Effect of vacuum-assisted closure on blood flow in the peristernal thoracic wall after internal mammary artery harvesting

Rainer Petzina, Lotta Gustafsson, Arash Mokhtari, Richard Ingemansson, Malin Malmsjö

Department of Medicine, Lund University Hospital, Lund, Sweden
Department of Cardiothoracic Surgery, Lund University Hospital, Lund, Sweden

Abstract

Objective: Vacuum-assisted closure (VAC) is a recently introduced method for the treatment of poststernotomy mediastinitis. The aim was to examine the effects of VAC negative pressure on peristernal soft tissue blood flow after internal mammary artery harvesting.

Methods: Microvascular blood flow was measured using laser Doppler velocimetry in a porcine sternotomy wound model. The effect of VAC negative pressure on blood flow to the wound edge was investigated on the right side, where the internal mammary artery was intact, and on the left side, where the internal mammary artery had been removed.

Results: Before removal of the left internal mammary artery, the blood flow was similar in the right and left peristernal wound edges, 2.5 cm from the edge (27/4 perfusion units (PU) on the right side and 32/3 PU on the left side, in muscle tissue). When the left internal mammary artery was surgically removed, the blood flow on the left side decreased (19/3 PU, in muscle tissue), while the skin blood flow was not affected. VAC negative pressure induced an immediate increase in wound edge blood flow both on the right side (43/9 PU, in muscle tissue at 75 mmHg), where the internal mammary artery was intact, and on the left side, where the internal mammary artery had been removed (49/11 PU, in muscle tissue at 75 mmHg). The increase in blood flow was similar on both sides at 75 mmHg and at 125 mmHg.

Conclusions: The peristernal wound edge microvascular blood flow is decreased when the left internal mammary artery is removed. VAC therapy stimulates blood flow in the peristernal thoracic wall after internal mammary artery harvesting.

Keywords: Animal model; Experimental surgery; Mediastinal infection; Vascular tone and reactivity; Wound healing

1. Introduction

Mediastinitis is a devastating complication in open-heart surgery. Vacuum-assisted closure (VAC) is a recently introduced technique that promotes the healing of difficult wounds, including poststernotomy mediastinitis [1]. The technique entails application of a negative pressure to a sealed, airtight wound. The suction force created by VAC therapy enables the drainage of excessive fluid and debris, which leads to the removal of wound edema, reduction in bacterial count and enhanced granulation tissue formation [1–4].

Enhancing blood flow to the soft tissue of the peristernal wound is presumably one of the mechanisms by which VAC therapy facilitates healing. Laser Doppler measurements have shown an increase in blood flow to a wound on the pig back when −125 mmHg is applied [4]. In a porcine sternotomy wound model, the peak increase in blood flow was observed at −75 and −100 mmHg. 2.5 cm from the wound edge, while high pressures, closer to the wound edge, induce hypoperfusion [5]. Negative pressure has been shown to induce an immediate increase in capillary diameter and blood flow on the dorsal side of rabbit ears [6], which may explain the mechanisms by which blood flow to wounds is stimulated.

The internal mammary artery is the bypass graft of choice due to its superior long-term patency [7]. Postoperative mediastinitis is more common when bilateral harvesting of the internal mammary arteries has been performed, especially in patients with diabetes and obesity [8–10]. The reason for the high risk of infection in these patients may be that the soft tissue is poorly perfused postoperatively. The blood flow and the subsequent nutrition of the wound edge may then not be sufficient to allow healing. It has already been shown that VAC therapy enhances blood flow to the soft tissue of the peristernal wound when the internal mammary artery is intact [5]. No study has yet been performed to examine the effect of VAC therapy on peristernal wound edge blood flow after internal mammary artery harvesting. In the present study, microvascular blood flow was measured using...
laser Doppler velocimetry in a porcine sternotomy wound model. The effect of VAC negative pressure on blood flow to the wound edge was investigated both on the right side, where the internal mammary artery was intact, and on the left side, where the internal mammary artery had been removed.

