Chapter 141

CRITICAL CARE OF THE LIVER TRANSPLANT PATIENT

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Intensive care of the liver transplant patient often begins even before an organ donor is found. Bleeding from esophageal varices, encephalopathy, intractable ascites, and coagulopathy may require intensive care support and urgent transplantation.

For most patients undergoing liver transplantation, the first phase of intensive care takes place in the operating room where the anesthesia team bears most of the responsibility for maintaining cardiodynamic stability, replacement of blood products, and correction of coagulation disturbances during the long, difficult surgical procedure (1,2).

THE OPERATIVE PROCEDURE

Liver transplantation takes from 6 to 24 hours to perform (average 8 to 10 hours), with blood replacement averaging 8 to 12 units (range, 2 to more than 200 units). The difficulty of the surgery and the blood product requirement are dependent upon the original disease process, a history of previous surgery, and how well the donor organ functions. Diseases such as chronic active hepatitis or Laennec's cirrhosis typically increase the difficulty of surgery because of the small shrunken liver with thickened, often highly vascularized ligamentous attachments and portal hypertension with extensive collaterals in the abdominal wall, omentum, hepatic hilum, and pericaval retroperitoneal tissues.

Previous surgery results in highly vascularized adhesions. Small children and infants who have had multiple operations in the hepatic hilum for biliary atresia are often the most difficult transplant patients because of these dense, highly vascularized adhesions.

The quality of early graft function is an important factor in the amount of blood loss. If early function is poor, a protracted coagulopathy may occur that will extend the time required to achieve surgical hemostasis. Usually the donor liver will begin making noticeable quantities of bile within an hour of revascularization. Failure of the liver to make bile is an ominous sign. The thromboelastogram has proved to be a valuable tool in the operating room for the assessment of the state of coagulation, and helps to monitor the need for clotting factors and fibrinolysis treatment.

The routine use of the heparin-free venous bypass during the anhepatic phase of the operation has made it much easier to maintain hemodynamic stability during the operation, and has also resulted in less blood loss (3,4). Decompression of the portal vein prevents massive splanchnic venous congestion with oozing from thin-walled, high-pressure collateral venous channels. Decompression of the infrahepatic vena cava prevents renal venous hypertension, and prevents sequestration of blood volume, potassium, and lactic acid in the peripheral venous circulation.

The use of the venous bypass is limited to patients weighing over 20 kg. Access is difficult in small children and infants, and flow rates are low, raising the risk of intravascular thrombosis. Fortunately, there is usually sufficient collateral circulation in these small patients for them to tolerate crossclamping of the vena cava and portal vein without need for bypass.

All patients are kept on a warming blanket during surgery; blood products and intravenous and irrigation fluids are warmed before administration. Nevertheless, there is significant loss of body heat during the long hours of surgery, and all patients are hypothermic as they arrive in ICU after surgery. Special attention to body temperature is required, especially for pediatric recipients. Since the head accounts for a large percentage of the body surface area in children, simple cellophane wrapping of the head will help prevent heat loss.

ROUTINE POSTOPERATIVE CARE

Once the patient has arrived in the ICU, strict attention is paid to fluid status, electrolyte balance, coagulation, liver and kidney function, and cardiopulmonary performance. Peripheral arterial, pulmonary artery wedge, and central venous pressures, arterial blood gases, cardiac rhythm and output, urine volume, and surgical drains are all monitored closely.

CBC, prothrombin time, partial thromboplastin time, platelets, sodium, potassium, chloride, and bicarbonate are monitored frequently. BUN, creatinine, calcium, phosphorus, bilirubin (total and direct), SGOT, SGPT, alkaline phosphatase, gamma GTP, amylase, and albumin are measured at least daily. In children, low serum calcium and magnesium are frequently seen, and must be promptly treated to prevent severe coagulation and CNS complications.

A nasogastric tube is kept to low continuous suction and irrigated hourly with saline. Antacid (Mylanta, 30 ml) is administered via the nasogastric tube every 4 hours. The patient is turned every 2 hours and postural drainage and clapping is done every 4 hours.

Antibiotics with a spectrum appropriate for biliary tract pathogens (*Klebsiella*, *E. coli*, and *Enterococcus*) are administered preoperatively and continued for 5 days after surgery. Ampicillin and cefotaxime, each given as one gram every 6 hours, has been our traditional regimen.

