. A.L.P. Markou)

SUMMARY AND CONCLUSIONS

There is growing interest in the use of NPWT on closed incisions after cardiothoracic surgery to prevent potentially severe SSIs in high-risk individuals. NPWT on closed incisions has been shown to reduce the risk of wound infection, wound dehiscence, and seroma in randomised, controlled studies of patients in orthopaedic settings.[47,51] NPWT also enhances graft adherence and survival after skin and biomatrix grafting.[43] Evidence is now accumulating that NPWT improves wound outcomes after cardiothoracic procedures.[28,44,45] Based on published data and clinical evidence, we recommend that NPWT should be considered in at-risk patients with the aim of preventing DSWI after surgery. Identifying at-risk individuals for whom prophylactic use of NPWT would be most cost-effective remains a challenge. However, several risk-stratification systems have been proposed,[13,28] and should be evaluated more fully. In the meantime, we believe that patients with one or more major risk factors or multiple intermediate risk factors are strong candidates for prophylactic use of NPWT and that any patient undergoing heart, lung, or heart/lung transplantation should receive this treatment. The availability of the peel-and-place, single-use CIM system offers surgeons a convenient and practical solution to overcome SSIs in high-risk patients, and CIM is recommended by the authors based on their own clinical experiences. Larger, randomised studies will help to clarify the precise role and benefits of NPWT on closed incisions after cardiothoracic surgery; however, initial data appear very promising.

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Conflict of interest

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Abbreviations

BMI	body mass index
CABG	coronary artery bypass graft
CI	confidence interval
CIM	closed incision management
DSWI	deep sternal wound infection
GFR	glomerular filtration rate
GOLD	Global initiative for chronic Obstructive Lung Disease
IMA	internal mammary artery
MRSA	methicillin-resistant Staphylococcus aureus
MVR	mitral valve replacement
NPWT	negative pressure wound therapy
RCT	randomised controlled trial
SSI	surgical site infection
SWI	sternal wound infection

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05

CAN POST-STERNOTOMY MEDIASTINITIS BE PREVENTED BY A CLOSED INCISION MANAGEMENT SYSTEM?

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ABSTRACT

Poststernotomy mediastinitis is a serious complication of cardiothoracic surgery and contributes significantly to postoperative morbidity, mortality, and healthcare costs. Negative pressure wound therapy is today's golden standard for post-sternotomy mediastinitis treatment.

A systematic literature search was conducted at PubMed until October 2012 to analyse whether vacuum-assisted closure technique prevents mediastinitis after clean surgical incisions closure. Today's studies showed a reduction of post-sternotomy mediastinitis including a beneficial socio-economic impact. Current studies, however, included only high-risk patients. Hence, larger randomised controlled trials are warranted to clarify the benefit of using surgical incision vacuum management systems in the general patient population undergoing sternotomy and clarify risk factor interaction.

INTRODUCTION

Poststernotomy mediastinitis is a serious complication of cardiothoracic surgery and contributes significantly to postoperative morbidity, mortality, and healthcare costs [1]. Negative pressure wound therapy is today's golden standard for post-sternotomy mediastinitis treatment due to oedema reduction, removing exudation, increase wound perfusion, stimulate granulation formation, and decrease microbial colonisation [1]. This positive effect on wound healing triggered the interest in using negative pressure wound therapy after the closure of clean surgical incisions in contrast with traditional wound care such as gauze dressings, hydrocolloids, growth factors or cultured skin to prevent surgical site infections, especially post-sternotomy mediastinitis. The surgical incision management system (Prevena Incision Management System, Kinetic Concepts, Inc. USA, San Antonio, TX, USA) is a single-use, battery-powered therapy unit that delivers negative pressure of –125mmHg [2]. Surgical incision management holds the incision edges together, reduces lateral tension and oedema, stimulates perfusion, and protects the surgical site from external infectious sources [3]. The skin interface layer containing 0.019% ionic silver, allows no direct contact of the foam, wicks fluid from the skin surface, and reduces bacterial colonisation within the fabric.

High-quality, multi-centre or single-centre, randomised controlled trials (level I based on the Evidence Rating Scale for Therapeutic Studies developed by the American Society of Plastic Surgeons) [4] in other clean surgery fields [5] showed positive outcomes by using incisional negative pressure wound therapy. These results encourage using surgical incision management, which is functionally equivalent to incisional negative pressure wound therapy, in high-risk patients undergoing median sternotomy to prevent post-sternotomy mediastinitis. Therefore a systematic of the literature was performed.

METHOD

The systematic literature search at PubMed was conducted through October 2012. The following keywords were included: "negative pressure wound therapy" and "sternotomy wound infection prevention" and "cardiac surgery". Excluded were case reports and articles not preventing surgical site infections but treated.

RESULTS

The largest prospective comparative study (Level II) was performed by Grauhan et al. [6] including 150 consecutive obese (body mass index>30 kg/m^2) patients with median sternotomy. Standard wound dressings were applied in the control group (n=75), while the treatment group received surgical incision management (n=75). This study showed a significant reduction in surgical site infections (SSI) after median sternotomy, respectively 16% versus 4% (OR 4.57, CI 95% 1.23–16.94; p=0.0266).

Atkins et al. [7] examined 57 adult cardiac surgery patients at higher risk for sternal wound infection, who were treated with incisional negative pressure wound therapy (Level III). The patient population included morbidly obese patients (77.2%), diabetics (54.4%), and patients who are both obese and diabetic (50.9%). Overall, 50.9% of patients underwent coronary artery bypass graft with one internal mammary artery and 14% with bilateral mammary artery use. Approximately 20% underwent coronary artery bypass graft with concomitant procedures. Since this study included no control group the estimated risk for post-sternotomy mediastinitis was based on risk scores, which predict SSI. Based on this system, the estimated average risk for developing postoperative post-sternotomy mediastinitis in this group of high-risk cardiac surgery patients was 6.1 ± 4.0%; therefore, at least three cases of post-sternotomy mediastinitis were expected in this study population. Ten patients (17.5%) required readmission within the first 30 days after discharge; however, no admissions were due to sternal wound complications. Therefore the authors recommend that incision negative pressure wound therapy should be strongly considered for patients with increased risk of surgical site infection.

Finally, Colli et al. [8] used surgical incision management over the surgical incisions of a small case series of ten patients at high risk for post-sternotomy mediastinitis following coronary artery bypass graft surgery (Level III). Surgical incision management was used for 5 continuous days immediately following sternal wound closure. This study also included no control group, and therefore the authors again utilised a risk score system finding a prediction of 6.4 ± 4.4% for post-sternotomy mediastinitis. This high-risk cardiac surgery population included diabetes in all, peripheral vessel disease in 90%, morbid obesity in 50%, chronic obstructive pulmonary disease in 30%, and renal failure in 20%. The left internal mammary artery was used in 100%, and bilateral mammary artery grafting was performed in 50%. The system was well tolerated, and all patients experienced complete wound healing with no evidence of early or late wound infections. The authors again recommend the use of surgical incision management in high-risk cardiac patients. These preliminary findings demonstrate the favourable efficacy and safety of surgical incision management systems in preventing wound complications after cardiac surgery in high-risk patients.

DISCUSSION

The remarkable infection-preventive effect raises the question of the possible causes. The bacterial density in wounds predicts the risk of wound infection with subsequent healing [9], [10], [11]. Therefore, it was obvious that negative pressure affects the bacterial colonisation. But some studies on acute and chronic wounds refutes that bacterial bioburden is consistently lessened during VAC therapy [12], [13]. In an in vitro wound model bacterial load of sponges with or without negative pressure did not differ [14]. The reduction in bacteria demonstrated in previous studies appears to be caused by other effects than physical suction alone. Since primary closed sternotomy wounds are not critically colonised, other mechanisms must be responsible. From a theoretical considerations point of view, following factors could affect a favourable outcome: (i) improved circulation and increased of vascularity [15], (ii) stimulation of

cell proliferation [15], (iii) immediate tight aseptic wound closure, (iv) microbiostatic activity of polyurethane-coated polyester fabric with silver and (v) optimal wound edges adaptation. Using a computer model, the hypothesis was generated, that micromechanical forces may stimulate wound healing through the promotion of cell division, angiogenesis, and local elaboration of growth factors [16]. These questions should be analysed in further studies in animal models.

CONCLUSION

All studies showed a reduction of post-sternotomy mediastinitis in high-risk cardiac surgery patients for SSI such as morbid obesity, including obesitas permagna, insulin-dependent diabetes, chronic renal failure, and bilateral mammary artery grafting. Additional risk factors including low body mass index (<18 kg/m2), long-term immunosuppressive therapy, high age and female sex, need to be investigated. Furthermore, larger randomised controlled trials are warranted to clarify exact benefit for the use of a surgical incision management system. These studies should not only include reduction of surgical site infection, including patient's morbidity and mortality but also investigate the social economic impact. Due to the complexity of SSI and multiple factors influencing poststernotomy mediastinitis, additional studies are needed to improve wound healing in cardiac surgery patients bringing prevention measures in proportion to risk factors.

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Conflict of interest

All authors declare that they have no conflicts of interest.

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06

CHALLENGES IN DESTINATION LVAD THERAPY, MANAGEMENT OF MEDIASTINITIS AND DEVICE INFECTION, A CASE REPORT

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ABSTRACT

Pump pocket infection and mediastinitis after LVAD surgery in patients with destination LVAD therapy are challenging. A potential surgical therapy can be surgical debridement followed by rectus abdominis coverage of the defects. In this case, there was no need to explore the driveline of the LVAD. In the case of destination therapy, this should be followed up by lifelong antibiotic therapy.

INTRODUCTION

Patients with therapy resistant heart failure remain a challenge for the clinician. Heart transplantation is only available for a limited group of patients due to comorbidities and shortage of donor hearts.(1) As an alternative, continuous-flow left ventricular assist devices (LVAD) are currently a clinical reality, resulting in a continuously growing number of patients. LVAD as destination therapy has an excellent early survival.(2) Nevertheless, it is well known that bleeding, thromboembolism, driveline infections and device failure are a source of concern for the long-term management of these patients.(3, 4)

Infectious complications have frequently been reported.(5) This is to be expected; patients often present with multiple organ insufficiencies and/or multiple comorbid conditions with prolonged hospitalisation. Any kind of infection in these patients will lead to poorer outcome. As the group of patients with destination therapy is rapidly growing, the numbers of infections in the surgical field will also increase. These infections can be superficial, limited to the driveline or deeper with extension to the pump itself. This case report shows a novel approach for the surgical treatment of mediastinitis and LVAD (pump and pocket) infection.

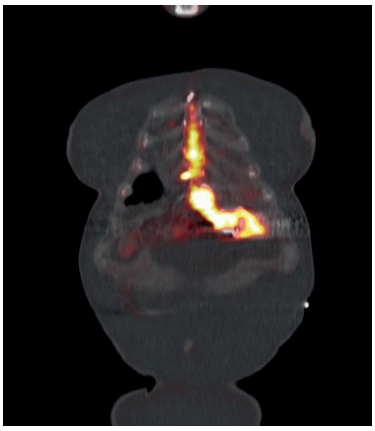
Case

A 75-year-old female with a long history of heart failure received a Heartmate 2 device (Thoratec, Inc.: Pleasanton, California, USA) as destination therapy for refractory heart failure. Her cardiac medical history shows a supraventricular tachycardia for which she received ablation in 1998. She has been known with a dilated cardiomyopathy since 2002. In the following years, she received an internal cardiac defibrillator. During the course of her disease, the cardiomyopathy led to ventricular arrhythmias and multiple admissions for decompensated heart failure. Her general medical history showed well-controlled asthma, rheumatic disease for which she is treated with long term low dose prednisone and a caesarian section.

The Heartmate 2 device was implanted on December 1st, 2015. Surgery was uneventful. A median sternotomy was performed, and the device was implanted under support of extracorporeal circulation. The driveline was placed in a subcutaneous loop to exit the abdominal wall at the lower left quadrant.

The postoperative course of the patient was initially uneventful. She was discharged home after 4 weeks. She was readmitted March 18th 2016 with elevated CRP and discharge from the wound. A small defect was observed in the caudal area of the sternotomy wound. The sternum was not dehiscent, nor was there redness. Cultures of the defect showed skin flora; no pathogen was cultured. The only positive culture was a sputum culture (Staphylococcus aureus) from November 2015. It was decided to treat this pathogen as the most likely pathogen involved. Flucloxacillin was started, as this is the preferred treatment for this pathogen with low antibiotic resistance in the Netherlands. During this treatment, the patient developed fever, and the antibiotic regime was changed to cefuroxime for broader coverage. The initially performed

CT scan showed a small retrosternal fluid collection. It was decided to perform a PET-CT scan 3 weeks after admittance. This showed an overwhelmingly elevated uptake in the sternum, retrosternal area and the pump pocket (Picture 1).

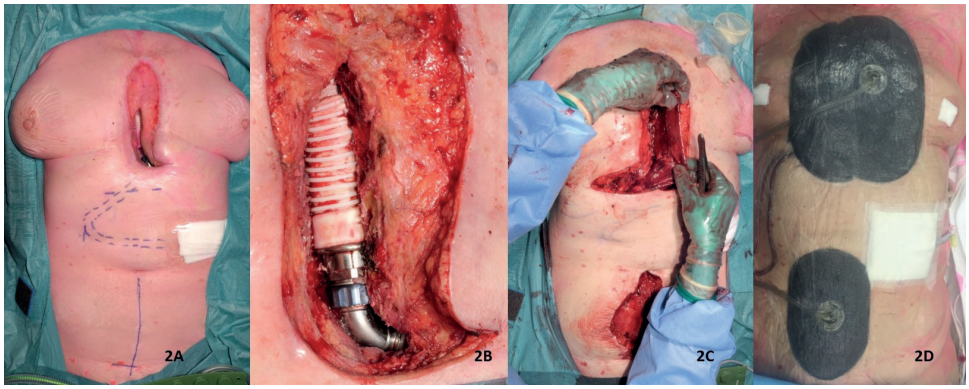


PICTURE 1. PET CT scan showing infectious activity in LVAD pocket and sternum area

In the multidisciplinary heart team, it was decided not to replace her pump but to debride, use negative pressure wound therapy and to treat antibiotically for mediastinitis. The patient was reoperated on March 14th 2016. A fistula was excised, and the tract of the fistula led to a retrosternal pus collection that led to the Heartmate 2 pocket. Inspection showed loosening of the ring around the bent of the Heartmate, and there was no sign of tissue adhesion around the bent. All the wiring of the sternum was removed, and the distal part of the corpus sterni was excised. The ring around the bent was also removed. Pus was evacuated and cultured. Negative pressure therapy (NPT) was initiated (V.A.C.® Therapy, Kinetic Concepts, Inc., San Antonio, TX, USA) at the end of surgery.

Postoperatively, during the negative pressure therapy, the wound was colonised with Enterococcus faecalis. Furthermore, the patient developed cystitis with a multiresistant Escherichia coli and candida albicans. The treatment was switched to meropenem and micafungin. During the usage of VAC therapy, the defect became smaller in size and no pus or edema was visualised in the wound area (Picture 2A).

Closure of the defect was performed June 8th 2016 using a pedicled rectus abdominis muscle. Thorough debridement of the sternal edges and area around the heartmate 2 (Picture2B) was performed and cultures were taken. The right rectus abdominis muscle was harvested through the scar in the lower abdomen and a horizontal incision over the insertion of the rectus adjacent to the defect in order not to jeopardise the vascularization of the skin in the upper abdomen. The anterior fascia of the rectus muscle was sutured using a PDF-loop, without a mesh. The muscle was tunnelled underneath the driveline and placed into the defect.

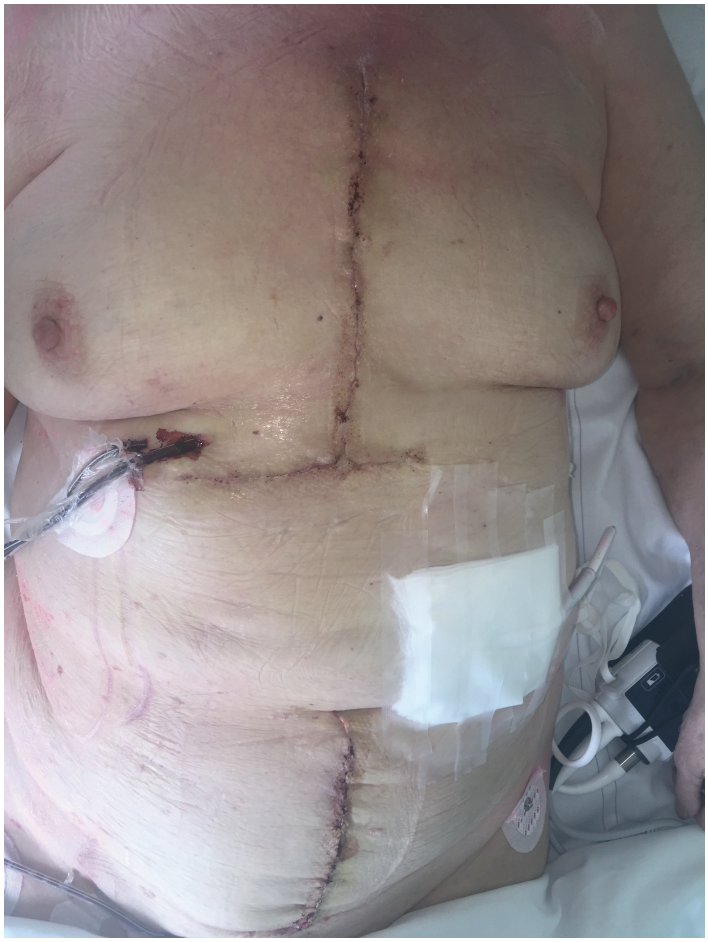


PICTURE 2. Perioperative photos using the right sided rectus abdominis muscle flap to close defect. In picture 2a the position of the drive line is shown

The exposed LVAD and mediastinal space were covered by the muscle. This completely obliterated the existing dead space. Thoracic and abdominal skin closure was performed after placement of suction drains. To prevent wound edge dehiscence so-called closed wound NPT (photo2D) (V.A.C.® Therapy, Kinetic Concepts,Inc., San Antonio, TX, USA) was applied. Negative pressure wound therapy uses a negative pressure unit and specific dressings that help to hold the incision edges together, redistribute lateral tension, reduce edema, stimulate perfusion, and protect the surgical site from external infectious sources. (6).

It was decided to give lifelong antibiotic therapy to provide suppressant therapy in this patient.

The patient was discharged two weeks after surgery with closed wounds and no signs of infection (Picture 3). The LVAD was working without errors and no signs of problems with the driveline. PET-CT scan 3 months after the closure of the defect, showed decreased intensity of FDG uptake around the LVAD .Patient follow-up at 6 months showed no signs of either a new infection or ongoing infection (no fever, low C-reactive protein levels). Clinically she is doing well, living at home with reasonable exercise capacity walking moderate distances near her house. She is without pain with normal wound healing.



PICTURE 3. Result 10 days after surgery with no signs of infection

DISCUSSION

Destination LVAD therapy is a reality. With growing numbers of patients, the number of patients presenting with severe wound complications will grow. In the group of patients with an LVAD as a bridge to transplantation, urgent transplantation is the definitive solution for the problem. In destination therapy, this is not possible and implanting a new LVAD in an infected area will only lead to ongoing infectious problems.

The literature on these infections and their treatment is scarce .(7, 8) Drainage remains the cornerstone of the surgical approach, often followed up by negative pressure therapy. In case of tissue infection, this can be done as either bridge to natural closure or bridge to surgical closure. In those cases in which the LVAD is also compromised, the treatment is more difficult. Two case reports show the current spectrum. The first one in a paediatric case with a large soft tissue defect in the area of the device.(7) The sternum was not dehiscent. Different to our case was the localisation of the drive line. This was placed in the right upper abdomen. A pedicled vertical rectus abdominus muscle with myocutaneous flap was used to cover the defect. This patient was transplanted 4 months after this surgery. The second case was an adult patient (52-year-old man) with dilated cardiomyopathy.(8) The LVAD was placed as bridge to transplant. Following the development of the infection, debridement was performed, and NPT was initiated. Omental transposition was used to cover and fill the pump pocket.

We have shown that a pedicled rectus abdominus muscle flap can be used successfully without the need to explore and or remove the drive line of the LVAD in the abdominal compartment. This muscle flap provides good coverage of the LVAD and, as in our patient, a large part of the sternal area as well. Using this approach gives the option to a minimal driveline manipulation approach. A (laparoscopic) omental transposition is an alternative. This will, however, lead to involving the abdominal cavity and potentially could result in infectious complications in that area and driveline failure due to manipulation. Scopic harvesting of the omentum can potentially prevent this complication but is complex and still leads to involvement of the abdominal cavity.

We have also applied the concept of closed wound NPT to prevent secondary infection, seroma and dehiscence of the wound. This system is easy to and can, in theory, reduce the chance of postoperative wound complications.

However, antibiotic treatment remains important. In our vision, this should be long-term suppressive antibiotics. The appropriate therapy was chosen by a multi-disciplinary team and in this case, will comprise of 6 weeks of vancomycin and after that levofloxacin.

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07

PAIN MANAGEMENT AFTER CARDIAC SURGERY: EXPERIENCE WITH A NURSE-DRIVEN PAIN PROTOCOL

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ABSTRACT

Objective: Management of postoperative pain is important for decreasing postoperative morbidity and mortality. After evaluating our pain score database of patients undergoing cardiac surgery (2007-2009) we revised our pain protocol. The new protocol allows nurses to administer analgesic medication without consulting the attending physician. The setting was a medium care unit, a nursing ward with additional monitoring of heart rate and rhythm. We investigated the effects of this revised pain protocol in a prospective consecutive cohort study.

Methods: We evaluated 193 patients treated according to the revised protocol (RP group) during the first 72 hours post-cardiac surgery on the medium care unit. As pain scoring system, the visual analogue scale (VAS) was used. These patients were compared with a control group (Ctrl-group) consisting of 1535 patients.

Results: Patients from the RP group had a mean VAS of 2.2 compared to a mean VAS of 2.8 of the Ctrl-group ($P<0.0001$). In the Ctrl-group 44% of patients with a VAS≥4 maintained this score for 8 hours afterwards. In contrast, in the RP group 81% had a reduction in VAS score within 3 h. Using the new protocol there were no adverse events requiring intervention such as medication or readmission to an intensive care unit.

Conclusions: This study shows that in post-cardiac surgery patients a significant reduction of VAS scores can be safely realised by a nurse driven protocol. Furthermore, a reduction of time to achieve an acceptable pain score (VAS<4) was realised.

INTRODUCTION

In 2009, in the Netherlands, over 19,000 patients underwent cardiac surgery. Management of postoperative pain is of concern for decreasing postoperative morbidity and mortality in this patient group.[1-2] Despite national guidelines, structural management of postoperative pain can still be seen as an underappreciated part of the postoperative treatment.[3-8] Pain after cardiac surgery is often described to be severe and seems most intense in the first 48 h after surgery and negatively influences health related quality of life.[9-10] Thus, the treatment of postoperative pain remains a point of interest and focuses on improving patient care and reducing mortality and morbidity.[3, 9-11] Requirements of Dutch healthcare organisations and government also form a base for the development of such an assessment tool.[12]

Especially nurses play a key role in the management of this postoperative sternotomy pain. However, frequently this does not result in the desired reduction of pain intensity.[8, 13] The management of postoperative pain is reported in only a few studies. Usually, these studies focus on intensive care settings instead of medium care units (a nursing ward with telemetric surveillance of heart rhythm). Thus, the best way to optimise postoperative pain management still needs investigation.

