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Cardiac Replacement with a Total Artificial Heart as a Bridge to Transplantation

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ABSTRACT

BACKGROUND

The CardioWest Total Artificial Heart orthotopically replaces both native cardiac ventricles and all cardiac valves, thus eliminating problems commonly seen in the bridge to transplantation with left ventricular and biventricular assist devices, such as right heart failure, valvular regurgitation, cardiac arrhythmias, ventricular clots, intraventricular communications, and low blood flows.

METHODS

We conducted a nonrandomized, prospective study in five centers with the use of historical controls. The purpose was to assess the safety and efficacy of the CardioWest Total Artificial Heart in transplant-eligible patients at risk for imminent death from irreversible biventricular cardiac failure. The primary end points included the rates of survival to heart transplantation and of survival after transplantation.

RESULTS

Eighty-one patients received the artificial-heart device. The rate of survival to transplantation was 79 percent (95 percent confidence interval, 68 to 87 percent). Of the 35 control patients who met the same entry criteria but did not receive the artificial heart, 46 percent survived to transplantation ($P<0.001$). Overall, the one-year survival rate among the patients who received the artificial heart was 70 percent, as compared with 31 percent among the controls ($P<0.001$). One-year and five-year survival rates after transplantation among patients who had received a total artificial heart as a bridge to transplantation were 86 and 64 percent.

CONCLUSIONS

Implantation of the total artificial heart improved the rate of survival to cardiac transplantation and survival after transplantation. This device prevents death in critically ill patients who have irreversible biventricular failure and are candidates for cardiac transplantation.

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*The CardioWest Total Artificial Heart Investigators are listed in the Appendix.

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THE INCIDENCE OF CONGESTIVE HEART failure, the final common pathway of myocardial dysfunction in most forms of cardiac disease, has increased by a factor of five in the past three decades and is currently increasing at a rate of 550,000 new cases per year. The nearly 5 million Americans who have heart failure generate annual health care costs of $38.1 billion.[1] Most of these patients are treated medically or with surgical therapy tailored to their cardiac disease. Unfortunately, even the most advanced pharmacologic and surgical treatments fail in some patients. Each year, nearly 300,000 Americans die of heart failure[1]; among them are 15 to 25 percent of those waiting for transplantation.[2] It has been estimated that 30,000 to 70,000 Americans each year could benefit from cardiac replacement.[3]

For the most severe forms of cardiac dysfunction, which lead to irreversible biventricular failure, cardiac transplantation has emerged as the only effective therapy affording longevity and quality of life, with survival rates at one and five years of up to 94 percent and 78 percent, respectively.[4] Unfortunately, demand for donor hearts has doubled in recent years, and the annual national supply has decreased from about 2500 hearts to about 2000.[2] Since 1998, the waiting time before transplantation among potential heart-transplant recipients has increased to more than one year. Nearly 75 percent of recent recipients require continuous intravenous inotropic support, and 54 percent are on life-support machines before transplantation.[2]

Many patients with end-stage congestive heart failure who are awaiting transplantation receive mechanical circulatory-support devices that have been approved by the Food and Drug Administration (FDA). Commercially available mechanical circulatory support devices include left ventricular assist devices and paracorporeal devices that may be used to support one or both ventricles. With the use of these devices, the rate of survival from the time of implantation to the time of transplantation has ranged from 51 to 71 percent.[5-9] Worldwide, more than 5000 patients have received these devices.

The CardioWest Total Artificial Heart is a biventricular, pneumatic, pulsatile blood pump that completely replaces the patient's native ventricles and all four cardiac valves orthotopically (Fig. 1).[10] It weighs 160 g and displaces 400 ml of volume. It is lined with polyurethane and has a four-layer, pneumatically driven diaphragm. At maximal stroke volume (70 ml), it delivers a cardiac output of more than 9 liters per minute. In the United States, the device is powered by a large console on wheels that prevents hospital discharge; portable drivers permitting discharge from the hospital are currently used in Europe. The device may be useful in patients for whom left ventricular assist devices and biventricular assist devices are contraindicated, including those with aortic regurgitation, cardiac arrhythmias, a left ventricular thrombus, an aortic prosthesis, an acquired ventricular septal defect, or irreversible biventricular failure requiring high pump outputs.

