Combined heart/liver transplantation

Bijan Eghtesad, M.D.

Hepatobiliary and Liver Transplantation Surgery

Dimensions in Cardiac Care  2014
Cleveland Clinic
Combined heart/liver transplantation

- Uncommonly performed and potentially life-saving
- Initial report *Lancet* 1984 (Starzl)
  - 6-year-old female with severe familial hypercholesterolemia
  - Heart failure due to coronary artery disease

- Indications:
  - End-stage cardiac and liver disease because of related causes
  - End-stage cardiac and liver disease because of unrelated causes
  - End-stage heart disease with liver transplantation performed to correct an underlying disorder*
Combined heart/liver transplantation

• OPTN National Data Transplantation Report:
  – 163 combined heart and liver transplant (CHLT)
    • 141 combined heart and liver
    • 13 combined heart, liver, and kidney
    • 12 combined heart, liver, and lung
  – Graft survival after CHLT is similar to isolated liver or heart transplantation
    • 80% at one year and 70% at 10 years

• Perioperative management and operative techniques have been reported from different centers
Patient evaluation in liver transplantation
The evaluation of patients for liver transplantation represents team efforts including hepatologists, transplantation surgeons, social workers, and consultants.
# Child-Turcotte-Pugh Score

<table>
<thead>
<tr>
<th></th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Encephalopathy: None</td>
<td>1, 2</td>
</tr>
<tr>
<td>Ascites: Absent</td>
<td></td>
</tr>
<tr>
<td>Bilirubin (mg/dl): 1-2</td>
<td></td>
</tr>
<tr>
<td>Albumin (g/dl): &gt;3.5</td>
<td>2.8-3.5</td>
</tr>
<tr>
<td>Prothrombin time (secs prolonged): 1-4</td>
<td>4-6</td>
</tr>
<tr>
<td>or (INR): &lt;1.7</td>
<td>1.8-2.3</td>
</tr>
<tr>
<td>Primary biliary cirrhosis/Primary sclerosing cholangitis: Bilirubin (mg/dl): 1-4</td>
<td>4-10</td>
</tr>
</tbody>
</table>
## Model for End-Stage Liver Disease (MELD)

- **MELD** - predict mortality while waiting for LTX
  - Based on three objective clinical lab values
  - \[ \text{MELD} = 3.8 \times \log_e(\text{bilirubin [mg/dl]}) + 11.2 \times \log_e(\text{INR}) + 9.6 \times \log_e(\text{creatinine [mg/dl]}) + 6.4 \]
  - Validated on UNOS datasets and Cervello cirrhotics

- **PELD** - adapted for pediatric patients based on other factors such as growth retardation
  - \[ \text{PELD} = 4.8 \times \log_e(\text{bilirubin [mg/dl]}) + 18.6 \times \log_e(\text{INR}) + 6.9 \times \log_e(\text{albumin [g/dl]}) + 4.4 (< 1 \text{ yr age}) + 6.7 (Z \text{ score <2 SD}) \]
Prediction of 90 Day Mortality and MELD/PELD
1963

First human liver transplant -
Dr. Thomas Starzl
(University of Colorado)
LIVER TRANSPLANTATION

FIRST PATIENT:

Three year old boy with biliary atresia;
he died on the table

Orthotopic homotransplantation of the human liver


1983

Liver transplantation is approved as a therapeutic modality by NIH Consensus Conference
Recipient Surgery
Incisions for liver transplantation
Veno-Venous Bypass

Inferior vena cava flow of up to 60% of cardiac output

Hepatic blood flow up to 2 liters per minute
“Standard” Cava

“Piggyback” Cava
Total adult liver transplants

SRTR 2013
Adult liver transplants

SRTR 2013
Deceased donor livers transplanted with another organ
Immunosuppression regimen at one year in adult liver transplant recipients, 2010
Immunosuppression use in adult liver transplant recipients
Organ Allocation
Combined heart/liver transplantation

- Allocation usually based on liver or heart and mainly local OPO
  - Organs recovered and packed separately
  - Absence of contraindication to the usage of organ
  - Usually not through expanded criteria donation
    - Immediate function of both organs
    - No stress on the heart after reperfusion of the liver
  - Heart implant first (reports on liver first in the presence of preformed antibodies)

- Implication for liver alone wait list mortality
  
  Swleowski et al. Transplantation 2014

  Allocating livers for CHLT bypasses liver candidates at the top of the wait list but is not associated with increased rates of wait list mortality or dropout
Combined heart/liver transplantation

• Do waitlisted patients require exception status?

