Editorial

Using skeletal muscle to assist the heart

The concept of using the contractile power of skeletal muscle to assist the heart was first proposed in 1959, but further work was initially discouraged by the finding that skeletal muscle fatigued rapidly if subjected to the continuous work necessary for cardiac assistance. An important development was the demonstration that cross-innervation of a fast-twitch muscle with the motor nerve of a slow-contracting muscle altered its functional characteristics to resemble the slow type muscle, which is more fatigue-resistant. Later, Salmons and Vrbova discovered that the same phenomenon could be achieved by subjecting a fast muscle to chronic, low frequency electrical stimulation. The possibility that this phenomenon might be exploited to adapt skeletal muscle for cardiac-type work was first suggested in 1981 and resulted in a considerable revival of interest in the subject.

Transformation
Muscle transformation of this type is characterised by biochemical and ultrastructural adjustments. There is a transition from fast myosin isoforms to those found in slow muscle fibres, and this, together with changes in calcium transport ATPase and calcium-binding proteins, results in reduced contractile speed of the muscle. Simultaneously, there is a shift in metabolism in favour of the oxidative rather than the glycolytic pathways, and ultrastructural reorganisation occurs, including a considerable increase in capillary density and mitochondrial volume fraction, and a reduction in sarcoplasmic reticulum. Studies with 31P-nuclear magnetic resonance confirmed that the decline in phosphocreatine and accumulation of inorganic phosphate, which characterise muscle fatigue, occur to a smaller extent in conditioned muscle. This considerable increase in the capacity for oxidative phosphorylation rivals that of cardiac muscle, and, together with changes in the bioenergetics of muscle contraction, results in more efficient coupling between the development and maintenance of tension and oxygen consumption. With appropriate electrical conditioning muscle transformation can be accomplished in six to eight weeks and is associated with a greatly increased resistance to fatigue.

Use of the latissimus dorsi
Attempts to provide myocardial support with skeletal muscle have focused mainly on the use of the latissimus dorsi muscle, which offers certain advantages suited to a cardiac assist role. Being supplied primarily by a single neurovascular pedicle, the muscle is easily mobilised and transposed within the chest without incurring significant impairment of shoulder function. In addition, the muscle has a bulk comparable with that of the left ventricle, and because skeletal muscle is capable of more work per unit weight than cardiac muscle, a single latissimus dorsi has the potential for assuming a major part of the workload of the left ventricle.

But after division of collateral blood vessels to the latissimus dorsi during its mobilisation from the chest wall, the distal half of the muscle becomes ischaemic. A three week vascular delay period, before chronic stimulation of the muscle, allows recovery of normal resting and exercise-induced blood flow. It has also been emphasised that, to generate cardiac-type work from skeletal muscle, a burst-pattern of stimulation of the motor nerve is necessary to induce mechanical summation of contractile force. Sophisticated, programmable pacemakers are now available that can sense the electrocardiogram and deliver an appropriately timed burst stimulus to the motor nerve of the muscle.

Cardiomyoplasty
Attempts to use skeletal muscle work to support cardiac function have become polarised into two main approaches. One is in the form of a cardiomyoplasty, in which the muscle is wrapped around the heart, such that it may directly augment myocardial contraction. The alternative method provides indirect assistance, often with aortic counterpulsation techniques. In the cardiomyoplasty procedure, the latissimus dorsi muscle is stimulated to contract synchronously with systole. This operation was first performed experimentally in 1959 with diaphragm muscle, and later, in 1968, using latissimus dorsi. It was applied for the first time clinically in 1985 to provide functional replacement of a large ventricular defect created by excision of a benign cardiac tumour. Subsequently, the technique was used for repair after aneurysmectomy or for simple reinforcement of damaged, hypokinetic myocardium. Enthusiasm is such that over 100 cardiomyoplasties have now been performed clinically (unpublished data).

While many patients have experienced an improvement in symptoms of heart failure, it has proved difficult to demonstrate a consistent haemodynamic improvement in terms of reduction of cardiac filling pressures or increases in cardiac output or ejection fraction. Attempts to document such changes in animals undergoing cardiomyoplasty have also provided conflicting results. This may
be related to the configuration of the muscle wrap, which encompasses a large radius of curvature, and thus (according to Laplace’s Law) acts at a mechanical disadvantage when the aim is to develop a significant pressure change within the left ventricle. In addition, electrical conditioning of skeletal muscle to a fatigue-resistant form reduces both the power output and shortening velocity; this will further prejudice the maximum tension developed by the muscle during the systolic interval. It may be that symptomatic improvement after cardiomyoplasty derives in part from a more passive role of the muscle flap, which prevents further dilatation of the heart and perhaps reduces myocardial wall stress by virtue of an effective increase in wall thickness.

