Complex Medical Inpatients with Good Outcomes in Transplant: Cardiac, Pulmonary, Kidney and Liver

Seema Khurana, DO
Quan Le, MD
Cristina Brea, MD
Armando Alvarez, MD MPH
Objectives/Goals:

- Explain types of organ donation and epidemiology of transplant
- Articulate the team members involved in transplants.
- Explain physical changes associated with transplantation
- Discuss methods of measuring qualities such as frailty, sarcopenia, malnutrition in transplant patients
- Discuss individual cases and rehabilitation considerations in each case
Important facts about transplant

113,000+
Number of men, women and children on the national transplant waiting list as of July 2019.

36,528
transplants were performed in 2018.**

20
people die each day waiting for a transplant.

We All Need to Register. Here’s Why:

95%
of U.S. adults support organ donation

but only

58%
are actually signed up as donors.

every 10 minutes
another person is added to the waiting list.

only 3 in 1,000
people die in a way that allows for organ donation.
The organ shortage continues...
What are the two types of organ donation and which organs can be donated?

- The two types of donation
  - Living donation
  - Deceased donation.
- The following organs can be donated:
  - Liver
  - Heart
  - Lung
  - Kidney
  - Intestine
  - Pancreas
  - Tissues
    - corneas, skin, veins, heart valves, tendons, ligaments and bones.
Directed versus non-directed donation

Directed donation.

- The donor specifically chooses who will receive the organ transplant.

Non-directed donation.

- The donor is neither related to nor known by the person in need.
Paired Donations

Kidney Swap

- Donor 1 (Husband)
  Blood Type A

- Donor 2 (Sister)
  Blood Type B

- Recipient 1 (Wife)
  Blood Type B

- Recipient 2 (Brother)
  Blood Type A
What organ is most commonly transplanted and needed for donation?

- Kidneys are the **most** commonly transplanted **organ**
- Kidneys are also the **most needed** organ
How long does it take to get an organ transplant?

- Once you are added to the national organ transplant waiting list, you may receive an organ fairly quickly or you may wait many years.
- In general, the average time frame for waiting can be 3-5 years at most centers and even longer in some geographical regions of the country.
Transplant team

- Transplant surgeon
- Transplant nephrologist/pulmonologist/ cardiologist
- Transplant coordinator
- Dietitian
- Social worker
- Financial coordinator
- Transplant pharmacist
- Physiatrist
- Therapists
Graft versus Host reaction

- Can occur after allogenic transplant
- Two forms
  - Acute versus chronic
- Immune condition that occurs in a patient after transplantation when immune cells present in donor tissue (the graft) attack the host's own tissues
Medical issues can increase after transplantation

- Liver transplants
  - Hypertension
    - 60-70% patients develop after transplant
  - Type 2 diabetes mellitus
    - Increases from 15% before OLT to 30% to 40% after transplant
  - Dyslipidemia
    - 45-69% after transplant
Important definitions that adversely affect morbidity and mortality

- Frailty
  - Clinical state of decreased reserve and decreased ability to endure stressors such as cumulative declines across multiple systems
  - Validated in cohorts of patients with chronic diseases
  - Associated with adverse health outcomes
  - Linked to increases in falls, fractures
  - Increases waitlist mortality and decrease quality of life in patients awaiting liver transplantation
Frailty assessments

- FFI
  - 5 domains of physical frailty
    - Weakness
    - Exhaustion
    - Weight loss
    - Low activity
    - Slowness
  - Three or greater on five-point scale independently associated with mortality in patient with ESLD
  - Pros: can be given in the office and short amount of time,
  - Cons: subjective
Short Physical Performance Battery

- Frailty assessment tool
- Objective instrument to evaluate lower extremity physical performance status
- Evaluates performance on three timed tasks
  - Walking speed
  - Standing balance
  - Chair stand test
- Pros: out-patient setting
- Poor performance in general population is associated with increased risk of all-cause mortality
Important definitions that adversely affect morbidity and mortality

- **Sarcopenia**
  - Progressive and generalized loss of skeletal muscles mass, strength and function
  - Component of frailty
  - Independent predictor of mortality in cirrhotic patients
  - Malnutrition and sarcopenia often present simultaneously given they have similar physiologic mechanisms

- **Systematic review and meta-analysis**
  - Impact of skeletal muscle mass assessed by cross-sectional imaging in patients awaiting or undergoing liver transplantation
  - Found that low muscle mass was independently associated with post-transplantation and waiting list mortality
Sarcopenia assessment