Immunosuppression is begun perioperatively. The first dose of cyclosporine is given orally, 17.5 mg/kg, just prior to surgery. Patients receive 1 gram of intravenous methylprednisolone at the time the graft is first revascularized. Postoperatively, cyclosporine is given as 2 mg/kg intravenously every 8 hours until the patient resumes oral intake. At this time oral cyclosporine, 17.5 mg/kg, is given in a divided dose every 12 hours and the intravenous therapy is reduced to twice a day. Blood trough levels of cyclosporine are monitored daily and the dosages adjusted accordingly to maintain therapeutic levels and minimize toxicity. Prednisone is administered starting at 200 mg on the first day in four divided doses, and is tapered by 40 mg/day until a maintenance dose of 20 mg/day is reached. In children weighing less than 30 kg, the dose of steroid is begun as 100 mg/day in four divided doses, and is tapered by 20 mg/day until a maintenance dose of 10 to 20 mg/day is reached.

Patients with poor renal function after surgery may be unable to tolerate conventional doses of cyclosporine. For these patients, the dose is reduced or cyclosporine may be temporarily withheld and treatment with another

agent substituted. Antilymphocyte antibody preparations, especially OKT, monoclonal antibody (Ortho Pharmaceuticals, Raritan, NJ), have been most frequently used for this situation as well as for the treatment of steroid-resistant rejection (5,6).

Oral and vaginal candidiasis are frequent problems in immunosuppressed patients. Mycostatin oral suspension is given four times a day, and for female patients, mycostatin vaginal suppositories are also given three times a day.

Fluid management in the early postoperative period is particularly important. Most patients arrive in the ICU with a much expanded extracellular fluid volume. Dextrose, 5% in 1/2 normal saline, is infused intravenously at 125 ml per hour. Excessive use of crystalloid can easily result in pulmonary edema. Plasma protein fraction or fresh frozen plasma is used to provide oncotic pressure and support volume. The central venous pressure is maintained at about 10 cm H_2O, and the urine output is maintained at 0.5 ml/kg·h. Hypovolemia must be avoided, as the combination of hypovolemia and cyclosporine may result in acute renal tubular necrosis.

Fluid replacement must be appropriately adjusted in children. A formula based on weight is followed in which 100 ml/kg for the first 10 kg, 50 ml/kg for the second 10 kg, and 20 ml/kg for weight in excess of 20 kg is given per day.

Aggressive correction of abnormal clotting parameters can be harmful and may precipitate hepatic artery thrombosis (7). We do not attempt to correct the prothrombin time unless it is greater than 25 seconds or there is significant clinical evidence of ongoing blood loss. The platelet count is frequently low after surgery; again, we do not treat unless the count is below 50,000 mm^3 or bleeding is a significant problem. Dextran 40, given at 20 ml/h for the first 100 hours after surgery, may be helpful in preventing hepatic arterial thrombosis.

Narcotics and sleep medications are generally avoided, as these medications depend upon hepatic metabolism. In children, small doses of morphine sulfate may be given frequently.

Most patients can be extubated within 36 hours of operation. An aggressive pulmonary regimen is maintained with frequent suctioning, turning, cupping, postural drainage, incentive spirometry, and early mobilization. Atelectasis is treated promptly with recruitment and, if needed, bronchoscopy.

If there are no special problems or complications, the patient is usually ready for transfer to the regular surgical floor on the second or third postoperative day.

COMPLICATIONS AFTER LIVER TRANSPLANTATION

Pulmonary Complications

The most common problems in the early postoperative period are respiratory, especially atelectasis and pleural effusion. Atelectasis may easily progress to lobar collapse, and even limited atelectasis can easily lead to pneumonia in the immunosuppressed patient and must be treated aggressively. A decision for early reintubation must be based not only on the patient's general overall status but also on the function of the newly transplanted liver. Frequent nasotracheal suctioning can result in serious bleeding.

Another very common problem is that of pleural effusions, particularly on the right side. When the suprahepatic cava is clamped, of necessity a portion of the right hemidiaphragm is usually included in the clamp, and this promotes the development of a right-sided pleural effusion. Less often, a right phrenic palsy may also result from crush injury to the nerve. A small pleural effusion will often resolve after several days of effective diuresis. If they are large, however, these effusions should be drained to prevent pneumonia in the underlying compressed lung. Great care must be taken in the placement of a chest tube, especially if the patient's coagulation profile is abnormal. These patients often have enlarged intercostal collateral vessels that can result in catastrophic bleeding if injured. A small, pigtail catheter, which is placed using guidewire technique, is a safe, effective way to obtain drainage.

