Can the Vineberg procedure improve blood supply to the latissimus dorsi muscle during cardiomyoplasty?

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Abstract

To evaluate the feasibility of implanting the internal mammary artery (IMA) in the latissimus dorsi muscle (LDM) during cardiomyoplasty to create a bipediculated muscle flap. Four dogs went under cardiomyoplasty with the right LDM. The IMA was dissected with the intercostal arteries branching from the IMA clipped except for the three most distal branches. The distal part of the IMA was tunneled in the LDM from ventral to dorsal and left to bleed in the muscle flap. The muscle flap was gradually stimulated to achieve stimulation every 10 heart beats in 10 days. Three months after surgery the dogs were evaluated with echocardiography and a selective angiogram of the IMA. Immunohistochemistry was performed to evaluate the density of capillaries in the LDM.

One dog died one week after the surgery due to thrombus in the iliac bifurcation. Three months after surgery, the IMA was patent in the remaining three dogs. Angiogram showed multiple collaterals from the IMA perfusing into the middle segment of the LDM in each dog. Immunohistochemistry showed that the density of capillary followed a gradient from distal to proximal in the LDM (p=0.1). Three months after surgery, stimulated beats had an aortic velocity increased by 19.2% and a left ventricular end systolic volume reduced by 36% when compared to non assisted beats. The IMA transposed in the LDM stimulated for cardiomyoplasty remained patent for three months. Multiple collaterals developed from the IMA seem to contribute to LDM perfusion.

Key words: Cardiomyoplasty, canine, skeletal muscle, blood flow, capillary, internal thoracic artery.

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Introduction

Skeletal muscle ventricles, dynamic cardiomyoplasty and aortomyoplasty utilize the power of a skeletal muscle to assist the myocardium during heart failure.[11,14,22] Long-term cardiac assist with a skeletal muscle has been difficult to achieve because the skeletal muscle deteriorates over time.[21,26]

Oakley et al[21] have shown that skeletal muscle deterioration is due to electrical stimulation, reduction of preload for the skeletal muscle and ischemia. Ischemia has been pointed has the major factor affecting the muscle long-term survival since the ischemia follow a gradient from proximal to distal along the muscle.[2,13,19,26,27] Power of the skeletal muscle flap is positively correlated to the muscle blood flow.[19] Vascular delay and electrical prestimulation have been associated with an improvement in muscle blood flow and performance during cardiomyoplasty.[1,5,6,12,13,38-40] After vascular delay and electrical stimulation the supply for the muscle flap is still based only on the thoracodorsal artery. Vascular delay and prestimulation requires two surgical procedures, which is not optimal in patients with heart failure.

Creation of a bipediculated muscle flap in one surgical intervention would more likely be optimal to improve blood flow of the middle and distal parts of the latissimus dorsi muscle. A bipediculated muscle flap can be created with vascular anastomosis. However, perforating arteries perfusing the middle and distal parts of the latissimus dorsi muscle are too small to provide a reliable improvement of blood flow. The Vineberg procedure with the internal mammary artery represents a reasonable alternative to create a bipediculated muscle

flap since it has been used to improve in the long-term perfusion of the ischemic myocardium.[8,37] The purpose of that study was to demonstrate the feasibility of the Vineberg procedure during cardiomyoplasty.

Materials and Methods

Four dogs weighting between 24.00 and 29.00 Kg were entered in the study. The study protocol was approved by the Animal Care and Use Committee of Colorado State University. After induction of general anesthesia dogs went under a dynamic cardiomyoplasty as described previously.[30] The right latissimus dorsi muscle was dissected on it thoracodorsal neurovascular pedicle. Intramuscular electrodes were placed in the proximal part of the latissimus dorsi to capture the thoracodorsal nerve. A fifth and second intercostal thoracotomies were performed. After partial resection of the second rib the latissimus dorsi muscle was introduced into the thoracic cavity. The proximal part of the latissimus dorsi muscle was sutured to the periosteum of the second rib. A vascular clamp was placed on the right internal mammary artery (IMA). The right IMA was then dissected along the border of the sternum. Distal branches were not ligated. The IMA was left attached to the brachiocephalic trunk. The distal part of the right IMA was introduced in a tunneled created in the middle portion of the latissimus dorsi muscle by blunt dissection (Figure 1). The vascular clamp was then released and the IMA left to bleed in the muscle. The skeletal muscle flap was applied around the heart in a clockwise fashion.[23,30] A cardiomyostimulator (Telectronics, Englewood, Colorado) was connected to the intramuscular electrodes and the sensing electrodes inserted in the right ventricle (Illini Group, Illinois). The cardiomyostimulator was inserted in a pocket in the abdominal wall. The intercostal thoracotomy was closed in a routine fashion with a thoracostomy drain and a subcutaneous drain. Postoperatively the dogs were maintained on aspirin (5 mg/kg every other day orally) for 14 days to prevent thrombosis of the IMA.

