Institutional report - Experimental

Effects of vacuum-assisted closure on central hemodynamics in a sternotomy wound model

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Abstract

Several authors have reported promising results with vacuum-assisted closure therapy in poststernotomy mediastinitis. The aim of this study was to investigate the hemodynamic outcome following the application of six negative pressures on an open sternotomy wound. Six 70-kg pigs underwent median sternotomy followed by vacuum-assisted closure therapy. Six negative pressures (−50, −75, −100, −125, −150, and −175 mmHg) were applied to each pig for 30 min each while hemodynamic parameters were measured. An increase in cardiac output was observed at −75 mmHg when compared to the other five pressures: −50 mmHg (P < 0.05; CI 0.12–1.13 l/min), −100 mmHg (P < 0.001; CI 0.34–1.32 l/min), −125 mmHg (P < 0.001; CI 0.51–1.52 l/min), −150 mmHg (P < 0.001; CI 0.50–1.47 l/min), and −175 mmHg (P < 0.05; CI 0.13–1.17 l/min). A decrease in systemic vascular resistance was observed at −75 mmHg when compared to −125 mmHg (P < 0.01; CI 108–552 dyn·s/cm²) and −150 mmHg (P < 0.01; CI 90–543 dyn·s/cm²), but not compared to the other pressures. No change (P = ns) was observed in heart frequency, mean arterial pressure or central venous pressure. Our data demonstrates that vacuum-assisted closure therapy of −50 to −175 mmHg does not impair the central hemodynamics in a porcine sternotomy model.

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1. Introduction

Recently, several studies have reported promising results following the use of VAC therapy in poststernotomy mediastinitis [1,2]. This therapy combines immediate stabilization of the open sternum with improved wound healing. Our group has previously demonstrated that delayed primary closure with VAC therapy can be guided by C-reactive protein [3]. Previous basic research on VAC therapy in pig models has demonstrated that −125 mmHg is the optimal negative pressure for wound healing [4], and therefore −125 mmHg has been adopted as a standard pressure in clinical use [1,2].

Vacuum-assisted closure was initially developed for wound healing in other areas in the body, and there are important aspects that require further consideration when it is applied to a sternotomy wound. Theoretically, VAC therapy might impair the right ventricular function, resulting in decreased cardiac output. There have also been reports of right ventricle rupture when using VAC therapy in poststernotomy mediastinitis [5]. Whether the application of VAC therapy to sternotomy wounds is detrimental to the central hemodynamics or not is of major concern since many patients with poststernotomy mediastinitis following cardiac surgery have reduced cardiac function. The aim of the present study was to evaluate the hemodynamic outcome during the application of VAC therapy at six different pressures (−50 to −175 mmHg) in a porcine sternotomy wound model.

2. Materials and methods

Six pigs with a mean body weight of 70±4 kg were used. All the animals received humane care in compliance...
with the European Convention on Animal Care. The experimental protocol for this study was approved by The Ethics Committee for Animal Research at Lund University, Sweden.

2.1. Anesthesia and surgical preparation

An intramuscular injection of ketamine (Ketalar™; Parke-Davis, Morris Plains, NJ) 30 mg/kg body weight was used for premedication. Anesthesia was induced with intravenous sodium thiopental (Pentothal™; Abbot Scandinavia, Stockholm, Sweden) 3–5 mg/kg body weight and maintained with a continuous infusion of 6 mg/kg/h pentobarbital (pentobarbital, Apoteksbolaget, Umeå, Sweden) in combination with 10 μg/kg/h fentanyl (fentanyl, Alpharma AB, Stockholm). In addition, nitrous oxide (65% in oxygen) was administered as an inhalation agent during mechanical ventilation. Pancuronium (Pavulon™; Organon Teknika, Boxtel, the Netherlands) was given intravenously (0.35 mg/kg/h) to achieve muscle paralysis. A Servo Ventilator 900 (Elema-Schönander, Sweden) was used for mechanical ventilation. Identical settings were used for all animals: volume-controlled, pressure-regulated ventilation, 10 l/min, 20 breaths/min, and an inhaled oxygen fraction of 35%. The arterial pressure was monitored via a catheter in the left carotid artery. A double-lumen central venous catheter was inserted into the left external jugular vein. A Swan-Ganz catheter (Abbott Laboratories, North Chicago, IL) was flow-directed into the pulmonary artery. The catheter was connected to a cardiac output monitor (Oximetrix 3, Abbott Laboratories, North Chicago, IL).

