Nutrition In Solid Organ Transplant Patients

Undernutrition In Transplant Patients
O. Abbasoglu (TR)
Undernutrition in Transplant Patients

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Disclosure

I have received financial relationships for speaking engagements from Baxter, Nutricia and Abbott.

No commercial relationships relevant to the topic being presented.
Outline

• Undernutrition and sarcopenia before and after transplantation
• Assessment of nutritional status
• Treatment of undernutrition
• Guidelines, conclusions
Similarities,

Differences,

Limitations...
Are transplant patients different?

- They are heterogeneous group of patients
- Chronic, longstanding debilitating diseases
- They are immunosuppressed

- Pathophysiology is similar
- No different assessment tools
Heterogenous group of patients

Organs transplanted annually (2015)

<table>
<thead>
<tr>
<th>Organ</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>85 000</td>
</tr>
<tr>
<td>Liver</td>
<td>28 000</td>
</tr>
<tr>
<td>Heart</td>
<td>7 000</td>
</tr>
<tr>
<td>Lung</td>
<td>5 000</td>
</tr>
<tr>
<td>Pancreas</td>
<td>2 300</td>
</tr>
<tr>
<td>Small bowel</td>
<td>200</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>127 000</strong></td>
</tr>
</tbody>
</table>

WHO Global Report 2015
Outline

• Undernutrition and sarcopenia before and after transplantation
• Assessment of nutritional status
• Treatment of undernutrition
• Guidelines, conclusions
## Risk of undernutrition in transplant candidates

<table>
<thead>
<tr>
<th>Condition</th>
<th>Risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis</td>
<td>40-90</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>45-60</td>
</tr>
<tr>
<td>Candidates for lung transplantation</td>
<td>60</td>
</tr>
<tr>
<td>Candidates for heart transplantation</td>
<td>45</td>
</tr>
</tbody>
</table>

*Mazurak VC. Liver Transplant 2017;23:1453*
*Tayyem RF. J Ren Nutr 2008;18:202*
*Calanas-Continente AJ. Nutr Hosp 2002;17:197*
*Godown J. Heart Lung Transplant 2013;32:S118*
Undernutrition in transplant candidate is multifactorial

- GI symptoms
- Malabsorption
- Anorexia
- Inadequate diet restrictions
- Dialysis-associated protein loss
- Insulin resistance
- Altered protein metabolism

Kerwin AJ. Surg Clin N Am 2011;91:565
Sarcopenia

• Loss of muscle mass
• Loss of muscle function

Sarcopenia has been identified as a risk for worse outcome after transplantation

Carey EJ. Nutr Clin Pract 2014;29:159
Sarcopenia is a predictor of survival in hemodialysis patients

Preserved muscle mass was associated with decreased mortality (HR, 0.52)

Sarcopenia is associated with mortality in cirrhosis

Patients with sarcopenia had higher waitlist mortality (HR, 2.21)

Montano-Loza AJ. Clin Gastroenterol 2012;10:166
Both sarcopenia and frailty determine suitability of patients for liver transplantation—A systematic review and meta-analysis of the literature

Judith Kahn1,2 | Doris Wagner3 | Nicole Homfeld1,2 | Helmut Müller1,2 | Daniela Kniepeiss1,2 | Peter Schemmer1,2

6 studies published between 2014-2017

Kahn J. Clin Transplant. 2018:e13226
Impact of frailty on waiting list mortality in liver transplantation

Sarcopenia and frailty were highly related to waiting list mortality

Kahn J. Clin Transplan. 2018:e13226
A limitation...

Organ allocation is based on MELD score,

3 laboratory tests: Bilirubin, INR, creatinine

Nutritional status, sarcopenia and frailty are not included!
Inclusion of Sarcopenia Within MELD (MELD-Sarcopenia) and the Prediction of Mortality in Patients With Cirrhosis

Aldo J. Montano-Loza, MD, MSc, PhD1, Andres Duarte-Rojro, MD, MSc, PhD2, Judith Meza-Junco, MD3, Vickie E. Baracos, PhD4, Michael B. Sawyer, MD3, Jack X.Q. Pang, MD4,5, Crystal Beaumont, BSc3, Nina Esfandiar, BSc3 and Robert P. Myers, MD, MSc4,5