In 2008, we started a database comprising of patient characteristics and postoperative pain measurements at the cardiothoracic surgery patient ward. Analysis of these data from 2008 revealed topics for improvement. A total of 34% of all pain measurements were found above an accepted upper-level for pain. Another important finding was that 60% of this group still scored above this upper-level eight hours afterwards. This initiated the change of the pain management protocol.

A task force, consisting of consultant-physicians from the departments of Intensive Care, Cardiothoracic Anaesthesia, and Cardiothoracic Surgery together with a nurse practitioner of the cardiothoracic surgery patient ward, an intensive care nurse and a safety officer from our hospital, rewrote the pain protocol. In contrast to the historical protocol, this revised protocol (Fig. 1) enabled nurses to administer pain medication to post operative patients without prior consultancy of the attending physician or nurse practitioner, under the condition that pre-set safety criteria are met. The aim of the present study is to investigate the effects of this revised pain protocol in a prospective cohort study of patients who underwent cardiac surgery in our hospital.

MATERIALS AND METHODS

Study setting and design

We performed a single centre prospective consecutive cohort study on the effectiveness and safety of a nurse-driven pain protocol (revised protocol; RP group) compared to a previously used conventional pain protocol (Ctrl-group), for postoperative pain management in Cardiothoracic surgery patients.

The two groups compared were consecutive patient groups without any change in operative techniques or changes in anaesthetic techniques during the duration of this study. Data collection was gathered from both the intensive care unit (ICU) and medium care unit (MCU). However, patients are sedated and mechanically ventilated during the largest part of their stay at the ICU. Thus, only a few hours being without sedation. Therefore, this study will only discuss the results on the medium care unit. The period of recording data on the MCU was set to 72 hours after admission to this unit and in accordance with the literature in which pain is reported to be most severe in the first 48 hours[3, 9-11] whereafter it decreases rapidly. Pain scores were collected using a Visual Analogue Scale (VAS) method as advised in the guidelines for acute pain management.[14-20] Using a ruler of 10cm, each postoperative patient was asked to make an assessment of his/her pain intensity at pre-defined moments. VAS scores of 4 and higher are regarded as levels associated with significant pain, whereas VAS scores below 4 are thought to reflect acceptable pain levels. [14-20]. For this reason 4 was chosen as the cut-off value to express pain. (Fig. 1).

The local ethics committee approved the study (MEC 2009-412). All included patients were adult. No exclusion criteria were used in the control group except non-cardiac surgery requiring sternotomy and the exclusion criteria implemented for the RP group and Ctrl group being a patient with delirium or not being able to speak Dutch or English. Patients with a complicated intensive care period requiring a longer stay on the ICU were excluded as well. Thus, all patients had an ICU-stay of less than 24 hours.

Clinical data

The conventional protocol consisted of a regiment of acetaminophen 1000mg, administered orally four times a day. If a patient had a VAS score of ≥4, morphine was prescribed by the attending physician in a routine of 4 times a day with a dose of 7.5mg subcutaneously (same for all patients). VAS scores were obtained three times a day at fixed times and were registered in an electronic patient data management system. The nurses were trained in using the VAS scale before implementation of the historical protocol.

Figure 1 illustrates the flowchart of our nurse driven revised pain protocol. It enables autonomous administration of analgesic medication by nurses. In short, it starts when patients arrive after ICU discharge. After obtaining a basic data set of hemodynamic and respiratory and neurological parameters, a nurse can intervene with a weight adjusted dosage of morphine when VAS≥4.

Safety parameters are included such as limitation of 0.2mg/kg of morphine per 8-hour shift. When the pain is significant and considered atypical, a physician or nurse practitioner should be consulted first before starting this protocol. Hemodynamic and pulmonary assessment was performed by standard care. The Ramsay score was used to evaluate the sedation level of the patients.[21] This score gives a numerical rating scale on which sedation levels can be measured and compared (Fig 1). Nurses at the Medium-Care ward had to be trained in using this method. This was the only variable for which additional training was necessary before implementation of the revised nurse driven pain protocol could be done.

In the study using the revised protocol data were collected in writing and in an electronic patient data management system during the first 72 hours on the medium care unit. Nurses followed the rewritten protocol to obtain the required clinical data.

Patient safety is an important factor in creating and evaluating a nurse-driven pain protocol. Forevaluation, patient safety was defined as no patients having a re-admission to an ICU, none having a systolic blood pressure below 100mmHg, and none having a respiratory rate below 12 breaths/min.

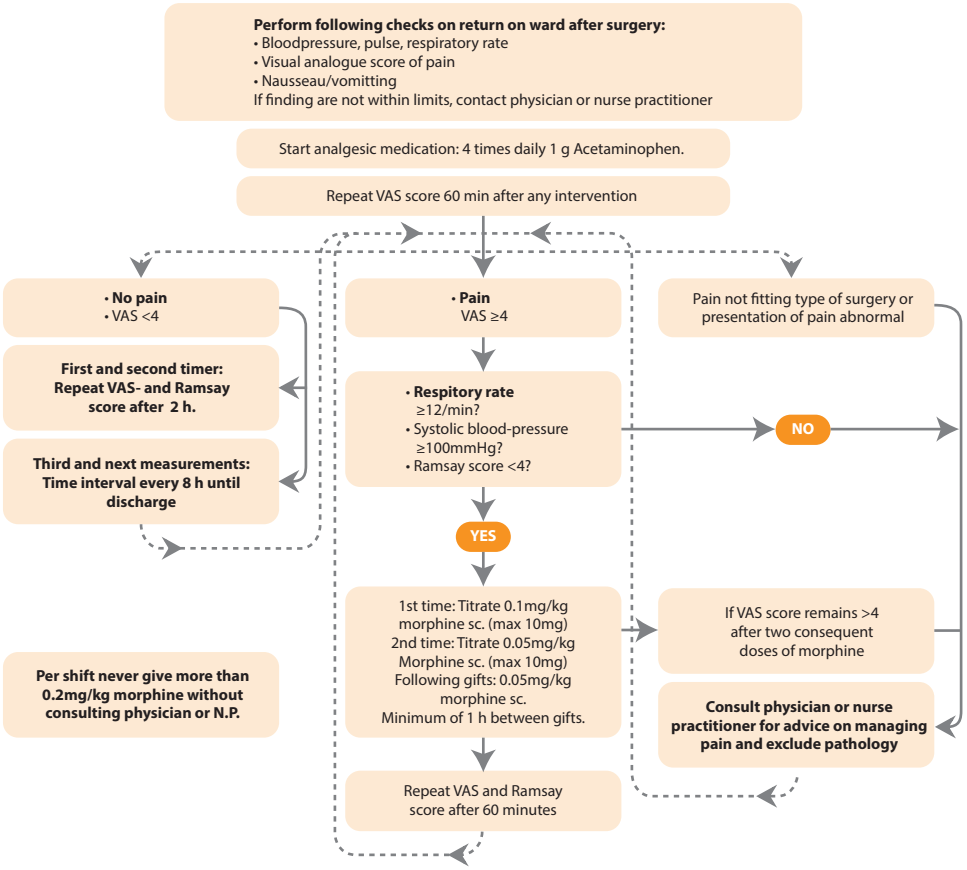
End points were defined as 1) patients reaching the 72-hour endpoint on the medium care unit, 2) patients requiring pain medication outside the protocol, or 3) patients needing re-admission to the ICU.

To evaluate the properness of our comparison of the Ctrl-group with the RP group, EuroSCORE® demographics were collected for each patient, as well as information about the type of cardiac surgery being performed. The EuroScore® provides an oversight of variables for scoring co-morbidity, e.g. kidney dysfunction, neurological dysfunction, chronic pulmonary disease etc., that give insight to the patient population being studied. [22]

Timing of data collection was based on the flowchart in the rewritten pain protocol (Fig. 1). This flowchart, also states when a physician or nurse practitioner should be contacted.

Statistical analysis

Continuous variables were compared using an unpaired Student's t-test. A Chi-square test was used for categorical variables. Data are presented as percentages unless indicated otherwise. A p value<0.05 was thought to represent statistical significance.



Ramsay score	
1. Agitation	Agitated
2. Awake	Cooperative, aware
3. Optimum	Follows commands
4. Optimum	Quick response
5. Slow	Slow response
6. Sedated	No response

Morphine dosage			
weight	**0,05 mg/kg**	**0.1 mg/kg**	**weight**
40-49	2.2 mg	4.4 mg	40-49
50-59	2.7 mg	5.4 mg	50-59
60-69	3.2 mg	6.4 mg	60-69
70-79	3.7 mg	7.4 mg	70-79
80-89	4.2 mg	8.4 mg	80-89
90-99	4.7 mg	9.5 mg	90-99
>100	5.0 mg	10 mg	>100

FIGURE 1. Flowchart medium care pain protocol.
This is the flowchart used by nurses on the medium care to administer analgesic medication. It starts when patients arrive after ICU discharge. After obtaining a basic data set of haemodynamic, respiratory and neurological parameters a nurse can intervene with a weight adjusted dosage of morphine if VAS ≥ 4. Safety parameters are included, such as a limitation of 0.2 mg/kg of morphine per 8-h shift. When the pain is not fitting the surgical intervention a physician or a nurse practitioner should be consulted first, before starting this protocol.

RESULTS

The RP group consisted of 193 consecutive patients undergoing cardiac surgery starting in September until December 2009 (a period of 10 weeks). The Ctrl group consisted of 1535 consecutive patients undergoing cardiac surgery between January 2008 and August 2009. This was the time-frame from which all patient data was collected within a patient data management system. Comparison of patient characteristics showed no significant differences between these groups (Table 1).

To compare the efficacy of both protocols, a design was developed in which both groups of patients were split up into two groups. One group of patients having VAS scores of 4 or higher at any moment during the 72 hours and one group with only VAS scores below 4. The demographics of the groups were compared using EuroScore® variables.

TABLE 1: Characteristics of Control group (Ctrl-group) group and Rewritten/new protocol group, (RP group)

	Ctrl-group n=1535 (%)	RP group n=193 (%)	P-value
Clinical presentation			
Age (mean [SD]) (yrs)	63 [13.6](17-88)	63 [14.6] (17-86)	0.85
Male	66%	72%	0.06
COPD	9%	10.2%	0,61
Creatinin (µmol/l)	94	91	0.53
Left ventricular function			
Good	67.3%	70.4%	
Impaired	20.8%	21%	
Moderate	12.0%	8.6%	
Cerebro-vascular accident history	4.1%	3%	0.51
Diabetes mellitus	20.1%	20.3%	0.52
EUROSCORE	4.90	5.02	0.61
Type of surgery			
CABG only	45%	50%	
CABG and valve	12.2%	12,4%	
Congenital	2.6%	6%	
Great vessels	13.6%	9.4%	
Valve	23.3%	21%	
Other	3.3%	1.2%	
Critical preoperative condition	2.9%	3.6%	0.07
Prior surgery	9.2%	9.0%	0.94

SD = Standard Deviation, COPD = Chronic Obstructive Pulmonary Disease, CABG = Coronary Artery Bypass Grafting

This reveals that patients with VAS 4 or higher were younger and in the Ctrl group, more often of male sex (Table 2). A lower overall EuroScore® was associated with higher VAS scores in the control group, whereas no such association was found in the revised protocol group.

The trends in percentage of obtained VAS scores and number of VAS scores of 4 or higher in all patients during the first 4 days after surgery are shown in Figure 2. Because of mechanical ventilation and intravenous sedation a large number of missing values of day 0 (day of surgery) was observed. A total of 20% of expected data could be retrieved from day 0. Patients are usually transferred to the Medium Care unit at day 1 at the end of the morning. Figure 2 shows that more than 89% of data on this unit (comprising of day 1 until day 4) could be collected.

TABLE 2: Characteristics of patients with VAS < 4 and patients with VAS ≥4

	Control group			Rewritten protocol		
	VAS ≥4 n=925	VAS < 4 n=610	P-value	VAS ≥4 n=107	VAS < 4 n=86	P-value
Clinical presentation						
Age mean [SD] (range)	61.3 [14.2] (17-88)	65.8 [12.7] (19-85)	<0.001	60.4 [15.2] (20-86)	67.0 [12.8] (17-84)	0.004
Male	62%	38%	<0.001	69%	31%	0.241
COPD	8.5%	9.9%	0.350	7.4%	13.9%	0.175
Creatinin (umol/l) [SD]	90.7 [58.4]	99.3 [58.6]	0.005	94 [23]	72 [39]	0.023
Left ventriculair function			<0.001			0.477
Good	71.2%	61.1%		73.1%	66.7%	
Impaired	18.9%	23.7%		20.4%	21.7%	
Moderate	9.9%	15.2%		6.5%	11.6%	
Cerebro Vascular accident history	3.8%	4.4%	0.534	1.1%	5.6%	0.093
Diabetes mellitus	17.9%	22.7%	0.022	23.4%	16.7%	0.286
EUROSCORE [SD]	4.4 [2.6]	5.6 [3.1]	<0.001	4.7 [3.2]	5.5 [2.8]	0.092
Type of surgery:			0.008			0.301
CABG only	47.3%	44.3%		50.0%	50.0%	
CABG and valve	10.7%	14.0%		9.6%	14.9%	
Congenital	2.8%	1.5%		9.6%	1.8%	
Valve	24.0%	22.2%		20.2%	23.6%	
Great vessels	13.6%	14.1%		8.5%	9.7%	
Other	1.5%	3.9%		2.1%	0%	
Critical preoperative condition	2.9%	2.8%	0.006	3.2%	4.2%	0.739
Prior cardiac surgery	8.8%	9.9%	0.4782	8.5%	9.7%	0.787

SD = Standard Deviation, COPD = Chronic Obstructive Pulmonary Disease, CABG = Coronary Artery Bypass Grafting

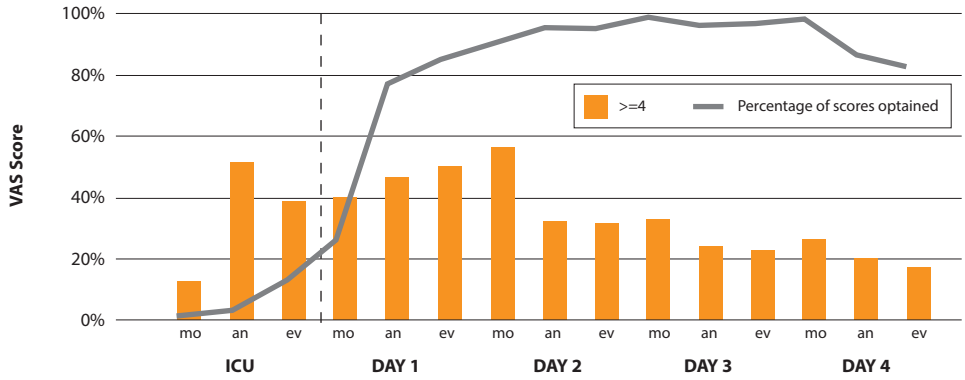


FIGURE 2. VAS score per day after cardiac surgery.
This figure shows the percentile of data acquired during a 4-day period. Furthermore, it shows how many patients score a VAS ≥ 4 in this period. Each day is split-up into three parts. A morning (mo), afternoon (an) and evening (ev) score. VAS = Visual Analogue Scale.

The missing 11% of values was due to non-compliance to protocol or not importing data into the written or electronic database. Noteworthy, refusal of pain medication (morphine) by patients was also examined. In 8.9% of all VAS scores that ideally should be followed by providing patients with medication according to the pain protocol, patients refused to take pain medication.

As in the Ctrl group, pain was measured every 8 hours whereas in the RP group pain levels are measured after 1 and then, consecutive, every 2 hours if needed, no direct comparison of patients benefits and time gain could be made. Evaluation of the data of both groups revealed that of all patients with a VAS≥4, in the Ctrl group 56 % had a reduction in VAS after 8 hours and 71% after 16 hours (2 consecutive measurements), whereas in the RP group this reduction was found in 64% after 1 hour and in 81% after 3 hours.

Figure 3 shows the mean VAS scores for patients from both groups at the first 3 postoperative days on the MCU. A continuous lower mean VAS score for the RP group in comparison to the Ctrl-group is found. Using a nurse-driven pain protocol, a 21% reduction of 175 VAS score was accomplished in postoperative cardiac surgery patients on a medium care unit, with a lowering of the average VAS score from 2.8 to 2.2.

Patient safety evaluation showed no readmission of patients to an ICU because of any factor related to administration of pain medication. Eight patients had an episode of hypotension. Evaluation showed that these patients had a baseline systolic blood pressure of around 100mmHg due to heart failure medication. None of the hypotension episodes were related to administration of morphine. Seven patients had a respiratory rate below 12 breaths/min. No relationship to previous morphine gifts on the ward was found. Neither intervention with opioid-antagonists, nor other respiratory support measures were necessary.

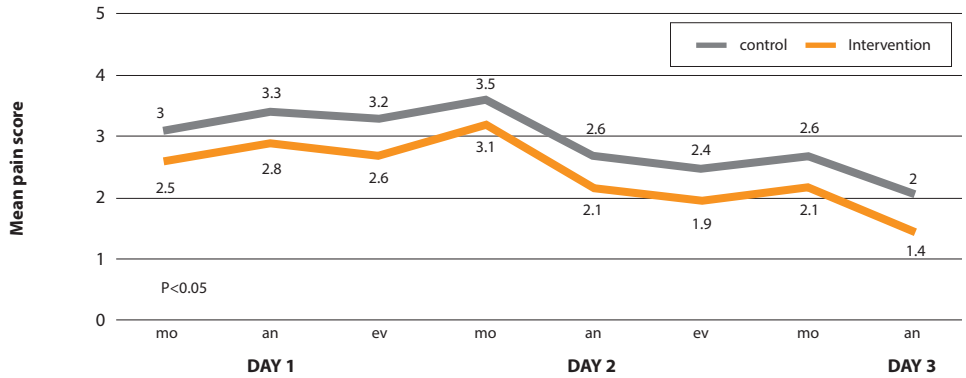


FIGURE 3. Effectiveness of the rewritten/new protocol measured in time.
This figure shows the time that is needed to get a patient with a VAS score ≥ 4 into an acceptable VAS (< 4). It also shows the time differences in which the historical protocol and the new nurse-driven protocol differ. In the old protocol a control of the VAS score was mandatory after 8 hours whilst in the new protocol this time is shortened to one hour.

DISCUSSION

Using a nurse-driven pain protocol on the MCU, a 21% reduction of VAS score was accomplished in postoperative cardiac surgery patients. Moreover, a reduction in VAS scores was obtained in more patients and less time as compared to the previous pain management protocol.

The reliability of a VAS score for evaluating acute pain is reported to have a good reproducibility when nurses and patients correctly use the instrument.[6-7, 19-20] Nurses in our department are well trained in taking a reproducible VAS score from patients for acute pain management. This training was performed before implementation of both protocols.

A remarkable finding was the number of patients refusing to take analgesic medication. A refusal rate of 8.9% by patients with a VAS score suitable for a morphine gift, according to the protocol. The most important reasons for refusing analgesic medication was fear of nausea (being a possible side effect of morphine) and fear of addiction to morphine. This is contradictory to studies that have reported nurses, with their perception of the intensity of pain of a patient, to be the major influence on inadequate response to postoperative pain.[7-8, 13, 23-25] Many reports stress the importance of patient control in pain medication which can be done by implementation of a protocol using patient controlled analgesia pumps (PCA-pump). It can be argued that PCA-pump is an option for patients after cardiothoracic surgery[26]. However, we chose a system where pain can be treated quickly but always after assessment of the patient by a trained nurse, because we wanted to maintain strict haemodynamic and respiratory observation by nurses in these postoperative cardiac surgery patient group.

We observed more postoperative pain in (slightly) younger patients. Within the Ctrl group, there was also a sex difference (men>women) for postoperative pain present. Furthermore, a lower overall EuroScore® was associated with more pain in the Ctrl group, however not in the revised protocol group.

The relation between age and pain has been presented before by Gjeilo et al.[10] However in our study, it were the younger patients who presented with higher VAS scores after surgery. A study on demographic and psychosocial predictors of acute peri-operative pain after total knee arthroplasty also described younger age being a predictor for more pre- and postoperative pain.[27] This is in accordance with our results. From literature it is also known that the relationship between sex and pain is not a simple one.[28] Although most population-based studies reveal a higher postoperative pain prevalence in women than in men, there are also studies that have found no such difference.[28] Our results for the Ctrl group are contradictory to this literature, indeed illustrating the difficulty of this relation. Our data on VAS and Euroscore® are not consistent between the groups. Unfortunately, we could not find studies paying attention to such a possible relation. We, therefore, think that this must be further explored in future studies.

In our study, we found no adverse events requiring ICU re-admittance. However, we did see patients having pain and a systolic blood pressure below 100mmHg before initiation of the rewritten protocol. In patients treated for heart failure, a well-regulated blood pressure treatment with a systolic blood pressure of 100mmHg or lower can be regarded as beneficial for patients and must not be seen as an adverse event. Thus, using a dynamic blood pressure range could be beneficial for these patients. Nevertheless, the protocol was strictly adhered to for reasons of practical usability. The protocol also allowed for a back-up, in which a physician or nurse practitioner could agree upon using the protocol despite the low systolic blood pressure.

A point of concern is the number of missing VAS score measurements due to non-compliance to follow the protocol. Evaluation of both groups showed 11% of data missing. Non-compliance to protocol is a point of interest, both for the safety of patients and for the (legal) safety of nurses and deserves further attention and warrants caution when implementing nurse-driven protocols.

Nurses in this study were asked to perform haemodynamic, respiratory and neurological controls one, two and four hours after a nurse-driven intervention is performed. In our study, the two and four-hour measurement points often were lacking from our database which creates possible safety issues for patients in using a nurse driven protocol.

Limitations and conclusion of our study

We did not measure anxiety in the peri-operative period. Combining pain and anxiety might deliver more information about patient's response to stress and pain after cardiac surgery. This might also give further insight to the responses of patients to pain and pain management programs.

Measuring pain and or discomfort of patients directly after surgery, while being intubated, remains a point of concern. Very few VAS scores were available within the first 24 hours post surgery. This is mainly due to using the Richmond Agitate and Sedation Scale (RASS) for evaluation at the ICU because the patients post surgery are still mechanically ventilated and requiring sedation.[29, 30] If possible, VAS scores were obtained at the intensive care unit. However because of a lack of data we choose not to discuss these scores within this study.

In conclusion, this study shows that in post-cardiac surgery patients, by using a nurse-driven pain protocol, an absolute reduction of VAS score can be realised together with a reduction in elapsed time to achieve an acceptable pain score. Furthermore, the implemented protocol not only showed to be effective but was found to be safe as well.

Conflict of interest

We have no conflict of interest to report.

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08

REAL-LIFE PERFORMANCE OF A NURSE-DRIVEN PAIN PROTOCOL AFTER CARDIAC SURGERY A 6-YEAR EXPERIENCE

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Submitted

ABSTRACT

Background: This study investigates the real-life performance of a nurse-driven pain protocol during a six-year period, with emphasis on effectiveness of the protocol and protocol adherence. The protocol allows nurses to administer morphine without consulting a physician after cardiac surgery.

