Transplantation for TTR Amyloidosis 2013

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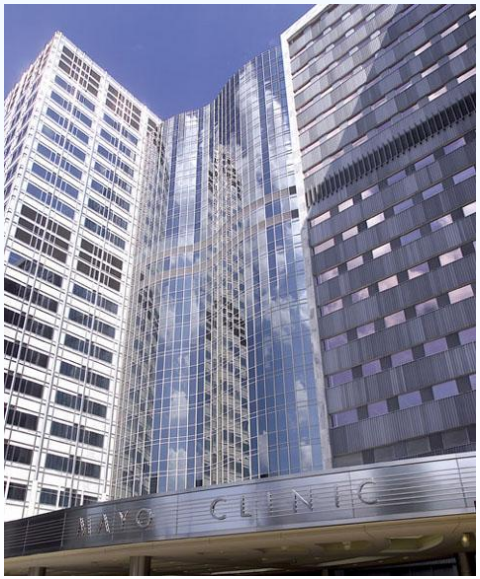

Rochester, Minnesota

Jacksonville, Florida

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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?**

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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

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Outcomes

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

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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

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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

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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

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Heart Transplant in ATTR

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

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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**

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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**

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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**

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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?**

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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**

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Future Directions

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

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Senile Systemic Amyloidosis (SSA)

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

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SSA

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