Artificial hearts and blood pumps in the treatment of profound heart failure

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ABSTRACT The recent clinical use of a pneumatic artificial heart at the University of Utah has focused attention on the role of blood pumps in the support of the circulation. Pneumatically powered assist pumps are now in clinical trials in patients with profound but reversible heart failure after open-heart surgery; survival rates as high as 50% in a heretofore lethal condition have been encouraging. The results of animal studies with the pneumatic artificial heart suggest that these devices are ready for clinical trials; the major application is likely to be as a bridge to cardiac transplantation. Implantable electric motor-driven assist pumps and artificial hearts are being evaluated in animals as permanent cardiac support or replacement devices; clinical use is projected to begin late in this decade. Initially, these devices will be employed in patients with end-stage cardiac disease who are not suitable candidates for cardiac transplantation or for whom donor hearts are not available. The availability of compact blood pumps will offer new forms of therapy to patients with certain types of profound heart failure.


IN 1982, after 24 years of development and laboratory research, members of Kolff’s group replaced the heart of a mortally ill patient with an artificial heart. The patient survived over 3 months and important information was learned. Because of the present technical limitations of this artificial heart, widespread use is not imminent. However, the observation is becoming increasingly clear that mechanical pumps can substitute for the function of the temporarily or permanently damaged human heart. Indeed, in the next decade, implantable blood pumps may assume an important role in the treatment of end-stage heart disease in the patient over 50 years of age in whom transplantation is not an effective form of therapy.

Four types of compact blood pumps are being developed to support the circulation (see figure 1 and table 1). Pneumatically powered ventricular assist pumps and artificial hearts represent the least engineering challenge and have progressed to useful, reasonably safe systems. The large size of the external power unit and the need for percutaneous tubes preclude prolonged use and have led investigators to search for a more optimal design. While still in an earlier stage of development, implantable motor-driven assist pumps and artificial hearts obviate the need for the bulky external power unit and for the large diameter percutaneous tubes. Accordingly, these systems will have a great advantage over pneumatic units when portability and prolonged use are required.

Pneumatic ventricular assist pumps. The most widely used type of compact blood pumps provides temporary (i.e., days) circulatory support for patients with profound ventricular failure after open-heart operations. First used successfully by DeBakey in 1963, these pumps are now available in six to eight medical centers in the United States and in fewer centers abroad. These temporary assist pumps have a valveless, flexible polyurethane, blood-containing chamber positioned within a rigid housing. When used as a left ventricular assist pump, the unit fills from the left atrium or left ventricle and ejects into the aorta; when used for right ventricular support, the pump fills from the right atrium and discharges into the pulmonary artery. The compact size of these blood pumps would permit implantation. However, no advantage to implantation has been apparent and, at present, the pumps are most conveniently positioned adjacent to the patient with the blood conduits passing through the body wall.

The indications for the use of temporary left ventricular assistance after a technically successful cardiac operation center around failure of the left ventricle to adequately support the systemic circulation as deter-
FIGURE 1. Comparison of the four types of blood pumps being developed to provide circulatory support. A, Pneumatic ventricular assist pump; B, pneumatic artificial heart; C, motor-driven ventricular assist pump; D, motor-driven artificial heart.

Table 1 lists the features of the different devices and provides information regarding indications for present or future application.

mined by a mean systemic arterial pressure lower than 60 mm Hg, a mean left atrial pressure greater than 25 mm Hg, and a cardiac output index of less than 1.8 l/min/m². Thus the assist pump forms a third "line of support" in a patient whose left ventricular failure is not responsive to drugs and the intra-aortic balloon. Similarly, the assist pump has been helpful in patients with right ventricular failure after a cardiac operation.