Methods: Between 2008 and 2015 a single-centre prospective consecutive cohort study was performed. The study was carried out on a cardiothoracic nursing ward during the first 72 hours after surgery. The protocol was the standard of care and used in all cardiac surgery patients fitting the criteria. The group of postoperative cardiac surgery patients evaluated during this 6-year period consisted of 4415 patients. The effectiveness of the protocol was compared to a cohort of patients operated on in the 2-year period before the introduction of the protocol (N=1535).

Results: Patients from the intervention group had a median VAS score of 1.6 compared to a median of 2.0 in the control group (P<0.001). In both groups, 60% of patients had at least one VAS score of 4.0 or higher. Administrative adherence to protocol was poor, 10% of required data was retrievable in the patient data management system (PDMS) after an intervention

Conclusions: A nurse-driven pain protocol resulted in sustained lower VAS scores after cardiac surgery, compared to a standardised physician-driven pain protocol. This was sustained throughout the investigated period. However, administrative adherence to this pain management protocol was poor during the study period.

INTRODUCTION

In the Netherlands, over 19,000 patients undergo cardiac surgery each year.(1) Although patients often describe pain after cardiac surgery as severe, effective pain management after cardiac surgery remains cumbersome.(2) Adequate pain management is crucial in patient care and helps to reduce postoperative morbidity and mortality.(2-5) After cardiac surgery, pain is described to be most severe in the first 48 hours. After this period pain decreases rapidly.(6-8) Therefore, a protocol was developed and implemented in order to enable nurses to administer pain medication to postoperative cardiac surgery patients without the prior consultation of an attending physician or nurse practitioner based on patient's rating of their pain. The pilot study showed a 21% reduction in Visual Analog Scale (VAS) score and a faster reduction in VAS score compared to a historical group. No safety issues were found.(9) The aim of the current study is to investigate the results of our nurse driven pain protocol over a prolonged (six years) time period. This is a study with emphasis on the effectiveness of the protocol in reducing postoperative pain, protocol adherence by nurses and performance of the protocol in different patient groups after cardiac surgery.

METHODS

Study design

Between 2010 and 2016 (72 months), a single-centre prospective consecutive cohort study was performed. The group of postoperative cardiac surgery patients evaluated during this 6-year time period is called the intervention group (N= 4415). Effectiveness of the protocol in daily patient care was compared to a cohort of patients operated in the 2-year period (2007-2008) prior to the introduction of the protocol (N=1535). This control group had been treated according to conventional physician-driven pain management regime. The intervention group of the pilot study is not included in this study, based on the fact that the pilot study does not reflect a real life situation. In both groups data was acquired prospectively.

Study period and setting

The study period spanned a period of 8 years. During the enrollment period there were no major changes in either surgical or anaesthesia techniques. Data were collected during the first 72 hours after the patients' admission to the medium care unit. This is a surgical ward with the option to perform continuous monitoring of heart rate and cardiac rhythm.

Study groups

In both groups, only patients with an intensive care stay shorter than 24 hours were included to assure the most homogenous group of patients. Baseline data for both groups, including comorbidities such as left ventricular function, previous surgery and emergency surgery, were collected. Furthermore, surgical variables, known to influence pain, were collected, such as the type of surgery.(10, 11) Pain scores were collected using VAS, as advised in guidelines for

acute pain management.(12-15) A VAS of 4.0 or higher was scored as significant pain (scores were measured in steps of 0.1). The EuroSCORE® risk model, based on logistic regression, was calculated to provide insight into the mortality risk and the comorbidities in the cohort.(16) All patients included in the study were adults.

The protocol was started in all patients after suitability of the patient was assessed by either physician or nurse practitioner. A prescription for morphine formalised the consent. This prescription stated that morphine would be administered according to the pain protocol. Exclusion criteria were an intensive care stay of more than 24 hours, haemodynamic instability, signs of neurological deficit or postoperative delirium.

Review board and standard of care

The protocol was standard of care in our department during the entire study period. Study approval was obtained from our institutional review board. The need for informed consent was waived (MEC 2009-412).

Pain management

In both groups, a regimen of acetaminophen (1000mg administered orally or rectal four times a day) was initiated on arrival on the ward.

The pain treatment regime in the *control group*, besides the acetaminophen, consisted of, morphine. Prescribed by the attending physician in a routine of 7.5mg, administered subcutaneously four times a day or if needed. The morphine was administered by the ward nurses based on VAS scores and at their discretion. VAS scores were obtained three times a day at fixed time points and were registered in a patient data management system (PDMS).

The pain treatment regime in the *intervention group* was based on a nurse-driven pain protocol (see Appendix 1) that allowed nurses to administer analgesic medication autonomously. The protocol starts when patients arrive at the medium care unit after ICU discharge. After obtaining a basic data set of haemodynamic, respiratory and neurological parameters, nurses can intervene with a weight-adjusted dosage of morphine when VAS scores are 4.0 or higher. The protocol also includes safety parameters, such as limiting the dose to 0.2 mg/kg of morphine per 8-hour shift and alerting a physician or nurse practitioner of hypotension with a systolic blood pressure below 100 mmHg.(9) When acute postoperative pain was persisting or considered atypical, a medical or nurse practitioner was consulted. Haemodynamic and pulmonary assessments were performed according to the standard of care. The Ramsay score, a numerical rating scale on which sedation levels can be measured and compared, was used to evaluate whether it was safe to administer morphine.(17)

Duration of protocol

The flowchart and registration of measurements were ended 72 hours after admission to the medium care unit. The protocol could be ended earlier if a patient needed more pain medication than a nurse was allowed to offer based on the protocol. The protocol was also ended when patients were re-admitted to an intensive care unit, for any reason.

Safety and effectiveness of protocol

Safety was monitored according to the mandatory perioperative complication registry of our department. The protocol's effectiveness was assessed in three ways. First, by measuring the percentage of patients who experienced significant pain at least once in the first 72 hours after admission to the ward. Second, by comparing median VAS scores in the intervention group with the control group. Third, by assessing the swiftness of pain relief per 8-hour time period.

Protocol adherence

Initially, adherence was measured by retrieving data from the PDMS, this is co called administrative adherence. This data contained the number of times VAS assessment was performed and blood pressure, pulse, oxygen saturation and Ramsay score. For each obtained parameter, the time of entering the data into the PDMS was also observed.

In each case of VAS greater or equal to 4.0, a response was expected within one hour. The result of this response should be within 1 to 2 hours (Appendix 1). In the case of VAS scores lower than 4.0, a new response was expected within 8 hours. Concerning the other parameters, the PDMS was searched for parameters within 1 hour after admittance to the ward and after 1 to 2 hours after a VAS greater or equal to 4.0.

In addition, a select number of patients were randomly selected and each nurse driven intervention was investigated with regard to protocol adherence and correct doses of morphine.

Lastly, semi-structured interviews were held with ward nurses to examine their attitudes towards the protocol and protocol adherence.

Potential risk factors associated with pain

The variables that were considered as potential risk factors for pain are shown in Table 1 and Table 2.

Statistical and additional analyses

Unpaired T-tests were used for continuous data (range, median and standard deviation). Non-normally distributed data (Kolmogorov-Smirnov test) were compared using the Mann-Whitney U-test. Categorical data are presented as frequencies and were compared using the Chi-Square test or the Fisher Exact test where appropriate.

To compare both groups, VAS scores were evaluated per group, per year and per standardised postoperative time point (every 8 hours during the 72 first hours on the ward). The effectiveness of the nurse-driven flowchart protocol was also compared by assessing all pain scores per patient. One measure of effectiveness is the swiftness of pain relief. Patients were considered to have pain if the VAS score was 4.0 or higher. The subsequent VAS scores (1st measurement versus 2nd measurement, 2nd versus 3rd, etc) were compared to assess the relief of pain (paired analyses). These scores were used to assess the percentage of patients with pain at each interval of 8 hours. Multivariate logistic analysis was performed to search for factors associated with pain after cardiac surgery. All significant variables were forced into the model. VAS score of ≥4.0 (having pain) was considered as the end point for the logistic regression analyses. Odds ratios (OR) and corresponding 95% confidence intervals (CI) are reported. A p-value of ≤0.05 was set to represent statistical significance. All data analyses were performed using SPSS version 23 (IBM, Armonk, NY, USA).

RESULTS

A total of 5950 consecutive patients were enrolled in this study. Between 2010 and 2016, a total of 4415 (74.2%) patients were treated according to the nurse-driven flowchart protocol (*intervention group*). The *control group* (n = 1535, 25.8%) was treated according to a physician-driven pain management approach (inclusion period 2007-2008). Significant differences were found in baseline characteristics between the intervention and control group for COPD, left ventricular function and logistic EuroSCORE(p=0.01, p=0.01 and p<0.001, respectively). Both groups predominantly consisted of men (66% and 68%, intervention and control group, respectively), the mean age was 63 years in both groups (intervention group SD 13.8 and range 18-82 years, control group SD 13.6 and range 17-84 years). Left ventricular function was good in the majority of patients (67.3% and 68.4%, intervention and control group, respectively)(Table 1).

Safety and effectiveness of protocol

There was one directly related morphine intoxication as a result of a pharmacological intervention by a nurse which required a gift of naloxon.

A non-significant number of patients (60% in both groups) reported a VAS score of 4.0 or higher within this time period. The median VAS score between the groups was significantly different (1.6 versus 2.0, P<0.001). Median VAS scores (in 8 hours blocks) during the 72 hour period of the protocol are shown in Figure 1.The percentage of patients with pain after 8 hours did not significantly differ in both groups (44% (control group) and 45% (intervention group), respectively). Further examination of the mean VAS scores during the first 72 hours on the ward showed that patients experienced the highest pain scores in the first 24 hours after their admission to the ward (Figure 2). After this period, VAS scores decreased rapidly.

TABLE 1: Characteristics of the control group and intervention group.

	Control group	Intervention group	P-value
	N = 1535	N = 4415	
Clinical presentation			
Age (mean [SD]) (years)	63 [13.6](18-84)	63 [13.8] (18-82)	0.64
Male	1013 (66%)	3002 (68%)	0.31
COPD	138 (9%)	525 (11.9%)	0.01
Creatinine (µmol/l)	94	93	0.31
Cerebrovascular accident history	63 (4.1%)	225 (5.1%)	0.10
Diabetes mellitus	304 (19.8%)	892 (20.2%)	0.08
Logistic EuroSCORE®	4.9	5.3	<0.001
Left ventricular function			0.01
Good	1035 (67.4%)	3020 (68.4%)	
Impaired	320 (20.9%)	772 (17.5%)	
Moderate	180 (11.7%)	623 (14.1%)	
Type of surgery			
CABG only	694 (45.3%)	1964 (44.5%)	0.28
CABG and valve	186 (12.2%)	486 (11.0%)	0.18
Congenital	39 (2.6%)	159 (3.6%)	0.09
Great vessels	208 (13.6%)	698 (15.8%)	0.11
Valve	357 (23.3%)	1002 (22.7%)	0.23
Other	51 (3.3%)	106 (2.4%)	0.36

Abbreviations: COPD: Chronic obstructive pulmonary disease, CABG: Coronary artery bypass graft.

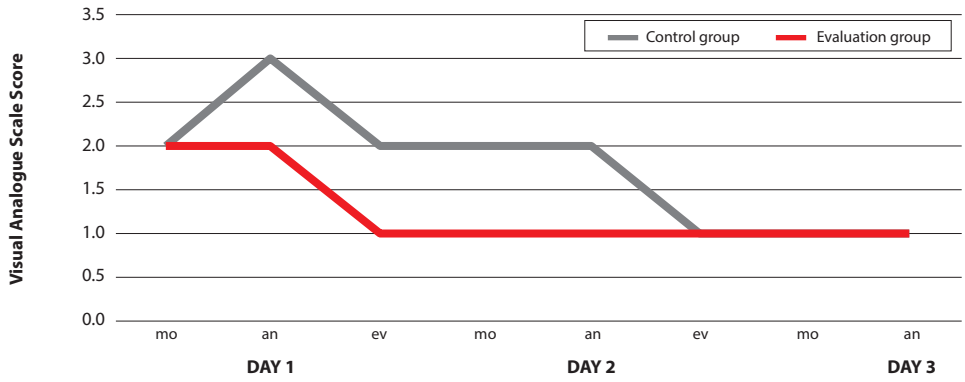
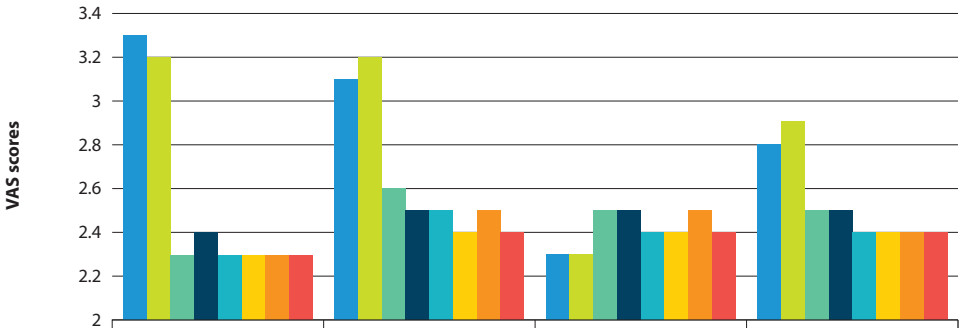


FIGURE 1. Distribution of median pain scores during the first 72 hours on the ward.



	Day 1	Day 2	Day 3	Average VAS score
2007	3.3	3.1	2.3	2.8
2008	3.2	3.2	2.3	2.9
2010	2.3	2.6	2.5	2.5
2011	2.4	2.5	2.5	2.4
2012	2.3	2.5	2.4	2.4
2013	2.3	2.4	2.4	2.4
2014	2.3	2.5	2.5	2.4
2015	2.3	2.4	2.4	2.4

FIGURE 2. Mean VAS scores per day in the 72 hours of protocol, measured over an 8-year period. Abbreviation: VAS = Visual Analogue Scale

Factors associated with pain

Higher pain scores were seen in male patients, younger patients, patients with impaired left ventricular function and those having higher logistic EUROscores. Furthermore, patients without a history of COPD or unstable angina had higher pain scores. Lastly, patients requiring emergency surgery had significantly higher pain scores (Table 2).

Protocol adherence

Initially, administrative adherence was measured by retrieving data from the PDMS. For 97% of patients, we could retrieve at least 3 VAS scores and blood pressure scores per day. It was also mandatory to register VAS scores after an intervention (meaning a morphine gift), but we were only able to retrieve those measurements in 10% after an intervention. The results for respiration rate and Ramsay scores were registered even more poorly; less than 1% was retrievable for both scores.

A number of 68 patients (70 interventions in this group) were randomly selected in order to assess the associated nurse-driven interventions. We checked all interventions in the PDMS for the necessary protocol variables and the correct dosages. Of these 70 interventions, 13 interventions showed irregularities. In 3 cases, the attending nurse administered more morphine than suggested by the protocol. In 10 cases, less morphine was administered than suggested by the protocol. The range of error varied between 1mg of morphine too little to 1mg of morphine too much.

To further examine data registration, a semi-structured interview session with five staff nurses was performed. All nurses agreed that the use of Ramsay score was very limited. They considered that interacting with the patient gave them enough insight into whether an additional dose of morphine would be safe. The nurses declared that they did look at the respiratory rates of patients before administering morphine. The consensus of the interviewed nurses was that time constraints prevented them from entering the data into the patient files.

TABLE 2: Multivariate analysis of predictors of pain after cardiac surgery.

	Odds Ratio	95% CI
Male	1.436	1.249-1.652
Age	0.984	0.979-0.989
Logistic EuroSCORE®	0.926	0.903-0.949
COPD	0.721	0.589-0.883
LVEF	0.912	0.836-0.995
Emergency surgery	1.188	1.060-1.331
Unstable angina pectoris	0.619	0.470-0.814

Abbreviation: COPD: Chronic Obstructive Pulmonary Disease, LVEF: Left Ventricular Ejection Fraction.

DISCUSSION

The results of this study show that a nurse-driven protocol with a tailored pain medication regime can result in less pain after cardiac surgery. However, it is also clear that administrative protocol adherence in time can become a challenge.

Pain

This study shows that the nurse driven protocol was more capable of reducing the intense pain in the first 48 hours after cardiac surgery compared to a physician-driven fixed dosage protocol. Pain scores towards the end of the 72 hours were low in both the intervention and control group. The higher VAS scores on day 1 and 2 can be contributed to the mobilisation of patients after surgery on day 1 and removal of wound drains on day 2. Further lowering pain scores around these periods should be a priority. These findings highlight the need to keep a vigilant pain monitoring system in place to facilitate early interventions to reduce pain.

Safety and effectiveness of protocol

Concerning the safety of the protocol, we assessed non-compliance by investigating the electronic records of all patients involved. In the pilot study, a non-compliance rate of 11% was observed. We concluded that this had potentially negative consequences for patient safety and

legal responsibility of nurses.(9) In the current study, non-compliance was poorer, both with regard to data registered as well as irregularities in dosages of morphine. Hence, it remains important to monitor and study protocol adherence further. It is also important to investigate how data entry can be made easier. Improving correct administration of the required flowchart data is difficult. The burden of checklists and bureaucracy seems to play a role in the poor administrative adherence.(18) Nurses in this study complained of time constraints in having to fill in the checklists and other paperwork not directly related to the patients.

Moreover, focussing on younger patients undergoing emergency surgery and on the pain induced by early mobilisation and the removal of thoracic drain-tubes seems useful to achieve and maintain lower pain scores after surgery.

In 19% of the pharmacological interventions (morphine administered by nurses), there was a discrepancy between the actual dosage and the dosage the protocol prescribed. The protocol offers two options: 0.1 or 0.05 mg morphine per kg of body weight. Some of the discrepancies can be attributed to weight averaging. The protocol averages the dose per 10 kg of body weight and is not clear whether to use preoperative body weight or the body weight at the time of administration. There is often a discrepancy of several kilogrammes because patients retain fluid after cardiac surgery. This phenomenon has been known for many years and is attributed to cardiopulmonary bypass use and hormone system activation.(19) In our hospital, the preoperative weight was chosen to use as the correct weight.

During the 6 years the intervention protocol was running, only one directly related morphine intoxication as a result of the pharmacological interventions by nurses occurred. In this case, the dosage of morphine was given despite rapid onset of acute-on-chronic kidney failure resulting in respiratory rate depression. This incident shows the importance of daily assessment of patients and their medication by clinicians. According to the guidelines, the usage of opiates should be short term and reassessed daily.(20, 21) The dosage of morphine in a patient with acute kidney failure may better be prescribed by a competent physician.

Risk factors for pain

The multivariate analysis of our cohort showed several discrepancies between our results and earlier studies. A recent study showed that being female or having younger age is associated with more postoperative pain.(2) Our study also found lower age as an independent predictor of more intense postoperative pain. However, being a woman was not associated with higher VAS scores in the large cohort of patients within this study. The relationship between pain and age was investigated by others as well, and their results show more pain for older patients.(22, 23) This proves that the relationship between sex, age and pain is difficult to explain. In-depth analysis of a large patient group could give more insight into these relationships. The nature of this study does not make it possible to do such an analysis. Another factor that can affect pain after surgery is sleep quality. This relationship has not often been investigated, but a small study from our Institute showed that quality of sleep and pain have an adverse influence on each

other. (24) Another issue that we did not take into account was the preoperative use of pain medication. Although, literature suggests that patients who were already using pain medication before surgery experienced more pain after surgery.(2)

The opinion of nurses

The experiences and views of nurses about the protocol were assessed during semi-structured interviews. The nurses concluded that the nurse-driven protocol enhanced the possibilities to optimise patient care. However, the nurses also state that they are under time constraints and that the protocol does not appreciate the clinical experience of nurses in assessing a patient before performing an intervention. Relying on this clinical experience can, however, cause problems in not correctly identifying patients at risk of an overdose (as shown in the patient with acute-on-chronic kidney failure) and puts nurses at risk for legal consequences. Following the protocol remains essential in providing safe and efficient care for patients.

Strengths and limitations

This study has a large cohort of patients and shows the performance of protocol over a prolonged period of six years. It also shows the strength and weaknesses of standardised protocols in patient care.

There are, however, limitations. Data was gathered from a patient data management system and was, therefore, not systematically collected. Furthermore, only a limited sample of patients was studied in-depth which could creat a selection bias. However, these patients were selected randomly to minimize the bias as much as possible. In addition, there were differences at baseline between the intervention group and the control with regard to COPD, left ventricular function and logistic EuroSCORE. This study did not take into account the effects of changes to the pain protocol in the intensive care unit, which were initiated at the same time as a separate part of the new pain protocol and which could influence initial pain scores on the ward. (9)

CONCLUSIONS

A nurse-driven pain protocol is associated with lower average VAS scores compared to a standardised physician-driven pain protocol, a change that is sustained even after 6 years of use. However, administrative adherence to this flowchart-driven pain management protocol was poor during the 6-year period of our study, which resulted in more patients with pain, slower pain relief for patients and variation in drug dosing. Maintaining a safe and adequate pain management system may be aided by making it easier for attending nurses to use IT tools, combined with an ongoing effort from the hospital organisation and the nurses to improve and use such systems for patient care purposes.

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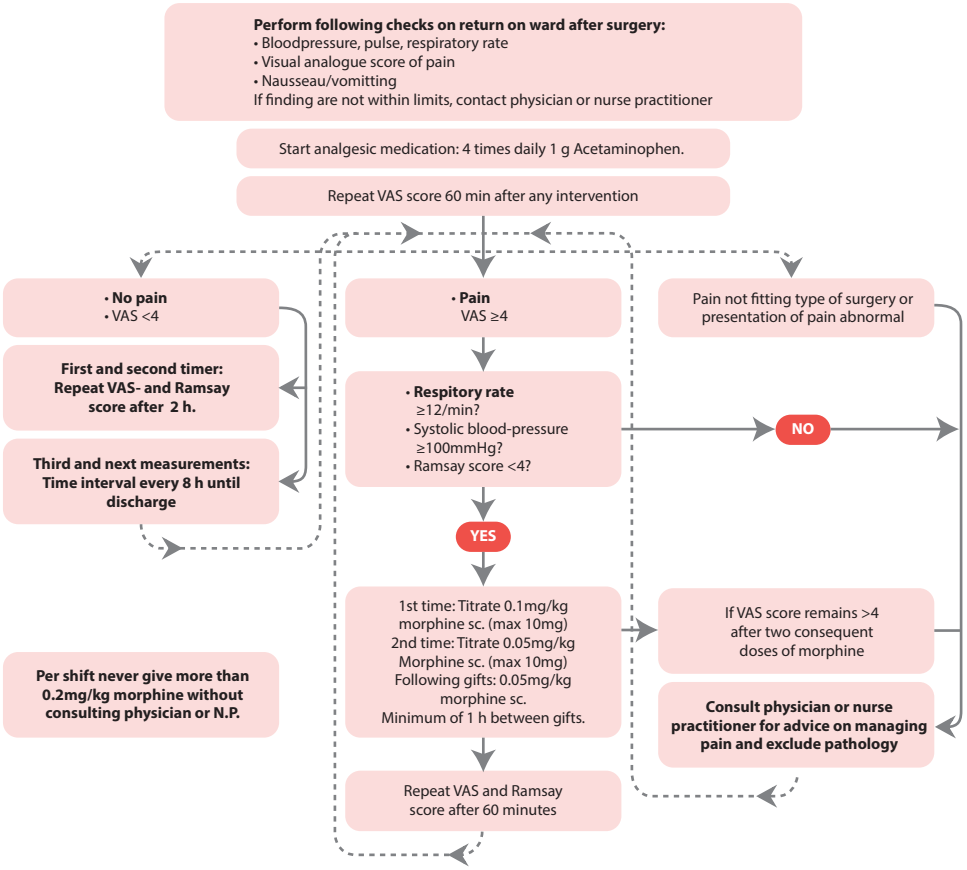

Ramsay score	
1. Agitation	Agitated
2. Awake	Cooperative, aware
3. Optimum	Follows commands
4. Optimum	Quick response
5. Slow	Slow response
6. Sedated	No response

Morphine dosage			
weight	**0,05 mg/kg**	**0.1 mg/kg**	**weight**
40-49	2.2 mg	4.4 mg	40-49
50-59	2.7 mg	5.4 mg	50-59
60-69	3.2 mg	6.4 mg	60-69
70-79	3.7 mg	7.4 mg	70-79
80-89	4.2 mg	8.4 mg	80-89
90-99	4.7 mg	9.5 mg	90-99
>100	5.0 mg	10 mg	>100

APPENDIX 1. Medium Care Cardio-thoracic surgery. Patients with epidural pain medication are excluded from this protocol

09

QUALITY OF SLEEP AT THE WARD AFTER CARDIOTHORACIC SURGERY

J. Pröpper, R. van Valen, R.T. van Domburg, M. Brunott, A.J.J.C. Bogers

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ABSTRACT

Objective: Sleeping problems are among the issues most mentioned by patients after cardiothoracic surgery. These problems can have a negative effect on duration of the hospital stay and recovery. In the ward of our cardiothoracic surgery department, a study was initiated to assess the quality of sleep after cardiothoracic surgery. The primary objective was to investigate the effect of cardiothoracic surgery on the quality of sleep. The secondary objective was to investigate the quality of sleep. Correlations with perioperative factors and related issues such as the type of surgery and medication were sought.