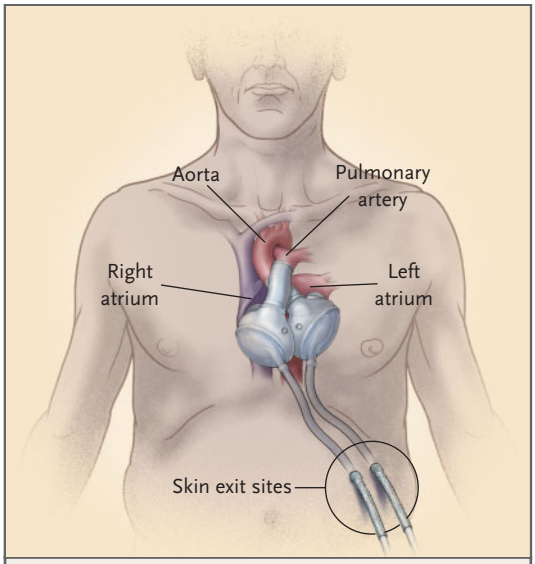

Figure 1. The CardioWest Total Artificial Heart.

METHODS

We conducted a prospective, investigator-initiated trial of the CardioWest Total Artificial Heart under an investigational-device exemption granted by the FDA. The study was initiated in January 1993 and completed in September 2002. The device is manufactured by SynCardia Systems (Tucson, Ariz.). The institutional review boards of the five participating institutions approved the protocol, and written informed consent was obtained from all patients or their representatives. The authors wrote the manuscript.

PATIENTS

There were 130 patients: 81 patients who met the protocol-inclusion criteria (the protocol group), 35 controls, and 14 patients who did not meet the

protocol-inclusion criteria but in whom the device was implanted on a compassionate-use basis (the off-protocol group) (Table 1). The median rate of accrual into the protocol group was 9 patients per year (range, 2 to 18). The patients selected for the protocol group were candidates for cardiac transplantation who were at high risk of imminent death due to irreversible biventricular cardiac failure. Implantation of a left ventricular assist device had been ruled out for the following reasons: 15 could not be weaned from cardiopulmonary bypass (with 12 of the 15 having had a prebypass cardiac arrest), 51 had central venous pressures greater than 18 mm Hg, 11 had right ventricular ejection fractions of less than 20 percent, 2 had ventricular tachycardia, 1 had an aortic prosthesis, and 1 had right ventricular damage sustained at the time of sternotomy.

The controls were patients who had been matched with the patients in the protocol group according to inclusion and exclusion criteria but who had not received any mechanical circulatory support. Data from the controls were used only for survival comparisons. Twenty-two were found on retrospective review of the participating centers' records for the period from 1991 to 1993. Three were prospective patients who had refused device implantation. Ten were identified by retrospectively screening 635 patients whose United Network for Organ Sharing (UNOS) status was 1 (indicating the need for continuous intravenous inotropic support or mechanical support) from participating centers' lists for the period from 1994 to 2001.

The baseline demographic factors, risk factors, hemodynamic measurements, and laboratory values of the patients in the protocol group and the controls are shown in Table 2. The selection process, based solely on the criteria listed in Table 1, resulted in groups that differed significantly in 12 of 65 baseline characteristics. Consequently, the control group is not an exact match and provides only a rough approximation of the natural history of patients with cardiogenic shock. An ischemic cause of heart failure, a history of smoking, use of anticoagulation, prior cardiac surgery, and current use of an intraaortic balloon pump were more prevalent in the control group, whereas the use of cardiopulmonary bypass was more common in the protocol group (19 percent, vs. 0 percent in the control group). The controls had a lower systolic pressure, pulmonary-artery mean pressure, central venous pressure, total bilirubin level, partial pressure of carbon dioxide, and bicarbonate level than the patients in the protocol group. Use of inotropic support was greater in the protocol group, in which 66 percent of the patients were receiving three or more inotropes; in contrast, 80 percent of the controls were receiving no more than two inotropes. The dosages of inotropes (dopamine, dobutamine, epinephrine, milrinone, and norepinephrine) did not differ significantly between the groups. The patients in the off-protocol group had distinctly different outcomes and are presented separately.

Table 1. Selection Criteria.

Inclusion criteria
Eligible for transplantation (according to institutional criteria)
New York Heart Association class IV
Body-surface area 1.7 to 2.5 m^2 or a distance of ≥10 cm from the anterior vertebral body to inner table of the sternum at 10th thoracic vertebra on computed tomographic scanning
Hemodynamic insufficiency according to either of the following definitions:
Cardiac index ≤2.0 liters/min/m^2 and one of the following: systolic arterial pressure ≤90 mm Hg or central venous pressure ≥18 mm Hg
Two of the following: dopamine at a dose of ≥10 μg/kg of body weight/min, dobutamine at a dose of ≥10 μg/kg/min, epinephrine at a dose of ≥2 μg/kg/min, other cardioactive drugs at maximal doses, use of an intraaortic balloon pump, or use of cardiopulmonary bypass
Exclusion criteria
Use of any vascular assist device
Pulmonary vascular resistance ≥640 dyn·sec·cm^{-5}
Dialysis in previous 7 days
Serum creatinine ≥5 mg/dl (440 μmol/liter)
Cirrhosis with total bilirubin ≥5 mg/dl (29 μmol/liter)
Cytotoxic antibody ≥10 percent

The total artificial heart was implanted with the use of simplified fitting, implantation, and explantation techniques, as previously described.[10-12] Coagulation monitoring and anticoagulation were also performed as previously described.[10]

Major efficacy end points included the rates of survival to transplantation, overall survival, and survival after transplantation, as well as a composite end point called "treatment success." Treatment was considered successful if the patient had the following characteristics 30 days after transplantation: he or she was alive, was in New York Heart Association class I or II, was ambulatory, was not dependent on a ventilator, and was not undergoing dialysis. Other efficacy end points included hemodynamic recovery, recovery of end-organ function (including the function of the kidneys and liver), the percentage of patients who were ambulatory, and the percentage of patients who could walk more than 100 ft (30.5 m).

Table 2. Characteristics of the Protocol and Control Groups at the Time of Entry into the Study.*

Characteristic	Protocol Group (N=81)	Control Group (N=35)
Age (yr)	51±10.3	52±9.8
Male sex (% of patients)	86	91
Ischemic cause of heart failure (% of patients)	53	74†
New York Heart Association class	IV	IV
Height (cm)	176±11.0	178±6.2
Weight (kg)	85±13.2	80±11.8
Body-surface area (m^2)	2.0±0.2	2.0±0.2
History of smoking (% of patients)	54	83†
History of excessive alcohol use (% of patients)	46	34
History of hypertension (% of patients)	32	17
Cardiac arrest within preceding 24 hr (% of patients)	37	26
Anticoagulation (% of patients)	47	69†
Cardiopulmonary bypass (% of patients)	19	0†
Intraaortic balloon pump (% of patients)	36	69†
Mechanical ventilation (% of patients)	42	34
Obtunded or drowsy (% of patients)	35	34
Prior cardiac surgery (% of patients)	38	60†
Prior percutaneous transluminal coronary angioplasty (% of patients)	15	6
Pacemaker (% of patients)	12	17
Automatic implantable cardioverter–defibrillator (% of patients)	30	11
Cardiac index (liters/min/m^2)	1.9±0.5	1.8±0.4
Cardiac output (liters/min)	3.9±1.1	3.5±0.9
Systemic vascular resistance (dyn·sec·cm^{-5})	1109±394	1283±611
Pulmonary vascular resistance (dyn·sec·cm^{-5})	222±117	203±113
Heart rate (beats/min)	101±21	105±22
Systolic arterial pressure (mm Hg)	93±15	86±11†
Mean arterial blood pressure (mm Hg)	68±9	66±9
Pulmonary-artery systolic pressure (mm Hg)	55±14	51±8
Pulmonary-artery mean pressure (mm Hg)	41±11	36±6†
Pulmonary-capillary wedge pressure (mm Hg)	30±11	28±6
Central venous pressure (mm Hg)	20±7	17±7†
Organ-perfusion pressure (mm Hg)	49±11	49±11
Serum sodium (mmol/liter)	132±6.6	130±6.3
Serum potassium (mmol/liter)	4.4±0.9	4.5±0.9
Serum chloride (mmol/liter)	96±6.7	94±7.5
Blood urea nitrogen (mg/dl)	36±19	41±25
Serum creatinine (mg/dl)	1.7±0.6	1.7±0.7
Total bilirubin (mg/dl)	2.0±1.3	1.3±0.7†
Serum aspartate aminotransferase (IU/liter)	189.9±773	50.4±48
White-cell count (per mm^3)	11,400±4100	10,300±3900
Hematocrit (%)	33.7±6.1	34.5±5.9
Platelet count (per mm^3)	213,000±94,000	242,700±104,000
Fibrinogen (mg/dl)	467±199	330±127
Prothrombin time (sec)	16.4±4	15.1±5
International normalized ratio	2.0±2	1.9±2
Partial-thromboplastin time (sec)	37.3±13	41.7±18
pH	7.5±0.1	7.5±0.1
Partial pressure of arterial oxygen (mm Hg)	115.2±83	118.5±72
Oxygen saturation (%)	95±4	96±3
Partial pressure of arterial carbon dioxide (mm Hg)	34.4±6.7	29.8±6.1†
Bicarbonate (mmol/liter)	25.1±5	21.6±5†