<table>
<thead>
<tr>
<th></th>
<th>Death (n=259)</th>
<th>Alive (n=410)</th>
<th>HR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascites</td>
<td>206</td>
<td>275</td>
<td>1.61</td>
<td>1.13-2.30</td>
<td>0.008</td>
</tr>
<tr>
<td>Albumin</td>
<td>31</td>
<td>33</td>
<td>0.98</td>
<td>0.96-0.99</td>
<td>0.04</td>
</tr>
<tr>
<td>Na</td>
<td>135</td>
<td>136</td>
<td>0.96</td>
<td>0.95-1.02</td>
<td>0.3</td>
</tr>
<tr>
<td>MELD score</td>
<td>16</td>
<td>13</td>
<td>1.05</td>
<td>1.03-1.07</td>
<td>0.001</td>
</tr>
<tr>
<td>Sarcopenia</td>
<td>139</td>
<td>159</td>
<td>2.26</td>
<td>1.73-2.94</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Montano-Loza AJ. Clin Transl Gastroenteol 2015 Jul 16;6:e102
In patients with low MELD scores, MELD-sarcopenia tended to outperform conventional MELD.

Survival of patients with and without sarcopenia

C-statistics for the prediction of mortality in patients with MELD <15:

- MELD: 0.69
- MELD-sarcopenia: 0.85

Log Rank, P<0.001

Montano-Loza AJ. Clin Transl Gastroentrool 2015 Jul;6:e102
After transplantation...
Clinical course of sarcopenia after transplantation

• Muscle mass: Decreased lean mass may persist
• Muscle function: Improves

Immunosuppressive drugs
- Tacrolimus, CyA
- Corticosteroids
- Rapamycin

Risk of sarcopenic obesity

Tsien C. J Gastroenterol Hepatol 2014;29:1250
• 1045 OLT
• Patients who survived at least one year
• 159 (17.9%) grafts were lost after the first year
Late graft loss causes:
- de novo malignancies
- cardiovascular diseases
- cerebral vascular accidents
Outline

• Undernutrition and sarcopenia before and after transplantation
• Assessment of nutritional status
• Treatment of undernutrition
• Guidelines, conclusions
**Assessment tools**

Antropometric measurements, BMI
Handgrip strength

Laboratory tests
  Serum proteins
  N balance/creatinine-height index
  Lymphocyte count

DEXA
Muscle mass (US, CT, MRI)

**Limitations**

Fluid retention
- 
Fluid retention
Poor liver/kidney function
Fluid retention
Immunosuppression
Not practical
Cutoff points in cirrhosis, and renal failure are not clear

Hasse JM. JPEN 2003;25:120
Tandon P. Hepatology 2017;65:1044
Cirrhosis specific screening and assessment tools

• Royal Free Hospital-Nutritional Prioritizing Tool (RFH-NPT) (Total score 7)
  - Alcoholic cirrhosis or tube feeding (score 6)
  - Fluid overload (Score 1)
    Different evaluation in the presence or absence of fluid overload

• Liver Disease Undernutrition Screening Tool

Arora S. J Hepatol 2012;56;S241
Amodio P. Hepatology 2013;58:325
How to assess then?

• SGA
• Muscle mass (CT) (quantitative)
• Handgrip strenght (functional)

SGA may be the best reliable tool!

Sezer S. Transplant Proc 2006;38:517
Outline

• Undernutrition and sarcopenia before and after transplantation
• Assessment of nutritional status
• Treatment of undernutrition
• Guidelines, conclusions
### Treatment of sarcopenia in pre-transplant patient is difficult

<table>
<thead>
<tr>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exercise</strong></td>
</tr>
<tr>
<td>- Fatigue, ascites, encephalopathy</td>
</tr>
<tr>
<td>- Risk of variceal bleeding</td>
</tr>
<tr>
<td><strong>Pharmacotherapy</strong></td>
</tr>
<tr>
<td>- Large studies are lacking</td>
</tr>
<tr>
<td><strong>Nutrition</strong></td>
</tr>
<tr>
<td>- Altered taste sensation, fluid overload</td>
</tr>
<tr>
<td>- May not reverse sarcopenia</td>
</tr>
</tbody>
</table>
Oral supplements can help to meet the nutritional goals
Meta-analysis: oral or enteral nutritional supplementation in cirrhosis

