Evaluation of stimulation parameters on aortomyoplasty, using Latissimus Dorsi muscle in a goat model: an acute study

Ardeshir Hakami\textsuperscript{b},*, William P. Santamore\textsuperscript{a}, Richard W. Stremel\textsuperscript{a}, Gordon Tobin\textsuperscript{a}, Vibeke E. Hjortdal\textsuperscript{b}

\textsuperscript{a}Department of Surgery, Division of Thoracic and Cardiovascular Surgery, University of Louisville, Louisville, KY, USA
\textsuperscript{b}Institute for Experimental Clinical Research, Skejby Hospital, Bredestrupsgaardsvej, Aarhus, Denmark

Received 21 December 1998; received in revised form 19 May 1999; accepted 25 May 1999

Abstract

Objective: Dynamic aortomyoplasty using Latissimus Dorsi muscle (LDM) has been shown to improve myocardial function. However, systematic examination of the effects of stimulation parameters on aortic wrap function has not been done. Thus, the present study measures the direct effect of stimulation voltage, pulse train duration, frequency of the pulses, and the duration of the stimulation delay from R wave on the aortic wrap function. Methods: In eight female goats, the left LDM was wrapped around the descending aorta. The muscle was then subjected to electrical stimulation, altering frequency of stimulation pulses (16.6, 20, 25, 33 and 50 Hz), amplitude (2, 4, 6, 8 and 10 V), and number of pulses (2, 4, 6, 8 and 10 pulses) in a train stimulation. Left ventricular, aortic pressure, and pressure generated by LDM on aorta (wrap pressure) was measured. The changes in hemodynamic parameters mentioned above were calculated and compared for different stimulation parameters during unassisted and assisted cardiac cycles. Results: Aortomyoplasty counterpulsation using LDM provided significant improvement in wrap pressure (78 mmHg ± 2), aortic diastolic pressure, and changes in aortic diastolic pressure from 2 to 4 V (P < 0.05). Further increase in amplitude did not make any significant improvements of the above mentioned parameters. Significant augmentation of wrap pressure (82 mmHg ± 2), aortic diastolic pressure (79 mmHg ± 3) and changes in aortic diastolic pressure (12 mmHg ± 1) occurred at 6 pulses (P < 0.05). Other changes in number of pulses did not show any significant improvements. Significant improvement of wrap pressure (80 mmHg ± 2), aortic diastolic pressure (73 mmHg ± 3) and changes in aortic diastolic pressure (12 mmHg ± 1) was observed with a frequency of 33 Hz. To examine a wide range of delays from the onset of the QRS wave to LDM stimulation, stimulation was delivered randomly. The exact delay was determined from the ECG signal and superimposed LDM stimulation pulses. Conclusions: In this study we present a new measurement, wrap pressure. We also present that in aortomyoplasty using LDM, the most significant improvement in wrap pressure, aortic diastolic pressure and changes in aortic diastolic pressure occurs when the stimulation consists of an amplitude of 4 V, a frequency of 33 Hz and a train stimulation of 6 pulses. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Aortomyoplasty; Electrical stimulation; Wrap pressure

1. Introduction

Intra-aortic balloon diastolic counterpulsation has been widely used clinically for the last 15 years to support the failing heart. However, the invasive nature of the balloon limits the duration of support. Several recent studies have demonstrated the feasibility of cardiac assistance using counterpulsation with the synchronous contraction of skeletal muscles [1,2]. Aortomyoplasty is a surgical procedure that consists of wrapping a pedicled muscle graft around the ascending or descending aorta and then synchronously electrostimulating the muscle mass in each diastole to compress the aorta. Aortomyoplasty offers a hope of long term support for the failing heart.