The hemodynamic data was collected with a data acquisition system (PowerLab, ADInstruments Ltd., Castle Hill, Australia). The cardiac output was measured by thermodilution and determined as the mean of three 10-ml saline bolus injections.

A midline sternotomy was performed and the polyurethane foam (KCI, Copenhagen, Denmark), was placed between the sternal edges. Evacuation tubes (KCI, Copenhagen, Denmark) were inserted into the foam layers. A second layer of foam was secured to the surrounding skin. The wound was sealed with a transparent adhesive drape (KCI, Copenhagen, Denmark). The two tubes were connected to a continuous vacuum source (V.A.C. pump unit, KCI, Copenhagen, Denmark).

2.2. Experimental protocol

After 1 h of stabilization baseline measurements were performed: mean arterial pressure, central venous pressure, and heart frequency. The cardiac output was measured and systemic vascular resistance was calculated. The baseline period was followed by the application of continuous negative pressure to the sternotomy wound. In order to eliminate time effects, the sequence of applying the six different negative pressures (–50, –75, –100, –125, –150, and –175 mmHg) was varied between the animals using a 6 by 6 Latin-square design. Each negative pressure was applied to the sternotomy wound for 30 min. Hemodynamic recordings were made on three occasions during the 30-min negative pressure period: after 10, 20, and 30 min of active vacuum therapy. A stabilizing 30-min baseline period without negative pressure was introduced before the application of each negative pressure. Baseline hemodynamic parameters were recorded on four occasions during each stabilizing period: immediately after vacuum disconnection, and after 10, 20, and 30 min without vacuum. In analogy with the active vacuum periods, only
the recordings after 10, 20 and 30 min without vacuum were included in the hemodynamic calculations.

2.3. Data analysis

A repeated-measurement general linear model was used to test the main effects of the treatment, minutes, subject, period and covariate (baseline) on cardiac output, heart frequency, mean arterial pressure, central venous pressure, and systemic vascular resistance. Posthoc testing of the treatment was performed using Tukey’s pairwise test. Analysis of the residuals was also performed to check for model adequacy. Anderson-Darling’s test was carried out to evaluate the assumption of normality and Levene’s test for heteroscedasticity was used to verify that the assumption of constant residual variance was justified. All $P$ values were adjusted with the Bonferroni procedure due to multiple analyses of the hemodynamic variables. A criterion level of $P<0.05$ was considered statistically significant. Significant $P$ values were presented together with a 95% confidence interval (CI).

3. Results

A higher cardiac output was observed during VAC therapy at $-75\, \text{mmHg}$ compared to the other pressures during the 30-min period, $-50\, \text{mmHg}$ ($P<0.05$; CI $0.12-1.13\, \text{l/min}$), $-100\, \text{mmHg}$ ($P<0.001$; CI $0.34-1.32\, \text{l/min}$), $-125\, \text{mmHg}$ ($P<0.001$; CI $0.51-1.52\, \text{l/min}$), $-150\, \text{mmHg}$ ($P<0.001$; CI $0.50-1.47\, \text{l/min}$), and $-175\, \text{mmHg}$ ($P<0.05$; CI $0.13-1.17\, \text{l/min}$) (Fig. 1). All six therapeutic pressures were compared to each other but no other pressure demonstrated an increase ($P=\text{ns}$) in cardiac output (Fig. 1).

A lower systemic vascular resistance was observed during VAC therapy at $-75\, \text{mmHg}$ during the 30-min period when compared to $-125\, \text{mmHg}$ ($P<0.01$; CI $108-552\, \text{dyn\cdot s/cm}^2$) and $-150\, \text{mmHg}$ ($P<0.01$; CI $90-543\, \text{dyn\cdot s/cm}^2$), but not when compared to $-50$, $-100$, or $-175\, \text{mmHg}$ ($P=\text{ns}$) (Fig. 2). No change ($P=\text{ns}$) in heart frequency (Fig. 3), mean arterial pressure (Fig. 4) or central venous pressure (Fig. 5) was observed during VAC therapy when all six pressures were compared to each other.

4. Discussion

Poststernotomy mediastinitis is a rare but serious and potentially lethal complication following cardiac surgery. The reported incidence of mediastinitis after sternotomy procedures in recent studies varies usually between 1 and 2% [6,7]. Mortality resulting from mediastinitis has been reported to range between 16 and 29% in recent studies [7–9].