Methods: A consecutive prospective cohort study was initiated (n=72). The study used validated questionnaires to assess sleep: the Pittsburgh Sleep Quality Index (PSQI), the Epworth Sleepiness Scale (ESS), the Verran Snyder-Halpern Sleep Scale (VSH) and the Factors Influencing Sleep Quality (FISQ).

Results: The PSQI showed that the quality of sleep one month after surgery was inferior to the quality of sleep before surgery (p-value: 0.03). The efficiency of sleep (time spent in bed) was higher after surgery than before surgery (p-value: 0.01). The VSH showed increased impaired sleep on the third night after surgery. The most disruptive factors were not being comfortable in a hospital bed, pain and the noise of medical devices.

Conclusions: The quality of sleep after cardiothoracic surgery is worse when compared with the preoperative situation. The main influencing factors are discomfort in bed, pain and disturbance from medical devices. The use of pain medication does not improve the quality of sleep.

INTRODUCTION

Although cardiothoracic surgery has led to improvements in life expectancy and quality of life for patients suffering from an array of cardiovascular problems and thoracic diseases, the quality of life after surgery is still negatively influenced by a number of factors. An important aspect of the quality of life is the quality of sleep, defined as a period of inactivity and the absence of consciousness. (1, 3) Lack of sleep influences the quality of life and well-being of patients. (1) Sleep deprivation, the lower overall sleep time and disturbance of sleep are common problems during either acute or chronic illness [2]. Surgical patients experience more sleeping problems than medical (nonsurgical) patients, with the exception of psychiatric patients. (3-4)

In the Netherlands each year about 19,000 patients undergo cardiac surgery. This kind of surgery is centralised in 16 hospitals. The Department of Cardiothoracic Surgery at the Erasmus University Medical Centre performs 1100 cardiac procedures and 350 thoracic procedures per year.

The department's protocol at the time of this study consisted of sleep medication on request by patients. Daily complaints by patients and a lack of recent literature into this relevant clinical problem constituted the basis of this study.

Earlier studies in patients undergoing cardiac surgery show that sleeping problems after surgery were a common complaint.(5, 8) The low quality of sleep and sleep deprivation lead to fatigue, sleepiness and a slower recovery, longer hospital stays and poor quality of life. (6, 9) Furthermore, it has been shown that poor quality of sleep increases the risk for the development of postoperative delirium in thoracic patients. It has also been demonstrated that the quality of sleep is related to a longer stay in hospital after surgical procedures. (9-11)

The aim of this study was to investigate the effect of cardiac or thoracic surgery on the quality of sleep using four validated questionnaires (PSQI, ESS, VSH and FISQ). The secondary aims were to determine what factors influenced sleep and the effects of hypnotics and pain medication on the quality of sleep. Furthermore, in order to assess the quality of sleep of our patients objectively, a comparison was made with the quality of sleep in the general population.

Cardiac surgery is here defined as any surgical procedure involving the heart and the thoracic aorta, which is performed to correct acquired or congenital defects, replace or repair diseased valves or bypass blocked vessels.

Thoracic surgery is here defined as any surgical procedure involving organs with the exception of the heart and thoracic aorta located in the thorax or chest.

METHODS

Study setting and design

Between January 1, 2013, and May 5, 2013, all consecutive patients meeting the inclusion criteria (>18 years old and capable of reading and answering questionnaires in Dutch) were included in this prospective study. All patients signed informed consent. The data was collected during the hospital stay of patients in the ward of the Department of Cardiothoracic Surgery and after discharge. There was a total of five measuring moments. Data was collected by using a flowchart which was applied to all patients (Figure 1). The day before surgery (T0) the first questionnaires were answered (PSQI and ESS). After discharge from intensive care and return to the ward at consecutive measuring moments T1 (first day after surgery), T2 (second day after surgery) and T3 (third day after surgery) the ESS, VSH and FISQ questionnaires were answered by patients. Three weeks after surgery all patients received the last questionnaires (PSQI and ESS) by mail at their home addresses (T4). If there was no reply within two weeks, the patients were called to remind them to answer the last questionnaires. The general and surgical details were retrieved from the electronic data management system. A total of 200 patients were asked to participate in this study, and of this population 72 (36%) patients agreed to participate. The complete study protocol was followed by 48 (67%) patients of this group. During the clinical period, data (T1, T2 and T3) were not completed by 24 (33%) patients. The loss of seven (10%) patients was due to complications, such as delirium, ischemic stroke or critical illness, but the major part of the lost data was due to patients not answering the clinical questionnaires, six (8%) patients listed pain as the reason for not answering the questionnaires, 2wo (3%) were too tired and another six (8%)

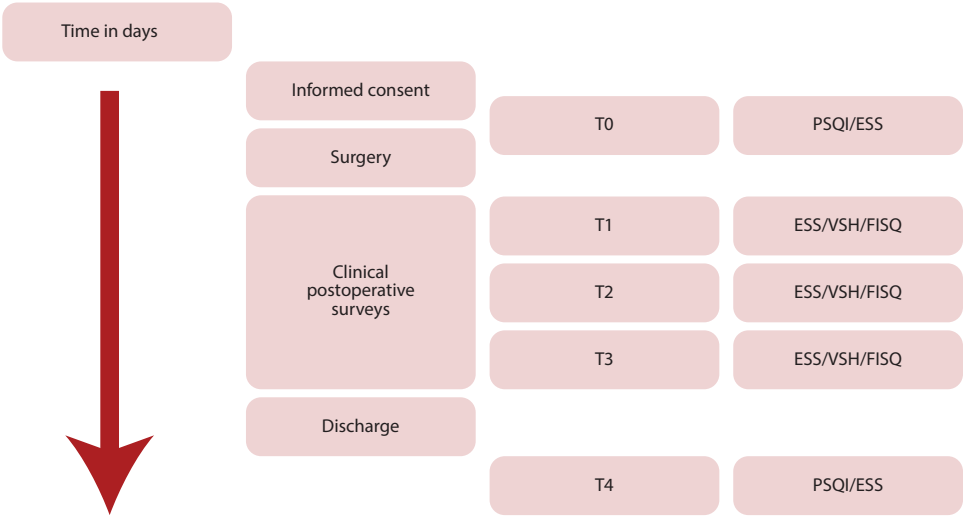

FIGURE 1. Oversight data-collection: T0 = before surgery; T1 = moment 1 after surgery; T2 = moment 2 after surgery; T3 = moment 3; T4 = moment 4 (one month after surgery). PSQI: Pittsburg Sleep Quality index; ESS: Epworth Sleepiness Scale; VSH: Verran Snyder-Halpem Sleep Scale; FISQ: Factors Influencing Sleep Quality.

patients forgot or were unable to return the needed forms. The outpatient data was retrieved for 56 (78%) pat
missing patients who were still admitted to hospital did not fit the research protocol. The other patients (19%) d
despite two attempts to invite them to participate.

The questionnaires

The following questionnaires were used to assess the quality of sleep in our patient population.

The Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index (PSQI) is a validated questionnaire and investigates different aspects of s
sleep, sleep disturbance, sleep latency, day dysfunction due to sleepiness, sleep efficiency, overall sleep qualit
medication. (12, 13) There are also questions for the partner of the patient, but these are not mandatory for c
index is used to interpret the quality of sleep during a 1-month period. A higher score indicates a worse quality

The Epworth Sleepiness Scale

The Epworth Sleepiness Scale (ESS) is also a questionnaire that is validated in Dutch and comprises eight questior
This scale was used to evaluate sleepiness in a clinical environment in an earlier study. (14) A score of more tha
sleepiness.

The factors influencing sleep quality

The Factors Influencing Sleep Quality (FISQ) is a questionnaire which is used to determine which variables in
hospital admission. The scale was validated in 1985 and demonstrated high validity in a previous study abo
surgery. (3, 15-16) The scale ranges from 0 (no disturbance) to 4 (extreme disturbance). The maximum score po
lowest possible score is 0.71.

The Verran Snyder-Halpern Sleep Scale

The Verran Snyder-Halpern Sleep Scale (VSH) is a scale which has been used in several studies of the quality of s
surgery patients. (17) It comprises of 15 questions and measures the disturbance of sleep, the efficacy of sleep an
sleep (sleeping during daytime). The scale was validated in 1987. For the disturbance of sleep the scale range
(bad), for efficacy of sleep from 0 (bad) to 40 (good) and need for additional sleep from 0 (good) to 40 (bad).

Statistical methods

The Statistical Package for Social Sciences version 20 (SPSS) was used for all statistical analysis. Variables were compared using an unpaired Student's t-test. A Chi-square test was used for categorical variables. Data are presented as percentages unless indicated otherwise. A p-value<0.05 was thought to represent statistical significance. ANOVA for repeated measurements was used for data collected at sequential measuring moments.

Ethics

The local Medical Ethics Committee of the Erasmus Medical Centre approved the study (MEC 2012-576).

RESULTS

The population predominantly consisted of males (81%) undergoing cardiac surgery. The most prevalent comorbidities among participating patients consisted of hypertension (35%), diabetes mellitus type II (15%) and previous myocardial infarction (13%) (Table 1). There was hardly any preoperative use of hypnotics (1%) or anxiolytics (6%).

PSQI

The quality of sleep four weeks post-surgery was rated lower than the quality of sleep before surgery (p-value: 0.03). This is calculated by comparing the total score on the day before surgery with that on Day 30 after surgery. The sleep efficiency (time spent in bed) at four weeks was higher in comparison to T0 (p-value: 0.01; Figure 2). When comparing the results of this study cohort to the results of the control group in the original validating cohort study, patients before and up to one month after surgery scored worse than the control group (the control group total score was 2.67 and the study group total scores were 5.9 and 6.7 at T0 and T4). (12)

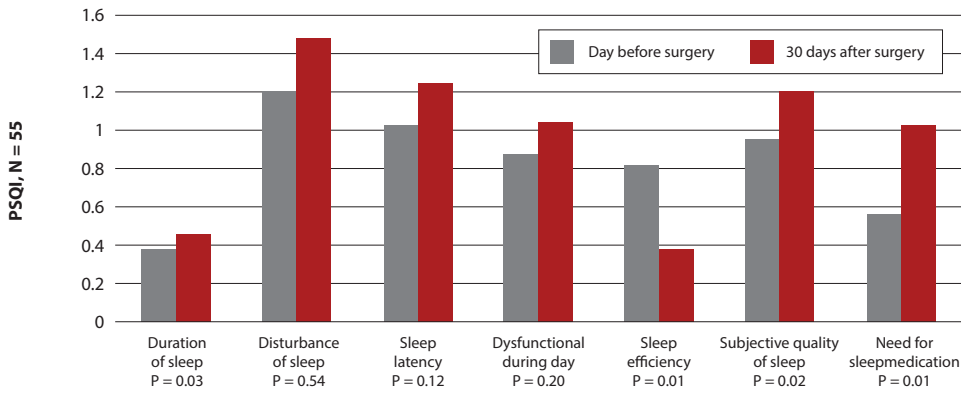

FIGURE 2. PSQI scores at the day before surgery and 30 days after surgery. Higher scores mean poorer quality of sleep. PSQI: Pittsburg Sleep Quality Index

TABLE 1. Demographic characteristics of patients. SD: Standard deviation, N: number of patients

Patient Characteristics (%)	
Male	81
Age, average (SD)	58 (14)
Body Mass Index, average (SD)	27 (5)
Medical History	
Atrial fibrillation	14
Other cardiac aritmia	1
Chronic obstructive pulmonary disease	8
Obstructive sleep apneu syndrome	3
Other sleep disorders	1
Diabetes mellitus	15
Mycardial infarction	13
Alcohol abuse	1
Heart failure	4
Hypertension	35
Psychiatric history	0
Cerebro-vasculair incident or transcient ischemic accident	10
Renal insufficiency	7
Previous cardiac surgery	10
Previous thoracic surgery	1
Perioperative Factors	
Endocarditis	1
Mediastinitis	0
Reason of Admittance	
Cardiac surgery	82
Lung surgery	14
Other cardio-thoracic surgery	4
Previous Used Sleep Medication, Antipsychotics or Anxiolytica Sleep medication	1
Antipsychotic medication	3
Anxiolytica	6

ESS

This score did not deviate during the five different measurements and was within normal parameters according to the ESS (Table 2).

TABLE 2. ESS: Epworth Sleepiness Scale, N: number, MIS: missing data, SD: standard deviation. A score of >10 indicates sleepiness

ESS	T0 n=73 MIS = 4	T1 n=48 MIS =0	T2 n=48 MIS = 0	T3 n=47 MIS = 0	T4 n=56 MIS = 1
Not sleepy, N (%)	65 (90)	44 (92)	46 (96)	43 (92)	53 (95)
Sleepy, N (%)	3 (4)	4 (8)	2 (4)	4 (8)	2 (4)
Average (SD)	3.7 ± 3.3	4.7 ± 3.4	4.2 ± 2.7	4.5 ± 3.5	3.6 ± 2.6

FISQ

The FISQ (Table 3) showed that the most disturbing factors of sleep were: Not being able or allowed to find a comfortable position in bed, pain and alarm signals from medical equipment.

TABLE 3. FISQ score of >1.44 is moderate to excess of disturbance in sleep. Maximum score possible is 3.54, lowest possible score is 0.71

	T1	T2	T3
Not being comfortable in bed or unable to move	2.85	2.60	2.32
Pain	2.54	2.69	2.11
Not being able to perform normal bed routine	2.27	1.88	1.66
Noise from medical devices	2.19	1.90	2.02
Noises from other patients, like coughing, snoring	2.10	1.81	1.96
Undergoing medical or nurse procedures	1.90	1.85	1.62
Not being in your own bed	1.85	1.79	1.77
Bed making noises	1.79	1.65	1.72
Noise made by healthcare providers	1.71	1.75	1.57

VSH

The results of the VSH showed that the worst overall quality of sleep occurred during the third night after surgery (T3). Disturbances of sleep were mainly seen on the first night after surgery (T1). This is shown in Table 4. Since pain medication is often used in this patient group, scores were divided into scores with and without pain medication. (18)

TABLE 4. Pain medication first night after surgery

T1	With pain medication average, SD n=25	Without pain medication average, SD n=23	p-value
VSH Total quality of sleep	73.6 ± 18.9	70.3 ± 21.3	0.57
Disturbance of sleep	35.4 ± 15.2	38.0 ± 16.1	0.57
Efficacy of sleep	16.1 ± 7.6	18.1 ± 8.0	0.39
Need for extra sleep	17.0 ± 7.1	19.8 ± 7.1	0.19
ESS	4.6 ± 2.7	4.7 ± 4.3	

VSH (Verran Snyder-Halpem Sleep Scale): Total score: lower = worse. Disturbance of sleep: Higher = worse. Sleep efficiency: lower = worse. Need for extra sleep: Higher = worse. ESS (Epworth Sleepiness Scale) Higher scores indicatie more sleepy.

This study also investigated the effect of pain medication and hypnotics on the quality of sleep. Pain medication was the most frequently administered medication (morphine in combination with acetaminophen). On T1 52% of all patients received pain medication, on T2 12% of patients still received pain medication and on the night of T3 10% received pain medication. There seems to be a trend towards a better quality of sleep after pain medication, though this is accompanied by a poorer efficacy of sleep. Analyses of VSH and ESS did not show any significant differences (p-values>0.1).

The administration of sleep medication showed an increase from 6% on T1 to 14% on T2 and then to 25% on T3 (Table 5). Patients receiving sleep medication scored worse on the quality of sleep compared to respondents not using sleep medication. Patients were also scoring lower on the efficacy of sleep and number of disturbances. However, there was no difference in sleepiness during the day.

In this study, not only cardiac surgery patients but also thoracic surgery patients (n=7) were included. The overall trend shows better VSH scores for the thoracic surgery patients. However, the small number of thoracic surgery patients included does not allow generalising about this trend.

TABLE 5. Effect of sleep medication on VSH and ESS on third night after surgery

T3 (third night)	With sleep medication average, SD n=12	Without sleep medication average, SD n=36	p-value
VSH Total quality of sleep	74.3 ± 20.8	79.3 ± 18.5	0.12
Disturbance of sleep	37.2 ± 16.3	34.1 ± 13.6	0.15
Efficacy of sleep	16.2 ± 11.1	18.3 ± 7.6	0.23
Need for extra sleep	14.7 ± 4.8	14.9 ± 5.7	0.81
ESS	3.3 ± 1.8	4.8 ± 3.8	

VSH (Verran Snyder-Halpem Sleep Scale): Total score: lower = worse. Disturbance of sleep: Higher = worse. Sleep efficiency: lower = worse. Need for extra sleep: Higher = worse. ESS (Epworth Sleepiness Scale) Higher scores indicatie more sleepy.

DISCUSSION

This study shows that quality of sleep after cardiothoracic surgery is worse up to one month after surgery compared to the preoperative situation.

Problems with sleep can be measured using VSH, which measures the disturbance of sleep, the efficacy of sleep and need to sleep during the day. That most disturbances are seen on the first night after surgery seems logical. Patients are still attached to wound drainage systems and cardiac surveillance equipment and are often physically examined by nurses and doctors. But the question of why patients experience the worst quality of sleep at night 3 (T3) is harder to answer. Monitor rounds are less frequent and wound drainage systems have been removed. One possible explanation is that not receiving additional pain medication (only 10% of patients still receive pain medication) accounts for the poorer quality of sleep. However, earlier studies in our centre show a decreased need for pain medication at this time. (18)

This effect of poorer sleep can be attributed to limitations after surgery (e.g. not being allowed to sleep on your side, or a different daily schedule).

Further analysis using the ESS (a self-reported measure of sleepiness) showed no deviation from the normal range. This result was unexpected. Patients have undergone major surgery with use of hypnotics and pain medication. It was expected that on day 1 and day 2 patients would experience more sleepiness. Objectifying sleepiness could be included in further research using equipment to either measure actual sleep [14] or by using wrist actigraphy. (19) The last technique has been validated for early detection of delirium by registering the amount of movement by patients and may also provide information on the amount of sleepiness and activity during the night.

Furthermore, the study shows that sleep is disturbed by many factors beyond the control of the patient (the FISQ questionnaire). Nurses should be aware of the disturbances that they cause during the night shift. Furthermore, there should be attention to the problems patients have with positioning and the amount of comfort in bed.

This study shows that these are persistent problems causing sleep issues.

Interventions in both nurses' behaviour but also the physical aspect of the ward need to be given more attention. After implementation of improvements, the results could be studied using the questionnaires of this study.

This study does not incorporate pain scores into the analysis. The department has a nurse-driven protocol which has been shown to result in lower pain scores (according to VAS). (18) The efficacy of pain medication and low VAS scores on the quality of sleep need further investigation. This study shows a trend towards better sleep with pain medication, in contrast with the trend towards worse quality of sleep despite using hypnotics after surgery. This relationship seems contradictory; with less pain, a better quality of sleep should be expected.

The ward comprises a high care and medium care facility. The usual pathway is one night of intensive care after surgery and then referral to the medium care facility. However, 24 patients were admitted to the high care facility after several hours in the ICU and before going to the ward. These patients answered T1 several hours earlier. This could affect the quality of sleep as these patients tended to be in greater pain and require more pain medication.

The poorer quality of sleep seems to continue in the complete follow-up. Comparing the scores to the benchmark set for the normal population continued to demonstrate worse scores. This study did not clarify why this cohort of patients continued to score worse.

A number of patients were unable to follow up for the complete study protocol. From the original 72 included patients only 47 filled in T1, T2 and T3. Using the four questionnaires to assess sleep and the protocol within the timeframe proved to be challenging for both patients and nurses. Therefore, there was an amendment after one week in which a flowchart was given to nurses and patients. The VSH proved to be difficult for most patients.

Redundancy or similarity in questions prompted patients to skip such questions.

In future studies, the usage of the questionnaires will need to be explained more in depth to patients.

Limitations

This study has several limitations. The number of patients enrolled was limited, and this made it harder to generalise the findings of this study to the overall population of cardiothoracic surgery patients. In follow-up studies, more patients should be enrolled in order to investigate sleeping issues after cardiothoracic surgery further.

Furthermore, enrolled subjects had problems with filling out the questionnaires. The redundancy or similarity in questions prompted patients to skip questions. Another reason for not following protocol was the number of questionnaires. This was addressed by a protocol amendment in which the patients and nurses involved received a flowchart with information on the required questionnaires and the timeframe of the questionnaires.

CONCLUSION

In conclusion, the quality of sleep after cardiac or thoracic surgery is poor. The influencing factors are discomfort in bed, pain and disturbance from medical devices. The use of pain medication does not improve the quality of sleep. Patients after cardiac surgery have a poorer quality of sleep than thoracic surgery patients do. Further research into how long these effects continue and if and when patients return to baseline needs to be formulated.

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10

ATRIO-ESOPHAGEAL FISTULA AFTER MINIMALLY INVASIVE VIDEO-ASSISTED EPICARDIAL ABLATION FOR LONE ATRIAL FIBRILLATION

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Thorac cardiovasc Surg, DOI: 10.1055/s-0036-1592436

INTRODUCTION

Minimally invasive video-assisted epicardial beating heart ablation for lone atrial fibrillation (AF) claims to be safe and effective.[1] We, however, report on 3 patients with an atrio-esophageal fistula (AEF) after this procedure.

