A New Configuration for Right Ventricular Assist With Skeletal Muscle Ventricle

Short-term Studies

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Background. Previous attempts to provide right heart assistance with skeletal muscle ventricles (SMVs) have been frustrated by the low preload supplied by the systemic venous blood pressure. In the present study, right ventricular pressure was exploited to provide more optimal preload, the SMV being connected by valved conduits between right ventricular free wall and the main pulmonary artery.

Methods and Results. SMVs were constructed from the right latissimus dorsi muscle in seven mongrel dogs. Following a delay period of 4 weeks, SMVs were preconditioned with 2-Hz continuous stimulation for 5–6 weeks. The SMV was then connected to the right ventricle using a porcine valved Dacron conduit. A similar valved conduit connected the SMV to the main pulmonary artery that had been ligated proximally. SMVs were stimulated with 33-Hz burst frequency to contract synchronously with ventricular diastole in a 1:2 mode. The stimulator was intermittently turned off to permit comparison of assisted and nonassisted circulation. Cardiac output increased by 27% at 1 hour (1,437±54 versus 1,140±64 ml/min, p<0.005) and by 30% at 4 hours (1,403±161 versus 1,074±99 ml/min, p<0.005), systemic arterial systolic pressure increased at 1 hour by 12% (87.1±4.9 versus 78.0±4.9 mm Hg, p<0.05) and by 13% at 4 hours (81.4±2.8 versus 72.3±3.4 mm Hg, p<0.005), and peak pulmonary arterial pressure increased at 1 hour by 35% (28.0±2.1 versus 20.9±1.8 mm Hg, p<0.01) and by 37% at 4 hours (31.5±2.6 versus 23.0±0.4 mm Hg, p<0.05). Peak SMV pressure was 52.8±2.0 mm Hg at 1 hour and 49.9±3.3 mm Hg at 4 hours (p=NS).

Conclusions. The improved preload supplied by this configuration of right ventricular assist enabled an SMV to provide stable and effective circulatory support throughout the 4-hour duration of the experiment. (Circulation 1991;84:2470–2475)

Skeletal muscle is receiving much attention as a potential means of improving cardiac function. It is readily available and not subject to tissue rejection, and it does not require a cumbersome and expensive external power source. Furthermore, skeletal muscle has the potential for growth, which may be relevant to its use in the area of congenital cardiac anomalies.

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In experimental models, considerable success has been achieved with skeletal muscle ventricles (SMVs) designed to act as auxiliary pumps within the circulation. In the systemic circulation, SMVs are capable of a level of continuous work applicable for a cardiac assist role. Attempts to provide right ventricular assist have proved more difficult because they have previously relied on systemic venous blood pressure for preload, which may be too low for optimal SMV performance.

The purpose of the present study was to determine whether right ventricular pressure could be exploited in such a manner that it could be used for SMV–right heart assist.

Methods

SMVs were constructed from the right latissimus dorsi muscle of seven mongrel dogs weighing between 20 and 30 kg. Animals were operated on in...
accordance with the Guide for the Care and Use of Laboratory Animals prepared by the National Academy of Sciences. Anesthesia was induced by intravenous thiamylal (12–18 mg/kg) and maintained by inhalation of isofluorane (1–2%). Prophylactic antibiotics were used, with intravenous cefazolin administered (1 g) before surgery, and cephalexin (60 mg/kg/day) given after surgery for 14 days. Pain was controlled with parenteral buprenorphine (0.02–0.04 mg/kg).

**Skeletal Muscle Ventricle Construction**

The right latissimus dorsi muscle was dissected from the chest wall and surrounding tissues, with care taken to safeguard the neurovascular pedicle. Its humeral insertion was left intact to minimize the risk of damage to the pedicle. All collateral blood vessels arising from the skin, chest wall, and adjacent muscles were ligated and divided. A modified unipolar cuff nerve electrode (Medtronic Inc., Minneapolis, Minn.) was then placed around the right thoracodorsal nerve. The muscle was wrapped in a spiral fashion around a conical Teflon mandrel (length, 9–10 cm; volume, 55–60 ml). A sewing ring fashioned from Teflon felt (USCI, Billerica, Mass.) was used to secure each layer of muscle to the base of the mandrel.

The nerve electrode was connected to a unipolar neural stimulator (Itrel model 7421, Medtronic Inc.) placed beneath the right rectus abdominis muscle. The SMV was placed on the outside of the chest wall, and the subcutaneous tissue and skin were closed over it.

The SMV was undisturbed for 4 weeks to allow muscle collateral blood supply to recover. After this vascular delay period, the stimulator was activated with a transcutaneous programmer (model 7431, Medtronic Inc.) to provide 2 Hz continuous stimulation, resulting in 120 twitches/min. Individual electrical pulses were of 210-μsec duration with an amplitude of 1.0–1.5 V (threefold that of threshold). Stimulation was continued for 5–6 weeks. This provided muscle conditioning that resulted in a more fatigue-resistant state.