• Schaffer et al. AJT 2014

• UNOS database (at one year)
  – Wait list mortality higher in CHLT than HRT 26% vs 12% (p=0.001)
  – Wait list mortality higher in CHLT than LT 26% vs 14% (p=0.005)
  – These differences persisted after stratifying by disease severity
  – Post Tx survival not different between CHLt and HRT or CHLT and LT
  – Multivariate model:
    • CHLT was associated with enhanced survival for CHLT candidates (HR 0.41; CI 0.21-0.79; p=0.008) but undergoing HRT alone was not
  – 90% of CHLT recipients were allocated an organ locally
    • 60% HRT candidates and 73% LT candidates (p<0.001)

• Current cardiac and liver allocation system may underestimate the risk of death for patients with concomitant end-stage heart and liver failure on the CHLT list
Combined heart/liver transplantation

INDICATIONS
### Combined Liver/Heart Transplantation

**Table 1.** Thirty-six patients, ordered by indication for OLT and age, who have undergone combined OHT-OLT in the United States, 1988–2006

<table>
<thead>
<tr>
<th>Age, sex</th>
<th>Indication for OLT</th>
<th>Pretransplant severity of illness</th>
<th>Pretransplant status</th>
</tr>
</thead>
<tbody>
<tr>
<td>36, M</td>
<td>Familial amyloidotic polyneuropathy</td>
<td>Old status 2</td>
<td>Alive 8 yr posttransplant</td>
</tr>
<tr>
<td>36, M</td>
<td>Familial amyloidotic polyneuropathy</td>
<td>MELD = 6</td>
<td>Alive 3 yr posttransplant</td>
</tr>
<tr>
<td>36, M</td>
<td>Familial amyloidotic polyneuropathy</td>
<td>UNOS status 3</td>
<td>Alive 3 yr posttransplant</td>
</tr>
<tr>
<td>37, M</td>
<td>Familial amyloidotic polyneuropathy</td>
<td>MELD = 24</td>
<td>Died 3.5 yr posttransplant</td>
</tr>
<tr>
<td>38, M</td>
<td>Familial amyloidotic polyneuropathy</td>
<td>UNOS Status 2b</td>
<td>Died 6 yr posttransplant</td>
</tr>
<tr>
<td>38, M</td>
<td>Familial amyloidotic polyneuropathy</td>
<td>MELD = 24</td>
<td>Died 3.5 yr posttransplant</td>
</tr>
<tr>
<td>40, P</td>
<td>Familial amyloidotic polyneuropathy</td>
<td>UNOS Status 2b</td>
<td>Alive 4 yr posttransplant</td>
</tr>
<tr>
<td>40, M</td>
<td>Familial amyloidotic polyneuropathy</td>
<td>UNOS status 3</td>
<td>Alive 7 yr posttransplant</td>
</tr>
<tr>
<td>41, M</td>
<td>Familial amyloidotic polyneuropathy</td>
<td>Old status 2</td>
<td>Died 6 yr posttransplant</td>
</tr>
<tr>
<td>43, M</td>
<td>Familial amyloidotic polyneuropathy</td>
<td>UNOS Status 2b</td>
<td>Alive 2 yr posttransplant</td>
</tr>
<tr>
<td>23, F</td>
<td>Cardiac cirrhosis</td>
<td>MELD = 11</td>
<td>Alive 6 mo posttransplant</td>
</tr>
<tr>
<td>26, M</td>
<td>Cardiac cirrhosis</td>
<td>UNOS status 1</td>
<td>Died 4 mo posttransplant</td>
</tr>
<tr>
<td>28, F</td>
<td>Cardiac cirrhosis</td>
<td>MELD = 26</td>
<td>Alive 3 mo posttransplant</td>
</tr>
<tr>
<td>35, M</td>
<td>Cardiac cirrhosis</td>
<td>UNOS Status 2b</td>
<td>Alive 3 yr posttransplant</td>
</tr>
<tr>
<td>45, F</td>
<td>Cardiac cirrhosis</td>
<td>MELD = 19</td>