- DEXA
  - Quantifies sarcopenia by measuring body fat, fat free mass and bone mineral content
- Bioelectrical impedance analysis
  - Evaluates body mass and sarcopenia by measuring the body’s resistance to flow of electrical current
  - Non-invasive
  - High interobserver reliability
  - Correlate with DEXA
Important definitions that adversely affect morbidity and mortality

- Malnutrition
  - Imbalance of energy, protein, and other nutrients
  - Negatively impacts patient outcomes
  - Example: preoperative malnutrition has been shown to negatively impact liver transplant outcomes after surgery
Important definitions that adversely affect morbidity and mortality

- **Malnutrition**
  - Can lead to decreased skeletal muscle mass
  - Caused by combination of decreased caloric intake
  - Increased protein requirements
  - Increased muscle protein catabolism
  - Decreased muscle protein synthesis
  - Poor absorption of nutrients
  - Not only does malnutrition affect post-transplantation it also affects quality of life
Malnutrition-
Subjective Global Assessment

- Developed in 1987
- Physical examination findings and history
  - Symptoms
  - Weight changes
  - Nutrient intake
- Simple
- Performed at bedside
- Non-invasive
- Neg: some items are subjective
- Prospective study by Stephson and colleague
  - Postoperative length of stay was significantly longer in those with severe malnutrition compared with patients with mild or moderate malnutrition
Exercise capacity

- Standard for measuring assessing exercise capacity is measurement of maximal oxygen consumption (VO2)
  - Can be due to decreased peripheral oxygen utilization in the setting of muscle wasting and decondition
- Dharancy and colleagues
  - Severely impaired pre-transplant exercise capacity, defined as peak VO2 values less than 60% predicted in patients with ESLD
  - It was independently associated with 1-year mortality after transplant
- Study:
  - Using 6-minute walk test
  - It was found that for every 100m increase in the walk distance at baseline there was a significant increase in survival in patients awaiting transplantation
Summary

- Sarcopenia, frailty and malnutrition are determinants of morbidity and mortality
- Modifiable risk factors
- Therefore gaining a better understanding of a patient’s muscles mass, muscle function and nutritional status is essential to individualizing nutritional and exercise interventions with the aim of improving patient outcomes
Rehabilitation in Cardiac Transplants
CNN: What is Cardiac Rehab

- https://www.youtube.com/watch?v=hnRWHsSpB8M
Patient Case

- 67 y/o gentlemen with PMH of OHT heart transplant on 10/11/19 secondary to Cardiac Sarcoidosis. Patient was at ALF when he developed diarrhea, diagnosed with Clostridium Difficile. He completed treatment with Vancomycin. Hospital course complicated by AKI, Stage 3 sacral ulcer and pneumonia.
- Patient presented to rehab for debility
Since the 1970s, one-year post-transplantation survival rates: 30% to almost 90%

Three- and five-year survival rates are now approximately 80% and 75%, respectively.

36% of heart recipients are hospitalized during the first year post-transplantation, and 61% are hospitalized within four years.
Post Transplant Challenges

- Exercise capacity remains diminished due to decreased chronotropic competence associated with cardiac allograft denervation
  - As a result of Vagus nerve denervation
- Impaired peripheral vascular function due to sympathetic response exacerbating vasocontraction
- Skeletal muscle strength and biochemistry due to post-transplant deconditioning or treatment with high-dose immunosuppressive therapy
Supervised Post Transplant Exercise

- High intensity Exercise have been proven to be safe in post transplant patients
- Skeletal muscle adaptation following exercise allows for optimal oxygen uptake. (increased Vo2 max)
- Multiple studies report improved psychological improvement and life satisfaction.
- Lifestyle modification with decreased systolic blood pressure
Sample Therapy Session

- Performed on treadmill under supervision by therapist
- 8 weeks consisting of 3 sessions each week
- 10 minute warm up
- Four 4 minute exercise with HR 85-95% max followed by 3 minutes recovery
Physiological Changes with High Intensity Exercise

Fig. 2. Changes in baseline systolic (SBP), diastolic blood pressure (DBP) and heart rate (HR) in the training and in the control group at different times of the study. *p < 0.01 vs first observation (before training).