Case presentation

During a 36 month time period (2013-2015), three patients with AEF after thoracoscopic ablation were treated in a university teaching hospital in the Netherlands. Characteristics of patients and the peri-operative details are shown in Table 1. In all patients, the ablation was done in accordance with the manufacturer's instructions (AtriCure©, West Chester, Ohio, USA).

TABLE 1. Characteristics of the patients and their surgery

	Patient 1	Patient 2	Patient 3
Age	65	67	68
Sex	Female	Male	Male
Type AF	Paroxysmal	Longstanding persistant	Longstanding persistant
Failed catheter ablation	Yes	Yes	Yes
Body mass index	22	27	25
Left ventricular function	Good	Moderate	Moderate
Medical history	Arthritis	Pulmonary embolism	2009 ST elevation myocardial infarction (rescue PCI), Hypertension, Hypercholesterolemia
Logistic Euroscore®	6.1%	3.9%	4.3%
Perioperative data			
Confirmed box lesion	Yes	Yes	Yes
Incision to skin closure time	4 hours 3 minutes	4 hours 25 minutes	3 hours 27 minutes
Length of stay (index surgery)	7 days	6 days	4 days

The first patient presented with signs of cerebrovascular accident 6 weeks after surgery. After admission, she developed heart failure and septic shock. CT showed air in the left atrium and left ventricle, suggestive for air-embolization (Figure 1A and 1B). Ultrasound of the heart showed a severely decreased left ventricular function which was previously normal. The next day her neurological deficit worsened as a result of shock and the treatment was stopped. The patient died the same day. An autopsy was denied. Review of the radiological findings and expert opinion (surgeon, cardiologist and radiologist) showed that an atrio-esophageal fistula was the most likely diagnosis. This was based on the time-path, the severe neurological deficit and the sepsis at presentation.

The second patient collapsed at home after a short period of fever 5 weeks after index surgery. This patient presented with a septic shock and signs of a cerebrovascular accident. His wife reported a short period of fever and later confusion. CT scan showed an indentation in the left atrium at the level of the esophagus (Figure 2A), suggestive for a hematoma due to the fistula. There was also air visualised in the left ventricle (Figure 2B).The decision was made to re-operate this patient despite his poor condition and unknown neurological status. On cardiopulmonary bypass, the fistula was found in the middle of the box created by the previous ablation. The left atrial defect was closed, and the esophagus was reconstructed (see below). The patient had a long and complicated intensive care stay and was admitted to a nursing home 34 days after his redo-surgery with an improved health status but with persistent neurological deficits. One year after the event, he is able to walk with an aid and has short term memory problems but reports a fair quality of life.

The third patient had his index thoracoscopic surgery in a different cardiac centre . He presented 8 weeks after index surgery with fever and developed neurological deficits in a general hospital. He showed progressive myoclonic seizures. The CT showed air in his heart and irregularities in the left atrium (Figure 3A and 3B). Based on our experience in the second patient, immediate surgery was performed in this patient. The fistula was also situated in the centre of the box lesion. The fistula was treated in a similar way by closing the left atrial defect and reconstructing the esophagus (see below). He also had persistent neurological deficits and was discharged to a nursing home. After six months the patient was still in a rehabilitation program with on-going need for nursing care. He was able to perform daily activities with some support and has persistent loss of strength of the left side. This patient was described recently for the Dutch general medical audience.[2]

The surgical approach in the two last cases was similar. Patients were placed on cardiopulmonary bypass. Cannulation for cardiopulmonary bypass (CPB) was performed in the groin. The surgical approach was a right lateral thoracotomy. Directly after the thoracotomy, an intercostal muscle pedicle was prepared for later usage. After initiation of the CPB, the left atrium was opened. The fistula was visualised and directly closed by a double row continuous Prolene® 4-0. The atrium was closed, and CPB support was weaned. After administering protamine and achieving a normal ACT, the area of the fistula was debrided, and the material sent for microbiological culturing. The esophageal part of the fistula was identified and the esophagus repaired in 2 layers with Dexon® stitches. The intercostal muscle pedicle was interposed between the left atrium and esophagus and used to reinforce the esophagus.

Both patients had a second thoracotomy due to empyema in the right chest cavity within three weeks after the surgery for fistula repair. In patient 2 the empyema developed 3 weeks after the thoracotomy. Cultures showed growth of Rothia species. The patient was treated for 6 weeks with moxifloxacin. Patient 3 developed an empyema with Staphyloccocus epidermidis and was treated with vancomycin.

Feeding was initially performed by a jejunal fistula which was placed in both patients. Oral feeding was reinstated after 6 weeks (mainly due to the neurological deficits of both patients).

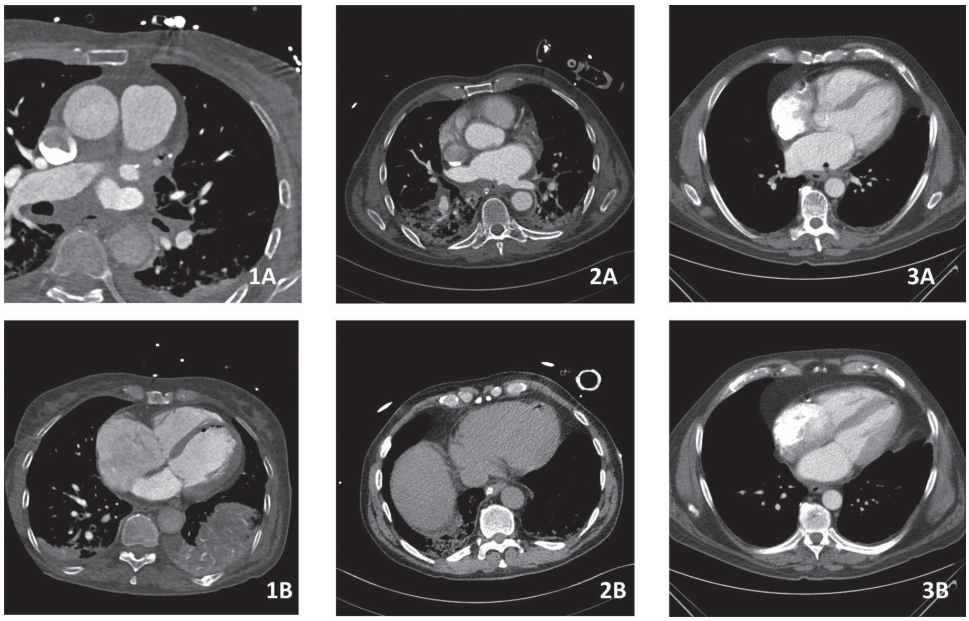

FIGURE 1. Showing air embolization and other CT characteristics in all three patients with AEF

DISCUSSION

Atrio-esophageal fistula first emerged in the field of electrophysiology as a rare complication of catheter-based ablations.[3] This condition is correlated with a high mortality rate of approximately 80%. These patients typically present between 2 and 6 weeks after catheter ablation. Common clinical features include dysphagia, nausea, heartburn, hematemesis or melena, high fever, sepsis, pericardial or pleural effusions, mediastinitis, seizures, and stroke. Survivors of this condition often have significant neurologic deficits as was also observed in the cases in our patient population. It is thought to be secondary to thermal injury along the posterior left atrium in both intra-operative cardiac surgery procedures and percutaneous catheter ablation procedures.

A literature search for this complication in the thoracoscopic surgical cohort only showed three other published cases. Two of these were seen in a small series using a trans-diaphragmatic approach.[4] Another case of atrio-esophageal fistula was reported in a patient undergoing concomitant mitral valve replacement and a MAZE procedure.[5] This procedure was done with a unipolar source. However, informally the issue seems to be better known. At several

national and international meetings, we discussed this complication, and other surgical centres confirmed this infrequent complication (personal communication at national surgical ablation meeting in Nieuwegein, the Netherlands, August 2014). There could be underreporting of this complication based on these findings.

The pathogenesis of this complication is unknown. The close anatomic relationship of the esophagus and the LA is the most important factor responsible for the pathogenesis of esophageal injury during AF catheter ablation. The esophagus is situated directly posterior to the LA, bounded by the aorta on the left and the vertebral column posteriorly.[3] The esophagus follows a variable course and can be found adjacent to the left or right pulmonary veins or the midportion of the posterior left atrial wall. In addition, the posterior LA wall, the fat pad, and connective tissue layer between the LA and the esophagus have variable thickness.[6] In all three patients, there was a normal course of the esophagus. Patients with LA dilatation have thinner fat pads and a larger contact area between the esophagus and the LA. In addition, a normal or lower than normal BMI is associated with a higher chance for damage to the esophageal structures.[7] These findings may be translated to catheter-based interventions. In the surgical based interventions, however, the source of energy is not directed at the esophagus and is applied under direct sight.

Another aspect of interest in this regard is the location and placement of the TEE probe. The probe can cause a hematoma. This is, in general, self-limiting and will manifest itself within 12 hours.[8] Moreover, the probe can act as an antenna and thus will attract energy toward the esophagus. This could cause heat transfer. These topics were discussed by Aryana and others as a result of an atrio-esophageal fistula in their series.[9] In our series, the TEE probe was in situ during the initial part of the procedure but was removed out of the field before the application of energy. Not having the probe in situ doesn't guarantee that fistulae will not form as seen in our series and reported in patients undergoing catheter-based ablations.[10]

CONCLUSION

This short communication discusses 3 cases of AEF after thoracoscopic surgical ablation of lone atrial fibrillation. One of these patients died, due to septicaemia and an infaust neurological prognosis. All patients presented around 6 weeks after surgery with either fever and/or neurological deficits. Diagnosis can be made by CT scan, air in the left sided cavities of the heart is highly suggestive, a secondary finding can be an irregularity in the wall of the left atrium. We advocate an aggressive surgical approach with closure of the atrial defect on cardiopulmonary bypass and closure and reinforcement of the esophagus with an intercostal muscle flap in a single stage surgery. Secondly due to bacteraemia broad antibiotic treatment should be initiated promptly. Due to air-embolization neurological deficits can be expected. This catastrophic complication is very rarely reported in literature, we have encountered three cases, underreporting of this complication cannot be excluded. Some caution as to the low-risk character of this procedure seems to be realistic.

Acknowledgements

We would like to thank Ricardo Budde, MD PhD (radiologist), for his assistance in assessing the CT scans.

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10.1

LETTER TO THE EDITOR I

R. van Valen, C. Kik, M.M. Mokhles, A.J.J.C. Bogers

Thorac Cardiovasc Surg 10.1055/s-0036-1597913

Dear editor,

We have read the letter to the editor concerning our article about atrio-esophageal fistula after thoracoscopic maze surgery with interest.

In this letter the occurrence of this catastrophic complication is attributed to our learning curve and the authors comment on the very rare character of this complication and the absence of this complication in their large series. Some comments from our side.

In our short communication we describe three cases.[1] The last case was from another hospital. The reason for referral to our hospital was our unfortunate "expertise" with this complication. We were somewhat surprised by the apparent need of one of the authors to disclose information about complications in our centre that are not relevant to the key message of this communication and are not mentioned in our report.

We fully agree that the occurrence of an atrio-esophageal fistula after thoracoscopic maze surgery is rare. However, it does happen and early recognition is vital. This is especially important because of the relative long time frame between initial surgery and occurrence of the complication (6 to 8 weeks).

The complication is well known in the cardiology world, as we discuss in the communication. The argument of the authors that the relative inexperience of our centre can play a role, is not relevant for our message. Even more, this procedure is introduced in more centres every day. With this fact, the number of inexperienced operators is growing, potentially leading to a higher chance of occurrence of this complication.

In this light, we advocate that our short communication is seen as a message of caution. Yes, this procedure is the most successful way of treating lone atrial fibrillation. And yes, in experienced hands it is a safe procedure. However, complications do occur and will remain to occur. Making transparency even more vital. The response of two surgeons, who have a financial relationship with Atricure, is off course welcome. It would, however, have been more constructive if these colleagues and Atricure would help to make this very rare complication well known. Giving patients with this complication the best possible chance for survival and quality of life. Cooperation instead of downsizing of the problem is the correct way to go towards truly safe thoracoscopic maze surgery.

So, we stand by our conclusion. The presumed safety of this procedure can be debated and timely recognition of the complication is vital.

R. van Valen, C. Kik, M.M. Mokhles, A.J.J.C. Bogers

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10.2

LETTER TO THE EDITOR II

R. van Valen, C. Kik, M.M. Mokhles, A.J.J.C. Bogers

Thorac Cardiovasc Surg 10.1055/s-0036-1597594

Dear editor,

With interest we read the letter-to-the-Editor by Suwalski regarding our short communication in The Thoracic and Cardiovascular Surgeon.[1] We would like to take the opportunity to response to some of the questions asked.

First of all, we would like to refer to our article and our response to the letter on this subject by van Putte et al.[2]

Once again, not all three patients had their TTMAZE surgery in our centre. This is clearly described in our short communication. Second, our centre has a proven track record, extending over 15 years, in performing surgery for lone atrial fibrillation and concomitant surgery for atrial fibrillation by a dedicated surgeon. In our open procedures, we have never encountered this complication.

We also like to state that the TTMAZE procedures were performed after a formal training and introduction program and were applied according to the instructions given by AtriCure. The difficulty with this complication is the low rate of occurrence and the relatively long time frame between initial surgery and the occurrence of the complication. In this light, we advocate that our communication is seen as a matter of caution. There is a small potential of a highly devastating, even lethal, complication with this procedure. We are convinced that these fistulas are not a single-centre problem. The exact mechanism of this complication remains unclear. As we described, the lesion is seen centrally in the posterior wall of left atrium, away from the ablation lines.[3] The fistula needs several weeks (6–8) to develop and to cause septicaemia and air embolism. This, in our view, seems to exclude a lesion caused by wrongly applied pressure or manipulation of tissue. Moreover, relatives of all the three patients reported well-being of patients until a day or even hours before collapse or neurological impairment. To conclude, we agree that TTMAZE shows good results in treating lone atrial fibrillation. We also agree that the track record of TTMAZE is excellent in high-volume centres.[4] We do, however, warn about the potential complication of an atrio-esophageal fistula and emphasize the need for stringent follow-up of all patients and further research into the pathogenesis of this complication.

Richard van Valen, Charles Kik, Mostafa M. Mokhles, Ad J.J.C. Bogers

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11

PROSTHETIC VALVE ENDOCARDITIS DUE TO *PROPIONIBACTERIUM ACNES*

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N.J. Verkaik, M.M. Mokhles, A.J.J.C. Bogers

Interact Cardiovasc Thorac Surg. 2016 Jul;23(1):150-5

ABSTRACT

Objective: To study the characteristics of patients with *Propionibacterium acnes* (*P. acnes*) prosthetic valve endocarditis (PVE) and required surgery.

Methods: A single-centre retrospective cohort study was conducted during a 7-year period. Patients with definite infective *P. acnes* endocarditis, according to the modified Duke criteria, were included. An extended culture protocol was applied. Information on medical health status, surgery, antibiotic treatment and mortality was obtained.

Results: Thirteen patients fulfilled the criteria for *P. acnes* endocarditis (0.53% of 2466 patients with valve replacement in a 7 year period). All patients were male and had a previous valve replacement. The health status of patients was poor at diagnosis of *P. acnes* PVE. Most patients (11 of 13, 85%) were admitted with signs of heart failure due to a significant paravalvular leak, 2 of 13 (15%) patients presented with septic emboli. Twelve patients needed re-do surgery, while one could be treated with antibiotic therapy only. The time between index surgery and presentation with *P. acnes* PVE varied between 5 and 135 months (median 26.5 months). Replacement and reconstruction of the dysfunctional valve and affected anatomical structures were mainly performed with a mechanical valve (n=5, 42%) or a (bio-)Bentall prosthesis (n=6, 50%). Antibiotic therapy consisted of penicillin with or without rifampicin for 6 weeks after surgery. Mortality in this series was low (n=1, 8%) and no recurrent endocarditis was found during a median follow-up of 38 months.

Conclusion: *P. acnes* PVE is a rare complication after valve surgery. Re-do surgery is often required. Treatment of the dysfunctional prosthetic aortic valve most often consists of root replacement, in combination with antibiotic therapy.

INTRODUCTION

With an incidence of 30 to 100 episodes per million patient-years, endocarditis might be a rare disease, but the risk of adverse outcome is high.(1, 2) The in-hospital mortality is around 20%, and more than one-third of patients will die within the first year of diagnosis, despite advances in diagnostic options, treatment and follow-up.(3-6)

Patients who are especially at risk for developing endocarditis are those who have undergone previous implantation of a prosthetic valve, device or lead. For this reason, prosthetic cardiac valves have been labelled as a predisposing cardiac condition for infectious endocarditis in all the key guidelines.(7)

Prosthetic valve endocarditis (PVE) is a complication with an even higher rate of mortality and morbidity than endocarditis in the absence of prosthetic material. In the literature, it is described as a relatively uncommon clinical entity. The reported incidence of PVE is between 0.3 and 1.2 cases per patient-year. Affecting 1% to 6% of patients with a cardiac valve prosthesis.(8) The mortality ranges between 21% and 74%.(9)

This paper focusses at *Propionibacterium acnes* (*P. acnes*) as the agent responsible for prosthetic valve endocarditis. *P. acnes* is a facultative anaerobic, non-spore-forming Gram-positive rod. It is considered to be normal flora of the human skin, but can also be found on conjunctive, in the oral cavity, intestinal tract and the external auditory canal.(10) This micro-organism tolerates oxygen for several hours and is able to survive in anaerobic conditions up to 8 months in vitro. It can also survive for long periods in human tissues with low oxidation potential.(11) Furthermore, it can resist phagocytosis and persist in macrophages.(12) *P. acnes* is most known as the causative agent of acne. It is generally considered to have a low level of virulence but can cause cerebral, ocular, spinal and postsurgical infections.(13) In cardiac surgery, it is a highly uncommon substrate for primary valve, prosthetic valve or conduit infection, with a description of only around 70 cases in English cardiac surgery literature to date.(14) Among these papers, several case reports and case series are reporting on this bacterium in relation to endocarditis. *P. acnes* seems to have a predilection for prosthetic valves. (15)

We report on our case series of 13 patients over a 7-year period with a proven *P. acnes* prosthetic valve infective endocarditis . To the best of our knowledge, it is the largest single-centre case series described in literature so far.

PATIENTS AND METHODS

Study setting and design

A retrospective study design was used. All patients operated at the Department of Cardiothoracic Surgery at the Erasmus Medical Centre, a large academic teaching hospital in the Netherlands, between January 2008 up to August 2015 were evaluated for the possibility of having *P. acnes* endocarditis. To define infective endocarditis, modified Duke criteria were used.(16) Patients or their legal representatives provided their written informed consent, and the local Medical Ethics Committee of the Erasmus MC approved the study (MEC-2015-232).

Baseline characteristics

Only cases that fulfilled the modified Duke criteria for the diagnosis of definite infective endocarditis were further investigated for index surgery, presentation at re-admission, re-do surgery characteristics, treatment modalities, mortality and outcome parameters such as a new episode of endocarditis, new valvular dehiscence or paravalvular leakage.

RESULTS

Patients

Within the period of investigation, no patients with a native valve *P. acnes* endocarditis were found. In the cohort of patients who underwent valve replacement (n=2466, male 60%) fourteen patients (0.54%) with an implanted cardiac valve prosthesis or conduit were eligible for the diagnosis *P. acnes* prosthetic valve endocarditis. All but one patient fulfilled modified Duke criteria for definite infective endocarditis (11 patients based on pathological criteria with or without clinical criteria; 2 patients based on clinical criteria). The 13 patients underwent their index cardiac surgery between 2002 and 2014. All but one patient underwent re-do surgery in the same centre, while one was treated with antibiotics. Characteristics of these patients and the surgery can be found in Table 1 and in depth in appendix 1.

Patient characteristics at re-do surgery

The 13 patients with definite infective *P. acnes* endocarditis were all male. The average age was 53 years (range 29-70 years) (Table 1). All patients had valve replacement in their history (11 aortic, 1 Bentall and 1 combined aortic and mitral valve replacement), in 2 patients for a congenital defect, in 11 for acquired valvular dysfunction. The time between index surgery and re-do surgery varied greatly (ranging from 5 to 135 months, Table 1 and as depicted in Figure 1). Heart failure based on massive paravalvular leakage of the prosthetic valve was the clinical presentation of the majority of patients (n=11, 85%). All patients were in poor clinical condition, and most of the patients (n=10, 77%) were admitted to a referring hospital before re-admittance at our department. The majority had an NYHA classification of III or IV at presentation (n=10, 77%). The left ventricular function was also poorer than before.

TABLE 1. Demographics finding of patients at index surgery and re-do surgery

	n=13 Index surgery	n=12 Re-do surgery
Clinical presentation		
Age in years (mean [SD]) (range))	53.4 [12.4] (29-70)	58.2[13.3] (30-71)
Male	13 (100%)	12 (100%)
Renal insufficiency (not requiring dialysis)*	2 (16%)	5 (42%)
Left ventricular function		
Good	10 (77%)	6 (50%)
Impaired	2 (15%)	5 (42%)
Poor	1 (8%)	1 (8)
Cerebrovascular accident history	0 (0%)	2 (17%)
Diabetes mellitus	1 (8%)	1 (8%)
Hypertension	5 (38%)	5 (42%)
Logistic EUROSCORE® (mean [SD]) (range))	4.9 [3.7] (10.2)	28.4 [23.6] (77.4)
Type of surgery		
Aortic valve replacement, bioprosthesis	1 (8%)	
Aortic valve replacement, mechanical valve	9 (69%)	4 (33%)
Aortic valve replacement bioprosthesis and CABG		1 (8%)
Mechanical aortic valve replacement and CABG	1 (8%)	
Mechanical aortic valve and root replacement (Bentall)	1 (8%)	4 (33%)
Aortic valve replacement, bioprosthesis, aortic root replacement (bio-Bentall)and CABG		1 (8%)
Bentall and mitral valve plasty		1 (8%)
Aortic and mitral valve replacement, mechanical valves	1 (8%)	
Mitral valve replacement composite valve		1 (8%)
Surgical characteristics		
Cardiopulmonary bypass time mean [SD] (min-max time)	2:15 [0:52] (1:19-4:10)	3:55 [2:05] (1:47-9:07)
Aortic clamp time mean [SD] (min-max time) (hr:min)	1:43 [0:40] (1:02-3.00)	2:35 [1:04] (1:27-5:16)
Peri-operative antibiotics regime (protocol followed)**	13 (100%)	7 (58%)
Continuation of antibiotic regime during surgery	0 (0%)	5 (42%)
Re-exploration for bleeding	0 (0%)	5 (42%)
Follow-up data		
Follow-up time since re-do surgery in months mean [SD] (range)		35 [26] (1-81)
Confirmed new paravalvular leak		2 (17%)
Confirmed re-endocarditis		0 (0%)

TABLE 1. (continued)

	n=13 Index surgery	n=12 Re-do surgery
Left ventricular function		
Good		8 (67%)
Impaired		3 (25%)
Poor		1 (8%)

*Renal insufficiency (not requiring dialysis) is a Glomerular Filtration Rate of less than 60ml/minute/1,73m^2
**protocol consists of a total of 4 gram of cefazolin during a 24 hour period.