The latissimus dorsi muscle was not stimulated for two days. Two days after surgery electrical stimulation was started at 5 volts, 0.1 ms, and two pulses per impulse. The cardiosynchronization ratio was set at 10:1. The number of pulses was increased to 4 after 2 days and then to 6 two days later.

After euthanasia, samples from the proximal, middle and distal third of the latissimus dorsi muscle were harvested for immuniohistochemical staining and evaluation of capillary density. Immunohistochemical staining was performed using standard techniques on an automated stainer (Discovery System, Ventanna Medical Systems, Tucson, AZ). All reagents were purchased from Ventana Medical Systems (Tucson, Arizona) and incubated at 37 ºC unless otherwise noted. Briefly, 4 micron sections were cut and mounted on positively charged slides. The sections were deparaffinized then rehydrated with descending alcohol concentrations to buffer. Antigen retrieval was with protease 1 incubation for 16 minutes. The sections were then incubated in the primary antibody for 4 hours. The primary antibody used was a polyclonal anti-Factor VIII Related Antigen antibody incubated for 30 minutes at a dilution of 1:500. A pre-diluted, universal biotinylated secondary antibody and a DAB MAP detection kit (Ventanna Medical Systems, Tucson, AZ) were utilized to detect the immunoreactive complexes. The slides were then counterstained with Mayer's haematoxylin.

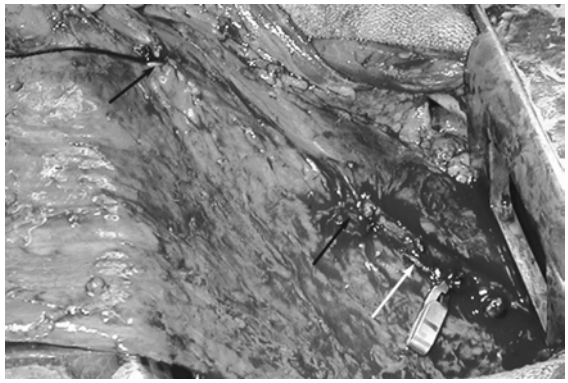

Figure 1: The IMA (white arrow) has been implanted in the latissimus dorsi muscle. The two black arrows show the length of tunnel for the IMA into the latissimus dorsi muscle.

Image analysis was performed using KS 400 system software from Carl Zeiss (Thornwood, New York.) For each tissue section five random images were taken using a Carl Zeiss Axioplan 2 imaging scope coupled with an AxioCam HRc Carl Zeiss camera. Selected images contained predominantly muscle tissue. Briefly, non-muscle portions of the image were cropped out. Using a threshold feature, DAB stained pixels were converted to white and unstained pixels to black yielding a binary image. Vascular density was then determined as the number of white pixels over total pixels. For standardization, the camera exposure and the threshold levels were constant for the acquisition and analysis of all images.

ANOVA test for repeated measures was used to evaluate the effect of stimulation on echocardiographic parameters. A Kruskal-Wallis test was used to evaluate the density of capillaries in the proximal, middle, and distal portion of the latissimus dorsi muscle. Level of significance was set at $p<0.1$ since the sample size was small.

Results

The four dogs entered in the study survived the procedure. One dog was euthanized one week after surgery because of a thrombus in the iliac bifurcation. On necropsy, the IMA was patent in the latissimus dorsi muscle.

