

Effect of Variable and Constant-Frequency Train in Latissimus Dorsi Muscle Stimulation

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Abstract

We tested the hypothesis that increased hemodynamic augmentation and mechanical performance could be achieved by using a variable frequency pulse train (VFT) to stimulate the latissimus dorsi muscle (LDM), compared to the conventional constant frequency pulse train (CFT) used in cardiomyoplasty. In dogs (n = 6), a vascular delayed LDM was wrapped posteriorly around the heart. LDM was conditioned for 9 weeks using implantable cardiomyostimulator. The hemodynamic parameters were recorded using VFT and CFT LDM stimulation with 7, 6 and 5-pulses, and compared to non-stimulated beats (NS). Both CFT and VFT LDM stimulation significantly increased pressures, flow, and stroke work. However, compared to CFT, VFT stimulation resulted in significant stroke power (20.6%), maximum peak aortic flow (20.1%) and maximum LV dp/dt (14.6%). These results suggested that stimulation of the LDM using VFTs is potentially greater beneficiary for application in cardiomyoplasty.

Key words: cardiomyoplasty, variable frequency, constant frequency, latissimus dorsi muscle.

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Dynamic cardiomyoplasty provides an optional therapy for chronic heart failure [8]. In current clinical practice, the latissimus dorsi muscle (LDM) is stimulated with a constant frequency pulse train (CFT), 6 uniformly spaced pulses with an interpulse frequency of 30 Hz [8, 9]. While CFT may be a reasonable choice, non-uniformly spaced nerve impulses are generally recorded during volitional contractions in a variety of muscles in both animals and humans [1, 12]. The use of variable-frequency trains (VFTs) that take advantage of the "catchlike" property of skeletal muscle has been shown to augment force and reduce fatigue compared with CFTs during isometric and non-isometric contractions [2-6, 14, 16, 18]. The catchlike property of skeletal muscle is the tension enhancement seen when an initial brief interpulse interval or burst of pulses added to the beginning of a subtetanic train of pulses [4-7].

In addition to the number of pulse trains per minute, the rate of fatigue of repeatedly stimulated skeletal muscle is partly determined by the number of pulses within the stimulus pattern [3]. In current practice, the LDM is converted into a fatigue-resistant phenotype through

chronic electrical stimulation. Unfortunately, this conversion process decreases muscle strength, speed, and power, thereby diminishing potential cardiac assist [15, 17]. If a stimulus patterns could be identified that used fewer stimulus pulses, but yet elicited similar or enhanced muscle contractile performance, decreased muscle fatigue may be possible. Thus, using an improved stimulus train may obviate the need for full conversion to a fatigue-resistant muscle and thereby reduce the decline in muscle performance presently noted.

This study investigated the application of VFT stimulation relevant to skeletal muscle cardiac assist and compared VFT to a CFT of 7, 6, 5-pulses, 30Hz burst.

Materials and Methods

All animals underwent routine sterile surgical procedures of vascular delay, LV dysfunction and cardiomyoplasty as described in our companion study in this special issue [Ref: Delay, frequency and pulses in cardiomyoplasty]. All monitoring devices, pharmacological interventions and anesthetic techniques were carried out

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as described in that study. We used the same animals ($n = 6$) for this study of VFT and CFT.

Instrumentations with variable and constant frequency trains

The hemodynamic measurement was carried out in closed chest after 9 weeks under general anesthesia as described earlier [13]. The pacemaker wire were dissected out and then connected to an external R wave-synchronous Grass cardiomyostimulator.

Stimulation protocol

At the terminal study, six pulse trains were tested. For the CFTs', a 7 pulse CFT with a 33 ms interpulse interval, a 6 pulse CFT of 33 ms (standard clinical CMP) and a 5 pulse CFT of 33 ms were examined. For the VFTs', the first 2 interpulse intervals was equal to 10 ms. For the 7 pulse VFT, the three remaining interpulse intervals = 42 ms, giving a train duration of 146 ms. For the 6 pulse VFT, the two remaining interpulse interval = 42 ms. For the 5 pulse VFT, the train was identical to earlier trains but two fewer pulses. The VFT patterns were chosen based on an earlier study [10].

Statistics

Statistical analyses were performed with a statistical program (Statview, Cricketgraph software, Inc.). All values were expressed as the mean $\pm$ standard deviation of the mean. A paired t -test was used to assess the differences between hemodynamic parameters following VFT, CFT stimulation in comparison with non-stimulated beats. 7, 6 and 5 pulse VFTs were also compared with 7, 6 and 5 pulse CFT, respectively. Significant differences were considered when the p value was < 0.05 .