Previous investigators have shown that aortomyoplasty improves mean aortic diastolic pressure [3], and subendocardial viability index [2–4]. However, the effects of stimulation parameters on aortic wrap function have not been systematically examined. Thus, the present study measured the direct effect of stimulation voltage, pulse train duration, frequency, and the delay for the onset of the QRS wave to skeletal muscle stimulation. We directly assessed muscle function by measuring the wrap pressure, the pressure induced by the muscle on aorta. Aortic wrap function was also assessed by measuring mean aortic diastolic pressure.
2. Methods

2.1. Preparation

All procedures were carried out in accordance with the ‘Guide for the Care and Use of Laboratory Animals’ prepared by the National Academy of Sciences (NIH publication No. 85–23, revised 1985). This study was also approved by Institutional Animal Care and Use Committee (IACUC).

Eight adult female goats, weighing 30–60 kg, were anesthetized using a pre-induction dose of xylazine (0.1 mg/kg) administered intravenously (i.v.) followed by an i.v. induction dose of xylazine–ketamine (0.08 mg/kg xylazine; 4 mg/kg ketamine). The animals were intubated and mechanically ventilated (Hallowel 2000, MA). Anesthesia was maintained with oxygen and isoflurane 2–4%.

With the goat in the right lateral decubitus position, the left LDM was exposed via a posterolateral thoracic incision along the anterior border of the LDM.

The perforators from the intercostal arteries to the distal portion of the muscle were ligated and cut. The number of perforators varied from two to three. The muscle was detached from its insertion and origin, preserving its neurovascular bundle.

2.2. LDM and configuration of extra-aortic wrap

The LDM was trimmed to 4–6 cm wide by removing the outer segments as previously described [4]. The thoracodorsal nerve was carefully free dissected and a nerve cuff electrode (Medtronic, Minneapolis, MN) was placed around the thoracodorsal nerve and secured from sliding by suturing it to the muscle. The nerve cuff leads were connected to an electrical pulse stimulator (model S8800, Grass, Quincy, MA). The muscle was then introduced into the thoracic cavity through a 2 cm window at the anterolateral portion of the second rib. A standard lateral thoracotomy at the level of fifth intercostal space was performed. The aorta was free dissected from its pleural attachments proximally to the origin of the left subclavian artery and distally to the level of the eighth intercostal arteries. The most proximal six to seven pairs of intercostal arteries were ligated at their origin from aorta and divided. The muscle was wrapped 1.5 times around the descending aorta in a spiraled counterclockwise (CcW) fashion, as viewed from the abdominal cavity, covering a total length of 10–12 cm of the aorta. The stability of the wrap was secured by suturing the muscle tight to itself. The wrap of the descending aorta was chosen in order to try to displace a large volume of blood by each contraction of the LDM. In some pilot studies, we measured the thoracic aortic diameter in the goats. The diameter varied from 1.2 to 1.7 cm. A 7F micromanometer tipped catheter (Millar Inc., Houston, TX) was placed in the ascending aorta from the right carotid artery to monitor the pressure in the ascending aorta. Left ventricular pressure was measured by a second Millar catheter introduced into the left ventricle (LV) through the left carotid artery. A third Millar catheter was placed between the muscle and the aorta in a fluid-filled balloon to monitor the pressure induced on the aorta by contraction of the LDM (wrap pressure (Fig. 1)). The wrap pressure enables us to evaluate the effect of muscle contraction on the descending aorta. A three limb lead ECG was obtained with the use of a bioamplifier (model BMA-931, CWE Inc., Ardmore, PA). Pressures, ECG, and stimulation pulses were continuously recorded to a paper recorder (Gould, TA11 coupler DC signal conditioner, Gould Inc., Valley View, OH).

2.3. Electrical stimulation of the muscle

In three different protocols variations of amplitude, numbers of pulses and interpulse frequency were performed. In each of the three protocols the two stimulation parameters not under investigation were kept constant.

To examine a wide range of delays from the onset of the QRS complex to LDM stimulation, stimulation was delivered randomly. The exact delay was determined from the ECG signal and superimposed LDM stimulation pulses.

2.4. Protocol

The effects of changing LDM stimulation parameters on wrap, aortic, and LV pressures were evaluated.