Although the precise role of cardiomyoplasty is currently uncertain, an important report has recently appeared from São Paulo, Brazil. Of 29 patients with dilated cardiomyopathy, 13 underwent cardiomyoplasty and 16, who refused the procedure, continued to receive medical treatment. Although this was not a randomised trial, the two study groups were comparable in other respects. In 10 of the 13 patients functional state (New York Heart Association classification) improved after cardiomyoplasty, and mean left ventricular ejection fraction increased by about 30%. However, of particular interest was the finding of improved 18-month actuarial survival in the cardiomyoplasty group compared with those treated medically (80% v 51%). This is the first study to suggest such a survival advantage.

Auxiliary pumping chambers

The alternative avenue of investigation has been the formation of separate skeletal muscle pouches or ventricles (SMVs), which function as auxiliary pumping chambers. They are constructed by wrapping the mobilised latissimus dorsi muscle around a conical Teflon stent that is later removed to create the pouch cavity. SMVs connected to an implantable mock-circulation device, capable of simulating predetermined conditions of preload and afterload, generated continuous stroke work intermediate between that of the left and right ventricles for several weeks. These results were later confirmed when SMVs were placed in a dog’s circulation via the thoracic aorta and stimulated in synchrony with diastole to create aortic counterpulsation.

One dog is alive a year after such a procedure, with the SMV continuing to provide effective aortic counterpulsation. The counterpulsation mode of assist had been chosen because the compliance of SMVs necessitated high preloads to generate optimal power output. However, with improvements in SMV design, based on previous laboratory experience and the use of mathematical models, the compliance of these pouches has been improved to the extent that SMVs have successfully supported or replaced right ventricular function at near physiological preloads in short-term experiments. Continued modifications in design have more recently enabled SMVs, in acute experiments, to generate a level of work greater than that of the left ventricle at low preloads. Thromboembolism and SMP rupture are among the major problems still to be overcome before this form of assist is applied clinically.

Other counterpulsation techniques

Other means for generating aortic diastolic counterpulsation powered by skeletal muscle have been suggested. The latissimus dorsi can be wrapped around the thoracic aorta, providing direct compression during stimulation, and this has resulted in circulatory assistance during short term studies. This method has the advantage that thromboembolic complications are avoided because foreign surfaces do not come into direct contact with blood. One disadvantage is that the degree of assist is limited by the volume of blood that can be displaced using this configuration. One answer is to enlarge the diameter of the aorta with a patch, so as to augment volume displacement.

An alternative method for generating counterpulsation has been to exploit the concept of the intra-aortic balloon pump, already a widely accepted form of clinical cardiac assist. A counterpulsation system powered by skeletal muscle has been devised. It consists of a cylindrical housing containing a silicone bladder that is anastomosed to the aorta. The inner bladder is displaced pneumatically by compression of a bulb placed either within an SMV or beneath the intact latissimus dorsi muscle. During muscle stimulation aortic diastolic pressure augmentation has been effective for up to several weeks. A major disadvantage of this device is that the vehicle used for transmitting pressure changes between the two chambers, whether gas or liquid, tends to leak from the system, thereby impairs the efficiency.

While conditioned skeletal muscle currently offers a realistic means of providing functional support for the failing myocardium, more research is required to define the optimal mode of assist for different patient subgroups. The mechanism by which cardiomyoplasty augments cardiac function is unclear, though an improvement in symptoms after the procedure is being increasingly reported, particularly in patients with dilated cardiomyopathy. SMVs, on the other hand, have the potential to replace left or right ventricular function, and have pumped effectively in the canine circulation for more than a year. With continued improvements in SMV design the future for this mode of support is promising. The efficacy of some other forms of circulatory support by skeletal muscle remains to be elucidated.

TIMOTHY L HOOPER
LARRY W STEPHENSON

Division of Cardi thoracic Surgery,
Wayne State University,
Harper Professional Building, Suite 228,
Detroit, Michigan 48201, USA

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T L Hooper and L W Stephenson

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