Recently, clinical studies have reported promising results with VAC therapy in patients with deep sternal wound infection [1,2]. Animal studies by Morykwas and colleagues have demonstrated that VAC therapy accelerates granulation tissue formation, enhances bacteria elimination and increases the blood flow in adjacent tissue [4]. The VAC technique provides excellent drainage and sternal stabilization in combination with complete coverage of the wound. The clinical standard pressure during VAC therapy in patients with poststernotomy mediastinitis...
is currently $-125 \text{ mmHg}$. This pressure has been suggested on the basis of laser Doppler measurements of blood flow over the spine in a porcine wound model which indicated a peak flow at $-125 \text{ mmHg}$ [4]. Furthermore, granulation tissue formation has been studied at different negative pressures with a maximum increase in growth rate at $-125 \text{ mmHg}$ [10]. However, it has not yet been clearly demonstrated that $-125 \text{ mmHg}$ is the optimal pressure in the mediastinum. The organs in the mediastinum are hemodynamically crucial, but also susceptible to external forces. An important issue is the interaction between the polyurethane foam and the surrounding tissue. A less negative pressure level might lead to insufficient stability of the sternum and thus promote shear and stretching between the sternal edges and the right ventricle, with an increased risk of rupture [11]. On the other hand, too high negative pressure on the cardiac wall might impair the right ventricular function or compromise the function of coronary by-pass grafts.

Recently, Conquest and colleagues presented an experimental study that demonstrated a decrease in cardiac parameters during VAC therapy at $-50$ and $-125 \text{ mmHg}$ [12]. However, they did not describe in detail how the polyurethane foam was placed in the sternotomy wound.
It might be that they have placed foam below the sternal edges. We believe that an excessive amount of foam below the sternal level can result in a tamponade effect. Our group has recently described the importance of correct foam application, between and above the sternal level, in order to avoid hemodynamic impairment [2].

We found no impairment in cardiac output during VAC therapy at pressures between $50$ and $175$ mmHg. Instead, we observed an improvement in cardiac output during VAC therapy at $75$ mmHg during the 30-min period of application (Fig. 1). Furthermore, we observed a lower systemic vascular resistance at $75$ mmHg compared to $125$ and $150$ mmHg, but not when compared to $50$, $100$, or $175$ mmHg (Fig. 2).

One theoretical explanation of the improved cardiac output could be that the heart adopts a hemodynamically more beneficial shape during the application of negative pressure. The polyurethane-splinted sternotomy increases the volume of the thoracic cavity and this thoracic expansion in combination with vacuum application might contribute to more favorable hemodynamic conditions. Another explanation could be an increase in cardiac contractility caused by the direct action of negative pressure on the cardiac wall. Previous basic research has demonstrated that transmembrane proteins (integrins) work as mechanotransducers and transform extracellular force to intracellular signals [13]. This promotes the intracellular release of second messengers such as prostaglandins, inositol phosphates, protein kinase C, and intracellular calcium. Therefore, the application of topical negative pressure to porcine myocardial cells might induce an increase in cardiac contractility due to an increase in the intracellular calcium levels. Previous in vitro studies in chick heart have indicated that stretch-activated, transmembrane ion ($Ca^{2+}$) channels open in response to the application of negative pressure [14]. A third explanation might be related to an increase in venous return to the thoracic cavity during the application of negative pressure. However, we could not demonstrate any increase in central venous pressure during the application of VAC therapy (Fig. 5). The decrease in systemic vascular resistance is probably due to an autoregulatory response to the increase in cardiac output since no change in arterial blood pressure was detected.

One limitation in the present study is the lack of echocardiography during the experiments. Therefore, we have not the opportunity to detect possible ventricular wall stress, the geometry of the heart, or sudden diastolic dysfunction at different negative pressures. However, in a future study our research group will repeat parts of this study in a clinical setting and evaluate the cardiac function with the help of echocardiography. A comparison could be performed in patients with normal and low left ventricular function, respectively, and study beat-to-beat changes during vacuum-assisted closure application. This may be performed during foam changes while the patient is anaesthetized.

In conclusion, VAC therapy is established as an alternative in the treatment of poststernotomy mediastinitis. Our study demonstrates that, with a proper foam application technique, pressures between $-50$ and $-175$ mmHg can be applied without compromising the central hemodynamics. The use of $-125$ mmHg is widely accepted in clinical practice and we believe this should be the standard pressure in poststernotomy mediastinitis since the primary goal is accelerated wound healing in combination with sufficient sternal support.
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References