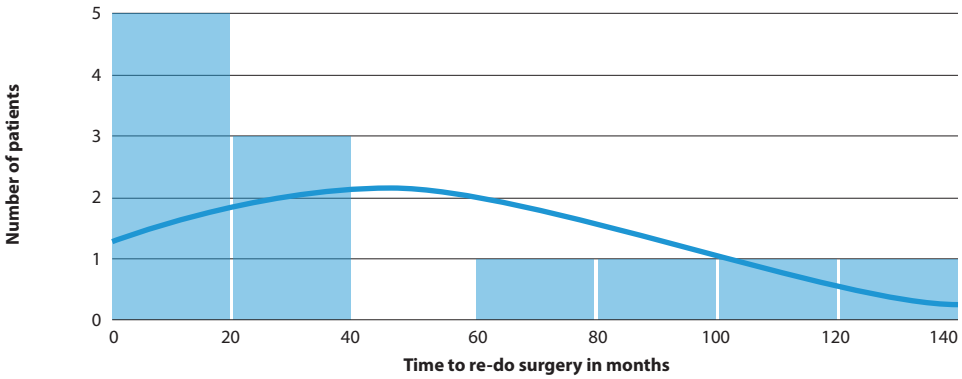

FIGURE 1. Time between index operation and re-do surgery in months

Of the 9 patients with a previously good left ventricular function, 3 had a poorer function at the time of re-operation for PVE (Table 1). Comparing the groups based on index surgery logistic EUROSCORE(17) and re-do logistic EUROSCORE reveals a large difference in calculated risk of mortality. The mean score was 4.9% at index surgery and 28.4% at re-do surgery. At redo-surgery, in all but 1 patient the aortic valve prosthesis was infected. Of these 12 patients 5 received a Bentall (42%), 1 a bio-Bentall, 4 patients received a mechanical aortic valve and 1 a bioprosthesis. One patient underwent replacement of the mitral valve mechanical prosthesis by a new mechanical prosthesis. Concomitant surgery can be found in Table 1. One patient did not undergo re-do surgery. The index surgery of this patient was an aortic valve replacement by a mechanical valve. There was no paravalvular leak at the diagnosis of PVE. Treatment consisted of a six-week regimen of penicillin and the patient recovered well. When comparing patients with endocarditis due to P. acnes and due to other microorganisms, who were operated between 2008 and 2015 in our centre, there were no significant differences between patient characteristics and 30-day mortality (Table 2).

TABLE 2. Demographics finding of patients with prosthetic valve endocarditis (PVE) between 2008 and 2015

	n=91 PVE complete population	n=12 PVE *P. Acnes*
Clinical presentation		
Age in years (mean [SD]) (range))	56.3 [13] (18-81)	58.2[13.3] (30-71)
Male	72 (79%)	12 (100%)
Renal insufficiency (not requiring dialysis)*	29 (32%)	5 (42%)
Left ventricular function		
Good	55 (60%)	6 (50%)
Impaired	31 (34%)	5 (42%)
Poor	5 (6%)	1 (8%)
Cerebrovascular accident history	14 (15%)	2 (17%)
Diabetes mellitus	7 (7%)	1 (8%)
Logistic EUROSCORE® (mean [SD]) (range))	27.3 [21.2] (82)	28.4 [23.6] (77.4)
30-day mortality	4 (4.4%)	0 (0%)

*Renal insufficiency (not requiring dialysis) is a Glomerular Filtration Rate of less than 60ml/minute/1,73m^2

Surgical findings

In 6 patients, the surgeon classified his findings as fitting with active endocarditis. In 2 patients, surgeons reported mainly calcifications but no signs of endocarditis. In 4 patients no obvious signs of endocarditis were observed. Valvular dehiscence was objectified in 11 of the 12 re-operated patients. The one patient without valvular dehiscence presented relatively short after index surgery (10 months). Another frequent finding was the formation of cavities. 75% of patients had small crypts or a true aneurysm (7 patients with crypts and 2 patients with a true aneurysm). The latter two required Bentall procedures as did 4 of the 7 patients with small crypts. Two patients had failure to wean from bypass. In one patient, coronary flow was impaired after placement of a Bentall prosthesis, requiring additional coronary bypass surgery and placement of a veno-arterial extracorporeal membrane oxygenation (ECMO) device. The patient could be successfully weaned from ECMO on the 6th postoperative day. The second patient developed heart failure with failure to wean from bypass requiring placement of an intra-aortic balloon pump and had high levels of inotropic and vasopressive support.

Antibiotic regime during and after re-do surgery

Nine patients (75%) received antibiotic treatment before surgery because of positive blood cultures with gram-positive rods. Six patients were treated with vancomycin, two patients with a penicillin and one patient with a ceftriaxone containing regime. After surgery, all patients were treated with antibiotics for a minimum period of 6 weeks. Different antibiotic regimens were used. 4 of 13 patients (31%) were treated with penicillin alone (2-3 ME 6 times daily). Seven of

thirteen patients (54%) were treated with a combination of penicillin (6 times daily 2-3 ME) and rifampicin 450mg 2 times daily. The other two patients received vancomycin (due to allergy) or penicillin in combination with gentamicin.

Follow-up

Median follow-up after re-do surgery was 36 months (range: 1 to 71 months). Only one patient died due to pneumo-sepsis, 2 years after surgery, not related to endocarditis. At the time of analysis, all other patients were alive and showed no signs of endocarditis. Ventricular function at follow-up was improved compared to before re-do surgery, implying ventricular remodelling after repair of the paravalvular leak. Two patients showed a small paravalvular leak on ultrasound in the follow-up. Both patients had received a prosthetic valve in aortic position after developing PVE. Haemolysis was minimal in both patients, and no reintervention was required. In both patients, no signs of recurrent PVR were found as proven by negative blood cultures.

DISCUSSION

In this study, patients with a proven prosthetic valve endocarditis with *P. acnes* were evaluated. All patients were male, and they all had previous valve replacement. The time between index surgery and presentation with endocarditis varied between 5 and 135 months. Twelve of 13 (85%) patients with *P. acnes* endocarditis presented with severe paravalvular leak. Crypts or true aneurysms were present in 75% (9 of 12) of patients reoperated on. Decreased left ventricular function was present in 40% of patients with a previous good left ventricular function. At presentation, patients were severely ill, but none of them died in the perioperative phase. Only one patient died at long-term follow-up.

The reason why *P. acnes* endocarditis is predominantly found in the male population, as also shown in other studies, is unknown. The difference might be explained by the fact that the absolute numbers of men receiving cardiac valves are higher, this is not only in literature but also in our own institute.(18) It is interesting that the same sex difference phenomenon has been described in studies on osteoarticular prosthesis infections with *P. acnes*,(19) especially in patients who have had shoulder surgery. Still, no clear explanation has been provided why men are affected more frequently than women.

What is the source of the *P. acnes* prosthetic valve endocarditis in these men? *P. acnes* is considered as an omnipresent and usual commensal of the human skin, but recently it has been shown that it can be a potential opportunistic pathogen.(20) *P. acnes* carries components on its surface which can trigger or mediate inflammatory processes or which can exhibit cell-adherent properties (dermatan-sulphate adhesion, thrombospondin type 3 repeat protein).(20) Contamination of prosthetic material at the time of implantation due to the presence of *P. acnes* from either skin flora of the patient, or from an exogenous source, as well as virulence factors, may be responsible for the increased risk of infection among patients with prosthetic valves. The extended period between index surgery and redo surgery might be explained by the low

virulence of this micro-organism. Patients with long time interval between index surgery and redo surgery (for example more than 11 years in this series and more than 23 years in known literature will most likely have occurred due to bacteraemia from a distant focus and secondary metastasis to prosthetic valves. (21)

The diagnosis of *P. acnes* PVE can be difficult. One of the major problems is the prolonged incubation time of this micro-organism. Prolonged aerobic and anaerobic cultures of blood and tissue for up to 2 weeks may be required to detect the organism.(24) In addition, diagnosis of *P. acnes* PVE is difficult because of non-specific clinical symptoms. In addition, the use of the modified Duke criteria is more complex, because of this particular micro-organism not included in the list of typical bacteria causing endocarditis.

Treatment of *P. acnes* PVE usually consists of surgical re-intervention in combination with antibiotics. Therapeutic strategies can be a challenge since surgical re-intervention can be associated with high risk of an unfavourable outcome and antibiotic regimens are hindered by the potential of *P. acnes* to form a biofilm.

In the past, it was common practice to replace an infected prosthetic valve with an allograft with an aortic root.(9) Even today the debate continues whether allograft or valve prosthesis is the best choice. Allografts have better reconstructive abilities in destroyed tissue and durability is no problem in the short and intermediate term. However long term durability is limited.(22) This small series showed that results of re-operation where a new prosthetic valve and root is placed are good. Those patients presenting with the forming of crypts or true aneurysms often required the placement of a conduit in aortic root position after precise and complete debridement of the affected area. There was no topical usage of betadine. The surgical treatment needs to be combined with an adequate antibiotic treatment.

Surgery times for the redo operation were significantly longer than index surgery and the peri- and postoperative course was complicated by the need for mechanical support devices due to heart failure in 2 patients and 42% (5 of 12) of patients needing re-exploration for bleeding. Both can be attributed to the more complex re-operation with adhesions, longer extracorporeal circulation and cross-clamp times. The preoperative condition of patients was also worse compared to the condition of patients at the start of the index surgery.

Patients in this series were predominantly treated with penicillin in combination with rifampicin, as has been proposed in literature.(23) In animal studies, rifampicin has shown to play a unique role in complete sterilisation of foreign bodies (in that case with *Staphylococcus aureus*), because of it's potential to penetrate in biofilms.(24) The resistance of pathogens can vary per country, but for now, this treatment regime seems adequate for patients with a *P. acnes* PVE.(20) Patients with a proven allergy to penicillin (1 patient in this series) can be treated vancomycin. The duration of 6 weeks from re-do surgery seemed adequate and was also propagated in other series.(21) In contrast to previous studies the mortality in this study was low. Literature reports a mortality between 15% to 27%, (25) fitting the calculated mortality risk using the logistic EURO-

score. This series had a 0% low mortality and 7.7% late mortality. This was, however, 2 years after the re-do surgery and was due to pneumo-sepsis. This overall very low mortality after PVE might be explained by advances in postoperative mechanical support. Furthermore, mortality in our centre for PVE is low. Table 2 shows the complete cohort of PVE patients in the same time period compared to *P. acnes* PVE patients. Showing similar high logistic EUROSCORE® scores and a low 30-day mortality.

A limitation of this study is the low number of patients. Still, this series is the largest single centre series described in literature. Overall, some 70 cases were described in literature before this series. The reason why our centre has such a large series to describe is open for debate. The general rate of prosthetic valve endocarditis is no higher than in other centres. Most likely the attention for this pathogen as a substrate for new paravalvular leakage plays a role. This presumption would imply that *P. acnes* PVE does occur more often, but would be undetected in many cases. This could be attributed to both the latency of this micro-organism in clinical features and the prolonged culture time it needs.

CONCLUSION

Patients with prosthetic valve surgery in their medical history are at risk for *P. acnes* endocarditis. Therefore, if such a patient presents with a new paravalvular leak, *P. acnes* PVE should be in the differential diagnosis, and it should be checked with the laboratory whether cultures are incubated for an appropriate time of 14 days. Therapy generally consists of re-do surgery, combined with antimicrobial therapy consisting of penicillin with or without rifampicin. Follow-up of the patients shows favourable outcomes, with improved ventricular function, no valvular revisions and low mortality. A good cooperation between cardiologist, surgeon and microbiologist is necessary to treat these patients appropriately.

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11.1

LETTER TO THE EDITOR

R. van Valen, N.J. Verkaik, M.M. Mokhles, A.J.J.C. Bogers

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We would like to thank Dr. Mestrovic and colleagues for their letter and kind words regarding our paper on prosthetic valve endocarditis (PVE) caused by *Propionibacterium acnes (P. acnes)*.(1) We would like to take this opportunity to further clarify the issues raised in this letter.

We fully agree with Dr. Mestrovic and colleagues that the diagnosis of PVE due to *P. acnes* can be challenging in the clinical setting and would like to take this opportunity to provide further information on our microbiological techniques as requested. Bactec aerobic and anaerobic culture bottles were used. The material was incubated for 14 days at 35 degrees Celsius in the Bactec FX blood culture system (Becton Dickinson). Cardiac valve tissue was incubated 14 days at 35 degrees Celsius on, amongst others, Brucella 5% blood agar anaerobic plates. *P. acnes* was identified on the basis of colony morphology and identification was confirmed by mass spectrometry (Maldi Biotyper, Bruker).

Concerning the question on neurological complications due to *P. acnes*. As shown in table 2 of our paper 2 patients presented with neurological deficit. This was a transient episode. The percentage of patients is comparable to the generic cohort of patients presenting with PVE in our institute and did not constitute a higher risk of mortality is this small series.

The PCR technique can indeed be very valuable to confirm the diagnosis, as Mestrovic argues, and can be performed in difficult cases. However, the technique is costly and is not standard of care in most countries. We would advocate proper culturing with a prolonged incubation time in patients with the likelihood of *P. acnes* PVE.

Using the current literature and our own experience we would not advocate longer terms of antibiotic treatment in patients with *P acnes* PVE or a conservative approach without surgery. (2, 3) Six weeks should be sufficient. If a patient is inoperable, the idea of suppression therapy with prolonged antibiotics could be entertained. In our series, we used a conservative approach in one patient. This patient did not show a dehiscence of his mechanical valve at presentation. This seems to be the pivotal point for a potentially successful treatment of PVE due to *P. acnes* without surgery.

Lastly, the importance of more studies, as also argued by Mestrovic, is there. In our article, we warn about the possible underdiagnoses of *P. acnes* PVE due to large differences in incubation periods for cultures and the wrongfully presumed innocence of *P. acnes*.

R. van Valen, N.J. Verkaik, M.M. Mokhles and A.J.J.C. Bogers

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VALVE DEHISCENCE AFTER BENTALL PROCEDURE: THE DETRIMENTAL TRAITS OF *PROPIONIBACTERIUM*

R.A.F. de Lind van Wijngaarden, R. van Valen, J.A. Bekkers, A.J.J.C. Bogers

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ABSTRACT

The case described exemplifies the detrimental traits of prosthetic valve endocarditis by *Propionibacterium acnes*. Having a congenital cardiac defect with truncus arteriosus type I with interrupted aortic arch and open ductus Botalli, he underwent several operations. Eighteen months after a Bentall procedure, he presented with major prosthetic dehiscence due to endocarditis. After receiving a high-risk reoperation performing a re-do Bentall procedure and treating him with intravenous antibiotic therapy consisting of vancomycin for five weeks and penicillin and rifampicin for six weeks after surgery, he was discharged from the hospital in good clinical condition. In conclusion, *Propionibacterium acnes* endocarditis of a prosthetic valve can be successfully treated with prompt surgery and antibiotic therapy.

INTRODUCTION

Prosthetic valve endocarditis (PVE) is an uncommon long-term complication of heart valve replacement with a lifetime occurrence of 1-6% of patients after prosthetic valve replacement. PVE can be a very dangerous complication with reported mortality rates of up to 74% (1) .

Propionibacterium acnes (P. acnes) as the bacterium responsible for endocarditis is rare with only 70 cases described in the literature. It is an anaerobic, non-spore forming Gram positive bacterium, which is slow-growing and can tolerate anaerobic conditions for a long time (2) . Despite the low virulence that is characteristic of this germ, it can cause detrimental infections of the brain, eyes, spine and surgical site. The next case exemplifies the devastating potential of this microorganism.

Case report

A 30-year old man with an elaborate history of surgical repair of congenital heart disease visited the outpatient clinic. His history consisted of a truncus arteriosus type I with interrupted aortic arch and open ductus Botalli, for which he underwent surgical reconstruction of the aortic arch by a modified subclavian flap procedure and reconstruction of the arterial trunk with ventricular septum defect closure and placement of a Hancock prosthesis, as a baby. In his puberty, the Hancock prosthesis showed stenosis and was replaced by a pulmonary homograft. Because of aortic root enlargement, he underwent a Bentall procedure with a SJM™ valved graft size 29 (St Jude Medical, Inc., St. Paul, MN, USA) 13 years later at the age of 29. The admission was uncomplicated, and he went home on the seventh postoperative day.

Eighteen months after this last operation, he presented with lower limb edema and a cold, pale left hallux in the outpatient clinic. He had no fever, and inflammatory markers were slightly elevated. Transthoracic echocardiography showed an uncertain picture of aortic valve dehiscence in combination with a vegetation. Transesophageal echocardiography showed dehiscence of the valved conduit surrounded by a space with blood flow (Fig. 1). CT angiography confirmed this finding, showing a large cavity with blood flow at the site of dehiscence next to the aortic root (Fig. 1). Blood cultures did not yield any bacterial growth, until after surgical intervention, when these turned positive for *P. acnes*. Nonetheless, based on his clinical condition, intravenous antibiotic therapy with vancomycin, gentamicin and rifampicin was initiated.

Six days later, the patient was reoperated again with deep hypothermia and circulatory arrest. During surgery, the proximal site of the valved conduit appeared to be completely dehiscent (Fig. 2). The old prosthesis was removed, and a new one was implanted onto the left ventricular outflow tract, SJM™ valved graft size 27 (St Jude Medical, Inc., St Paul, MN, USA). Furthermore, ascending aorta replacement was performed with a Gelweave™ Ante-Flo graft (Vascutek Ltd., Inchinnan, United Kingdom).

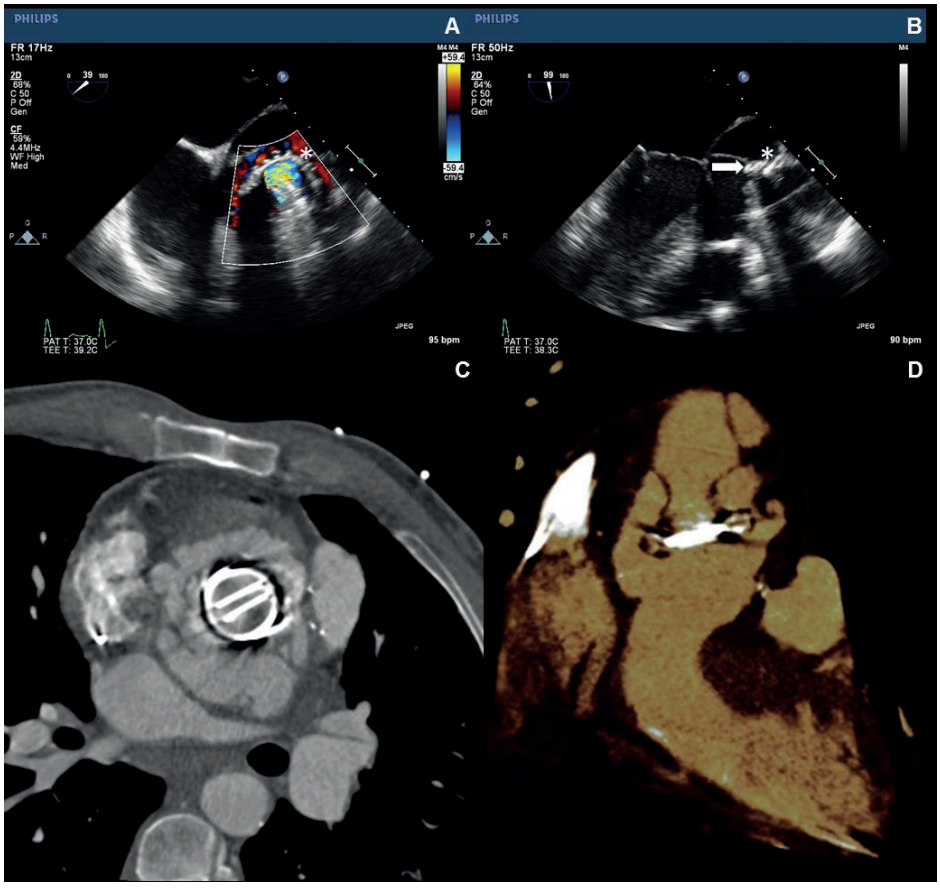

FIGURE 1. Transesophageal echocardiography image of fully dehiscent valved conduit after Bentall procedure. A: In the short axis view, the stitches of the prosthesis are clearly visible and are surrounded by free space with blood flow: pseudoaneurysm formation (*). B: In the long axis view, the prosthesis is clearly detached from its surroundings and placed further from the left ventricular outflow tract than normally expected (⟶) and pseudoaneurysm formation is clearly visible (*). C: Transverse plane and D: sagittal plane of preoperative CT scan showing dehiscence of the valved conduit with pseudoaneurysm formation.

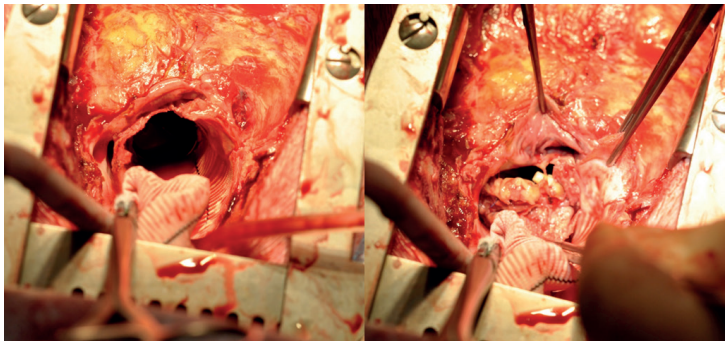

FIGURE 2. Perioperative image of valved conduit with fully circumferential dehiscence

Immediately after surgery, he showed a cerebrovascular accident of the right medial cerebral artery with paresis of the left arm and dysarthria, which resolved spontaneously. He was transferred from the ICU to the ward on the first postoperative day. His course was complicated by atrial fibrillation for which ventricular rate control was achieved by beta blockers, thereafter spontaneous conversion into sinus rhythm was achieved. Perioperative cultures confirmed the presence of *P. acnes*. After the culture turned positive one week after surgery, gentamicin was replaced by penicillin. After intravenous antibiotic therapy with vancomycin for five weeks and penicillin and rifampicin for six weeks after surgery, after which he was discharged from the hospital in good clinical condition.

Within a year after surgery, he underwent percutaneous closure of a pseudoaneurysm at the site of the reimplantation of the left main stem in the prosthesis without signs of infection but jeopardising the flow to the left coronary artery. In the following years, he showed recurrent cerebral infarction with complete recovery and underwent ablation for recurrent septal focal atrial tachycardias. In four years of follow-up, he has had no signs of recurrent endocarditis.

DISCUSSION

A major threat to the lifespan of mechanical heart valves is valve dysfunction. This can be due to structural or non-structural failure. Most often, dysfunction is caused by thrombus, pannus overgrowth or endocarditis. Prosthetic mechanical valves can be dysfunctional in the form of stenosis, central or paravalvular insufficiency or valve dehiscence.

In severe cases, endocarditis can result in dehiscence of a valve prosthesis. This is a very serious disease and should be dealt with promptly. Morbidity is high with reported complications of surgery up to 79% at 30 days and significant mortality (3) . If dehiscence evolves over a period of time, a false aneurysm develops without massive bleeding. Such a false aneurysm can result in compression of cardiac structures and in thrombus formation due to turbulence in low flow compartments.

Although *P. acnes* is considered a usual commensal of the human skin, it has the potency of acting as an opportunistic pathogen (4). Prosthetic material can be contaminated by *P. acnes* from the patient's skin or an exogenous source. In a permissive environment, *P. acnes* can mediate inflammatory responses. But, since it is of low virulence, it can take a long time before PVE becomes clinically overt. In literature, the longest time between index surgery and *P. acnes* prosthetic valve endocarditis is 23 years (5). A long period might also be explained by secondary infection from a distant focus.