Results

Both CFT and VFT stimulation significantly increased aortic and left ventricular pressure, stroke volume, work and power, aortic flow, and LV dP/dt. However, VFT stimulation caused significantly greater increases in stroke power, maximum aortic flow, and LV dP/dt compared to CFT stimulation. Figure 1 shows the percent changes in stroke power, aortic flow, and LV dP/dt caused by LDM stimulation. For the same number of

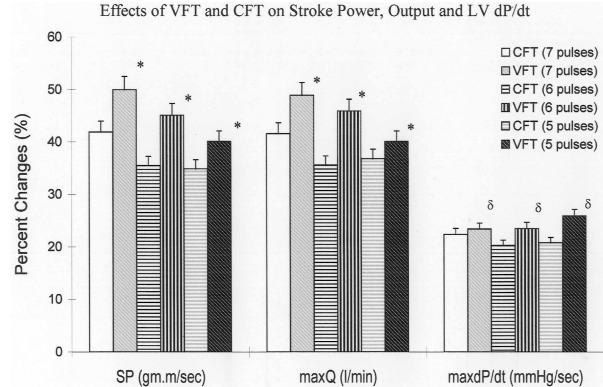


Figure 1. The percent changes in stroke power, aortic flow, and LV dP/dt caused by VFT and CFT LDM stimulation. For the same number of pulses, VFT stimulation resulted in greater increases. VFT: variable frequency train, CFT: constant frequency train; SP: stroke power; maxQ: maximum peak aortic flow; and LV dP/dt: maximum first peak derivative of left ventricular pressure (* $p < 0.05$ and $\delta p < 0.01$ when CFT LDM stimulation was compared with VFT).

pulses, VFT stimulation resulted in greater increases. Compared to CFT, VFT increased peak systolic aortic pressure by 7.3% ($p = \text{NS}$), peak systolic left ventricular pressure by 6.5% ($p = \text{NS}$), stroke volume by 2.8% ($p = \text{NS}$), stroke work by 9.7% ($p = \text{NS}$), stroke power by 20.6% ($p < 0.05$), maximum peak aortic flow by 20.1% ($p < 0.05$) and max LV dP/dt by 14.6% ($p < 0.01$).

Table 1 summarizes the absolute hemodynamic changes following CFT and VFT stimulation. VFT stimulation caused significant greater increases in stroke power ($p < 0.05$), maximum aortic flow ($p < 0.05$) and maximum LV dP/dt ($p < 0.01$).

VFT stimulation tended to provide greater or equivalent hemodynamic increases with fewer pulses than the CFT trains. For example, Figure 2 presents the percent changes in the hemodynamic data following a 5 pulse VFT and 6 pulse CFT LDM stimulation. In this figure, the hemodynamic increases resulted from a 5 pulse VFT are equivalent or greater than a 6 pulse CFT. 5 pulse VFT LDM stimulation caused greater significant percent

Table 1. The absolute changes of the hemodynamic data using VFT, CFT LDM stimulation. AoP: peak systolic aortic pressure; LVP: peak systolic left ventricular pressure; SV: stroke volume; SW: stroke work; SP: stroke power; MaxQ: maximum peak aortic flow; maximum LV dP/dt: maximum left ventricular contractility. CFT: constant-frequency train; VFT: variable-frequency train. * $p < 0.05$ and $\delta < 0.01$ when CFTs was compared to VFT LDM stimulation changes.

Absolute changes	AoP (mmHg)	LVP (mmHg)	SV (ml)	SW (gm·m)	SP (gm·m/sec)	MaxQ (l/min)	Max dP/dt (mmHg/sec)
CFT	11.8 $\pm$ 0.3	13.0 $\pm$ 0.3	3.5 $\pm$ 0.3	7.4 $\pm$ 0.6	76.0 $\pm$ 0.6	2.5 $\pm$ 0.1	246.8 $\pm$ 5.6
VFT	12.2 $\pm$ 0.3	13.9 $\pm$ 0.5	3.7 $\pm$ 0.1	8.2 $\pm$ 0.3	93.2 $\pm$ 3.7*	3.0 $\pm$ 0.1 δ	275.9 $\pm$ 6.9*

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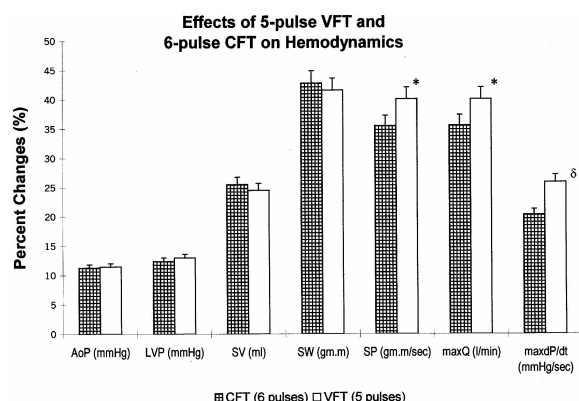