In the best series, over half of the patients in whom the pump has been implanted have been provided good circulatory support. An overzealous effort to exhaust every possible drug and combination of drugs before use of the assist pump results in a prolonged cardiopulmonary bypass time, excessive bleeding, and reduced renal function, each of which reduces the chances of a favorable outcome. In those patients with good circulatory support, return of ventricular function has been progressive, with satisfactory recovery requiring 3 to 5 days for right ventricular recovery and as long as 9 days for left ventricular recovery. The mechanism of recovery is not known, but progressive reduction of myocardial edema and rebuilding of the intracellular high-energy phosphate content are thought to play important roles in functional recovery.

When adequate myocardial function has been verified by intracardiac pressure and cardiac output index measurements after gradual weaning and during brief periods of cessation of pump support, the patient is
TABLE 1
Comparison of the four types of blood pumps being developed to provide circulatory support

<table>
<thead>
<tr>
<th>Ventricular assist pump</th>
<th>Artificial heart</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temporary use after open-heart operation</td>
<td>Pneumatic</td>
</tr>
<tr>
<td>Supports circulation while malfunctioning heart recovers</td>
<td>Major use will be to support patients while donor heart located</td>
</tr>
<tr>
<td>Pumps blood from left atrium (ventricle) to aorta</td>
<td>Requires 2 similar blood pumps</td>
</tr>
<tr>
<td>Place outside body</td>
<td>Pumps are implanted in chest after heart removal</td>
</tr>
<tr>
<td>Required for up to 10 days</td>
<td>Two 1.3 cm diameter tubes carry air pulses through chest to pumps</td>
</tr>
<tr>
<td>Removal requires reoperation</td>
<td>Requires bulky pneumatic power unit</td>
</tr>
<tr>
<td>Currently available at 6–8 medical centers in United States</td>
<td>Has been used in 3 patients (Houston, 2; Salt Lake City, 1)</td>
</tr>
<tr>
<td>Best survival rate: about 50%</td>
<td>Projected use: less than 500/yr in U.S.</td>
</tr>
<tr>
<td>Projected use: 1000/yr in U.S.</td>
<td></td>
</tr>
</tbody>
</table>

Motor-driven

| Designed for certain patients with end-stage left heart failure | Designed for certain patients with left and right heart failure |
| Permanently implanted motor-powered pump located in chest or abdomen | Consists of 2 motor-powered pumps implanted in chest |
| Pumps blood from left ventricle to aorta                       | Requires thin electrical wire to cross chest wall |
| Requires a thin electrical wire to cross chest wall             | Uses 12–15 W of power |
| Can be energized by a portable external battery pack           | Patient will be fully mobile |
| Natural heart provides “back up”                               | No “back up” system envisaged |
| Patient will be fully mobile                                   | Animal studies are just starting |
| Animal studies to date: duration up to 6 mo                     | Clinical use: beyond 1990 |
| Clinical use: anticipated in 1988                              | Projected use: depends on effectiveness of electric assist pump and heart transplant |
| Projected use: 10,000/yr in U.S.                                |                                                       |

returned to the operating room. The chest is reopened, the inflow cannula is removed (atrial) or divided (ventricular), the arterial cannula is disconnected, and the chest is closed. Attempts have been made to eliminate the need for a repeat operation by dividing the cannulas just below the skin line and occluding the lumen with an obturator. However, this latter technique presents a risk of a burrowing infection, starting at the skin and ultimately entering the vascular system, that far outweighs the risk of a reoperation with removal of the cannulas.

Since 1979, we have used the techniques described above in 19 patients. Left ventricle support has been used in 14 patients with a 57% survival, while right ventricle support has been used in two patients with 100% survival. We have not had a survivor in any of the three patients who required biventricular support.

In the future, the indications for the use of short-term ventricular assist pumps will be broadened to include not only patients who have profound cardiac failure after cardiac operations but also certain patients with myocardial infarction and cardiogenic shock.