The three other dogs survived for 3 months. Angiogram of the IMA showed that the three arteries

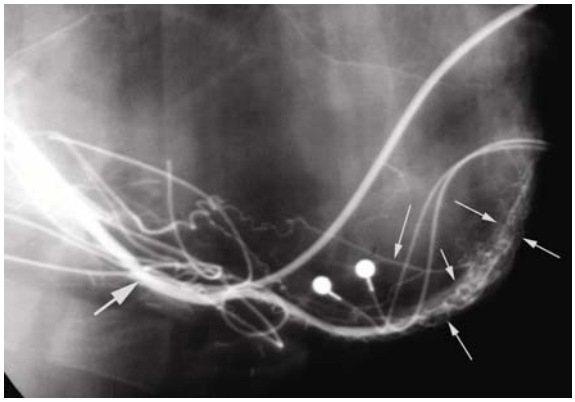

Figure 2: Angiogram three months after implantation of the IMA (large arrow) in the latissimus dorsi muscle. Multiple collaterals developed form the IMA (small arrow) are perfusing the middle and distal part of the latissimus dorsi muscle.

were patent (Figure 2). The angiogram also showed that angiogenesis was present in the distal part of the latissimus dorsi muscle. Measurement of density of capillaries showed a gradient from distal (0.71 ± 0.30) to proximal (0.30 ± 0.10) (p=0.100) (Figure 3). The density of capillaries was 0.20 ± 0.10 in the middle part of the LDM. The density of capillaries was double in the distal part compared to the proximal part.

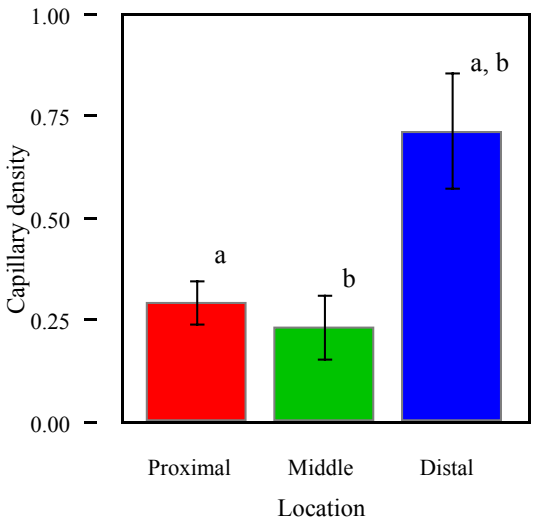

Figure 3: Capillary density in the proximal, middle and distal third of the latissimus dorsi muscle. P=0.1

On echocardiography three months after surgery, stimulated beats had an ejection fraction increased by 5%, an aortic velocity increased by 19.2% and a left ventricular end systolic volume reduced by 36% when compared to non assisted beats (Table 1).
the improved blood flow still follows a gradient from proximal to distal in the latissimus dorsi muscle. The

Discussion

Table 1: Echocardiographic data of assisted and non- assisted beats recorded in three dogs treated with cardiomyoplasty and the Vineberg procedure

Parameter	non-assisted	assisted	p
EF (%)	59.90 ± 16.20	63.00 ± 16.50	0.042
LVESVI (ml/m^2)	40.50 ± 36.60	26.00 ± 28.80	0.086
LVEDVI (ml/m^2)	40.90 ± 10.70	38.40 ± 8.90	0.150
AV (cm/sec)	1.30 ± 0.60	1.50 ± 0.40	0.148

SF: Shortening Fraction; EF: Ejection Fraction; LVESVI: Left Ventricular End Systolic Volume Index; LVEDVI: left Ventricular End Diastolic Volume Index; AV: Aortic Velocity

The internal mammary artery implanted in the latissimus dorsi muscle at the time of cardiomyoplasty remained patent after three months of continuous cardiac assist. The Vineberg procedure resulted in an increase number of capillaries seen on angiogram and immunohistochemistry in the distal segment of the latissimus dorsi muscle. The Vineberg procedure allows the creation of bipediculated muscle flap suitable for cardiomyoplasty, aortomyoplasty, and ventricular pouch.

Vascular delay and prestimulation have been used to improve blood flow to the latissimus dorsi muscle by increasing the number of capillaries within the muscle flap.[13,36,40] Even after vascular delay and prestimulation Vineberg procedure seems to be able to provide a density of capillaries with a gradient from distal to proximal, which should translate into an augmentation of blood flow in the distal segment of the muscle flap.

The blood supply to the latissimus dorsi muscle after vascular delay and electrical prestimulation is only based on one pedicle, the thoracodorsal artery. The Vineberg procedure provides, with the IMA, a second source of arterial blood supply to the latissimus dorsi muscle. We did not measure the blood flow in this study however, since it has been shown that a bipediculated muscle flap has a better blood flow than a single pedicle muscle,[24,31] we can assume that the Vineberg procedure

will be more efficient to improve blood flow than vascular delay and/or electrical prestimulation.