A curious pulmonary complication that occasionally occurs is severe metabolic alkalosis with compensatory respiratory acidosis. This is usually seen in cases of primary graft failure. If the patient is awake and making urine, the liver will usually recover.

Primary Graft Failure

Urgent retransplantation of the liver is required if the graft fails to function. Primary graft failure presents with a variety of problems. In its mildest form it presents with decreased quality and quantity of bile, decreased urine output with increasing serum creatinine, increased arterial pH and PCO_2, and elevated hepatic transaminases. The patient nevertheless shows minimal ill effects and improves as the liver recovers. In severe cases, the patient remains comatose, anuric, and alkalotic. Prothrombin times are markedly prolonged and serum transaminases in the 5,000 to 10,000 IU range may be seen. The ammonia level is markedly increased, and pH and HCO_3 levels are in the 7.60 and 35 to 45 mEq/L range, respectively. Infusion of 0.2 N HCl is required to maintain acceptable blood pH. Acetazolamide cannot be used because of poor renal function, and dialysis may be required. Hypertension must be prevented since these patients are at high risk for intracerebral hemorrhage. The blood glucose, which may be high initially, falls to dangerous levels, requiring infusion of hypertonic glucose. Prompt retransplantation, crossing ABO blood groups if necessary, is the only way to save these patients (8).

Severe, Early Rejection

Hyperacute, antibody-mediated rejection of the liver, if it occurs at all, is a rare event, but accelerated cell-mediated rejection does occur and can be severe enough to require early retransplantation (9). It presents 48 to 72 hours after transplantation, and is characterized by an increase in prothrombin time, bilirubin, and liver enzymes. A cholangiogram and ultrasound are obtained to rule out biliary tract complications or vascular accidents. It may be difficult to differentiate ischemic injury from early rejection without a liver biopsy; however, the prolonged prothrombin time and thrombocytopenia may make biopsy hazardous.

More commonly, acute cellular rejection presents 10 to 14 days after transplantation with elevated bilirubin, with or without elevated transaminases. A needle biopsy is almost always possible and confirms the diagnosis. The first treatment of acute rejection is high-dose steroids, but if there is not a prompt response, OKT3, a murine antihuman T-cell monoclonal antibody, is our treatment of choice and will reverse rejection in 70% to 80% of the cases (5,6).

Graft-Versus-Host Disease

If transplantation of the liver is done across ABO blood groups, the transplanted liver may produce antibodies to recipient ABO antigens. This may cause a mild, short-lived graft-versus-host reaction manifested by hemolytic anemia with or without thrombocytopenia and/or leucopenia (8,9). Transfusion support may be required for a limited period. Splenectomy was required in one case in our experience for refractory thrombocytopenia.

Hepatic Artery Thrombosis

Arterial thrombosis complicates approximately 7% of the liver transplants and is most common in children, especially infants (10) (Marsh et al., unpublished observations). Unexplained fever and sepsis with or without an increase in hepatic transaminases is the hallmark, and a Doppler ultrasound is almost always diagnostic (11). If hepatic artery pulsations cannot be clearly identified, an arteriogram is indicated. Bile leak, bile peritonitis, or intrahepatic bile abscess may result from the ischemic injury to the bile duct system. Blood and bile (if a T tube is present) are cultured, and broad-spectrum antibiotics are begun. Liver abscesses can often be drained percutaneously. Many patients, especially children, can be maintained on conservative therapy for many months, but virtually all will eventually require retransplantation because of irreversible ischemic injury to the biliary tract. Some patients will present with frank hepatic gangrene and require urgent retransplantation.

Portal vein thrombosis is rare. Patients at highest risk include very small children (weight less than 10 kg) with hypoplastic portal veins, and adults with low flow through the portal vein secondary to previous thrombosis, phlebitis, or portosystemic shunts. Acute portal vein thrombosis is usually a catastrophic event, with bacterial and fungal sepsis and severe liver failure.