2. Material and methods

2.1. Animals

An uninfected porcine sternotomy wound model was used for the present study. Six domestic landrace pigs of both genders, with a mean body weight of 70 kg, were fasted overnight with free access to water. The study was approved by the Ethics Committee for Animal Research, Lund University, Sweden. The investigation complied with the ‘Guide for the Care and Use of Laboratory Animals’ as recommended by the U.S. National Institutes of Health and published by the National Academies Press (1996).

2.2. Anesthesia and surgical procedure

Ketamine and xylazin were used for premedication. An infusion of propofol and fentanyl was given to maintain anesthesia and atracuriumbensylate was given to achieve muscle paralysis. A midline sternotomy was performed and the pericardium was opened. The left hemisternum was elevated and prepared for surgical removal of the left internal mammary artery and left untouched for 10 min for the microvascular blood flow to stabilize. Baseline blood flow measurements were then recorded (as described in the following text). The left internal mammary artery was dissected free as a wide pedicle (which took 12–15 min) and a new series of measurements were performed immediately. After these experiments, the sternotomy wound was prepared for VAC therapy. A polyurethane foam dressing was placed between the sternal edges and two non-collapsible drainage tubes were inserted into the foam. The open wound was then sealed with a transparent adhesive drape. The drainage tubes were connected to a purpose-built pump unit, KCI, Copenhagen, Denmark, which was set to deliver a continuous pressure of 75 mmHg.

2.3. Laser Doppler velocimetry

Microvascular blood flow was measured using laser Doppler velocimetry, with a multichannel PeriFlux System 5000 (Perimed, Stockholm, Sweden). Laser Doppler velocimetry is a technique that quantifies the motion of red blood cells in a specific volume, and has been applied extensively to measure blood flow in flaps during plastic surgery procedures [11]. In this method, a fiberoptic probe carries a beam of laser light. Light reflected from moving blood cells undergoes a change in wavelength (Doppler shift) while light reflected on static objects is unchanged. The magnitude and frequency distribution of these changes in wavelength are directly related to the number and velocity of the blood cells. The information is collected by a returning fiber, converted into an electronic signal and analyzed. For the current experiments, recordings were made with three parallel probes. Two 0.5 mm filament probes (Probe 418-1, Perimed, Stockholm, Sweden) were used to measure microvascular blood flow in muscle tissue, and a skin probe was used to measure skin blood flow.

The aim of this study was to examine the stimulatory effects of negative pressure on blood flow after internal mammary artery removal. A distance of 2.5 cm from the wound edge was chosen for the measurement, since peak blood flow responses have been demonstrated at this location in a previous study [5]. Filament probes were inserted into the muscle tissue between the corpus and manubrium sterni, posterior to the bone, 2.5 cm from the wound edge. A skin probe was placed on the skin, 2.5 cm from the wound edge, to measure blood flow before and after left internal mammary artery removal.

In the VAC experiments, pressures of −75 and −125 mmHg were applied to the wound, and microvascular blood flow was measured continuously by the filament probes in the muscle tissue. To monitor systemic microvascular blood flow changes, a reference probe was placed on the skin, 10 cm from the wound edge. It has been demonstrated that subatmospheric pressure only has local effects on blood flow and, at 10 cm from the wound edge, only systemic effects contribute [5]. The pressures of −75 and −125 mmHg were chosen on the basis of previous experiments showing that the increase in blood flow is greatest at −75 mmHg [5], while −125 mmHg is the pressure of choice for the clinical treatment of poststernotomy mediastinitis [12]. During the entire experiment the wound edge skin temperature was recorded, to ensure that the tissue temperature did not change.

2.4. Calculations and statistics

The laser Doppler velocimetry experiments were performed on six pigs. The output was continuously registered using PeriSoft software (Perimed, Stockholm, Sweden). Microvascular blood flow was expressed in terms of ‘perfusion units’ (PU). Calculations and statistical analysis were performed using GraphPad 4.0 software. Statistical analysis was performed using the Mann–Whitney test when comparing two groups and the Kruskal–Wallis test with Dunn’s test for multiple comparisons when comparing three groups or more. Significance was defined as ‘’P<0.05, ‘’’P<0.01, ‘’’’P<0.001 and P>0.05 (not significant, n.s.). Values are presented as mean±the standard error on the mean (SEM).