<td>Re-O LT; alive 9 d posttransplant</td>
</tr>
<tr>
<td>37, M</td>
<td>Cardiac cirrhosis</td>
<td>MELD = 10</td>
<td>Alive 6 mo posttransplant</td>
</tr>
<tr>
<td>28, M</td>
<td>HCV-associated cirrhosis</td>
<td>UNOS Status 2b</td>
<td>Died 3 wk posttransplant</td>
</tr>
<tr>
<td>36, M</td>
<td>HCV-associated cirrhosis</td>
<td>MELD = 16</td>
<td>Alive 3 mo posttransplant</td>
</tr>
<tr>
<td>38, F</td>
<td>HCV-associated cirrhosis</td>
<td>MELD = 23</td>
<td>Alive 2 yr posttransplant</td>
</tr>
<tr>
<td>40, F</td>
<td>HCV-associated cirrhosis</td>
<td>MELD = 12</td>
<td>Alive 2 wk posttransplant</td>
</tr>
<tr>
<td>36, M</td>
<td>HCV-associated cirrhosis</td>
<td>MELD = 12</td>
<td>Alive 2 mo posttransplant</td>
</tr>
<tr>
<td>38, F</td>
<td>Alcoholic liver disease</td>
<td>UNOS status 1</td>
<td>Alive 8 yr posttransplant</td>
</tr>
<tr>
<td>43, M</td>
<td>Alcoholic liver disease</td>
<td>UNOS Status 2</td>
<td>Alive 4.5 yr posttransplant</td>
</tr>
<tr>
<td>47, M</td>
<td>Alcoholic liver disease</td>
<td>Old Status 2</td>
<td>Died 5 yr posttransplant</td>
</tr>
<tr>
<td>49, M</td>
<td>Alcoholic liver disease</td>
<td>MELD = 17</td>
<td>Alive 6 mo posttransplant</td>
</tr>
<tr>
<td>26, M</td>
<td>Iron storage disorder</td>
<td>UNOS Status 1</td>
<td>Alive 8 yr posttransplant</td>
</tr>
<tr>
<td>25, M</td>
<td>Iron storage disorder</td>
<td>Old Status 2</td>
<td>Alive 11 yr posttransplant</td>
</tr>
<tr>
<td>49, M</td>
<td>Iron storage disorder</td>
<td>UNOS status 3</td>
<td>Alive 8 yr posttransplant</td>
</tr>
<tr>
<td>47, M</td>
<td>Iron storage disorder</td>
<td>UNOS Status 1</td>
<td>Re-O LT; alive 7.5 yr posttransplant</td>
</tr>
<tr>
<td>49, M</td>
<td>Primary biliary cirrhosis</td>
<td>UNOS status 1</td>
<td>Re-O LT; alive 1 yr posttransplant</td>
</tr>
<tr>
<td>36, F</td>
<td>Primary biliary cirrhosis</td>
<td>UNOS Status 2b</td>
<td>Alive 5 yr posttransplant</td>
</tr>
<tr>
<td>36, F</td>
<td>Cryptogenic cirrhosis</td>
<td>Old Status 2</td>
<td>Died 5 yr posttransplant</td>
</tr>
<tr>
<td>38, M</td>
<td>Alpha-1 antitrypsin</td>
<td>UNOS Status 2a</td>
<td>Died 1 d posttransplant</td>
</tr>
<tr>
<td>31, M</td>
<td>Primary sclerosing cholangitis</td>
<td>MELD = 11</td>
<td>Died 2 yr posttransplant</td>
</tr>
</tbody>
</table>

MELD: Model for End-Stage Liver Disease score.
Combined heart/liver transplantation
Indications

• Familial amyloid polyneuropathy
• Hemochromatosis (iron storage disease)
• Familial hypercholesterolema
  – Homozygous
  – Heterozygous
• Ischemic heart disease and congenital heart disease with cardiac cirrhosis
• Alcoholic liver disease and heart failure
• Other causes of cirrhosis and heart failure
Amyloidosis

- Disorder of protein metabolism (autologus protein)
- Acquired or inherited

- Deposition of extracellular, insoluble fibrils in various organs “amyloid”

- Maybe focal, localized or systemic
  - Visceral involvement involving: kidneys, adrenals, thyroid, heart, eye, and intestine.