Primary Biliary Complications

Biliary leaks or strictures are the most common biliary complications (12). Bile leaks at the anastomosis or from a T-tube insertion site typically present with fever, chills, right upper quadrant pain, sepsis, increased serum bilirubin, bilious drainage, or *Candida* cultured from the abdominal drains. In the absence of systemic candidiasis, a positive *Candida* culture from an abdominal drain invariably means a bile or bowel leak. CT scans have been unreliable in making this diagnosis, and the absence of enteric pathogens in cultures can also be misleading. Surgical correction of the leak is required. A leak from a T-tube insertion site can often be fixed by simple suture reinforcement, but a leak from a duct-to-duct reconstruction requires conversion to a Roux-en-Y choledochojejunostomy.

Bile duct strictures are usually late complications from ischemic injury to the biliary tree, premature removal of the T-tube or biliary stent, or the normal cicatricial healing process. Percutaneous dilation may relieve the stricture, but usually definitive surgical revision is ultimately required (12).

Again, it is emphasized that biliary tract complications are often secondary to hepatic arterial thrombosis, and this diagnosis must always be suspected and ruled out.

Renal Failure

Acute renal failure after liver transplantation is much less common since the routine use of the venous bypass was instituted. However, acute renal failure still complicates cases with severe pre-existing renal disease, hepatorenal syndrome, cyclosporine toxicity, drug reaction, or, most commonly, acute tubular necrosis.

Pre-existing hepatorenal syndrome is common and usually resolves rather quickly in the presence of good graft function. Patients whose grafts fail to function well are usually oliguric or anuric until the graft recovers function or until the patient is successfully retransplanted. Simultaneous liver-kidney transplantation has been performed in ten of our cases for patients on dialysis with chronic renal failure from liver disease or from intrinsic renal disease.

Cyclosporine toxicity is difficult to distinguish clinically from acute tubular necrosis. It commonly presents in the early postoperative period while patients are on intravenous cyclosporine but certainly can occur in patients taking only oral cyclosporine. Acute tubular necrosis usually occurs in the intraoperative setting of hypotension and massive transfusions. It is exacerbated by cyclosporine (and other nephrotoxic drugs) and is likely to resolve more quickly if cyclosporine dosage is reduced (13). Early dialysis is instituted if needed.

Nervous System Complications

Problems of the nervous system are often perplexing and difficult to deal with. These include seizures, strokes, "dulled mentation," peripheral neuropathy, and brachial plexus injuries.

Seizures are the most common neurological complication, are more common in children than in adults, and are usually grand mal in type. CT scan and lumbar puncture are usually negative and the need for further treatment is unusual. Occasionally, patients will have seizures due to an intracranial bleed, hyponatremia, or cyclosporine combined with hypervolemia. If cyclosporine toxicity is suspected, it is not necessary to discontinue the drug, but reduction in dosage is prudent. If there is no metabolic or anatomical abnormality, the seizures usually do not recur.

Intracranial bleeding is a rare but devastating event. It usually happens early in the postoperative period while the patient is hypertensive and still has a relative coagulopathy. Strict attention must be given to postoperative hypertension, avoiding mean arterial pressures above 100 mm Hg in adults and 90 mm Hg in children.

"Dulled mentation" is mentioned for lack of a better term. Some patients, especially those with Laennec's cirrhosis, are often very slow to return to their preoperative mental status baseline. Fortunately, eventual complete return is usually achieved. Confusion, disorientation, and delirium result from cyclosporine toxicity, especially in older patients.

Peripheral neuropathy may result from toxic doses of cyclosporine. It is usually limited to the lower extremities and can range from mild tingling to severe sensory and motor dysfunction. A reduction in cyclosporine dosage is all that is required, but other causes such as the Guillain-Barré syndrome should be ruled out.

Brachial plexus injuries are rare and can result from stretch or direct injury during dissection of the axillary vein. Simple stretch injuries from prolonged hyperextension of the arm are almost always partial, and full recovery can be expected with time. Nerve conduction studies are helpful in reassuring the patient that the nerves are intact and that function will return.

Surgical injury to the brachial plexus can be stretch,

thermal, or crush injury, or a complete or partial transection. Recovery depends upon the nature of the injury.