LDM stimulation voltage was varied randomly between 2 and 10 V in steps of 2 V (2:4:6:8:10). During this test, the LDM was stimulated on every fifth heart beat with a pulse train. Each pulse train had 6 pulses (each pulse 210 µs) with an interpulse frequency of 33 Hz.

Next the number of pulses per pulse train was varied randomly from 2 to 10 in steps of 2 (2:4:6:8:10). The stimulation voltage was set to 8 V and the interpulse frequency was held constant at 33 Hz. Thus pulse train duration changed.

![Fig. 1. Placing of the Millar catheters and the muscle wrap around the aorta.](image-url)
Finally, the interpulse frequency was varied randomly from 16.6 to 50 Hz (16.6, 20, 25, 33, 50). Each pulse train had 6 pulses and the stimulation voltage was set to 8 V. Thus, for this test, the pulse train duration changed without a change in the number of pulses per train. The order of interventions was randomized.

At the end of the experiment, the animal was euthanized with Beauthanasia-D special (390 mg pentobarbital, 50 mg phentoin sodium).

2.5. Statistics

Values are given as mean ± SEM. Variants of analysis and Newman Keul tests were used. A significant level of 0.05 was chosen.

3. Results

Aortic diastolic (ADP) and LV pressure in the anesthetized goats were 60 ± 10 mmHg and 110 ± 20 mmHg, respectively.

The wrap function was measured by wrap pressure. The unstimulated wrap pressure was measured 45 ± 5 mmHg.

Increasing the stimulation amplitude to 2 V did not induce any changes in wrap pressure, but further increase to 4 V raised the wrap pressure to (78 ± 1.5). There was no significant rise of wrap pressure, 5–7 mmHg, when the stimulation voltage was increased from 4 to 10 V (Fig. 2). Stimulation amplitude of 2 V did not induce any changes in ADP. However, using a stimulation amplitude of 4 V induced a significant increase of ADP (80 ± 1.3 mmHg). Further increase of amplitude had no significant effect on ADP. According to the above, changes in ADP were significant when a stimulation amplitude of 4 V was used.

Stimulation with 6 pulses (frequency 33 Hz 1.5, 8 V) did induce the highest value in wrap pressure (82 ± 2.1 mmHg), (Fig. 3) and changes in aortic diastolic pressure (12 ± 1 mmHg). Further increase of the number of pulses did not seem to improve either the aortic wrap pressure or the aortic diastolic pressure. We were not able to show any significant difference in ADP with application of different number of pulses.

The stimulation frequency of 33 Hz induced the highest value in wrap pressure (80 ± 1.7 mmHg), (Fig. 4), ADP (73 ± 3.2 mmHg) and changes in ADP (12 ± 0.7 mmHg), further increase in the frequency did not induce any significant changes in wrap pressure and ADP.

This experiment shows that a train stimulation of 6 pulses with a pulse frequency of 33 Hz and a stimulation amplitude of 4 V induces the highest rise in wrap pressure, ADP and changes of ADP.

4. Discussion

In 1959 Kantrowitz and McKinnon [5] mobilized the diaphragm and wrapped it around the descending thoracic aorta. Electrostimulation of the muscle resulted in a temporary increase in diastolic pressures of up to 26.5%, but muscle fatigue was a major problem. Salmon showed that chronic electrical stimulation of the muscle makes it fatigue resistant [6]. Since then several investigators have used LDM for aortic counter-pulsation [7–10]. Experimentally, skeletal muscle has been used as a counter-pulsation device similar to an aortic balloon pump or in a skeletal muscle ventricle configuration. These studies have helped define stimulation parameters for cardiomyoplasty and have produced augmented cardiac function. Descending aortomyoplasty has also been used by several investigators. The feasibility and efficacy of this procedure have been demonstrated in acute and chronic animal studies [11–15] and one clinical case report [16].

Previous investigators have shown improvements in cardiac function with aortomyoplasty. However, they have not systematically examined the effects of LDM stimulation parameters.