- Clinical manifestations, prognosis, and therapy vary greatly depending on the specific type of amyloid and structural and functional derangements in the affected organs
Amyloidosis

- Familial amyloidosis:
  - Precursor protein is a mutant form of transthyretin
  - Is transmitted as an autosomal dominant with high penetration (1% of cases of amyloidosis)
  - Presentation occurs from the 3rd decade on, and commonly after the age of 40
  - Deposits predominantly in the peripheral nerves
  - Polyneuropathy and dysautonomy
  - Cardiac amyloid is either absent or limited to the conduction system, most frequently manifesting as sinus node dysfunction
HEREDITARY SYSTEMIC AMYLOIDOSIS
FAMILIAL AMYLOID POLYNEUROPATHY

• Diagnosis
  – Biopsy of clinically affected tissue, e.g. >80% involvement of the rectum,
  – Characteristic congo red staining.
  – Immunohistochemical staining
  – Electron microscopy suggestive but not diagnostic
  – PCR for mutated gene.
HEREDITARY SYSTEMIC AMYLOIDOSIS
FAMILIAL AMYLOID POLYNEUROPATHY

- Evaluation
  - Cardiac function: echocardiography, Holter monitoring, right heart catheterization
  - Gastrointestinal motility
  - Nerve conduction and autonomic function
  - Renal function
Heart with amyloid infiltration

R H Falk  Circulation  2005; 112:2047-2060
Rationale for liver transplantation
- Eliminate site of abnormal protein synthesis
- Stabilize or reverse stigmata of amyloid infiltration
- Prevent accumulation of amyloid in other transplanted organs
Familial Hypercholesterolemia

• A genetic disorder due to mutation in the LDL receptor gene
• Cardiovascular disease is generally the revealing sign, especially in homozygous patients in whom symptoms appear in childhood
• Usually, patients die from severe heart disease before the age of 20
• Heterozygous occurs in 1 in 500 of population
  – Heart disease appears between the 4th and 5th decade with cholesterol levels lower than homozygous patients
Familial Hypercholesterolemia

• Treatment:
  – Low-fat diet
  – Cholesterol (statins, cholestyramine, nicotinic acid, ..)
  – Aggressive interventions such as LDL apheresis, ilial bypass, and liver transplantation
  – Cases with terminal chronic heart disease despite aggressive treatment may require heart transplant
  – Combined liver/heart in selective cases
Combined heart-liver transplantation for hemochromatosis

- Disorder of excess iron deposition in tissues
- May cause multiorgan dysfunction
- Hereditary or secondary according to the underlying etiology
  - Increased absorption of iron from gastrointestinal tract
- Hereditary: autosomal recessive genetic disorder
- Secondary: excessive oral intake or parenteral iron overload
- 1 in 200 population
- Male:Femal 8:1
- Men present earlier than women
- Cirrhosis, cardiomyopathy, diabetes, arthralgia, hypogonadism, skin hyperpigmentation,
- Chelating therapy
- Main cause of death: liver failure, liver cancer
- Liver transplantation is the primary treatment
- Liver-heart transplantation in patients with advanced cardiomyopathy
Combined heart/liver transplantation

- 26 combined transplant
  - Age 46 ± 13 years, 26% females
  - Chronic renal insufficiency 38%
  - Etiology of heart failure (inotrop3 38.4%)
    - Nonischemic 69.2%, Ischemic 7.7%, Congenital 23.1%
  - Etiology of liver failure (MELD score 16.8 ± 6.8)
    - Cardiac cirrhosis 88.5%, Hepatitis C 7.7%, A-1-A def. 3.8% (No amyloid!)
  - No primary graft dysfunction
  - Thirty day survival 96%
  - 1-, and 5-year survival 87% and 83%
  - 88.5% free of rejection
  - Hospital LOS 25 ± 11
Combined heart/liver transplantation

- *Barbara et al. Transplantation 2014*

- 27 patients (4 patients simultaneous kidney Tx)
  - Age 53.8 ± 9.7 (29-66)  16/27 Males
  - Etiology of heart failure (70% on inotrope)
    - Amyloidosis 21(78%), CHD 2(7%), restrictive cardiomyopathy 2 (7%),
  - Etiology of liver failure (MELD score 12 ± 4.7)
    - Amyloidosis 21 (78%), congestive hepatopathy 6(22%)
  - 30-day survival 96%
  - 12 livers from amyloid patients were used as domino transplant
  - Hospital LOS 24.6 ± 27.8  (8-134)
Combined heart/liver transplantation

