LIVER TRANSPLANT OVERVIEW

- General trends in liver transplantation
  - Living donor liver transplantation
  - MELD score and hyponatremia
  - Chronic HCV
  - HCC
  - NASH
- Chronic HCV and renal transplant
**LIVER TRANSPLANT**

**TRANSPLANTS PERFORMED**

- **Donor Type:** Deceased, Living

- **Living donor liver transplants:**
  - Started in children ~1990
  - Started in adults in ~2000
  - Accounts for ~2-5% of LT
  - 9 centers have performed over 90% of LDLT to date
  - Survival similar to DDLT
  - Bile duct complications more common
  - Risk of donor mortality

- UNOS.
  - [https://optn.transplant.hrsa.gov/data](https://optn.transplant.hrsa.gov/data)

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**LIVER TRANSPLANT WAITING LIST**

- **Mean waiting time by MELD at time of listing:**
  - <10: 1776 days
  - 11-18: 639 days
  - 19-24: 106 days
  - 25+: 20 days

- **% Transplanted by blood group:**
  - O = 55%
  - A = 57%
  - B = 63%
  - AB = 76%

- **MELD implemented**

- UNOS.
  - [https://optn.transplant.hrsa.gov/data](https://optn.transplant.hrsa.gov/data)
LIVER TRANSPLANT MELD SCORE

N=12,996
Risk of death from LT vs remaining on the LT waiting list

Establishes MELD of 15+ as minimal MELD for listing

HYPONATREMIA AND CIRRHOSES IMPACT ON SURVIVAL

LIVER TRANSPLANT
IMPACT OF HYPONATREMIA

- UNOS modified MELD to include NA in 1/2016
- Accounted for decline in survival with hyponatremia
- Especially with low MELD

AE Ruf, et al.

LIVER TRANSPLANT
DISEASE TRENDS

- NASH: Up 71% in 10 yrs
- AIH, PBC, PSC: Up 82% in 15 yrs
- HCC: Up 82% in 15 yrs
- ETOH
- HCV: Down 33% in 10 yrs

UNOS.
https://optn.transplant.hrsa.gov/data
LIVER TRANSPLANT
CHRONIC HCV

- 33% decline in patients listed for LT in past 10 years
- Potent oral therapy achieves high SVR rates in patients with cirrhosis before and after they decompensate
- By 2020 chronic HCV will be an uncommon indication for liver transplantation
- CAUTION
  - Treating HCV in patients with advanced cirrhosis
  - MELD purgatory

HCV WITH ADVANCED CIRRHOSIS
SIMEPREVIR-SOFOSBUVIR

120 patients with cirrhosis
Genotype 1A: 69%
Prior PEGINF/RBV+PI: 36%, 15%
Child class B, C: 21%, 12%
Platelet <70,000: 20%
Hemoglobin <10 gm: 10%
Variceal bleed: 15%
Ascites: 10%
Hepatic Encephalopathy: 22%
Prior HCC: 3%
Age >65 years: 20%
Serum creatinine >1.5 mg: 5%
PEGINF/RBV Intolerant: 15%

ML Shiffman et al
Am J Gastroenterol 2015;110:1179-1185
DECOMPENSATED CIRRHOSIS
IMPACT OF HCV TREATMENT

A B = 73%

SVR 78%

No SVR 22%


No Treatment: 4%
HCC: 5%
6-15 mos: 2.5%
LT: 12%
0-6 mos: 4%
Death: 3%
0-6 mos: 18%
Decomp: 16%
6-15 mos: 7%
No treatment: 28%

DECOMPENSATED CIRRHOSIS
IMPACT OF HCV TREATMENT

LDV/SOF
SVR= 86%

LDV/SOF
SVR= 87%

Mean change in
MELD = -1.2

Mean change in
MELD = -1.5

HCV WITH CIRRHOSIS
AVOIDING MELD PURGATORY

M Charlton, et al.