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Nutritional supplement</th>
<th>Placebo</th>
<th>Total</th>
<th>Weight</th>
<th>Risk ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>1.10.1 Enteral nutrition</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>De Ledinghen 1996</td>
<td>3</td>
<td>12</td>
<td>2</td>
<td>10</td>
<td>1.25 [0.26, 6.07]</td>
</tr>
<tr>
<td>Dupont 2012</td>
<td>17</td>
<td>44</td>
<td>19</td>
<td>55</td>
<td>1.12 [0.66, 1.88]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>20</td>
<td>56</td>
<td>21</td>
<td>65</td>
<td>1.13 [0.69, 1.85]</td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.90); I² = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.49 (P = 0.63)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>1.10.2 Oral nutrition</th>
<th>Nutritional supplement</th>
<th>Placebo</th>
<th>Total</th>
<th>Weight</th>
<th>Risk ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>Bunout 1989</td>
<td>2</td>
<td>17</td>
<td>5</td>
<td>19</td>
<td>0.45 [0.10, 2.01]</td>
</tr>
<tr>
<td>Hirsch 1992</td>
<td>3</td>
<td>26</td>
<td>6</td>
<td>25</td>
<td>0.48 [0.13, 1.72]</td>
</tr>
<tr>
<td>Le Cornu 2000</td>
<td>2</td>
<td>42</td>
<td>7</td>
<td>40</td>
<td>0.27 [0.06, 1.23]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>7</td>
<td>85</td>
<td>18</td>
<td>84</td>
<td>0.40 [0.18, 0.90]</td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.00; Chi² = 0.35, df = 2 (P = 0.84); I² = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 2.21 (P = 0.03)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>141</td>
<td>149</td>
<td>100.0%</td>
<td>0.75 [0.42, 1.32]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>27</td>
<td>39</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.10; Chi² = 5.18, df = 4 (P = 0.27); I² = 23%</td>
<td></td>
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<tr>
<td>Test for overall effect: Z = 1.01 (P = 0.31)</td>
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<tr>
<td>Test for subgroup differences: Chi² = 4.58, df = 1 (P = 0.03), I² = 78.2%</td>
<td></td>
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</tr>
</tbody>
</table>

RR: 0.75 (0.42 - 1.32), P = 0.31

Ney M. Aliment Pharmacol Ther 2013;37:672
Nutrition recommendations in cirrhosis....

• Periods of starvation should be kept short by consuming 3 to 5 meals a day and a late evening snack

• Caloric intake: 35-40 kcal/kg/day
  Protein intake: 1.2-1.5 g/kg/day

Do not restrict proteins!

Plauth M. ESPEN guidelines: liver disease
Other interventions to ameliorate malnutrition

- Branched-chain amino acids (BCAA)
- Fish-oil
- Zinc supplementation
- Probiotics
- Growth hormone

Debatable

Mazurak VC. Liver Transplant 2017;23:1453
In liver transplant recipient....
Long-term .... main problems:

- Hyperlipidemia
- Diabetes mellitus
- Sarcopenia
- Hypercholesterolemia
- Obesity
- Osteoporosis
- Hypertension

Sanchez AJ. Liver Transpl 2006;12:1310
Long-term ....prevention:

• Avoid/decrease corticosteroids

• Close monitoring of immunosuppressive medications

• Resistance exercises

• Nutritional counselling: Increased risk of DM, dyslipidemia, HT
Vitamin and micronutrient deficiencies

• Fat-soluble vitamins
• Water-soluble vitamins  No evidence for routine
• Magnesium  supplementation
• Zinc
• .......

Correction if there is deficiency
Difference in renal transplants

- Vitamin D deficiency: As high as 60%

Osteoporosis

Sgambat K. Pediatr Transplant 2011;8:790
Rosina KTC. Br J Nutr 2017;117:1279
Outline

• Undernutrition and sarcopenia before and after transplantation
• Assessment of nutritional status
• Treatment of undernutrition
• Guidelines, conclusions
• Malnutrition is a major factor influencing outcome after transplantation, so monitoring of nutritional status is recommended. In malnutrition, additional oral nutritional supplements or even tube feeding is advised.

• Recommendations for living donor and recipient are not different from those for patients undergoing major abdominal surgery.
Take-home messages (1)

• Malnutrition is an independent predictor of poor clinical outcome after transplantation

• Sarcopenia is the most common nutritional variable associated with mortality

• During the long preoperative waiting period, there is time to try to replete patients nutritionally
Take-home messages (2)

• Pre- and post- transplantation nutritional treatment and rehabilitation programs are crucial. Oral supplements and artificial nutrition may be needed in some patients.

• Nutritional counselling and improved parameters of nutritional status may affect post-transplant outcome.
Finally...

Patients should be referred to transplantation centers before getting too sick and malnourished.
Further reading: