Variations of Electrical Stimulation Regimens for Acute Thoracic Aortomyoplasty in a Canine Model

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Abstract
Our previous studies in a sheep model demonstrated that when electrical stimulation (ES) was applied to a newly mobilized latissimus dorsi muscle (LDM) in a work-rest regimen and a rate of 15 contractions per minute (cpm), it did not damage this muscle. This regimen was employed twice during 60 minutes daily for 16 days with no LDM damage. The goal of our current investigation was to study this identical regimen in a canine model and, if it proved successful, to apply this regimen in studies of acute thoracic aortomyoplasty.

In two experimental groups, we mobilized the LDM but left it in situ. Two hours later, contractile force (CF) testing (20 g/kg preload, 6 impulses per burst) was performed until CF dropped to 50% of baseline. Recovery time needed to completely restore CF was calculated. In one group (6 dogs) we applied continuous ES; in another (6 dogs) we applied ES in a work-rest regimen (one-minute work-one minute rest). In two other groups (of 6 dogs each) aortomyoplasty was performed after which the LDM flap was subject to ES immediately postoperatively (6 impulses per burst, ventricular-LDM delay 290 ms). Again, one group received continuous ES, the other work-rest ES.

In the mobilized LDM under continuous ES, CF decreased to 50% of baseline values after 52±18 min and returned to baseline after 84±16 min. Under the work-rest regimen, this decrease took 105±28 min and the return to baseline 25±6 min (p<0.05). In LDM subjected to work-rest ES, light microscopy revealed no additional damage in LDM tissue than was seen immediately after mobilization. However, LDM subjected to continuous ES had evidence of increased basophilic degeneration and wavy fibers. After acute thoracic aortomyoplasty, assisted hemodynamic values under continuous ES exceeded unassisted values for only 40 min compared with the 100 min for work-rest ES (p<0.05).

Our study showed that a work-rest regimen of electrical stimulation can be started safely immediately post procedure.

1. Introduction
A key problem in cardiac bioassist is the conditioning of the latissimus dorsi muscle (LDM). For several weeks after subtotal mobilization, it remains in a state of ischemic shock, which sometimes continues for months. In addition, the LDM suffers if it is made to contract synchronously with heart rate (>60 contractions per min [cpm]), leading to muscle degeneration that may compromise the results of the operation. To overcome these problems, a new device, the LD-PACE II (Centro del Construccion de Cardioestmuladores del Uruguay, Montevideo, Uruguay) has been created with the ability to change the power and timing of muscle contraction and to allow the LDM to rest between contractions.

Using a cardiosynchronization ratio of 1:2, we investigated the hemodynamic efficiency of different ES regimens: 1) conventional continuous ES and 2) work-rest ES (one minute of work followed by one minute of rest).

1.1. Previous Work
To achieve the aims of our investigation, we performed our studies in two series of dogs. In series 1 (feasibility studies), we compared the results of a work-rest regimen with those of a continuous regimen for applying ES to newly mobilized LDM. Based on these results, we progressed to series 2. In this second series, we studied application of ES immediately post acute thoracic aortomyoplasty over a short duration.

Electrical Stimulation of Newly Mobilized LDM: Comparison of Regimens
A. Surgical Preparation: Canine Model
Twelve adult dogs were studied in this series: 6 subjected to the continuous ES regimen, 6 subjected to work-rest ES. With the dog in a right lateral decubitus position, a 25-cm longitudinal skin incision was made from the posterior edge of the auxiliary region to the
midpoint of the twelfth rib to expose the left LDM. The LDM was detached from all insertions while carefully preserving the thoracodorsal neurovascular pedicle and the distal attachment to the ribs. All vessels supplying the LDM except the thoracodorsalis artery were dissected, after which it was left in situ. Several sutures were placed to reattach the LDM to the distal attachment to the ribs. Two intramuscular probes were inserted into the proximal part of the LDM 5 cm apart from each other and connected to the LD-PACE II cardiomyostimulator.

Baseline measurements for contractile force (CF) and for fatigue resistance (FR) were taken two hours after LDM mobilization. For these measurements, animals were placed into one of two groups to compare ES regimens. Both regimens used muscle contraction at a rate of 35 cpm to match the cardiosynchronization ratio of 1:2 to be used in thoracic aortomyoplasty: 1) continuous muscle contraction or 2) work-rest contraction cycle (one minute work at 35 cpm, one minute rest). During testing, we measure CF every 10 minutes, continuing until CF reached 50% of baseline value. Upon completion of this fatigue test, CF recovery was measured during 10 seconds at 5-min intervals until return to baseline. The time needed for CF to recover to baseline value was calculated and recorded to evaluate FR for subsequent studies.

Electrical Stimulation during Thoracic Aortomyoplasty: Comparison of Regimens

In 12 adult dogs, the dissected LDM was relocated into the chest and a median sternotomy was performed. The ascending part of the aorta was moved up to the truncus brachiocephalicus, just below which the LDM was wrapped counterclockwise: the LDM was positioned under the aorta, which was completely wrapped, and a suture line of muscle was formed on the front surface. Next, the fibers of the LDM were laid perpendicular to the longitudinal axis of the aorta. To test for cardiosynchronization, a detection electrode was implanted on the front surface of the right ventricle, and the free ends of this electrode and of stimulation electrodes were connected to the cardiomyostimulator, the LD-PACE II.

The following stimulation settings were used: pulse amplitude 5.6 V; pulse width 0.244 ms; pulse interval 15.6 ms; pulses per burst 6, ventricular refractory period 484 ms; ventricular-lattissimus dorsi delay 290 ms, ratio 1:2. To compare hemodynamic efficiency, animals (6 per group) were subjected to one of the following stimulation regimens: 1) conventional continuous ES or 2) work-rest ES (one minute of work followed by one minute of rest). The following were then measured: heart rate, peak diastolic aortic pressure, end-diastolic aortic pressure, mean diastolic aortic pressure, and counterpulsation index. When counterpulsation was stopped (when results of assisted and unassisted ES were similar), we continued to monitor these hemodynamic parameters, switching every 5 min for 10 seconds in counterpulsation mode to monitor levels of diastolic aortic peak pressure, end-diastolic aortic peak pressure, and mean diastolic aortic peak pressure to determine when these reached the same levels as had been present immediately after starting assisted counterpulsation.

Results

Newly Mobilized LDM: Comparison of Continuous and Work-Rest Regimens

Series 1: Continuous Contraction Regimen

For the first 30 min CF decreased at the same rate for all dogs, beginning with a rapid drop to 75±8% of baseline after the first 10 min, to 68±6% after the next 10, then to 62±7% by the end of 30 min. Following this, in 3 dogs it took 15-20 additional min for CF to reach 50% of baseline value, 55-60 min for the remaining 3 dogs (mean testing time for this regimen was 52±8 min). CF returned to each dog’s baseline value after 84±16 min.

Series 2: Work-Rest Contraction Regimen

For the first 30 min CF decreased at the same rate for all dogs, beginning with a more gradual drop to 94±3% of baseline after the first 10 min (vs. series 1, p<0.05), to 80±3% after the next 10 (vs. series 1, p<0.05), then to 71±5% by the end of only another 20 min. Following this, it took 20 additional min for CF to drop to 60±4% of baseline value, and another 30-43 min to reach 50% of baseline value (mean testing time for this regimen was 105±8 min). CF returned to each dog’s baseline value after 25±6 min (vs. series 1, p<0.05).

Thoracic Aortomyoplasty: Comparison of Continuous and Work-Rest Regimens

Series 1: Continuous Counter-Pulsation Regimen

Thoracic aortic counterpulsation resulted in significantly improved hemodynamic parameters during the first 20 min of testing: diastolic aortic peak pressure increased from 56.93±5.20 to 74.63±6.21 mmHg (p<0.05); diastolic aortic mean pressure increased from 50.88±5.10 to 60.33±6.21 mmHg (p<0.05); end-diastolic aortic pressure decreased from 45.62±5.75 mmHg to 39.71±4.86 mmHg (p<0.05). Although all hemodynamic values for the next 20 min were worse than those of the first 20 min, they continued to be better than those for unassisted animals. However, after 60 min, hemodynamic values decreased to pre-assist levels.