**Pneumatic artificial heart.** Pneumatically powered blood pumps have progressed to the point where two intrathoracically placed units can be used to replace the heart, thereby providing both a systemic and pulmonary circulation. Every group doing research in this field now uses two separate, smooth-surfaced, segmented polyurethane, sac-type pumps. Clinical style concavoconvex disc-type prosthetic inflow and outflow valves provide unidirectional blood flow in the two ventricles. Each pump is energized by pulses of air generated by an external pneumatic unit and transmitted through percutaneous tubes. Artificial heart implantation technique is similar to that used for cardiac transplantation; 2 to 3 hr of cardiopulmonary bypass are required. The operative mortality associated with animal implantation is low and similar to that seen with other major large animal operations. Successful maintenance of the circulation with an artificial heart requires unimpeded ventricle filling, some technique to balance the output of the two ventricles, and an adequate cardiac output index. The calves with the implanted pumps generally stand on the evening of operation and begin eating soon thereafter. Their weight gain approximates that of an unoperated calf.

Three research groups have each achieved survival periods in calves exceeding 6 months. One major cause of death appears to have been overcome during the past 2 years. Improved design and use of smooth-surface atrial sewing cuffs have eliminated tissue overgrowth (pannus) and associated infection at the inflow.
valves. Other problems that lead to death in young growing calves with artificial hearts are polyurethane sac calcification and the limited pump output relative to the rapid animal growth. Although these problems do not appear to have a clinical counterpart, they do limit the long-term evaluation of the artificial heart in animals and have proved to be extremely costly. Accordingly, investigators are directing their attention to the use of an adult animal preparation in an effort to extend the longevity of animal studies to 1 year or more. The ultimate limit to the duration of pumping will be the flex life of the blood sac. The segmented polyurethane currently being used has an extremely long flex life; in vitro flex tests have exceeded several years. However, no data are available as to the functional limit in actual animal use, nor have efforts been made to optimize design or material for this application.

Initial clinical use of the artificial heart has been directed to interim support of the circulation in a potential transplant candidate while a suitable donor heart can be procured. The present experimental results with the pneumatic artificial heart indicate that this is an appropriate and timely application and is likely to remain so. The use of cyclosporin A for immunosuppression reduces the need for steroid therapy and thus the risk of infection at the percutaneous tube sites in a patient undergoing sequential heart transplantation. In spite of the optimism regarding this approach, application will be limited. There is no "shortage" of potential cardiac transplant recipients at present. Most groups performing cardiac transplantation are intent on achieving the best results possible. Accordingly, there will be hesitancy to use a scarce donor heart in a patient having an additional risk factor of an artificial heart. Clearly, use of the artificial heart in this application is intimately related to the future role of cardiac transplantation as a therapeutic option.

The patient over 50 years of age with end-stage heart disease has had no alternative to optimal drug therapy. The recent elective use of a pneumatic artificial heart in such a patient is serving as a "toe in the water" to test the acceptability of a device that is capable of supporting the circulation but has the drawbacks of two percutaneous tubes with their risk of infection, a bulky pneumatic pulse generator that curtails patient mobility, and a functional life that has not been proved to exceed 9 months. The use of the pneumatic artificial heart at this stage of development depended on the personal philosophy of the developers and on a personal desire of the patient. All who work in this field carefully followed the course of this patient to ensure that their research would be directed to satisfying the clinical needs of the patient with end-stage cardiac disease. Already clear is the need for a compact, portable pneumatic unit, which will eliminate one serious drawback of the current system. Such a unit has been developed and is undergoing initial testing in calves with artificial hearts.7

Motor-driven ventricular assist pump. The compact implantable blood pump being developed for support of the systemic circulation in the patient with an irreparably damaged left ventricle is believed to be the most practical form of permanent circulatory support being developed and the form that will receive the widest use. Indeed, this concept has been supported over and over again by committees of experts assembled by the National Heart, Lung and Blood Institute (NHLBI). Conservative but realistic estimates have been made, which indicate that as many as 10,000 patients per year could benefit from such a device. Accordingly, during the past 15 years the NHLBI has targeted funds to develop suitable implantable blood pumps. In its most general form, the implantable left ventricular assist pump consists of a valved, pusher-plate activated blood sac, filling from the left ventricle and ejecting blood into the aorta.8 The pusher-plate movement is achieved by a brushless electric motor or solenoid unit. The pumps are being designed to be implanted in the peritoneal space or the thorax. The 12 to 15 W required for pumping will be supplied through percutaneous wires or by wireless connection with inductive coupling techniques. Thus the patient with this type of system will be required to remain close to an electrical outlet or, if tether-free function is desired, to carry a battery pack. Moreover, to ensure continuous pumping during a period of loss of external power, a compact, sealed, implantable battery will be an integral system component and will provide energy capable of powering the unit for over 30 min.

Long-term animal studies are now in progress in five laboratories in the United States. Most groups have achieved over 100 days of continuous pumping, but to date no animal has been supported for 200 days. A variety of minor but important improvements are being made by each group to extend the period of continuous pumping. The concern regarding this general approach is reflected by the virtual absence of experimental animal trials of implanted left ventricular assist pumps abroad.

The systems being developed continue to show great promise. However, clinical use is about 5 years away. The initial applications will be in patients over 50 years of age, who are not transplant candidates. In addition
to simplicity, the implantable assist pump has an advantage over the artificial heart in the fail-safe nature of the assist system, analogous in some ways to a pacemaker. Thus if the pump should fail, the left ventricle, albeit damaged, will support the circulation for a period long enough for a patient to report to a hospital and for the unit to be changed.

**Motor-driven artificial heart.** One obvious step beyond the implantable motor-driven assist pump is to add a second pump to the unit and employ it for a complete heart replacement. These hearts will have many design features in common with the assist pumps, but will be used initially in patients with biventricular failure who are not transplant candidates or in cases in which urgent heart replacement is required and suitable time does not exist to obtain a compatible donor heart.

Research in the motor-driven artificial heart has lagged behind the units described above. However, several compact systems have been assembled and are now being evaluated on the laboratory bench. The unit being developed by our group is shown in figure 2. Suitable stable control techniques have been developed, based on lessons learned with pneumatic hearts. As a result, animal implant studies are proceeding; their duration has only recently exceeded 5 months. Unless research in this area increases, units of this type will not be available for patient therapy until the 1990s.

**Conclusion**

A series of blood pumps are being developed that will undoubtedly play an important role in the treatment of the patient with serious forms of heart disease. As with other forms of therapy, each of the devices described has specific indications. The appropriate pump for a specific patient will be the simplest unit that will provide the circulatory support required. The temporary (days to 1 week) ventricular assist pump is the only unit that has been shown to be lifesaving in clinical application; it will see wider application within the next several years.

The units designed for prolonged use are being designed with a 2-year functional life requirement. As laboratory and clinical experience is gained, gradual improvement will be made that will extend the functional life to a decade.

A complex interrelation exists between the cardiac transplant and the permanent mechanical support device. Since the rejection problem presently precludes transplantation in patients over 50 years of age, a particularly clear division of "turf" appears to exist. However, as advances occur in both fields, the division or overlap is certain to be altered in a way not now predictable. It is clear that research in the two fields has complementary rather than competitive aspects.

No discussion of the application of high-technology devices to medical care today can be complete without reference to the costs involved. No component of any device discussed here has a rare or inherent complex nature by current standards. The use of modern integrated-circuit components and microprocessor control electronics has provided stable, practical systems at what all would agree are low costs. To provide an example of the cost of a motor-powered assist pump or total artificial heart, we summed the cost to purchase components and to build a single prototype unit, including the pump, mechanical components, motor, and electronics. The cost of $20,000 (1983) could be reduced by about one-third with volume purchase and production fabrication. When industrial setup costs, management fees, overhead costs, product liability, insurance, and profit are added, the price will increase rapidly. However, the commercial unit cost will not be out of line with health costs now being incurred. Every indication at present suggests the benefits obtained will be well worth the costs incurred.
References

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