Because of the low virulence of this pathogen, clinical presentation is usually accompanied by significant patient's and doctor's delay, since symptoms can be non-specific for a long time. Another challenge in *P. acnes* prosthetic valve endocarditis is the diagnosis, since this microorganism may reveal itself as long as 14 days after incubation (6).

Reoperation in combination with antibiotic treatment is usually a successful treatment. Replacement of the infected prosthetic material and damaged structures is accompanied by a high risk of morbidity and mortality, whereas an antibiotic therapeutic regimen can be hindered by the formation of a biofilm by *P. acnes*. The risk of the operation on this patient was reflected by high-risk scores with a Euroscore II of 7.02 and Euroscores I of 11.73 (logistic) and 8.00 (additive), which is just below a reported mortality of 15-27% in literature (5). This patient was successfully treated with penicillin and rifampicin due to its potential to penetrate biofilms, as proposed in literature (7, 8).

In conclusion, patients with prosthetic valve surgery in their past are at potential risk for *P. acnes* endocarditis. When patients present with an infection and new paravalvular leak or false aneurysm formation, *P. acnes* infection should be considered, and cultures should be incubated for 14 days. The appropriate treatment for this endocarditis is redo surgery in combination with adequate antibiotic treatment (in this case penicillin and rifampicin). However, reoperation comes with significant risk of morbidity and mortality.

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GENERAL DISCUSSION AND FUTURE PERSPECTIVES

In this thesis, the effects of two different protocols on quality of care and patient safety were investigated. The first study explored the effect of a protocol for pain management after cardiac surgery and the second study investigated the daily clinical effects of cessation of anticoagulants and platelet-inhibiting medication before cardiac surgery according to protocol.(1) In addition, options for preventing wound infections in high-risk patients were explored using the concept of negative topical wound therapy on closed incisions (ciNPWT).(2, 3)

Whereas the first chapters of this thesis aim to prevent complications and improve patient care, the final chapters work towards a better understanding of rare complications and the necessary interventions to optimise patient outcomes after these complications.(4, 5) All topics in this thesis emphasise the importance of the multidisciplinary team. In this chapter, we will discuss the role of the nurse practitioner within this team.

Blood loss

In Chapter 2, we investigated the real-life effects of protocol violations concerning cessation of anticoagulants and antiplatelet medication before cardiac surgery. We presented the effects of protocol violations on blood loss, use of blood products, re-explorations for excessive blood loss and mortality.

The investigated protocol was initiated within our department in 2009.(6) The majority of patients were using either anticoagulants or antiplatelet medication (72.7%, N=1190) according to protocol. A major potential side effect of stopping these types of medication are thromboembolic complications.(7, 8) Our study showed that stopping anticoagulants before cardiac surgery according to protocol was safe, with no thromboembolic complications. If medication was continued, that might be a result of guidelines (for example a recent implantation of a drug-eluting stent) or of an error (for example, forgotten by the patient, incorrect instructions). The study showed that violation of the protocol led to significantly more blood loss. The secondary effects of protocol violations were increased use of fresh frozen plasma, red blood cell transfusions and thrombocyte transfusions. These findings were in line with previous research.(9) However, we found no difference in the need for re-exploration or in 30-day mortality. These results were not in line with previously published studies, which showed more re-explorations and higher mortality.(10-12)

In the current antiplatelet therapy guidelines, there is a tendency to further expand the indication for continued use of single or double antiplatelet therapy before surgery in high-risk patients.(13) This is, for example, the case in patients with acute coronary syndrome or recently placed drug-eluting stents. In these patients, guidelines advocate the use of double antiplatelet therapy.(13) Our study shows that continuation of this medication can be justified with no increase in the serious complications of re-explorations or mortality. However, it may result in more blood loss and a higher use of blood products. In this study, we did not investigate the use of new P2Y12 inhibitors such as ticagrelor. This drug was not yet used in the time frame of our study. Recent literature has shown that these highly effective drugs lead to more blood loss compared

to the drugs used during our study period.(14) In the process of deciding to go for urgent or emergency surgery, the potential for higher blood loss is something that needs to be taken into account by the heart team.

Healthcare cost is an important issue nowadays. Our study showed that violation of the protocol does lead to higher costs. We observed significantly more use of red blood cells, thrombocytes and fresh frozen plasma when the protocol was violated. The costs of blood products (and the relative shortage of blood products such as thrombocytes) should make stringent adherence to protocol a priority. Our study indicates a potential savings of €30,000 per year in costs of red blood cells for our department alone. A recent study showed that more savings could be accomplished by using a blood transfusion guideline in addition to stringent protocol adherence.(15) The investigated protocol in our study did not have a guideline for transfusion of blood products. Adding this could potentially lead to more savings as a result of a uniform blood transfusion policy.(15)

Pain management after cardiac surgery

Adequate pain management after cardiac surgery is essential.(1, 16, 17) Patients experiencing pain have a higher risk for pulmonary complications and are more likely to develop chronic pain. We present two studies on this topic in this thesis (Chapter 7 and 8). Our work shows that nurses can efficiently and safely manage pain in cardiac surgery patients. In the first study (presented in Chapter 7), we showed that a 21% reduction of the Visual Analogue Scale (VAS) pain score can be accomplished postoperatively in cardiac surgery patients.(1) Furthermore, this reduction in VAS score was achieved in more patients and in a significantly shorter time compared to the control group. The control group consisted of patients on a physician-driven pain protocol with a standard amount of pain medication and standard timing. Safety of the nurse-driven protocol was determined by assessing the number of interventions needed for either hemodynamic or respiratory complications. Compared to other studies, our results showed overall lower VAS scores when compared to physician-controlled or true patient-controlled pain regimes after cardiac surgery.(18)

Our second study (Chapter 8) explored the effectiveness of the nurse-driven pain protocol over a prolonged period. We showed that our nurse-driven protocol resulted in sustained lower median VAS scores during the first 72 hours on a nursing ward after cardiac surgery, compared to a physician-driven pain treatment protocol. However, although statistically significant, the results of this study were less convincing than the results of the first study (Chapter 7). The percentage of patients with pain at any moment increased to 60% of patients, similar to the control group. The swiftness of pain relief also declined. In both the control and the intervention group, speed of pain relief was comparable. Even with decreased effectiveness, the overall results were still better than those presented in other studies with either nurse-controlled or patient-controlled analgesia.(18) This demonstrates that nurse-driven protocols, even with the concerns described in this thesis, are an effective tool to improve patient care.

Another important finding was the decline of administrative adherence to protocol during the 6-year study period after implementing the protocol. Each nurse-driven intervention required a number of measurements as stated in a flowchart (for example, the VAS score, blood pressure and sedation score). Adherence was assessed by investigating the percentage of measurements that could be retrieved from the patient data management system. We showed a sharp decline in retrievability, which was accompanied by lower effectiveness as measured in time to pain relief. The interventions by nurses were still safe: only one complication was observed during the study period that was directly related to a nurse-driven intervention. This complication was seen in an elderly patient with rapid-onset kidney failure. After an appropriate dose of morphine, she developed hypoventilation that required a morphine antagonist. Most likely, the complication arose as a result of the rapid deterioration of kidney function combined with the administration of morphine. In our study, we advised that in such situations, pain medication should be monitored and prescribed by a physician or nurse practitioner.

We investigated the reasons for decreased protocol adherence and less efficient pain management over time by holding semi-structured interviews with the nurses involved. The interviews showed a relationship with the administrative workload of nurses. A high administrative burden led to poorer registration of the performed interventions and the measurements that should be taken before and after the interventions.

Another important question is whether the protocol performs adequately in different patient groups. The results of multivariate analysis showed that the ability of the protocol to provide sustained and efficient pain management to all patients after cardiac surgery is limited. In both studies, younger and male patients had more pain compared to other patient groups. Furthermore, patients who had had emergency surgery showed higher levels of postoperative pain. The first finding is in contrast to other studies that showed more pain for women after cardiac surgery.(19) We argue that a protocol aims to protect the frailest group. Therefore, the morphine dosages may be on the low side for more robust groups of patients (younger patients and males). Patients undergoing emergency surgery may have higher pain scores because they did not have time to prepare or read instructions to reduce postoperative pain.

During the same time frame, another study (Chapter 9) was undertaken to explore the quality of sleep after cardiac surgery. This study showed a relationship between poorly regulated pain and poor quality of sleep. Using various validated questionnaires, the quantity and quality of sleep after cardiac surgery was explored. The strong relationship between pain and poor quality of sleep is particularly evident on night three on the ward. This is the first night after cessation of the pain protocol. We observed a tendency towards better sleep with pain medication. Another important finding is that nurses can play a vital role in creating the right environment for patients to sleep. The three most important factors for poor sleep are not being able or being allowed to find a comfortable position in bed, pain and alarm signals from medical equipment. Simple interventions (such as timely checks of equipment and infusions) could prevent alarms and help create a minimal-noise environment during the night shift.(20) This study also showed that

quantity and quality of sleep remain poor up to one month after surgery. This is to be expected, as lifestyle adjustments are needed in the period after cardiac surgery. For example, patients are advised to sleep in a supine position during the first six weeks after surgery.

Prevention of wound infections

Surgical site infections (SSIs) are among the most serious complications after cardiothoracic surgery, contributing significantly to postoperative morbidity, mortality, and healthcare costs. (21-23) Rates of SSIs range from 0.5% to 22.2% after cardiac surgery.(24, 25) Incidence rates of deep sternal wound infection (DSWI) range from 0.4% to 2.6%, with mortality rates between 7% and 35%. Recently, there has been growing interest in the concept of negative-pressure wound therapy as a preventative measure in those patients at high risk for wound complications after surgery and especially after orthopaedic, vascular and cardiac surgery. This technique has been named closed-incision negative-pressure wound therapy (ciNPWT). (2, 26) Negative-pressure wound therapy was initially introduced to assist in the treatment of chronic open wounds. The therapy uses a negative-pressure unit and specific dressings that help hold the incision edges together, redistribute and reduce lateral tension, reduce oedema, stimulate perfusion, and protect the surgical site from external infectious sources.(27-29) Randomised clinical trials investigating negative-pressure wound therapy on closed incisions in orthopaedic settings have shown it to reduce the risk of wound infection, wound dehiscence and seroma. There is accumulating evidence that the technique also improves wound outcomes after cardiothoracic surgery. The challenge is that the scientific evidence in cardiac surgery consists primarily of large case series.(27, 30, 31) Despite the lack of controlled studies in this field, the concept of this therapy has been adopted in several important guidelines on prevention of SSIs.(32, 33)

Several risk factors have been found to be associated with a higher risk of postoperative wound infection after cardiac surgery. Diabetes mellitus, especially poorly controlled diabetes mellitus, is a strong predictor for wound complication.(34, 35) Obesity is another important precursor for complications. (36) Both diabetes mellitus and obesity are linked with several major inhibitors in wound healing. Ageing and its associated frailty can contribute to higher rates of wound complications. Medication can also play a role in the development of an SSI. Usually, this involves medication that affects the immune system in a negative way.(36) Another important factor is malnutrition. This is primarily seen in patient groups who are already at risk for impaired wound healing: elderly patients, patients with chronic health problems and patients with a very limited (one-sided) diet.(37)

Surgical risk factors include the use of one or two internal mammary artery (IMA) grafts (especially bilaterally), duration of surgery and perfusion time, prolonged mechanical ventilation, use of an intra-aortic balloon pump, postoperative bleeding, re-operation, sternal rewiring, extensive electro-cautery, shaving with razors, and use of bone wax.(21, 38)

In recent decades, enormous progress has been made in the absolute reduction of SSIs after cardiac surgery. However, the high-risk patients still have an SSI rate of up to 15% after cardiac surgery, clearly showing the importance of continued efforts to reduce the risk of SSIs.(39)

Chapters 3 and 4 of this thesis consist of a review of the current literature on devices for prevention of wound infections after cardiac surgery and recommendations for using ciNPWT in daily practice. A risk system consisting of minor, intermediate and major risk factors was formulated and offers a risk stratification system for using ciNPWT devices. This system can aid clinicians in choosing a ciNPWT device for high-risk patients.

The risk score model has not yet been validated, so future research will be needed to see if using this model helps identify those at the highest risk and to balance hospital economics and patient benefits. The importance and need for further randomised clinical trials cannot be underestimated. Further reduction of wound infections is paramount. However, interventions should be evidence-based and cost-effective. Not all patients require ciNPWT, but it can be an aid to reduce the risk of wound complications after cardiac surgery.

Chapter 5 discusses whether ciNPWT can help in reducing DSWI. All previously discussed case reports show reduction of DSWI in the examined population. The effect of negative-pressure therapy, however, only has an influence on the first centimetre of tissue below the foam or dressing, dissipating exponentially beyond this point.(40) A panel of experts was asked to review the literature. We concluded that there is no simple answer to this question. The effect of lower DSWI is seen, but cannot be explained by ciNPWT only. Both experimental and clinical research should further explore the link between ciNPWT and reduced DSWI.

Management of rare complications

Complications as a result of cardiac surgery are mostly seen in the immediate postoperative phase and include re-operations due to excessive blood loss and wound infections.(14, 41-43) These complications are often easy to detect and have a clear and direct relationship with the surgery. There are, however, rare complications that only are seen after an intermediate to long period after surgery.

This thesis presents two of these complications. The first one is prosthetic valve endocarditis due to *Propionibacterium acnes*.(5) With an incidence of 30 to 100 episodes per million patient-years, endocarditis might be a rare disease, but the risk of adverse outcome is high. (44, 45) The in-hospital mortality is around 20%, and more than one-third of patients will die within the first year of diagnosis, despite advances in diagnostic options, treatment and follow-up.(46-49)

Patients who are especially at risk for developing endocarditis are those who have undergone previous implantation of a prosthetic valve, device or lead. For this reason, prosthetic cardiac valves have been labelled as a predisposing cardiac condition for infectious endocarditis in the guideline on management of infective endocarditis.(50)

Prosthetic valve endocarditis (PVE) is a complication with an even higher rate of mortality and morbidity than native valve endocarditis. In the literature, it is described as a relatively uncommon clinical entity. The reported incidence of PVE is between 0.3 and 1.2 cases per patient-year, affecting 1% to 6% of patients with a cardiac valve prosthesis.(51) The mortality

ranges between 21% and 74%. (52) *P. acnes* is a very rare cause of prosthetic valve endocarditis, with fewer than 100 described cases in the literature.(53-57) Based on observations within our institute, a retrospective review of all positive *P. acnes* cultures resulted in a cohort of 13 patients in 10 years. Our study showed the difficulty in diagnosis. This difficulty is caused by, first, the relatively long delay to presentation; in one patient, the endocarditis was diagnosed more than ten years after surgery. Second, *P. acnes* is often viewed in the clinical setting as contamination of a culture instead of a harmful pathogen.(58, 59) Third, *P. acnes* is a so-called slow grower. The standard time that cultures are investigated (7 days) is, in most cases, too short to culture *P. acnes*. Tissue cultures and blood cultures should have a follow-up of 10 to 14 days. Fourth, there was no harmonised antibiotic regime. The results of our study indicate that patients with this condition should be treated with penicillin in combination with rifampicin for 6 weeks to treat this infection adequately.

Another example of a rare complication after cardiac surgery is that of the atrio-esophageal fistula after thoracoscopic ablation for atrial fibrillation (TTMAZE).(4, 60) TTMAZE is offered to patients with lone atrial fibrillation who have failed medical treatment or catheter-based ablation by a cardiologist. The atrio-esophageal fistula is a rare but potentially lethal complication after this procedure. The fistula forms between the left atrium and the oesophagus, causing air embolism in the heart and aorta with neurological complications and sepsis due to the introduction of bacteria into the bloodstream. This complication is well known in the field of electrophysiology and has been seen after ablation for atrial fibrillation using intra-cardial catheters.(61-63) We have treated three patients with this complication in our hospital after surgical treatment of their lone atrial fibrillation. The complication was seen 6 to 8 weeks after surgery. At that time, patients developed the complication without precursors in the time period before the complication. One of these patients died within 24 hours after admission due to neurological complications of air embolism. Serious neurological deficits were also seen in the two surviving patients. The literature on this topic has shown that without swift intervention, mortality rises to almost 80% within a short time period.(61) Chapter 10 presents the approach to surgical repair of the fistula in our hospital and a discussion on the importance of imaging if these patients present with a neurological deficit or a septic profile. More importantly, we believe that this complication might be underdiagnosed. First, due to the relatively long time period between surgery and the occurrence of events, patients may die unexpectedly or become septic with bowel bacteria, while the cause is not attributed to the TTMAZE. Second, the events mimic a cerebral vascular accident that is often seen in patients with a history of atrial fibrillation.(64, 65) To create awareness for this complication, we presented our findings to the general medical audience in the Netherlands and the cardiac surgery audience.(4, 60) This message is even more urgent as the number of TTMAZE procedures and the evidence of the effectiveness of the procedure grows.(66) This could potentially lead to a higher number of patients presenting with this catastrophic complication. These articles created discussion within the surgical community, resulting in several letters to the editor. In our answers to these letters, we emphasised the importance of awareness of this complication and the need for swift diagnosis. It could be argued that the TTMAZE procedure should only be undertaken by large-volume centres. Previous studies have shown that large-volume centres have better outcomes in the different cardiac surgery procedures, because of

experience and optimal patient pathways.(67, 68) In the reports from large-volume TTMAZE centres, this complication has not been reported.(69) We advocate standardised follow-up of patients for a prolonged period with particular attention to mortality and morbidity. Not only sustained sinus rhythm should be the outcome for long-term follow-up, but also complications.

Innovative roles for allied professionals

The work in this thesis was the result of a longstanding multidisciplinary team effort within the Department of Cardiothoracic Surgery to improve patient outcomes by performing scientific research and contributing to evidence-based medicine. Traditionally, research in this field was done by physicians, and adoption of the science for use in daily clinical practice by nurses and allied professionals was slow. The scientific body of knowledge within the field of nursing in surgery has been developing over the last 20 years. The emphasis has first been on best practice and later on evidence-based nursing. The introduction of nurse practitioners and physician assistants led to a crossover not only of tasks but also of research in both nursing science and medicine.

In the last decade, scientific work by nurse practitioners has been increasing. The fields of cardiology and cardiothoracic surgery clearly show this crossover effect. For example, in his thesis on telemedicine for heart failure, de Vries (a NP) combined practical issues with relevant parameters for patient safety while following the most recent guidelines for heart failure.(70-72)

Another good example is the work of Koster (also a NP) on delirium after cardiac surgery.(73-75) She validated a predictive risk model and investigated the outcomes on the patient level. This risk score is still widely used in Dutch hospitals, confirming the added value of the crossover function of NPs.

In daily patient care, adding an NP to the multidisciplinary team leads to a consistent factor on the ward or outpatient clinic. This consistency and the knowledge of the NP about the normal clinical course after cardiac surgery procedures results in early recognition of deviations from the normal postoperative course. This enables early interventions and will lead to better outcomes. As mentioned in the title of this thesis, this development will help patients and multidisciplinary teams in "getting better". A good example is the *P. acnes* paper. Observations of this very infrequently occurring bacteria in cultures from patients that required a redo of surgery emerged every few years and led to the research question on prevalence and treatment of *P. acnes* prosthetic valve endocarditis.

An NP does, however, need time to evolve into these different roles.(76) Developing these roles requires time, and mentoring by experienced nurse leaders and physicians is essential. The result will be better cooperation between both professions. Both patients and healthcare teams can benefit significantly from this development. The role of nurses as team members was recognised many years ago, but their role as researchers still needs to be expanded. This is the challenge that awaits NPs in the coming years and decades.(76-78)

General observations and future perspective

The aim of the first part of this thesis was to improve outcomes for patients after cardiac surgery. A protocol on cessation of anticoagulants and platelet inhibitors was investigated as well as a protocol to support nurse-driven pain management.

Both studies showed a difference between using a protocol in a controlled research environment and in a clinical setting. For example, the pain protocol showed impressive results during the pilot study, both in the reduction of average pain score and the speed of pain reduction. In daily clinical practice, the effects were less convincing, as shown by higher average pain scores and slower pain relief in patients. This is partly due to the Hawthorne effect: being actively involved in new research and implementation of new protocols leads to positive effects. In recent years, there has been some debate on the Hawthorne effect, but the positive effect has been seen over and over.(79) The challenge for researchers and clinicians is to maintain the positive effect of new protocols and guidelines after the implementation phase. To achieve this, it is necessary to know and understand human factors and behaviour in everyday clinical practice and the result of these factors on outcomes and protocol adherence. In the last decade, awareness has grown of the application of protocols in daily clinical practice. For example, research into the real-world effects of guidelines showed only limited success in improving guideline adherence.(80) It is vital that we learn more about the reasons for poor adherence to guidelines and poor adoption of guidelines in daily practice.

Research on this topic should lead to improved real-world performance of protocols and discovery of ways to maintain adherence in daily practice, even years after implementation. The effectiveness of protocols in real life is also influenced by the administrative burden on the users. The effect goes beyond reduced effectiveness of protocols and retrievability of data and applies not only to nurses. Physician burnout has also been linked to administrative burden.[9]

In the Netherlands, several initiatives aim to reduce administrative workload. In 2014, the Dutch national society of nurses (V&VN) launched a campaign for awareness of this topic.[10] However, it remains important that data be retrievable. Not only from a legal perspective, but also to enable evaluations of protocols.

The second challenge of protocols is the large difference in individual patient characteristics. The problem of making a protocol and flowchart that is both safe and effective for all patients is shown in the pain studies. We were able to provide a protocol that is safe for those with the highest risk of developing complications: the elderly and more frail patients. However, this came at a cost: younger and male patients had more pain using this protocol. In modern medicine, there is a trend towards individualised and tailor-made solutions for patients. This seems to contradict the generalised protocols advocated in this thesis. It is clear are limits to adapting protocols to deliver personalised interventions. A protocol needs to be safe for patients and, equally important, usable and understandable for the users. For example, increasing the amount of morphine to be given to a patient in pain will lead to more morphine intoxications in the elderly and in patients with renal insufficiency.(81) Future research should be directed at managing

these complex but clinically very relevant questions. Possible alternatives to generic protocols could be computer applications (apps) that calculate the correct dosage of pain medications for each patient by looking at age, kidney function, hemodynamic and respiratory profile and weight. These apps could then advise nurses about each specific patient, providing tailor-made solutions for patients based on proven and safe protocols. Patient data management systems and these apps should be able to communicate with each other, reducing the administrative burden for health care workers and improving data registration.

Options to reduce the number of the surgical site infections were also investigated in this thesis. Current research has shown that no single intervention or device results in a sustained reduction in the number of wound infections. The most recent guidelines on prevention of SSIs by the World Health Organisation show the current spectrum of interventions.(82) Successful programmes have incorporated several of these recommendations, which has resulted in a feedback loop. (83, 84) This feedback loop provides users (such as surgeons) with regular updates on the number of infections and rate of protocol violations. The feedback should not "shame and blame" those involved but instead encourage them to investigate the differences and to improve their results. This concept has been introduced in several surgical fields with encouraging results.(85) The ciNPWT technique has the potential to help further reduce the SSI rate in cardiac surgery, but further research is needed to validate this. It is also important to realise that no single device can stop SSIs. Further reduction in the number of SSIs will require the constant awareness of all team members that their actions and those of the whole team are crucial.