**Connection to Circulation**

After the electrical preconditioning period, a second surgical procedure was performed. Animals were anesthetized as described previously. An incision was made over the most ventral aspect of the SMV, and the mandrel was removed. A median sternotomy was then performed to expose the heart. Two screw-in epicardial electrodes (SP 6917, Medtronic Inc.) were placed on the left ventricle to detect the R wave of the electrocardiogram. Two 16-mm porcine valved Dacron grafts (Hancock, Medtronic Inc.) were then anastomosed separately—one to the main pulmonary artery and the other to the right ventricular outflow tract—using side-biting vascular clamps. Partial resection of the right second and third ribs enabled the two conduits to be connected to the SMV (Figure 1).

No artificial lining was used within the SMV itself apart from the smooth fibrous inner surface reaction induced by the Teflon mandrel over several weeks. Animals were heparinized with 300 units/kg i.v. before release of the clamps. Ligation of the proximal main pulmonary artery with umbilical tape ensured obligatory flow through the SMV. Heparin (1,000 units i.v.) was subsequently administered every hour.

**Skeletal Muscle Ventricle Stimulation Protocol**

After the SMV was connected to the circulation, the Itrel pacemaker (Medtronic Inc.) was replaced with an implantable rate-responsive synchronized pulse train stimulator (Prometheus, Medtronic Inc.). The pacemaker was programmed to deliver a 33-Hz burst frequency, 25% of RR interval burst duration, 4-V amplitude, and 55% of RR interval delay. The pacemaker was programmed to stimulate the SMV at 1:2 when the heart rate was less than 160 beats/min and 1:3 for heart rate of more than 160 beats/min. As a result, the SMV contracted at a rate of 1:2 throughout most experimental protocols.

**Measurements**

Femoral artery pressure, ascending aortic flow, pulmonary artery (PA) pressure, and central venous pressure (CVP) were measured. An ultrasonic flow probe (Transonic Systems, Inc., Ithaca, N.Y.), placed around the ascending aorta, was connected to a two-channel flowmeter (T-201, Transonic Systems, Inc.) for measurement of pulsatile and average flows. Cardiac output was calculated from the integrated aortic blood flow curve, using a digitizing pad (GAP1, GTCO Corp., Rockville, Md.) linked to a portable computer (T3200S, Toshiba, Irvine, Calif.). A 5F microtransducer-tipped catheter (Millar Instruments, Inc., Houston, Tex.) was placed in the SMV and the main pulmonary artery.

SMV stimulation was interrupted briefly to permit measurements to be made without SMV assist. Measurements were recorded hourly for a total of 4 hours.
Rectal temperature was monitored and maintained above 37°C with a heating blanket.

Statistical Analysis

All data are reported as mean±SEM. Statistical analysis was carried out with the Wilk-Shapiro test for normality. A Student's t test was performed on paired data with RS/1 statistical software (Bolt, Beranek, and Newman Inc., Cambridge, Mass.) on a portable computer (T3200SX, Toshiba).

Results

Seven dogs were entered into this experiment. One sustained thoracodorsal nerve damage at the time of surgery; in another, the main pulmonary artery could not be ligated proximal to the graft for technical reasons. Both animals were, therefore, excluded from further analysis. The remaining five animals tolerated the surgical procedures well and remained hemodynamically stable during the 4-hour experiment.

The hemodynamic effects observed during SMV stimulation are shown in Figures 2–4. Representative recordings from one dog are provided in Figure 5.

Peak PA pressure at 1 hour was increased by 35% with the stimulator on (28.0±2.1 versus 20.9±1.8 mm Hg, p<0.01) compared with the stimulator off. After 4 hours of continuous SMV pumping, the same degree of augmentation of PA pressure was apparent (31.5±2.6 versus 23.0±0.4 mm Hg, p<0.05) (Figure 2). CVP was slightly decreased during the pacemaker compared with it off, but this failed to achieve statistical significance (7.1±0.9 versus 7.4±1.1 mm Hg at 1 hour; 6.8±0.9 versus 7.6±1.1 mm Hg at 4 hours).

Cardiac output at 1 hour increased by 27% with the stimulator on (1,437±54 versus 1,140±64 ml/min, p<0.005), and at 4 hours increased by 30% (1,403±161 versus 1,074±99 ml/min, p<0.005) (Figure 3). Arterial systolic pressure at 1 hour increased by 12% (87.1±4.9 versus 78.0±4.9 mm Hg, p<0.05), and at 4 hours by 13% (81.4±2.8 versus 72.3±3.4 mm Hg, p<0.005) (Figure 4). Peak SMV pressure was 52.8±2.0 mm Hg at 1 hour and 49.9±3.3 mm Hg after 4 hours (p=NS) (Figure 6).