Postoperative Infection

Infection is the most common postoperative cause of death after liver transplantation (14). Infections early in the postoperative period are rare and limited mostly to wound infections, especially in children with a previous enterostomy from a Kasai procedure. It is in this same group of children that the dreaded late complication of infected and ruptured vascular grafts occurs. It is therefore preferable that enterostomies be closed prior to transplantation. In adults, wound infections are quite rare and usually occur subsequent to intra-abdominal infections such as from bowel or bile leaks. As previously mentioned, CT scans have not been reliable in detecting either of these complications. Prompt reoperation is indicated if either is suspected. Positive cultures for *Candida* in closed abdominal drains are a strong indication for abdominal exploration.

Bacterial pneumonia is fairly uncommon but there is a predisposition to it in adults with pre-existing lung disease (chronic bronchitis, emphysema, cystic fibrosis, and alpha-1-antitrypsin deficiency). Antibiotic treatment is based on the results of specific cultures.

Occasionally, it is learned that the donor had a positive blood culture. In these cases, especially for Gram-negative infections, the recipient is treated as though he or she, too, were positive for this organism.

Viral screening is routinely performed, but it is rare to find evidence of viral infection early after surgery. Positive titers for cytomegalovirus (CMV) are common after the first month and can result from new infection or reactivation. CMV-positive donors, whenever possible, are used only for CMV-positive recipients.

Of the three most common viral infections, CMV, herpes simplex virus (HSV), and Epstein-Barr virus (EBV), CMV is the most prevalent (Breinig et al., Ho et al., and Makowku et al., unpublished observations). CMV infection is characterized by fever, malaise, anorexia, abnormal liver function tests (bilirubin, transaminases), and leucopenia. Steroids are reduced to a minimal dose (5 to 10 mg/day), and cyclosporine is reduced modestly. Severe cases of fulminant viral hepatitis, with or without pneumonitis, duodenitis, gastritis, and colitis, usually require withdrawal of all immunosuppression. The virus itself has an immunosuppressive effect and fulminant rejection is rare. Failure to promptly withdraw immunosuppression in the face of severe, systemic viral infection is fatal. The severe leucopenia that is often seen with viral infections can lead to secondary bacterial infection. If immunosuppression is withdrawn early enough, complete recovery is often possible. In some cases, overwhelming hepatitis has been successfully managed by retransplantation.

Occasionally, in patients without any clinical symptoms of viral infection, evidence of virus is found on liver biopsy, usually in conjunction with rejection. In this setting, the virus is usually ignored and the patient is treated for rejection.

We have had little experience with DHPG for the treatment of CMV infection. It seems useful for the treatment of CMV retinitis and GI infections, but results for hepatitis, encephalitis, and pneumonitis have been disappointing (15).

Herpetic infections range from rises in titers alone to skin lesions, hepatitis, or encephalitis. Any sign of HSV infection should be treated with acyclovir. Limited, accessible cutaneous lesions can be treated with topical cream but other lesions require systemic therapy. Withdrawal of immunosuppression is based on the clinical severity of the disease. Herpes encephalitis has been uniformly fatal, even with acyclovir and the withdrawal of immunosuppression.

EBV infections are the least often appreciated and range from asymptomatic rises in titers, to a mononucleosis-like picture, to true lymphoma (16). All EBV infections are treated with acyclovir. Patients presenting with lymphadenopathy or masses suspicious of a pseudo or true lymphoma should be biopsied to determine the clonality of the tumor. Acyclovir, surgical resection, and withdrawal of immunosuppression are the treatment options, depending upon the stage of the disease (17). Since we believe that these lesions are an iatrogenic complication of immunosuppression, the withdrawal of immunosuppression rather than chemotherapy is the proper approach to management.

Fungemia, particularly with *Candida albicans*, is an all too frequent manifestation of an overcompromised host. We recommend that patients who have had long operations with large amounts of blood replacement or significant violations of the GI tract also be considered for 6 weeks of maintenance therapy with amphotericin (10 to 15 mg per day). Patients with established systemic *Candida* infections may require higher dose therapy (25 to 30 mg/day). Positive blood cultures should not be dismissed as "line sepsis." The dose of amphotericin is adjusted to accommodate the level of renal function.

