

Transplantation for TTR Amyloidosis 2013

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Rationale

- **Why liver transplant?**
 - **Removing source only known cure**
 - **Majority of circulating TTR made in liver**
 - **Not for asymptomatic gene carriers**
- **What about transplanting other organs?**

Liver Transplant

- **First liver transplant performed in Sweden 1990**
- **The FAP World Transplant Registry:**
 - **Updated 12/31/11**
 - **2008 liver transplants performed worldwide**
 - **120 transplants/year**
 - **Portugal, France and Sweden account for over two-thirds**

Outcomes

- **Low mortality rate (3%)**
- **Predictors of outcome:**
 - **mBMI**
 - **Disease duration (?)**
 - **Mutation (V30M vs non-V30M)**
 - **Autonomic neuropathy**

V30M Outcomes

- **Neuropathy stable or improved in up to 40%**
- **Nutrition improves in up to 80%**
- **Cardiac progresses in most**
- **Kidney involvement unaffected**
- **Eye deposits progress**

Non-V30M Outcomes

- **Small numbers make prediction difficult**
- **Neuropathy – autonomic most likely to improve, sensory variable**
- **GI improves in most**
- **Eye and brain can worsen due to local production of variant TTR**

Non-V30M Outcomes

- **Cardiac progresses in many**
- **Evidence that pace of deposition can increase after transplant**
- **Cardiac deposits develop in those with no heart involvement at dx.**
- **New deposits contain normal TTR made by transplanted liver**

Heart Transplant in ATTR

- **FAPWTR:**
 - **Liver + heart 37**
 - **Liver + previous heart 11**
 - **Liver + sequential heart 1**
 - **Liver + heart + kidney 3**

Heart Transplant in ATTR

- **Survival better than those that did not receive transplant, but slightly worse than average**
- **Some centers advocating combined heart/liver transplant in non-V30M**
- **Controversy over timing (combined vs. sequential)**
- **Bridging with LVAD available**

Kidney Transplant in ATTR

- **Kidney involvement in most at diagnosis**
- **Only symptomatic in ~10%**
- **FAPWTR: Liver + kidney 46**
- **Survival worse than liver alone, but related to low mBMI**

What Does It All Mean?

- **Known:**
 - **Survival improved with liver transplant in V30M**
 - **Most effective if early**
 - **Major benefit is nutrition**
 - **Combined liver + heart and liver + kidney feasible**

What Does It All Mean?

- **Unknown:**
 - **When is it futile?**
 - **Which mutations benefit?**
 - **If heart involved need combined heart + liver?**
 - **Is amyloid halted, slowed, reversed or accelerated?**

Implications

- **ATTR clear indication for liver transplant**
- **Early and accurate diagnosis critical**
- **Possibility of domino shortens wait time**
- **Need for multiple organs lengthens wait time**

Future Directions

- **Better follow-up needed to answer important questions (disease progression, etc.)**
- **Impact of new treatments (alternative to transplant vs. adjunct to transplant)**

Senile Systemic Amyloidosis (SSA)

- **Deposits formed by normal (wild-type) TTR**
- **Systemic deposits**
- **Affects predominantly heart in elderly males**

SSA

- Liver transplant not curative in SSA
- Heart transplant possible, but mean age at diagnosis of SSA around 70
- Potential benefit from novel therapies