Discussion

The concept of using skeletal muscle contractile power to augment cardiac function was first proposed in 1959, but muscle fatigue during continuous, cardiac-type work appeared to be a major obstacle to further progress. The discovery that with appropriate electrical conditioning the muscle could be transformed to a fatigue-resistant state more suited to a cardiac assist role has generated a great deal of enthusiasm in this field during the past decade.

To date, efforts have focused on two main methods of augmenting cardiac assist. In the dynamic cardiomyoplasty procedure, skeletal muscle is wrapped around the heart and stimulated to contract synchronously with systole, thus reinforcing ventricular ejection. Alternatively, specially constructed SMV may act as an auxiliary heart to augment the circulation. Although dynamic cardiomyoplasty is the only form of assist to have been applied clinically, with resulting improvement in symptoms of heart failure in most patients, objective improvement in measured

FIGURE 2. Plot of peak pulmonary arterial pressure as a function of time. SMV ON, stimulation of skeletal muscle ventricle (SMV) with 33-Hz burst stimulation; SMV OFF, no stimulation of the SMV.

FIGURE 3. Plot of cardiac output over time. SMV ON, stimulation of the skeletal muscle ventricle (SMV) with 33-Hz burst stimulation; SMV OFF, no stimulation of the SMV.

FIGURE 4. Systolic blood pressure is shown over time, during stimulation of the skeletal muscle ventricle (SMV) with 33-Hz burst stimulation (SMV ON) and no stimulation of the SMV (SMV OFF).
Skeletal Muscle Ventricle for Right Heart Assist

Figure 5. Representative hemodynamic tracings recorded during stimulation of the skeletal muscle ventricle (SMV) with 33-Hz burst stimulation and without stimulation of the SMV (SMV OFF). Top panel: Recorded at paper speed at 50 mm/sec. Bottom panel: Recorded at paper speed of 5 mm/sec to highlight the impact of SMV assist.

Hemodynamic variables have been an inconsistent finding in many studies.\textsuperscript{16,31,32} In contrast, SMVs have been shown to be capable of sustained cardiac-type work at levels intermediate between that generated by the normal left and right ventricles.\textsuperscript{2–10} SMVs have been able to achieve a work output equal to that of the left ventricle in acute studies.\textsuperscript{33} When placed within the systemic circulation, SMVs have pumped effectively for as long as 18 months as aortic diastolic counterpulsators.\textsuperscript{11–13}
FIGURE 6. Peak skeletal muscle ventricle (SMV) pressure recorded during SMV stimulation.

Providing right heart assistance with SMVs has proved a more difficult problem. The reason relates to the filling pressures provided by systemic venous return, which generates an inadequate preload to allow optimal SMV performance. Recent improvements in SMV design have been accompanied by better compliance characteristics, which have, in turn, led to improved SMV function at lower preloads. Others have previously capitalized on such advances to achieve successful total or partial right heart replacement with SMVs in short-term experiments, although at the expense of an appreciably elevated CVP of almost twice the normal value. Other investigators have tried to overcome the problem of inadequate SMV preload by using a spring-assembly mechanism to aid filling.

To overcome this problem, we attempted to use normal right ventricular pressures to generate higher SMV preload, instead of depending on systemic venous pressures. The configuration we used is based on the concept of the right ventricle–pulmonary artery valved conduit originally proposed by Rastelli for correcting transposition of the great arteries. It differs fundamentally from previous attempts at right heart assist in that instead of bypassing the right heart, the SMV provides assistance “in series” with the right ventricle.

Significant improvement in cardiac function was observed when the SMV was contracting, as judged by increases in cardiac output and systemic and pulmonary arterial pressures. Systemic venous pressures remained normal. Furthermore, SMV function remained stable throughout the 4-hour duration of continuous right heart assist. A 4-hour period was chosen on the basis of our previous experience in this laboratory using acute open-chest models of this type. Progressive deterioration and hemodynamic instability invariably occur beyond this time period in acute experiment of this type due to the complications associated with systemic anticoagulation, bleeding, and prolonged anesthesia.

Conclusions

This new SMV configuration appears better suited to satisfy the preload requirements necessary for effective right ventricular assistance. Our previous experience indicates that a skeletal muscle assist system such as this, which remains hemodynamically stable over 4 hours, is likely to function well chronically. Clearly, the next two logical steps with this model include long-term testing and evaluation in the setting of right ventricular failure. This SMV assist system may have application in patients with severe right ventricular dysfunction.

References


**KEY WORDS** • muscle, skeletal • assisted circulation
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