Figure 2. The percent changes following 5 pulse VFT and a 6 pulse CFT LDM stimulation on hemodynamics. Compared to CFT, VFT increased peak systolic aortic pressure by 7.3% ($p = ns$), peak systolic left ventricular pressure by 6.5% ($p = ns$), stroke volume by 2.8% ($p = ns$), stroke work by 9.7% ($p = ns$), stroke power by 20.6% ($p < 0.05$), maximum peak aortic flow by 20.1% ($* p < 0.05$) and maximum LV dP/dt by 14.6% ($^{\delta} p < 0.01$).

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Discussion

In cardiomyoplasty, the current clinical practice uses CFT stimulation to provide cardiac assistance. However, in many patients, the LDM is stimulated every other beats (1:2 mode) to prevent the diastolic filling impairment due to slow or incomplete LDM relaxation [11]. The present study tested for the first time in CMP whether VFTs with different pulses and shorter duration could exert comparable or better mechanical performance than CFT stimulation.

Comparison to literature

Several other experimental studies have examined VFT stimulation. Burke et al. showed that VFT increased performance compared to CFT stimulation in the slow motor unit of the cat triceps surae muscle [6], and in fast and slow motor units of the cat gastrocnemius muscle [7]. Kwende et al. showed similar effects in the rabbit tibialis anterior muscle [14] and Stein et al. showed VFT improved performance in the cat soleus muscle [16]. These studies did not measure VFT effects after repeated muscle stimulation. George et al. [10] measured the VFT effects after repeated muscle stimulation. Their study measured peak muscle force, peak displacement, and velocity. VFT stimulation resulted in 25% greater peak power and 15% greater mean power compared with CFTs. They showed better performances by 6-pulse VFT than 6-pulse CFT when the muscle was fatigued. In addition, they showed significantly of

greater peak power and mean power using 5 pulse VFT when compared to 5 pulse and 6-pulse CFTs, similar to the results of the present study.

In a previous study, we showed that vascular delay improves the outcome of cardiomyoplasty surgery [13]. Our goal in this study was to compare mechanical performance using VFT with the traditional CFT used in current cardiomyoplasty practice. Both CFT and VFT stimulation significantly increased pressure, flow, and stroke work. However, as compared to CFT, VFT stimulation caused significantly larger increases in stroke power, maximum peak aortic flow and maximum LV dP/dt. Further, VFT had a shorter pulse train duration. Thus VFT may have less effect on subsequent diastolic filling. These indicate better mechanical performances and contractions by LDM using VFTs.

However, our study on VFTs is consistent with earlier work showing that VFT stimulation produces greater augmentation in slow-twitch motor units than in fast-twitch motor units [7, 10]. It suggests that in the fully conditioned LDM, transformed into slow fibers and after vascular delay of the LDM, VFT may be useful. It was encouraging that muscle performance can be manipulated and potentially enhanced by adjusting the inter-pulse intervals within the stimulus pattern. A beneficial effect of VFT stimulation was demonstrated in this study.

It has been suggested that the rate of fatigue may be related to the number of pulses used to stimulate the muscle [3, 7]. In this study, a 5 pulse VFT produced similar effects as a 6 pulse CFT. Thus, it may be possible to stimulate the LDM with fewer pulses, thereby reducing the muscle fatigue while maintaining mechanical performance. This is especially important in the early post-operative period after cardiomyoplasty surgery. If used appropriate, VFT along with vascular delay of the muscle could diminish fatigue, provide earlier cardiac assistance, and achieve better hemodynamic performance.

Limitations of the study

This study shows the advantage of VFT stimulation over CFT. However, we probably did not examine the optimal stimulation pattern. In this special issue, Stuart et al. showed that doublet frequency stimulation (DFTs) produced a 49% augmentation over the traditionally used 6-pulse CFT and a 23% augmentation over the 6-pulse VFTs [5]. If we had employed DFT, we may have observed even greater increases in pressures, flow and work with LDM stimulation.

The mechanism of VFT augmentation is not yet known because of lack of understanding mechanics of muscle force generation. However, rearranging the stimulus pulse pattern to form a VFT can produce greater power than the CFTs. VFT takes advantage of the catchlike property of skeletal muscle for activation.

Thus, use of VFT stimulation improves muscle contractile performance, reduces contraction duration and muscle fatigue. Further investigation into the effects of LDM using pulse patterns on muscle mechanics for skeletal muscle cardiac assist should be carried out.

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