Series 2: Work-Rest Counter-Pulsation Regimen

In this series, as with the other regimen (series 1), thoracic aortic counterpulsation significantly improved
hemodynamic parameters during the first 20 min of testing but all values improved (none of these improvements was statistically significant) compared with the series 1 regimen: diastolic aortic peak pressure increased from 55.43±4.86 to 72.11±6.08 mmHg; diastolic aortic mean pressure increased from 51.24±3.34 to 58.22±2.69 mmHg (p<0.05); end-diastolic aortic pressure decreased from 46.17±5.03 mmHg to 40.01±4.27 mmHg. The counterpulsation index increased from 0.9563±0.139 to 1.098±0.147.

All values for the next 20 min were the same as those obtained in series 1 (not statistically significant). However, in the 20 min that followed next (i.e., for a total of 60 min of counterpulsation) the difference between series 1 and series 2 did become statistically significant. In series 2, diastolic aortic peak pressure was 68.093 vs. 46.27±5.03 mmHg (p<0.05). The continuous regimen yielded better results than did the work-rest regimen after the first 20 min of work. But the apparent advantage of continuous ES disappeared in the next 20 min: results of work-rest were better than those of the continuous regimen. Moreover, work-rest results were practically the same as our findings with the work-rest regimen after the first 20 min. At 60 min of continuous ES, this regimen proved ineffectual, but the work-rest regimen continued to yield statistically significant results that were better than those of the unassisted mode.

In comparing results of continuous vs. work-rest ES for counterpulsation, it must be remembered that we were investigating a newly mobilized LDM in situ. After 52±8 min of continuous ES, light microscopy of LDM tissue revealed a high proportion of swollen fibers, progression of basophilic degeneration, markedly pronounced leukocyte margination, and many wavy, shrunken fibers. No such damage was revealed in tissue subjected to work-rest ES for 105±8 min. (twice the work of the continuous ES LDM).

These studies also demonstrated that a work-rest regimen makes it possible to initiate LDM cardiac assist immediately after aortomyoplasty and to continue the work portion of the cycle for up to 60 min (during 5-60 min), then to repeat the work cycle after adequate rest, leading to incremental increases in the amount of time the muscle is used for cardiac assist and to incremental decreases in the length of rest periods.

Our investigations indicate that a work-rest regimen of electrical stimulation can be used safely immediately post aortomyoplasty and to continue the work portion of the cycle for up to 60 min (during 5-60 min), then to repeat the work cycle after adequate rest, leading to incremental increases in the amount of time the muscle is used for cardiac assist and to incremental decreases in the length of rest periods.

2. Summary and Conclusions

In our investigations reported here, we needed to determine if the hemodynamic improvement post aortomyoplasty from one minute of work would be comparable with that of continuous ES. To answer this question, we devised the series of experiments to study thoracic aortomyoplasty and found that with continuous contraction (a cardiosynchronization ratio of 1:2) all hemodynamic values were better after the first 20 min compared with no cardiac assist. These results correlated with our findings for CF of a newly mobilized LDM.

Our next step, to employ the above ES protocol immediately post aortomyoplasty, required construction of a specially designed stimulator (the LD-PACE II) that would allow variable programming of the work-rest periods, a feature unavailable in conventional stimulators. In this step, we could pursue the goal of aortomyoplasty research: to provide cardiac assist as soon as possible after surgery by initiating ES training of the LDM immediately after its mobilization for wrapping around the aorta.

However, after 60 min of work, we found that hemodynamic values for both cardiac assist and nonassist were identical, indicating that the LDM becomes ineffectual at this point.

The continuous regimen yielded better results than did the work-rest regimen after the first 20 min of work. But the apparent advantage of continuous ES disappeared in the next 20 min: results of work-rest were better than those of the continuous regimen. Moreover, work-rest results were practically the same as our findings with the work-rest regimen after the first 20 min. At 60 min of continuous ES, this regimen proved ineffectual, but the work-rest regimen continued to yield statistically significant results that were better than those of the unassisted mode.

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Our investigations indicate that a work-rest regimen of electrical stimulation can be used safely immediately postprocedure for cardiac assist and that this can be repeated several times daily, opening a new horizon for the clinical application of aortomyoplasty.

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