The second section of this thesis aimed to help recognise and treat rare complications after cardiac surgery. Chapters 10 and 11 clearly illustrate the importance of prolonged follow-up and stringent screening for complications after surgical procedures. National and international societies should advocate stringent follow-up. This thesis also shows the importance of the multidisciplinary team, for example regarding *P. acnes* endocarditis. It is reasonable to assume that this micro-organism was seen as a contaminant in many cases, and as not very likely to cause an endocarditis. A heart team of cardiologists and cardiac surgeons could be assisted by a microbiologist so everyone fully understands the potential harm *P. acnes* can do to a prosthetic heart valve.

Multidisciplinary teams are being advocated in current guidelines and will help to better recognise and treat these rare complications.(86) Another good example of the positive effect a multidisciplinary team can have is the comprehensive advice we formulated on treatment (both surgical and preferred antibiotic treatment).

The same principle applies to patients with complications after TTMAZE. Collaboration between the various departments will help improve awareness of the existence of atrio-esophageal fistula, which will hopefully lead to reduced mortality and morbidity for patients who develop this complication.

In summary, this thesis has not only been written to improve outcomes after cardiac surgery but also to show the importance of a team effort in cardiac surgery. All disciplines can help in areas of prevention (for example pain reduction), reducing the rate of complications and finally in identifying patients who have developed complications after cardiac surgery. Allied professionals and nurses need to have an integral role in these teams. Emancipation and integration are the challenges for these groups in the coming years. If successful, multidisciplinary teams will become truly multidisciplinary, and the combined knowledge and perspective of all involved will help improve outcomes for patients.

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14

SUMMARY
NEDERLANDSE SAMENVATTING

SUMMARY

Chapter 1 gives a general introduction to the topics in this thesis. The aims of this thesis are presented and an outline of the work within this thesis is given.

Chapter 2 describes the effects of protocol violations in cessation of anticoagulants and platelet-inhibiting medication before cardiac surgery. We investigated the consequences of the violations on blood loss, use of blood products, surgical re-explorations for blood loss and mortality. The results of this study show that not following protocol leads to increased blood loss and greater use of blood products. There was no significant increase in the number of surgical re-explorations for blood loss or mortality in this cohort in patients with protocol violation. Based on the results of this study, we recommend that physicians should adhere to protocol but that deviation of the protocol can be justified in individual cases if the calculated risk of protocol violation for the involved patient is acceptable.

Chapter 3 gives an overview of factors that can lead to wound complications after surgery. Despite many innovations and investigations to reduce the number of surgical site infections (SSI) during the last decades, no significant reduction in SSIs has been achieved. In this chapter, a novel technique to prevent wound complications is discussed. It is known as closed-wound negative-pressure wound therapy (ciNPWT). With this technique, after normal closure of the surgical wound, a negative-pressure device and dressing is placed on the wound. The dressing is left in place for five to seven days, and there is evidence that this reduces the chance of an SSI. Current guidelines recognise this therapy and state that the use of this therapy can be entertained by surgeons to use in high-risk patient populations.

Chapter 4 summarises the current literature on the technique of ciNPWT and is a consensus document by experts in the field of negative-pressure therapy. The document helps identify patients at risk for wound infections and offers a model to predict which patients could benefit from the ciNPWT technique.

Chapter 5 presents a literature review and an expert discussion on the question whether ciNPWT can prevent post-sternotomy mediastinitis. Several case series show a lower incidence of mediastinitis in the group of patients who were treated with ciNPWT. Experimental studies, however, demonstrated that the effect of the negative pressure is limited to a maximum of one centimetre below the skin. Group consensus was that this question cannot be answered without more research. This should be done both in a clinical setting and in experimental studies.

Chapter 6 shows the potential of the ciNPWT technique. CiNPWT was applied in a patient with a high-risk profile for wound complications. The patient received a left ventricular assist device (LVAD) in an earlier session and developed mediastinitis and LVAD pocket infection. She was a chronic corticosteroid user. The case report shows the use of ciNPWT to prevent a new

infection after surgery and describes a novel approach to closing the sternal wound and LVAD pocket using rectus abdominis muscle with minimal manipulation of the drive line, reducing the chances of drive-line dysfunction.

Chapter 7 introduces a novel approach for pain management after cardiac surgery. In the past, patients were treated by a physician-driven pain protocol with fixed doses of pain medication. In this pilot study, a nurse-led pain protocol was initiated. Nurses were allowed to give an individualised dosage of pain medication to patients with pain, and to repeat this if pain scores remained high. The study showed that this was efficient and safe. There were no complications recorded related to a nurse-driven intervention.

Chapter 8 shows the performance of the nurse-driven pain protocol over a prolonged period. Over a six-year period, pain scores, complications and protocol adherence were monitored. The evaluation showed that median pain scores remained lower compared to the physician-driven protocol and comparable protocols described in literature. Pain scores were, however, higher compared to the pilot study. The swiftness of pain reduction was slower and was once again comparable to the physician-driven protocol. Protocol adherence was significantly poorer. Interview with staff nurses showed that they attributed this to a high administrative workload and limitations in the patient data management system.

Chapter 9 investigates the quality of sleep after cardiac surgery. Sleep can be affected by many factors. Using validated questionnaires, the study revealed that quality of sleep is poor during the first weeks after surgery. The study shows that sleep is affected by pain, the position in the bed and factors such as noise on the ward and medical devices.

Chapter 10 describes a rare complication after surgical treatment of atrial fibrillation (AF). In patients with lone AF, there is no concomitant heart disease or other known reason for AF. These patients can undergo a surgical treatment to restore sinus rhythm and thus improve quality of life. During a three-year period, three patients were seen with an atrio-oesophageal fistula. In the literature, only one case was described with the same complication. Patients with this complication develop a fistula (opening) between the left atrium of the heart and the esophagus. This fistula leads to air embolisation and introduction of bacteria into the bloodstream. All patients presented relatively late after surgery (six to eight weeks) without prodromes in the days before developing the complication. Mortality and morbidity were high in these patients. The article emphasises the importance of early recognition and swift surgical treatment. One of the patients described died without undergoing surgery. The two other patients underwent correction of the fistula and survived. However, both of these surgically treated patients had permanent postoperative neurologic impairments.

Publication of this article has led to two letters to the editor by colleagues. Our response to these letters is also presented in this chapter.

Chapter 11 discusses another rare complication after cardiac surgery. *Propionibacterium acnes (P. acnes)* is a skin bacteria that is usually seen as benign. In the field of orthopaedics, *P. acnes* has been linked to infected implanted materials. In this article, a cohort of 13 patients is described after valve surgery. All patients presented with valve dehiscence or heart failure due to endocarditis with *P. acnes*. Patients presented late after surgery, one patient even after ten years. This article describes the presentation and surgical and antibiotic therapy of this complication. Bases on the results, we concluded that these patients should be re-operated and treated for at least six weeks with penicillin in combination with rifampicin.

After publication of this article, a letter to the editor was received. Our response to this letter is also presented in this chapter.

Chapter 12 presents a patient with *P. acnes* endocarditis and shows the detrimental traits of this bacteria. Presentation, surgical treatment and outcomes are described.

In **Chapter 13**, the general discussion, the results that were presented in this thesis are discussed. Future developments in the field of prevention, recognition and treatment of complications after cardiac surgery are also discussed as well as research questions that remain after this thesis.

NEDERLANDSE SAMENVATTING

In **hoofdstuk 1**, de algemene introductie, wordt de achtergrond van het onderzoek beschreven en worden het doel en de onderzoeksvragen uiteengezet.

Hoofdstuk 2 laat de resultaten zien van een studie naar de effecten van protocolafwijkingen bij het staken van bloedverdunners voor hartoperaties. Er werd onderzocht wat de gevolgen zijn voor bloedverlies, verbruik van bloedproducten, aantal heroperaties en mortaliteit. Patiënten bij wie van het protocol afgeweken werd, hadden significant hoger bloedverlies. Deze patiënten hadden ook meer bloedproducten nodig. Er was geen significant verschil in het aantal heroperaties en mortaliteit tussen de onderzochte patiëntengroepen. Op basis van de resultaten van deze studie adviseren we om zoveel mogelijk het protocol te volgen. In sommige situaties kan het echter nodig zijn om van het protocol af te wijken. Deze studie toont aan dat dit kan met beperkte extra risico's voor de betrokken patiënt (extra bloedverlies en meer verbruik van bloedproducten).

Hoofdstuk 3 geeft een overzicht van bekende factoren die wondgenezingstoornissen kunnen geven bij patiënten die chirurgie ondergaan. Ondanks vele jaren van innovaties en verbeterde technieken daalt het aantal wondinfecties niet significant. In dit hoofdstuk word een innovatieve techniek besproken die mogelijk kan helpen om wondcomplicaties te voorkomen. Deze techniek staat bekend als closed-incision negative-pressure wound therapy (ciNPWT). Dat betekent dat de chirurg de wond op de normale manier sluit na de operatie en dat er vervolgens een negatief druksysteem op de primair gesloten wond wordt aangebracht. Huidige richtlijnen geven aan deze techniek overwogen kan worden bij patiënten met een sterk verhoogd infectierisico na operatie.

Hoofdstuk 4 geeft een overzicht van de bekende literatuur op het gebied van ciNPWT. Vervolgens worden indicaties voor het toepassen van deze therapie bij patiënten na hartchirurgie voorgesteld door een groep experts op dit gebied. Om de juiste patiënten te selecteren voor deze therapie is een risicomodel gemaakt en gepresenteerd.

Hoofdstuk 5 geeft de groepsdiscussie weer van de expertgroep op gebied van ciNPWT over de vraag of deze techniek ook diepe sternale wondinfecties kan voorkomen. De literatuur laat bij herhaling zien dat deze complicatie minder vaak voorkomt bij patiënten behandeld met ciNPWT. Studies laten echter zien dat de invloed van ciNPWT beperkt is tot 1 à 2cm onder de incisie. De conclusie is dat, gezien de complexiteit van deze materie, deze vraag nu niet te beantwoorden is. De noodzaak tot verder onderzoek, zowel in klinische setting als in het laboratorium, is evident.

Hoofdstuk 6 laat een voorbeeld zien van het gebruik van de ciNPWT-techniek bij een patiënt met een sterk verhoogd risicoprofiel. Het betreft een patiënte met een geïnfecteerd steunhartsysteem en mediastinitis. Deze patiënte gebruikte chronisch corticosteroïden. Dit

artikel toont hoe ciNPWT in een patiënt met hoog risico gebruikt kan worden. Tevens wordt een innovatieve methode van wondbedekking en -sluiting na mediastinitis geïntroduceerd, waarbij de drive line van het steunhart van de patiënt minimaal gemanipuleerd hoeft te worden.

Hoofdstuk 7 beschrijft een pilotstudie met als doel betere pijnbestrijding na hartchirurgie door een pijnprotocol gedreven door verpleegkundigen. Met dit protocol kunnen verpleegkundigen patiënten met pijn na hartchirurgie zelfstandig een aangepaste dosering pijnbestrijding geven. De studie toont aan dat dit veilig en effectief is met afgenomen pijnscores en snellere daling van de pijnscores in vergelijking met voorgeschreven doseringen door de arts.

Hoofdstuk 8 laat zien wat de resultaten van het protocol zijn gedurende een langere periode. Gedurende zes jaar werden van patiënten pijnscores bijgehouden. De evaluatie laat zien dat de mediane pijnscores nog altijd lager zijn vergeleken met door de dokter voorgeschreven pijnbestrijding en resultaten van soortgelijke protocollen in bekende literatuur. De scores zijn echter duidelijk minder gunstig dan in de pilotstudie. De snelheid waarmee pijnreductie werd bereikt is duidelijk afgenomen en is nu vergelijkbaar met de resultaten van door de dokter voorgeschreven pijnmedicatie. Daarnaast werd het protocol duidelijk minder strikt gevolgd: de verplichte scores werden significant slechter bijgehouden. Verpleegkundigen gaven aan dat dit komt door werkdruk en moeizaam invoeren van data in het patiëntdata-managementsysteem.

Hoofdstuk 9 beschrijft de effecten van hartchirurgie en ziekenhuisopname op slaapkwaliteit. Middels een aantal gevalideerde vragenlijsten werd aangetoond dat de slaapkwaliteit in de eerste weken na operatie beduidend slechter is. Het ervaren van pijn, de houding in bed en apparatuurgerelateerde factoren (piepende apparaten) werden als enkele redenen gevonden voor deze observatie.

Hoofdstuk 10 beschrijft een zeldzame complicatie na chirurgische behandeling van boezemfladderen, ook wel bekend als atriumfibrilleren (AF). Bij patiënten met solitair AF zonder structurele hartafwijkingen of andere verklaringen voor het AF biedt een totally thoracoscopic MAZE (TTMAZE) een chirurgische oplossing om sinusritme te herstellen en daarmee een betere kwaliteit van leven te verkrijgen. Gedurende drie jaar werden drie patiënten gezien die een atrio-oesophageale fistel ontwikkelden na deze procedure. In de literatuur was deze complicatie éénmaal eerder beschreven. Bij deze complicatie ontstaat een fistel (een niet-natuurlijke gang) tussen de linkerboezem van het hart en de slokdarm, waarbij lucht en bacteriën in de grote bloedsomloop komen. De patiënten presenteerden zich laat na chirurgie (6 tot 8 weken) en hadden een hoge mortaliteit en morbiditeit. Het artikel beschrijft het belang van onderkenning en de chirurgische behandeling die wij hebben toegepast bij twee van de patiënten. Eén van de patiënten overleed zonder chirurgische behandeling. De twee geopereerde patiënten overleefden maar hadden blijvend neurologisch letsel. In het artikel wordt het belang van snelle onderkenning van de complicatie en zorgvuldige follow-up van patiënten benadrukt.

Naar aanleiding van dit artikel hebben collega's uit andere centra twee brieven ingezonden. Ons antwoord op deze brieven wordt eveneens weergegeven in dit hoofdstuk.

Hoofdstuk 11 beschrijft een tweede zeldzame complicatie na hartchirurgie. De *Propionibacterium acnes*-bacterie is een huidcommensaal die veelal als onschuldig wordt gezien. Al langere tijd is binnen de orthopedie bekend dat dit micro-organisme ernstige infecties kan veroorzaken bij patiënten met kunstmateriaal. Dit artikel beschrijft een cohort van 13 patiënten na klepchirurgie die zich laat na chirurgie (in een enkel geval meer dan 10 jaar na operatie) presenteren met een kunstkleploslating of hartfalen. Het artikel laat zien dat deze patiënten succesvol kunnen worden geheropereerd. Op basis van de resistentiepatronen van de bacterie bij de verschillende patiënten wordt een antibioticaregime met penicilline en rifampicine geadviseerd met een minimale duur van 6 weken.

Naar aanleiding van dit artikel hebben collega's uit een ander centrum een brief ingezonden. Ons antwoord op deze brief wordt eveneens weergegeven in dit hoofdstuk.

Hoofstuk 12 presenteert een casus van een patiënt met *P. acnes*-endocarditis. Dit hoofdstuk beschrijft de presentatie van deze ziekte, de chirurgische aanpak en de antibioticabehandeling.

In **hoofdstuk 13** volgt de algemene discussie naar aanleiding van de diverse stukken in dit proefschrift. Tevens worden resterende en nieuwe onderzoeksvragen en toekomstperspectieven beschreven op het gebied van preventie, onderkenning en behandeling van complicaties na hartchirurgie. Hiermee komt het belangrijkste doel van dit proefschrift naar voren, namelijk patiënten helpen beter te worden en behandelteams beter te laten worden in het voorkómen, onderkennen en behandelen van complicaties.

15

PHD PORTFOLIO
ABOUT THE AUTHOR
DANKWOORD
LIST OF PUBLICATIONS

PHD PORTFOLIO

Name PhD student: Richard van Valen
Erasmus MC Department: Cardiothoracic Surgery
Research School: COUER

PhD period: 2011-2017
Promotor: A.J.J.C. Bogers, MD PhD
Supervisor: M.M. Mokhles, MD PhD

1. PhD training	Year	ECTS
General courses		
Arrhythmia Research Methodology	2016	1.5
Research Integrity	2016	0.3
Basic introduction course on SPSS	2017	1.0
BROK hercertificering	2016	1.0
Seminars and workshops		
SCTS Advanced Cardiothoracic Course	2011	1.0
Masterclass Research voor Nurse Practitioners en zorgonderzoekers	2012	2.0
ERCATHAN: functional and applied cardiac anatomy	2013	0.3
Presentations (National)		
Wound complications after cardiac surgery (Amsterdam)	2011	0.6
Cardiac surgery and kidney function (Utrecht)	2012	0.6
Surgical treatment of atrial fibrillation (Utrecht)	2013	0.6
Surgical AVR versus TAVI (Rotterdam)	2015	0.6
Nurse practitioners in internal medicine (Maastricht)	2015	0.6
Presentations (International)		
Topical negative-pressure therapy in daily practice (Lisbon, Portugal)	2011	0.6
Long-term effectiveness of a nurse-driven pain protocol (Amsterdam, the Netherlands)	2015	0.6
Propionibacterium acnes and mechanical valves (Birmingham, United Kingdom)	2016	0.6
Complications in cardiothoracic surgery, the nursing perspective (Paris, France)	2016	0.6
Pain management after cardiac surgery (Belfast, Northern Ireland)	2017	0.6
Closed incision negatieve-pressure therapy (Vienna, Austria)	2017	0.6

National and international conferences

Annual meeting EACTS (Lisbon, Portugal)	2011	1.5
Annual meeting EACTS (Barcelona, Spain)	2012	1.5
Annual meeting EACTS (Vienna, Austria)	2013	1.5
Annual meeting ESTS (Copenhagen, Denmark)	2014	1.5
Annual meeting EACTS (Milan, Italy)	2014	1.5
Annual meeting EACTS (Amsterdam, the Netherlands)	2015	1.5
Annual meeting SCTS (Birmingham, United Kingdom)	2016	1.2
Annual meeting EACTS (Barcelona, Spain)	2016	1.5
Annual meeting SCTS (Belfast, Northern Ireland)	2017	1.2
Annual meeting EACTS	2017	1.5

Other

Organising committee Thoraxcenter Rotterdam	2012-2017	5.0
Organising committee nurses and allied health EACTS (chair)	2012-2017	6.0
Reviewer McMaster Online Rating of Evidence	2011-2014	2.0
Reviewer abstracts EACTS annual meeting	2012-2017	2.0
Prevena Advisory Panel	2012	1.0
National guidelines use topical negative-pressure therapy	2012	1.0
Faculty LVAD coordinator course	2014	1.5
Faculty CT forum SCTS	2017	1.5

2. Teaching

	Year	ECTS
Lecturing		
University applied sciences Leiden	2011-2017	6.0
Training Institute Erasmus Medical Center	2011-2017	6.0
Supervising practicals and excursions, tutoring		
University of applied sciences Leiden	2011-2017	4.0
Other		
Advisor e-learning chest drainage	2013	1.0

Total ECTS points: 65.1

ABOUT THE AUTHOR

Richard van Valen was born on 21 May 1977 in Sliedrecht, the Netherlands. He graduated from the Willem de Zwijger College in Papendrecht in 1995. Afterwards, he worked towards a bachelor degree in Nursing from the University of Applied Sciences in Rotterdam. In 1999, his career in cardiothoracic surgery began on the nursing ward of the Erasmus Medical Center. After completing several nurse specialisations on medium and intensive care nursing, he was asked to help form the nurse practitioner profile within the Department of Cardiothoracic Surgery. He obtained his Master of Arts in Advanced Nursing Practice degree from the University of Applied Sciences in Leiden in 2005. After his graduation from Leiden, Richard has been involved as teacher and examiner in the programme for nurse practitioners.

His research career started in 2009, after he joined a task force to improve pain management after cardiac surgery. His field of interest involves protocol adherence, nurse-driven interventions, prevention and management of infectious complications after surgery, and multidisciplinary teams.

During his career, he has been working towards further expanding the role of nurse practitioners within the clinical setting. He has helped develop the role on a hospital, national and international level.

On a hospital level, he has worked with the department of pharmacy and the medical staff towards nurse prescribing and guidelines for medical interventions by NPs. On a national level, he has been involved in writing guidelines, for example on the use of negative-pressure wound therapy. Internationally, he has been involved in creating the nurses and allied health portal for CTSNet, which acts as a forum for all involved in cardiothoracic surgery. He was part of the team that created the LVAD coordinator course for the European Association of Cardiothoracic Surgery (EACTS) and has been asked as reviewer for several peer-reviewed journals and international meetings. He has also been the chair of the allied health and nurses committee of EACTS. This team created a well-received postgraduate course, which acts as a platform to present research for nurses and allied health researchers. Richard has been invited to speak at several national medical and nursing societies and to contribute during annual meetings.

He has been married to his wife Anika since 2009 and they are the proud parents of two children, Lotte (2010) and Niels (2014).

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De verpleegkundige staf, niets is zo essentieel voor goede patiëntenzorg. Maar ook toegepaste wetenschap kan niet zonder hulp van deze uitzonderlijke groep mensen. Jullie hebben mij mede-gevormd in de eerste jaren van mijn carrière. Bijzondere mensen als Bas, Norma, Slawitsa, Roel en vele anderen ben ik daarvoor eeuwig dankbaar.

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De verpleegkundig specialisten Thoraxchirurgie. Maaike, wij kennen elkaar al sinds 1999. Sinds 2007 werken wij samen. Samen hebben wij ook de verpleegkundig specialist een essentieel onderdeel gemaakt van de afdeling Thoraxchirurgie. Yin en yang omschrijft ons goed: samen kunnen wij de afdeling, en alles wat daarbij hoort, aan. Ik wil je bedanken voor je vriendschap, begrip en steun in de afgelopen jaren. Jozefine, wat heb ik aan je moeten wennen. Wat een uitzonderlijke vrouw. Van je voorgeschiedenis en voorliefde voor science fiction tot aan je heldere en duidelijke inzichten. Een verrijking voor ons team en een fijne vriendin. Mijn dank voor je vriendschap, begrip en steun in de afgelopen jaren.

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I would also like to thank the very talented group of nurses with whom I have the honour to organise the annual meetings for nurses and allied health professionals during the meeting of European Association for Cardiothoracic Surgery (EACTS). It is an honour to work with people like Tara Bartley, Christina Bannister, Dorthe Bordinggaard, Lene Haus, Cristina Ruiz Segria and others. I look forward to continuing our mission to unite cardiac and thoracic surgery nurses on an European level. Working with you has helped me to become the person, nurse and researcher I am today.

De treinclub: in 2003 begonnen wij samen aan ons Master of Arts avontuur. 2 jaar lang deelden wij lief en leed en wisten wij ook nog de opleiding tot een goed einde te brengen. Iedere lesdag samen in de trein van Dordrecht naar Leiden en terug. Wie had verwacht dat wij elkaar 14 jaar later nog regelmatig zouden zien en nog altijd lief en leed delen. Lieve Tanja, Anneke en Suzan, wat zijn jullie toppers en wat ben ik blij dat wij al zoveel jaren alles kunnen bespreken en dat jullie mij hebben gesteund bij dit avontuur. De treinclub houden wij in ere! En Tanja, om het maar op papier te zetten: ik verwacht een uitnodiging voor je eigen promotie over enkele jaren.

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