3. Results

Before removal of the left internal mammary artery, the microvascular blood flow was similar in the muscle tissue on the right and left side (27±4 on the right and 32±3 on the left side, P=n.s.). When the left internal mammary artery had been surgically harvested the blood flow in the muscle tissue on the left side (2.5 cm from the wound edge) was less, while the blood flow in the skin on the left side (2.5 cm from the wound edge) was not affected (Figs. 1 and 2).
VAC therapy induced an immediate increase in the blood flow in the muscle tissue both on the left side, where the internal mammary artery had been removed, and on the right side, where the internal mammary artery was intact (Figs. 3 and 4). The blood flow after VAC application (both for $-75$ and $-125$ mmHg) was similar on the right and the left side (Fig. 3).

The skin blood flow, 10 cm from the wound edge, was not affected by VAC therapy, indicating that the changes in blood flow were localized to the wound and no systemic effects contributed. The basal blood flow was $27 \pm 3$ PU in the skin and $24 \pm 3$ PU in the muscle tissue.

4. Discussion

The aim was to analyze the effect of internal mammary artery harvesting on peristernal soft tissue microvascular blood flow and to evaluate the effects of VAC therapy. The left internal mammary artery was harvested and blood flow was measured using laser Doppler velocimetry in muscle tissue and in the skin, 2.5 cm from the wound edge. Before internal mammary artery harvesting, the blood flow was similar in the right and left peristernal wound edges. After left internal mammary artery removal, the blood flow in the muscle tissue on the left side was less, while the blood flow in the skin was not affected. The sternum is supplied with blood from three different types of vessels: (1) branches of the internal thoracic artery that supplies both the sternum and the pectoralis major (‘sternal/perforating branches’), (2) branches of the internal thoracic artery that supplies both the sternum and an adjoining intercostal space (‘sternal/intercostal branches’) and (3) posterior intercostal arteries that do not anastomose with an internal thoracic artery branch but continue past the internal mammary artery to reach the sternum [13]. When the internal mammary artery is surgically removed with a wide pedicle, only the ‘sternal/perforating branches’ remain to supply blood to the peristernal muscle tissue, which may explain the decrease in flow. It has been shown previously that internal mammary artery dissection causes sternal ischemia [14], which may
result in insufficient nutrition for healing of the wound edge. This is probably the reason for postoperative mediastinitis being more common when bilateral harvesting has been performed [8—10]. In the present study, the blood flow to the skin was not affected by internal mammary artery removal. Blood is supplied to the skin from skin arteries that have no connection with the internal mammary artery. Previous animal studies have shown beneficial effects of subatmospheric pressure on wound edge microvascular blood flow. In a wound on the back of pigs, the blood flow increased four times above baseline values when a pressure of \(-75\) mmHg was applied, whereas it was inhibited at pressures of \(-400\) mmHg and greater [15]. In a recent study, using a porcine sternotomy wound model, we demonstrated that the changes in blood flow to the wound edge due to VAC therapy varied with the distance from the wound edge and the pressure applied [5]. High negative pressures induced hypoperfusion close to the wound edge [5]. Maximum increase in blood flow was observed 2.5 cm from the wound edge at \(-75\) mmHg [5], and these parameters were therefore chosen for the present study. Since \(-125\) mmHg is the pressure of choice for the clinical treatment of poststernotomy mediastinitis [12], effects at this pressure were also investigated.

Pressures of \(-75\) and \(-125\) mmHg induced an immediate increase in blood flow both on the right side, where the internal mammary artery was intact, and on the left side, where the internal mammary artery had been removed. The blood flow after VAC application was similar on the right and on the left side. We can only speculate about the reason for this massive increase in blood flow during the application of negative pressure on the left side, despite prior internal mammary artery harvesting. Presumably, VAC therapy recruits blood from collateral circulation including the ‘sternal/perforating branches.’ Furthermore, it has been shown that internal mammary artery dissection results in hypoperfusion and ischemia of the peristernal tissue [14], which may elicit the release of vasorelaxant factors that dilate blood vessels to restore blood flow.