The Vineberg procedure cannot improve/immediately the blood flow in the muscle because it requires angiogenesis and connection with preexisting capillaries. However, the Vineberg procedure has been used successfully clinically and the internal mammary artery is the gold standard conduit for revascularization of the ischemic myocardium. The combination of electrical stimulation with the Vineberg procedure would likely be very beneficial. Electrical prestimulation has been shown to improve the number of capillaries within the muscle flap in less than three weeks.[5,6] Electrical prestimulation should enhance the Vineberg procedure by providing an optimal environment the IMA to establish anastomosis with a greater number of capillaries. It will have the potential then to improve blood flow in a larger part of the latissimus dorsi muscle.

In this study, the IMA was implanted in the middle part of the latissimus dorsi muscle flap. However it could be implanted in the distal part of the muscle, which is the segment that suffers the most from ischemia during cardiomyoplasty.[13,36] Implantation of the IMA in the muscle flap could be performed before or after completion of the wrap depending of the proximity of the segment of the muscle recipient of the artery to the IMA.

After releasing the clamp, bleeding within the skeletal muscle around the artery resulted in an hematoma that might affect the compliance of the muscle in the early postoperative period. We did not notice in these dogs any deterioration of the cardiac function. However, a failing myocardium might be susceptible to modification of the compliance of the muscle. It has been shown that after cardiomyoplasty the skeletal muscle produces an embarrassment for the failing heart. Cardiac function has been reduced up to 50% by the skeletal muscle wrapped around the failing heart immediately after surgery.[9,10,17,18] More likely, this embarrassment is resulting from edema occurring within the muscle flap after dissection of thoracodorsal pedicle. The Vineberg procedure has also the potential to worsen the edema within the muscle flap because the drainage of the muscle is not improved until enough collateral circulation develops.

In the last decade, muscle preservation during cardiac assist has been significantly improved with vascular delay, in situ electrical prestimulation, better training and stimulation of the skeletal muscle.[3,4,32-34,36,39,40] The Vineberg procedure should contribute to the improvement of blood supply and survival of the latissimus dorsi muscle during long-term cardiac assist. Addition of ventricular defibrillator has been shown to improve survival of patients treated by cardiomyoplasty.[15,16,35] The most recent data with cardiomyoplasty has shown that survival after cardiomyoplasty is as good as with heart transplantation.[32] Combination of these different procedures should result in a more viable and more powerful muscle to support the failing heart. Cardiomyoplasty became out of favor for the treatment of heart failure because of lack of long-term improvement of cardiac function. Since major improvements have been made in muscle physiology, muscle perfusion and training, it would be worth having a second look at the cardiomyoplasty to assist the failing heart.[7] The amount of work produced by the skeletal muscle is a function of the blood flow in the muscle.[19] Therefore, the utilization of a skeletal muscle with a significant improvement of its blood flow and better stimulation protocol should significantly improve cardiac assist and provide sustained systolic augmentation. Cardiomyoplasty should still be considered as a valuable option for the treatment of patients in heart failure.

A limitation of the study is the limited number of experiments and the absence of control. This study is a pilot study to show that the concept of the Vineberg procedure can be applied to skeletal muscle during cardio-biossist. Blood flow was not measured during the experiment, which should be the ultimate data to collect to confirm the improvement in perfusion of the latissimus dorsi muscle. However the augmentation of capillary density is already an indication of more likely an augmentation of blood flow.[13,36,40] The density of capillary doubled in the distal segment of the latissimus dorsi muscle when compared to the proximal segment. This augmentation was not significant more likely because of the limited number of experiments. This is confirmed by the low power of the study.

The Vineberg procedure by creating a bipediculated muscle flap could be used to improve the skeletal muscle function during cardiomyoplasty or aortomyoplasty. Since the internal mammary artery is a robust graft extensively used for long-term coronary bypass we can expect the Vineberg procedure to create a bipediculated muscle flap suitable for long-term cardiac assist. Patients with myocardial infarction treated with the Vineberg procedure had sustained an improvement of their cardiac function over many years.[20,25] Cardiac function was improved on echocardiography between assisted and non-assisted beats after three months of continuous stimulation with a cardiosynchronization ratio of 10:1. However, improvement of cardiac function can be due to augmentation of blood flow within the muscle,[19] the training protocol[28,29] or the short-term follow up. The Vineberg procedure should be tested in a longer-term study with a model of failure.

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