* Plus–minus values are means ±SD. To convert the values for blood urea nitrogen to millimoles per liter, multiply by 0.357. To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for bilirubin to micromoles per liter, multiply by 17.1.
† $P<0.05$ for the comparison with the protocol group.

Safety was measured by prospectively recording previously defined adverse events.[13] Data from all 95 patients in whom a total artificial heart was implanted (the 81 patients in the protocol group and the 14 in the off-protocol group) were used in the analysis of adverse events.

STATISTICAL ANALYSIS

All the data generated by this study were collected and maintained by an independent monitoring group (Research Technology Management, Scottsdale, Ariz.). Statistical analyses were carried out by Synteract (Carlsbad, Calif.). For dichotomous variables, Fisher's exact test was used to test the null hypothesis (i.e., the hypothesis that there was no difference between the protocol group and the control group). P values of less than 0.05 were considered to indicate statistical significance. Kaplan–Meier curves were used to display time-to-event distributions.

RESULTS

SURVIVAL

Survival to transplantation was achieved in 79 percent of the patients who received a total artificial heart according to protocol (95 percent confidence interval, 68 to 87 percent), as compared with 46 percent of the controls (P<0.001). The mean time from entry into the study to transplantation or death was 79.1 days among all the patients who received an implant and 8.5 days among the controls (P<0.001).

The overall survival rate at one year was 70 percent (95 percent confidence interval, 63 to 77 percent) among the patients who received an implant according to protocol, as compared with 31 percent among the controls (P<0.001) (Fig. 2). Survival rates one and five years after transplantation among the controls were 69 percent and 34 percent, respectively, and among patients in the protocol group they were 86 percent and 64 percent, respectively; in comparison, contemporary UNOS data[2] from more than 4000 patients include one- and five-year survival rates of 84.7 percent and 69.8 percent, respectively. Treatment success was achieved in 69 percent of the patients who received an implant, as compared with 37 percent of the controls (P=0.002).

OTHER END POINTS

In the protocol group, patients' hemodynamic status improved immediately after implantation of the total artificial heart, with a sustained increase in the cardiac index from a baseline value of 1.9 to 3.2 liters per minute per square meter of body-surface area. Other signs of hemodynamic recovery that occurred immediately after implantation and that persisted included the mean systolic arterial pressure, which rose from 93 to 122 mm Hg; the mean central venous pressure, which fell from 20 to 14 mm Hg; and the organ-perfusion pressure (mean arterial pressure minus central venous pressure), which rose from 49 to 68 mm Hg. Renal and hepatic function and the levels of blood urea nitrogen, creatinine, bilirubin, and liver enzymes returned to normal within three weeks after implantation. Other laboratory values, such as electrolyte levels, the platelet count, and the white-cell count, also returned to normal at three to four weeks.

The quality of life among the patients who received an implant according to protocol improved significantly. One week after implantation, 75 percent of these patients were out of bed. Mobility, defined as the ability to walk more than 100 ft two weeks after entry into the study, was observed in 60.5 percent.