LIVER TRANSPLANT
POST-LT HCV TREATMENT

- Virtually all patients with recurrent HCV post-LT have been treated
- In the future all patients will be treated soon after the LT
- LDV-SOF-RBV has no interaction with immune suppression
- Patients with CTP C cirrhosis after LT require 24 weeks

M Charlton et al.
HEPATOCELLULAR CARCINOMA
STAGE AT DIAGNOSIS

Stage 4: 35%
Stage 3: 27%
Stage 2: 33%
Stage 1: 5%

Why not LT candidate:
• Advanced HCC at diagnosis
• HCC growth/recurrence
• Cardio-Pulmonary disease
• Psycho-social support
• Other

21%

Patients with HCC who ultimately undergo LT

LIVER TRANSPLANT EFFECT ON SURVIVAL IN HCC

• Liver transplant within Milan criteria
• Stage 1 → Stage 2
• Stage 2
• Stage 3 → Stage 1 or 2
• Pre-LT management:
  ▪ TACE
  ▪ Radioembolization
  ▪ RFA
  ▪ Until no viable HCC seen by imaging
LIVER TRANSPLANT
MELD EXCEPTION

- The vast majority of patients with stage 2-3 HCC have stable Child class A cirrhosis and a MELD score under 15
- Receive exception from MELD so they may undergo LT
- Priority for patients with HCC was too high
- Prevented patients with high MELD from ESLD from getting a LT

Prior to October 2015 | After October 2015
--- | ---
Assigned MELD 22 | List at true MELD
3 months 25 | 6 months 28
6 months 28 | 9 months 31
9 months 31 | 12 months 33
12 months 33 | Capped at 34
Capped at 34 | Capped at 34

https://optn.transplant.hrsa.gov

END STAGE RENAL DISEASE
SURVIVAL

NIH: Kidney Statistics for the USA
Last updated: 2010
END STAGE RENAL DISEASE
RENAL TRANSPLANTATION

Deceased Donor
Living Donor

NIH: Kidney Statistics for the USA
Last updated: 2010

CHRONIC HCV AND ESRD
DAYS TO TRANSPLANT

Recipient + Donor +
Recipient - Donor -
Recipient + Donor -

JR Scalea, et al.
Transplantation 2015;99:1192-1196
CHRONIC HCV AND ESRD IMPACT ON MORTALITY

- Observational Study
- 49,762 hemodialysis patients
- Evaluated 1996-2011
- 9.5% HCV positive
- Only 1% treated for HCV
- Only 13% waiting for HCV
- Only 3% of those waiting for RT were treated for HCV


CHRONIC HCV IN ESRD GRAZAPREVIR / ELBASVIR

<table>
<thead>
<tr>
<th>N</th>
<th>122</th>
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<tbody>
<tr>
<td>Male</td>
<td>75%</td>
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<tr>
<td>HCV GT1A</td>
<td>52%</td>
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<tr>
<td>Prior treatment</td>
<td>17%</td>
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<tr>
<td>Cirrhosis</td>
<td>6%</td>
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<tr>
<td>Diabetes</td>
<td>36%</td>
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<tr>
<td>Dialysis</td>
<td>75%</td>
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<td>SVR (ITT)</td>
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<td>SVR (Per Protocol)</td>
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<tr>
<td>GT1A</td>
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<tr>
<td>GT1B</td>
<td>98%</td>
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<tr>
<td>Frequency of Resistant mutations:</td>
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<tr>
<td>NS3/4 mutations</td>
<td>32%</td>
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<tr>
<td>NS5A</td>
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</table>

All patients treated with GZV/EBV for 12 weeks

CHRONIC HCV IN ESRD
ALGORITHM

Renal Transplant Candidate

Yes

Living Donor

Yes

No Living Donor

Cirrhosis

Treat HCV Now

Consider Combined LT/RT

No Cirrhosis

No

Treat HCV

Take HCV positive Kidney

Treat HCV After RT

TRANSPLANTATION MEDICINE
SUMMARY

• Hyponatremia:
  ▪ An important determinant of mortality in patients with cirrhosis and is now factored into MELD

• Chronic HCV:
  ▪ The number of patients needing a liver transplant is declining and will be and HCV will be an uncommon indication for LT by 2020
  ▪ Great benefit can be achieved by treating patients with decompensated cirrhosis
  ▪ Beware of placing a patient into MELD purgatory
TRANSPLANTATION MEDICINE
SUMMARY

- LT trends:
  - The incidence of HCC and NASH as indications for LT are increasing
  - HCC is up 82% in 15 years
  - NASH is up 71% in 10 years
- HCV in patients with ESRD:
  - Determine if the patient is a candidate for a renal transplant before initiating HCV treatment
  - It might be best to defer HCV treatment in a patient with ESRD until after the renal transplant