Pneumocystis pneumonia is the most common life-threatening, opportunistic, nonviral infection. Treatment with trimethoprim/sulfamethoxazole (TMP/SMX) should be begun on suspicion. Bronchoalveolar lavage is helpful in establishing the diagnosis (18,19). Open-lung biopsy is reserved only for cases in which the diagnosis is unclear and it is dangerous in patients requiring high levels of positive end-expiratory pressure (PEEP) to maintain oxygenation. Immunosuppression should be severely reduced or withdrawn until significant clinical improvement occurs. Pentamidine can be used instead of TMP/SMX in patients with resistant infections or allergy to sulfa drugs. Prophylaxis with TMP/SMX is effective in reducing the incidence of *Pneumocystis* infection in the immunosuppressed patient.

CONCLUSION

The care of the liver transplant patient is formidable but highly rewarding. With proper care, the typical patient will recover rapidly and intensive care is required only for the first few days after surgery. However, when problems do occur, care of these patients requires the highest level of skill and dedication.

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Chapter 142

HEART TRANSPLANTATION

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INTRODUCTION

In June 1986, the United States Congress authorized Medicare to provide financial coverage for patients in need of cardiac transplantation who were covered by this agency. In this way, cardiac transplantation was given the same official recognition, as a therapeutic modality, that was given to renal transplantation for the treatment of end-stage renal failure in 1971. This Federal intervention came when there had already been an incredible proliferation of heart transplant centers in the United States. In 1980, there were six medical centers in which this procedure was performed. By June 1986, this number had increased to about 90. If it is exciting to see an increasing enthusiasm for heart transplantation, and if we do agree that this procedure should be performed in many medical centers in order to make it available for a larger number of patients, we also believe that a few centers in the United States should continue to display a particular commitment to the experimental and clinical research in heart transplantation in order to improve the knowledge in this field of transplantation which, in many aspects, has not been explored.

In this chapter we will present the historic background, experimental and clinical, and the present state of the art of cardiac transplantation. The present indications, the surgical technique, the postoperative management, and the results will be presented, referring in particular to the Pittsburgh experience.

HISTORICAL BACKGROUND

Clinical cardiac transplantation flourished from the experimental work of Lower and Shumway (1). More than 20 years ago, they developed in a dog model a surgical technique for orthotopic cardiac transplantation that, with only slight modification, is still used. Christian Barnard in December 1967 performed the first human heart transplant in Capetown (2). This event was followed in the United States by a period of great enthusiasm during which the procedure was attempted in several centers. In January 1968, Shumway et al. (3) performed the first cardiac transplant in the United States and were followed by Cooley et al. (4), who performed their first successful transplant in May 1968. This enthusiasm was of short duration because the results were drastically hampered by an excessive short-term mortality related to an uncontrollable rate of infections or rejection. As a consequence of these poor results, clinical experimentation was continued during the 1970s in only a few centers and, in particular, at Stanford University. In the late 1970s at Stanford, with the introduction of cyclosporine as a new immunosuppressive agent, improvement in the 1- and 5-year survival rates to 65% and 40%, respectively, resulted in the consideration that transplantation was no longer experimental, but therapeutic.

As a consequence of these improved results, a renewed interest in the procedure came about; since 1980, the number of centers performing cardiac transplantations has been steadily increasing (Fig. 142–1). The number of potential candidates seems to increase as the indications for the procedure widen. It is estimated that, in the United States, 4000 patients per year could benefit from cardiac transplantation. If the proliferation of heart transplant centers should be welcomed as a way to make this procedure more easily available to a larger number of patients, the care of the heart transplant recipient requires such a multidisciplinary approach that the cost effectiveness of performing only a few procedures per year in any center must be considered, especially in a time when funds for medical care seem to be limited and waning. We will leave aside these medico-economic considerations and focus on the medical aspects of cardiac transplantation.

PATIENT SELECTION

The classic indications for cardiac transplantation have been end-stage ischemic or idiopathic cardiomyopathy, equivalent to Class IV categorization by the New York Heart Association. While early in our experience idiopathic cardiomyopathy was the prevalent indication, since 1984 older patients have been treated, and ischemic cardiomyopathy has been more common (Fig. 142–2). Most patients with ischemic cardiomyopathy have had one or two previous coronary artery bypasses. Of 204 patients who underwent cardiac transplantation between July 1982 and June 1986, 110 had ischemic cardiomyopathy and 74 had idiopathic cardiomyopathy (Table 142–1). We have included patients with end-stage valvular heart disease (n = 12), isolated amyloidosis (n = 1), and sarcoid-