Fourteen patients received a total artificial heart on an off-protocol basis. Reasons for off-protocol implantation included inability to document fulfillment of inclusion criteria (in four cases), the pres-

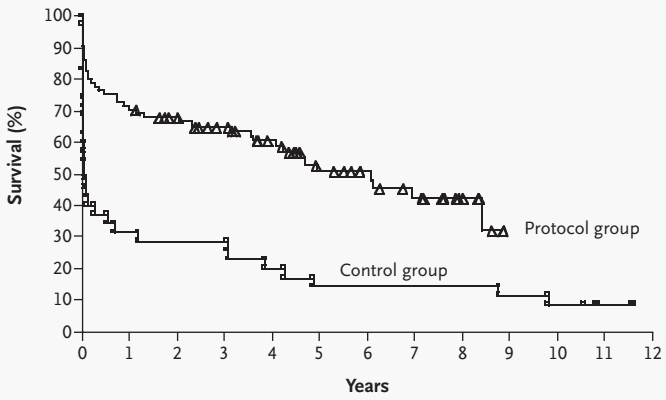

Figure 2. Overall Survival Rate from the Time of Study Entry to the Termination of the Study among the Patients Who Received a Total Artificial Heart According to Protocol and the Controls.

The Kaplan–Meier curve for the controls extends two and a half years beyond that of the patients in the protocol group because the recruitment of controls began in 1991 and that of patients for the protocol group began in 1993. There was a large difference in the early mortality rate between the two groups, but the survival curves became parallel after transplantation. The symbols on each curve indicate the points at which data were censored.

ence of a ventricular assist device (in three), conditions likely to preclude survival (in two), dialysis (in two), contraindications to heart transplantation (in two), and a previous heart transplantation (in one). The rate of survival to transplantation among these patients was 50 percent. Causes of deaths during the period when the total artificial heart was in use (all of which occurred within 20 days after the procedure) were pulmonary edema (in two cases), bleeding (in two), multiorgan failure (in two), and sepsis (in one).

ADVERSE EVENTS

Table 3 lists the adverse events among all 95 patients who received a total artificial heart and among the subgroup of 81 patients who received the implant according to protocol. The implant was used for a total of 7515 days (20.6 years) in the overall group and 6407 days (17.6 years) in the protocol group.

There were 102 bleeding events, 55 of which occurred during implantation. These 55 events were described as mediastinal bleeding or tamponade necessitating repeated surgery (23 events in 21 patients [21 percent]), the need for 3 units of blood within a 24-hour period after the first 48 postoperative hours (18 events), the need for 8 or more units of blood during surgery (13 events), and abdominal bleeding necessitating surgery (1 event). All but one of the repeated operations took place within the first 21 days after implantation. Two patients died from bleeding, one at the time of device implantation and one at the time of transplantation.

One serious device malfunction — a perforation in one of the four layers of the device's left ventricular diaphragm — resulted in the death of a patient on day 124 after implantation. No other serious device malfunctions occurred during more than 12,000 patient-days of use of the device. A complication of fitting occurred in five patients. In three of these cases the fit was corrected by repositioning or repeated surgery. A poor fit contributed to death in two patients.

The cardiac index fell to less than 2 liters per minute per square meter for four or more hours in association with eight events during the first 11 days after implantation. These events included one fitting problem, four episodes of hypovolemia, one case of pneumothorax, one of tamponade, and one of catheter entrapment. The five other instances in which the cardiac index fell were attributed to a single patient on the 117th day and were the result of a device malfunction. The systolic arterial pressure fell to less than 90 mm Hg for four or more hours 27 times in 18 patients as a result of sepsis (12 events), hypovolemia (12), an antihypertensive medication (1), aspiration (1), and pneumothorax (1).

There were 125 infections during use of the total artificial heart: 50 were respiratory infections, 28 were genitourinary infections, 17 involved the drive line, 12 were gastrointestinal infections, 7 were blood infections, 6 involved the infusion catheter, and 5 were mediastinal infections. In 68 of the 81 patients in the protocol group (84 percent), infection neither delayed transplantation nor contributed to death. Infection delayed transplantation in five patients in this group (6 percent) (two of whom had drive-line infections and one each of whom had a blood, respiratory, or mediastinal infection). Infection contributed to death in seven patients in the protocol group (9 percent) (five of whom had a respiratory infection, one of whom had an infection involving the infusion catheter, and one of whom had a mediastinal infection) and caused death in one patient (1 percent) (who had a respiratory infection). Sixty-two percent of the infections occurred during the first 28 days after the implantation procedure. There were 17 superficial drive-line infections, with none ascending to the mediastinum.