*Nelson et al. Clinical Transplantation 2012*

- CHLT in 7 patients with familial amyloid cardiomyopathy
  - Leu 111 Met variant (Primarily cardiac amyloidosis)
  - 48.3 ± 4.2 years with mean follow up 55 months
  - No perioperative mortality
  - Two patients died in the first year (infection and MSOF)
  - 71% cumulative 4.5 year survival
  - No liver rejection One cardiac rejection
  - LV EF 61% for the survivors
  - No recurrent cardiac amyloid
Combined heart/liver transplantation


• Five patients received CHLT
  – 4 HCV and one Amyloid    Age $49 \pm 20$    MELD $17 \pm 5$
  – All nonischemic cardiomyopathy
  – 3/5 on inotrop    One on total artificial heart
  – No cardiac or liver graft dysfunction
  – 100% survival
Combined heart/liver transplantation

- Cannon et al. Transplant International 2012
- UNOS database CHLT compared to heart and liver transplant alone
  - 1987-2010
  - 97 reported cases of CHLT in US  68 males
    - Amyloid the most common indication
    - MELD 13.8 ± 5.4
    - Inotropes 24.7%
  - Liver graft survival , 1, 5, and 10 years: 83.4%, 72.8%, and 71% compared to liver alone  79.4%, 71%, 65.1%  p=0.894
  - Cardiac allograft 1, 5, and 10 years: 83.4%, 73.2%, 71% compared to heard alone: 82.6%, 71.9%, 65.1%  p=0.341
Combined heart/liver transplantation

Combined heart/liver transplants performed by year in the United States

Cannon et al. Transplant International 2012
Combined heart/liver transplantation

Liver graft survival of patients undergoing combined heart/liver transplantation versus isolated liver transplantation

Cannon et al. Transplant International 2012
Combined heart/liver transplantation

Heart graft survival of patients undergoing combined heart/liver transplantation versus isolated heart transplantation.

Cannon et al. Transplant International 2012
## Combined heart/liver transplantation

<table>
<thead>
<tr>
<th></th>
<th>Amyloid indication</th>
<th>Other indications</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Liver graft survival</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 year</td>
<td>92.2%</td>
<td>80.2%</td>
<td>0.585</td>
</tr>
<tr>
<td>3 years</td>
<td>86.4%</td>
<td>67.8%</td>
<td></td>
</tr>
<tr>
<td>5 years</td>
<td>79.7%</td>
<td>67.8%</td>
<td></td>
</tr>
<tr>
<td><strong>Heart graft survival</strong></td>
<td></td>
<td></td>
<td>0.328</td>
</tr>
<tr>
<td>1 year</td>
<td>92.3%</td>
<td>80.3%</td>
<td></td>
</tr>
<tr>
<td>3 years</td>
<td>86.5%</td>
<td>68.1%</td>
<td></td>
</tr>
<tr>
<td>5 years</td>
<td>79.9%</td>
<td>68.1%</td>
<td></td>
</tr>
<tr>
<td><strong>Patient survival</strong></td>
<td></td>
<td></td>
<td>0.375</td>
</tr>
<tr>
<td>1 year</td>
<td>92.3%</td>
<td>81.5%</td>
<td></td>
</tr>
<tr>
<td>3 years</td>
<td>86.5%</td>
<td>69.1%</td>
<td></td>
</tr>
<tr>
<td>5 years</td>
<td>79.9%</td>
<td>69.1%</td>
<td></td>
</tr>
</tbody>
</table>

Patient and graft survival for patients undergoing simultaneous cardiac-liver transplantation for amyloidosis versus other indications

Cannon et al. Transplant International 2012
Domino liver transplantation
Combined heart/liver transplantation

Conclusions

• No consensus statement on combined OHT-OLT exists
• Acceptable survival (like either of the organs alone)
  – 81% 1-year-survival
  – 72% 4-year-survival
• Indications are well known
• Early diagnosis of the problem and early liver transplantation (certain indications) could prevent further deterioration of other organs, e.g. *Heart* and decrease need for combined transplantation
## Table 2. Previously-published reports of combined transplantation of the heart and liver (n=34)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year of publication</th>
<th>Age, sex</th>
<th>Indication for OHT-OLT</th>
<th>OLT technique</th>
<th>Survival</th>
<th>Effect on primary disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suttorp (2)</td>
<td>1984</td>
<td>67, F</td>
<td>HIV, young familial hypercholesterolemia</td>
<td>CPB</td>
<td>Alive at 12+ months</td>
<td>Cholesterol improved</td>
</tr>
<tr>
<td>Shaw (3)</td>
<td>1985</td>
<td>2, M</td>
<td>Bilary hypoplasia and cardiac dysplasia</td>
<td>CPB</td>
<td>Died within days</td>
<td>(unknown)</td>
</tr>
<tr>
<td>Oubrier (4)</td>
<td>1994</td>
<td>26, M</td>
<td>Familial hypercholesterolemia</td>
<td>CPB</td>
<td>Died soon after</td>
<td>(unknown)</td>
</tr>
<tr>
<td>Rela (5)</td>
<td>1995</td>
<td>26, F</td>
<td>Familial hypercholesterolemia</td>
<td>CPB</td>
<td>Alive at 2 mo</td>
<td>Improved</td>
</tr>
<tr>
<td>Kela (6)</td>
<td>1995</td>
<td>61, F</td>
<td>Familial amyloidotic polyneuropathy</td>
<td>CPB</td>
<td>Alive at 4 mo</td>
<td>Improved</td>
</tr>
<tr>
<td>Zhao (7)</td>
<td>1996</td>
<td>19</td>
<td>Hyperproteinaemia and heart failure</td>
<td>Piggyback</td>
<td>Alive at 90 mo</td>
<td>Worsened</td>
</tr>
<tr>
<td>Detry (8)</td>
<td>1997</td>
<td>28, M</td>
<td>Familial hypercholesterolemia and heart failure</td>
<td>Piggyback</td>
<td>Alive at 6 mo</td>
<td>Improved</td>
</tr>
<tr>
<td>Surakakomol (9)</td>
<td>1997</td>
<td>47, M</td>
<td>Hemochromatosis and heart failure</td>
<td>VVBP</td>
<td>Alive at 48 mo</td>
<td>Improved</td>
</tr>
<tr>
<td>Belfer (9)</td>
<td>1999</td>
<td>47, M</td>
<td>Alcohol cirrhosis and heart failure</td>
<td>VVBP</td>
<td>Alive at 36 mo</td>
<td>Improved</td>
</tr>
<tr>
<td>Belfer (9)</td>
<td>1999</td>
<td>39, F</td>
<td>Cryptogenic cirrhosis and heart failure</td>
<td>VVBP</td>
<td>Alive at 36 mo</td>
<td>Improved</td>
</tr>
<tr>
<td>Belfer (9)</td>
<td>1999</td>
<td>45, M</td>
<td>Alcohol cirrhosis and heart failure</td>
<td>VVBP</td>
<td>Alive at 12 mo</td>
<td>Improved</td>
</tr>
<tr>
<td>Ruygrok (10)</td>
<td>2001</td>
<td>60, M</td>
<td>Familial amyloidotic polyneuropathy</td>
<td>Not reported</td>
<td>Alive at</td>
<td>Not reported</td>
</tr>
<tr>
<td>Hofstad (11)</td>
<td>2001</td>
<td>46, F</td>
<td>Familial hypercholesterolemia</td>
<td>CPB</td>
<td>Alive at 48 mo</td>
<td>Cholesterol normal, ed</td>
</tr>
<tr>
<td>Murali (12)</td>
<td>2001</td>
<td>—</td>
<td>Familial amyloidotic polyneuropathy</td>
<td>(unknown)</td>
<td>(unknown)</td>
<td>(unknown)</td>
</tr>
<tr>
<td>Murali (12)</td>
<td>2001</td>
<td>—</td>
<td>Familial amyloidotic polyneuropathy</td>
<td>(unknown)</td>
<td>(unknown)</td>
<td>(unknown)</td>
</tr>
<tr>
<td>Murali (12)</td>
<td>2001</td>
<td>—</td>
<td>Primary biliary cirrhosis with heart failure</td>
<td>(unknown)</td>
<td>(unknown)</td>
<td>(unknown)</td>
</tr>
<tr>
<td>Murali (12)</td>
<td>2001</td>
<td>—</td>
<td>Primary biliary cirrhosis with heart failure</td>
<td>(unknown)</td>
<td>(unknown)</td>
<td>(unknown)</td>
</tr>
<tr>
<td>Murali (12)</td>
<td>2001</td>
<td>—</td>
<td>Hemochromatosis</td>
<td>(unknown)</td>
<td>(unknown)</td>
<td>(unknown)</td>
</tr>
<tr>
<td>Nardo (12)</td>
<td>2004</td>
<td>60, M</td>
<td>Familial amyloidotic polyneuropathy</td>
<td>Piggyback w/VVBP</td>
<td>Alive at 42 mo</td>
<td>Improved</td>
</tr>
<tr>
<td>Nardo (12)</td>
<td>2004</td>
<td>53, M</td>
<td>Familial amyloidotic polyneuropathy</td>
<td>Piggyback</td>
<td>Died at 2 mo</td>
<td>(unknown)</td>
</tr>
<tr>
<td>Nardo (12)</td>
<td>2004</td>
<td>45, M</td>
<td>Familial amyloidotic polyneuropathy</td>
<td>Piggyback</td>
<td>Died at 20 mo</td>
<td>Worsened</td>
</tr>
<tr>
<td>Nardo (12)</td>
<td>2004</td>
<td>43, M</td>
<td>Familial amyloidotic polyneuropathy</td>
<td>VVBP</td>
<td>Alive at 1 mo</td>
<td>Improved</td>
</tr>
<tr>
<td>Haynes (14)</td>
<td>2004</td>
<td>40, M</td>
<td>Hemochromatosis and heart failure</td>
<td>VVBP</td>
<td>Alive at 6 wk</td>
<td>Improved</td>
</tr>
</tbody>
</table>

CPB, cardiopulmonary bypass; VVBP, veno-venous bypass.

Barshes et al. Transplantation 2007;83:95-98
Amyloidosis

- Familial amyloidosis
  - More than 70 mutations have been described
    - Thr-60-Ala: presents with a predominant cardiomyopathy
      - Heart failure
      - Conduction system disturbances
      - Minimal neuropathy
    - Val-122-Iso: mainly cardiac presentation
      - Approximately 4% of the AA population in the US is heterozygous for this mutation
      - Late-onset cardiomyopathy in either sex
      - Progressive congestive heart failure
      - Remarkably consistent features among patients
      - Infiltrative/restrictive cardiomyopathy with predominant signs of right heart failure with ascites and peripheral edema
<table>
<thead>
<tr>
<th>Type of Amyloidosis</th>
<th>Amyloid Protein Component</th>
<th>Current Therapy</th>
<th>Goal of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>AL or AH (primary)</td>
<td>Immunoglobulin light chain (AL) or (occasionally) heavy chain (AH)</td>
<td>Melphalan plus dexamethasone; alternative is autologous stem-cell transplantation in selected patients with limited organ involvement who are candidates for the procedure</td>
<td>Eradicate clonal plasma cells that are the source of immunoglobulin protein</td>
</tr>
<tr>
<td>AA (secondary to chronic inflammation or familial Mediterranean fever)</td>
<td>Serum amyloid A protein</td>
<td>Treatment of underlying infection or inflammation; colchicine for familial Mediterranean fever</td>
<td>Reduce level of serum amyloid A protein</td>
</tr>
<tr>
<td>Mutant ATTR (familial)</td>
<td>Mutant form of transthyretin</td>
<td>Liver transplantation</td>
<td>Eliminate source of mutant transthyretin</td>
</tr>
<tr>
<td>Senile systemic amyloidosis</td>
<td>Wild-type form of transthyretin</td>
<td>No therapy</td>
<td></td>
</tr>
<tr>
<td>Other forms of familial amyloidosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrinogen α-chain</td>
<td>Mutant form of fibrinogen α-chain</td>
<td>Hepatorenal transplantation</td>
<td>Eliminate source of fibrinogen α-chain (liver) and replace affected organ (kidney)</td>
</tr>
<tr>
<td>Lysozyme</td>
<td>Lysozyme</td>
<td>Undefined</td>
<td></td>
</tr>
<tr>
<td>Apolipoprotein</td>
<td>Apolipoproteins A-I and A-II</td>
<td>Renal transplantation</td>
<td>Replace affected organ</td>
</tr>
</tbody>
</table>