The pressure of choice for clinical treatment of poststernotomy mediastinitis is \(-125\) mmHg. This pressure was chosen on the basis of a small animal study on a peripheral wound [4]. Positive effects on the blood flow in the peristernal thoracic wall [5], hemodynamics [16] and biochemical pathways involved in granulation tissue formation [17] have been observed at less negative pressures (\(-75\) to \(-100\) mmHg) than at the clinically adopted negative pressure (\(-125\) mmHg). When VAC therapy is used in a sternotomy wound, patients sometimes experience pain and the pressure has to be reduced [12]. In the present study we show that the blood flow at \(-75\) mmHg and at \(-125\) mmHg is similar. These results support the use of less negative pressures for VAC treatment of sternotomy wounds.

Unilateral or bilateral harvesting of the internal mammary arteries is a common practice in thoracic surgery. Postoperative mediastinitis is more common when bilateral harvesting has been performed, especially in patients with diabetes and obesity [8—10]. The reason for the high risk of infection in these groups of patients may be that the soft tissue is poorly perfused postoperatively. The blood flow and the subsequent nutrition of the wound edge may then not be sufficient for healing. Stimulating blood flow to the sternotomy wound edge in these patients may be crucial to ensure healing. Further studies aimed at optimizing blood flow to the sternotomy wound edge may lead to the development of safe techniques for wound closure in patients at high risk of postoperative mediastinitis, e.g. performing delayed primary wound closure following a brief period of VAC therapy.

One limitation of the present study is that the blood flow was only monitored during a short period of time and the effects may be temporal, with the patient and the wound edge eventually acclimatizing to the treatment [18]. Studies must be performed on the long-term nature of the effects on blood flow before recommendations can be made regarding delayed primary wound closure following VAC therapy in patients at high risk of postoperative mediastinitis. Furthermore, the current study was performed on uninfected animals that lacked the systemic and local conditions associated with active sternal wound infection. VAC therapy has been shown to be advantageous in infected or non-healing chronic wounds but not in acutely injured wounds [9]. An infected wound is often edematous and perfusion is decreased, leading to decreased nutrition of the wound margins. VAC therapy decreases wound edema [2] and improves blood flow, as shown in the present study. It is possible that the effects of VAC therapy may be even more pronounced in an infected wound than in this experimental setup employing an uninfected acute sternotomy wound.

The exact mechanism by which negative pressure stimulates blood flow is not known. In a study on wounds...
on the dorsal side of rabbit ears VAC was shown to induced an immediate increase in capillary diameter and blood flow velocity [6]. VAC also stimulated endothelial proliferation and angiogenesis [6]. Negative pressure is believed to induce mechanical stress and a pressure gradient between the wound and the surrounding tissue, which may cause a surge of blood to the wound, promote blood flow velocity, dilate capillaries and open up the capillary beds [19,20]. Mechanical forces and increased blood flow affect the cytoskeleton in the vascular cells and is known to stimulate endothelial proliferation, capillary budding and angiogenesis [21].

In conclusion, VAC therapy induces prominent stimulatory effects on blood flow in the peristernal wound edge after internal mammary artery dissection. VAC therapy may be especially beneficial for the treatment of sternotomy wounds where unilateral or bilateral internal mammary artery harvesting has been performed.

Acknowledgments

We thank Roland Hetzer, MD, PhD, at the German Heart Institute in Berlin for valuable support. This study was supported by the Åke-Wieberg Foundation, the Magnus Bergvall Foundation, the Swedish Medical Association, the Royal Physiographic Society in Lund, the Swedish Medical Research Council, the Crafoord Foundation, the Swedish Heart-Lung Foundation, the Swedish Government Grant for Clinical Research and the Swedish Hypertension Society.

References