During the period that the total artificial heart was in use, there were 26 neurologic events among patients in the protocol group, including stroke (11 events in 10 patients [12 percent]), transient ischemic attacks (4 events), anoxic encephalopathy (5), metabolic encephalopathy (1), seizure (4), and syncope (1). The actuarial rate of freedom from any neurologic event among patients in the protocol group was 0.91 at day 7, 0.88 at day 14, 0.85 at day 28, and 0.67 at day 168. The curve remained flat (at 0.67) after three months. The linearized rate of stroke was 0.05 event per month. Six of the strokes had no residual effect after 48 hours, four had neurologic residual effects of a minor nature, and one caused a fixed deficit (hemiplegia) and delayed transplantation. There were no deaths from neurologic complications.

Technical or procedural complications occurred in three patients. In these patients, the mechanical tricuspid valve of the total artificial heart became obstructed as a result of migration of the central venous catheter, and the complication either caused

Table 3. Adverse Events, Including Those That Affected Outcomes, from the Time of Study Entry to 30 Days after Transplantation.

Adverse Event	All Patients Who Received an Implant (N=95)			Patients Who Received an Implant per Protocol (N=81)	
	All Events		Event Affecting Outcome	Event Delaying Transplantation	Event as Primary Cause of Death
	no. of events		*number of patients (percent)*		
Bleeding	102	59 (62)	15 (16)	8 (10)	1 (1)
Device malfunction	19	16 (17)	1 (1)	1 (1)	1 (1)
Fitting complication	5	5 (5)	2 (2)	2 (2)	0
Reduced cardiac index	13	9 (9)	2 (2)	0	0
Reduced blood pressure	27	18 (19)	8 (8)	5 (6)	2 (2)
Hemolysis	5	4 (4)	0	0	0
Hepatic dysfunction	37	35 (37)	13 (14)	9 (11)	0
Infection	172	73 (77)	18 (19)	13 (16)	1 (1)
Neurologic event	35	26 (27)	6 (6)	5 (6)	0
Operation	31	23 (24)	2 (2)	2 (2)	0
Peripheral thromboembolism	18	13 (14)	3 (3)	2 (2)	0
Renal dysfunction	34	29 (31)	16 (17)	12 (15)	0
Respiratory dysfunction	61	34 (36)	15 (16)	11 (14)	0
Technical or procedural problem	11	3 (3)	2 (2)	1 (1)	1 (1)
Other problem	10	9 (9)	6 (6)	3 (4)	1 (1)

or contributed to death. Central venous catheters in the right atrium of this total artificial heart are contraindicated.

Nineteen of the 35 control patients (54 percent) and 17 of the 81 patients in the protocol group (21 percent) died before transplantation. Causes of death before transplantation among the controls were cardiac arrest (in seven), heart failure (in seven), multiorgan failure (in three), graft failure or acute rejection (in one), and pulmonary edema (in one). Causes of death before transplantation in the protocol group were multiorgan failure (in seven patients), procedural or technical complications (in four), bleeding (in two), sepsis (in two), congestive heart failure (in one), and pulmonary edema (in one). After transplantation and before discharge in the control group, in which 16 patients remained at the time of transplantation, there were 2 deaths (1 due to acute rejection and 1 due to multiorgan failure). During the same interval in the protocol group, in which 64 patients remained at the time of transplantation, there were 6 deaths (3 due to graft failure, 1 due to sepsis, 1 due to procedural or technical complications, and 1 due to multiorgan failure).

DISCUSSION

Implantation of the total artificial heart improved outcomes in dying patients by providing immediate hemodynamic restoration and clinical stabilization, leading to end-organ recovery and thus eventually allowing cardiac transplantation. Among the patients who received the device on a per-protocol basis, the rate of survival to transplantation was 79 percent. Previous studies of approved devices[5-9] have reported rates of survival to transplantation of 51 to 71 percent with left ventricular assist devices and 58 to 61 percent with biventricular assist devices.

The overall survival rate was 70 percent one year after transplantation. The one- and five-year survival rates among transplant recipients were 86 percent and 64 percent, similar to those reported by UNOS.[2] All end points with respect to survival and treatment success significantly favored the pa-

tients who received an implant as compared with the controls.