Thus, the present study measured the effect of stimulation voltage, pulse train duration, and interpulse frequency on the aortic wrap function. We also introduced wrap pressure, a new measurement which enables us to evaluate the direct effect of LDM contraction on aorta. We used this to evaluate
the effect of muscle contraction together with other hemo-
dynamic parameters such as aortic pressure and left ven-
tricular pressure. Aortic diastolic pressure was highest at 4 V
and further increasing to 10 V did not induce any improve-
ment in aortic diastolic pressure, probably because of
muscle fatigue. Stimulation with 6 pulses (frequency 33
Hz: 1.5, 8 V) induced the best value in wrap pressure and
changes in aortic diastolic pressure. Further increasing of
number of pulses did not seem to improve either the aortic
wrap pressure or the aortic diastolic pressure. There could
be two reasons for that, one is probably the muscle fatigue,
and the other reason could be that a long train duration will
go further to next QRS complex, and therefore a contraction
during the next systole. This is not beneficial for diastolic
pressure augmentation. The relationship between frequency
and wrap pressure and aortic diastolic pressure indicates that
a frequency of 33 Hz is the most desirable frequency to
obtain the best wrap pressure and aortic diastolic pressure.
We found by looking at wrap pressure and changes in aortic
diastolic pressure that the optimal stimulation protocol
entails a combination of 6 pulses of 4 V with an interpulse
frequency of 33 Hz in which the stimulation were delivered
at every fifth heart beat.

Our study shows that function of LDM in an extra-aortic
wrap can be measured by some direct measurements and
that it is dependent upon the stimulation protocol which is
used. It should be mentioned that in case of tachycardia we
would not have been able to deliver an optimal delay by
using the Grass pulse generator and the authors suggest the
use of an physiologic stimulator which can stimulate the
muscle at a variable delay.

Some important questions are not answered by this study
and require further investigation.

• All animals in this study had normal ventricular function.
The significance of our model in an animal with heart
failure was not ascertained.

• We are not able to determine from this acute study when
or whether the muscle flap will eventually fatigue,
because the muscle is not preconditioned fatigue resistant
muscle. In order to evaluate the effect of wrap pressure
on aorta in a chronic study, the Latissimus Dorsi muscle
should be preconditioned. Although we should keep in
mind that preconditioning of a muscle to a fatigue resis-
tant type reduces the force of contraction of the muscle
fibers and consequently causes a minor pressure on aorta
when applying aortomyoplasty. By using Preconditioned
muscle we would have expected a longer stimulation of
the muscle without muscle fatigue, but a smaller increase
in hemodynamic parameters.

Acknowledgements

With thanks to The Danish Heart Association, Aarhus
University Research Foundation, Danish Research Council,
NYCOMED and Fulbright Commission, for their financial
support of this project.

References

[1] Mannion JD, Acker MA, Hammond RL, Faltemeyer W, Duckett S,
Stephenson LW. Power output of skeletal muscle ventricles in circu-
aortomyoplasty to assist left ventricular failure. Ann Thorac Surg
[3] Lazarri RR, Trumble DR, Magovern JA. Autogenous cardiac assist
with chronic descending thoracic aortomyoplasty. Ann Thorac Surg
pulsation for up to 28 days with autologous latissimus dorsi in sheep. J
Morse CC, Kelly AM, Stephenson LW. Skeletal muscle ventricles in
circulation: one to eleven weeks experience. J Thorac Cardiovasc
[8] Neilson IR, Brister SJ, Khalafalla AS, Chiu RC. Left ventricular
assistance in dogs using a skeletal muscle powered device for diastolic
powered by transformed fatigue-resistant skeletal muscle. J Thorac
experimental results and early clinical experience. Ann Thorac Surg
[11] Lee KF, Dyke CM, Wechsler AS. Theoretical considerations in the
use of dynamic cardiomyoplasty to treat dilated cardiomyopathy. J
terpulsation with a latissimus dorsi flap: hemodynamic effects in a