Since 1982, there have been over 430 implantations involving this type of device worldwide.[10] Previous studies of the CardioWest device[14-16] have summarized results for 219 patients, of whom 70 percent to 93 percent survived from implantation to cardiac transplantation; 93 percent to 100 percent of those patients survived from transplantation to hospital discharge. A retrospective comparison of the device and two of the currently approved devices in very sick patients with heart failure documented an advantage for the total artificial heart.[17]

Among the patients in this study who received a total artificial heart according to protocol, the cardiac index rose to and remained at 3 liters per minute per square meter or higher, systolic arterial pressure rose above 120 mm Hg, central venous pressure fell to less than 14 mm Hg, and organ-perfusion pressure rose to 68 mm Hg. As a consequence of hemodynamic restoration, serum creatinine, blood urea nitrogen, bilirubin, liver enzymes, and other laboratory values returned to normal within three weeks. Seventy-five percent of these patients were out of bed within one week.

Adverse events were broadly defined and thus frequently reported. However, the outcomes for most patients were good and were similar to those found with left ventricular and biventricular assist devices. There were no deaths from neurologic causes. During the implantation period, 12 percent of the patients had strokes; six of the strokes had no residual effect 48 hours after onset. Reported rates of stroke in patients with ventricular assist devices have varied: 0 to 12 percent for the HeartMate device,[5,8,9] 20 to 58 percent for the Novacor device,[7-9] and 24 percent for the Thoratec device.[8]

In this study, bleeding caused death in 2 patients and necessitated repeated surgery in 21, for a combined frequency of 28 percent. Published studies[5-9] have documented rates of similarly defined end points (death or repeated surgery) of 35 to 48 percent (for the HeartMate left ventricular assist device), 22 to 40 percent (for the Novacor device), and 23 to 33 percent (for the Thoratec biventricular assist device). Among the patients in the protocol group in this study, infection caused one death and contributed to seven others, but most infections neither delayed transplantation (84 percent, no delay) nor had a major clinical effect (81 percent, no clinical effect). Device malfunction, causing a perforated diaphragm, resulted in one death and (in a single patient) five episodes of a reduced cardiac index. Fitting complications, despite well-defined guidelines for fitting the device,[10] contributed to two deaths. In three cases, the tricuspid valve of the device became obstructed by the central venous catheter, causing death in two of the cases and contributing to death in the third and thereby underscoring the contraindication to right atrial catheters in these patients. As expected in this group of very sick patients, most of the deaths before transplantation in the control group were due to end-stage heart disease, whereas most deaths in the protocol group were related to multiorgan failure, technical problems, sepsis, or bleeding during the first four weeks after implantation.

In conclusion, implantation of the CardioWest Total Artificial Heart was a successful bridge to cardiac transplantation in many patients with heart failure in whom inotropic therapy had failed and who were not candidates for the use of a left ventricular assist device. Implantation of the total artificial heart helped to restore hemodynamic function, promoted end-organ recovery and mobility, and was associated with a post-transplantation survival rate very similar to national survival rates five years after transplantation. For patients with biventricular cardiac failure whose condition had continued to deteriorate despite maximal inotropic support, the device helped to prevent death and afforded clinical stabilization. Its safety and efficacy have been documented. With this device, a considerable number of potential cardiac-transplant recipients who have no other suitable options may successfully await cardiac transplantation.

Supported from 1991 to 2001 by CardioWest Technologies and thereafter by SynCardia Systems with respect to the costs of data collection.

Dr. Copeland reports owning equity in SynCardia Systems, the manufacturer of the CardioWest Total Artificial Heart. Mr. Smith and Dr. Slepian report owning equity in SynCardia Systems and being paid for part-time employment by the company.

APPENDIX

The CardioWest Total Artificial Heart Investigators and their institutions are as follows: J.G. Copeland and F.A. Arabia (University Medical Center, Tucson, Ariz.), B. Foy (Loyola Medical Center, Chicago), J. Long and D. Doty (LDS Hospital, Salt Lake City), A. Tector (St. Luke's Medical Center, Milwaukee), and R. Kormos (University of Pittsburgh Medical Center, Pittsburgh).

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