<table>
<thead>
<tr>
<th></th>
<th>Exercise group</th>
<th>Sedentary group</th>
<th>p-Value*</th>
<th>p-Value** group difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
<td></td>
<td>Before</td>
</tr>
<tr>
<td>N</td>
<td>14</td>
<td>14</td>
<td>NS</td>
<td>13</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.3 ±</td>
<td>26.0 ±</td>
<td>NS</td>
<td>26.1 ±</td>
</tr>
<tr>
<td></td>
<td>3.4</td>
<td>3.0</td>
<td></td>
<td>6.1</td>
</tr>
<tr>
<td>Hip-waist ratio</td>
<td>1.02 ±</td>
<td>1.05 ±</td>
<td>NS</td>
<td>1.03 ±</td>
</tr>
<tr>
<td></td>
<td>0.11</td>
<td>0.11</td>
<td></td>
<td>0.14</td>
</tr>
<tr>
<td>VO2max (mL/kg/min)</td>
<td>23.9 ±</td>
<td>28.3 ±</td>
<td>&lt;0.001</td>
<td>24.6 ±</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>142 ±</td>
<td>127 ±</td>
<td>0.02</td>
<td>141 ±</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>85 ± 7</td>
<td>82 ± 9</td>
<td>NS</td>
<td>82 ± 9</td>
</tr>
<tr>
<td>Heartrate (min⁻¹)</td>
<td>76 ± 11</td>
<td>76 ± 7</td>
<td>NS</td>
<td>78 ± 7</td>
</tr>
</tbody>
</table>
Physiological Changes with High Intensity Exercise

### Table 1: Changes in Cytokine Levels

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Initial</th>
<th>Final</th>
<th>NS</th>
<th>Final</th>
<th>NS</th>
</tr>
</thead>
<tbody>
<tr>
<td>hsCRP (mg/mL)</td>
<td>1.41 ± 0.81 ± 0.017</td>
<td>0.87 ± 1.14 ± NS</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IL-6 (pg/mL)</td>
<td>0.42 ± 0.31 ± NS</td>
<td>0.41 ± 0.41 ± NS</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNF-α (pg/mL)</td>
<td>4.51 ± 4.35 ± NS</td>
<td>3.77 ± 4.14 ± NS</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1:** Change in upper and lower extremity strength after 12 weeks of supervised exercise training or no-training (values between lines are between group adjusted change and 95% confidence interval).
Limitations

- Contradictory evidence: Possibility of re-innervation
- Improvement of HR due to natural time progression
- Myocardial ischemia may be silent due to denervation
- Importance of individualized exercise program while understanding that rehabilitation requires an interdisciplinary approach.
Rehabilitation in Pulmonary Transplant Patients
A 66-year-old male underwent bilateral sequential pulmonary transplant due to severe Idiopathic Pulmonary Fibrosis. His immediate post-operative course was complicated by third degree heart block, coronary arrest with pulseless electrical activity and subsequent placement of a cardiac pacemaker and implantable cardioverter defibrillator. He also had respiratory failure requiring prolonged mechanical ventilation and was status-post tracheostomy placement. Further, he had dehiscence of his sternotomy incision necessitating negative-pressure wound therapy.

He was admitted to inpatient rehabilitation with the goals of improving functional mobility, self-care management and medical management of his multiple co-morbidities.
Pre-transplant: Acute hospitalization

**Outpatient:**
- **Exercise training**
  - Using FITT-P: Aerobic, resistance, flexibility
- **Oxygen titration**
  - to support exercise/activity

**Inpatient:**
- **Modified exercise and mobility program**
  - on ward/ICU as tolerated
- **Oxygen titration**
  - to support exercise/activity

Post-transplant: Early (1-6 mo)

**Early mobility**
- On ICU and ward

**Progression to independent function**
- (transfers, walking, self-care, stairs)

**Exercise training**
- Aerobic, resistance, flexibility exercise as tolerated
- **Oxygen titration**
  - to support exercise/activity

Post-transplant: Uncomplicated course

**Exercise training**
- using FITT-P:
  - Aerobic, resistance, flexibility

**Complicated Course** (Long-stay ICU/acute care):
- **Progression to independent function**
  - (transfers, walking, self-care, stairs)
- **Referral to inpatient rehab** (if required)
- **Exercise training**
  - Aerobic, resistance flexibility exercise as tolerated balance training

Post-transplant: Long-term (> 6 mo)

**Exercise training**
- Home and community programs

**Education** on long-term maintenance of exercise

**Physical activity**
- Counseling: Identify barriers and motivators, relapse planning, restarting after illness or injury
- Return to leisure activities, sports, etc.

**Transplant games and charity events**
Initial FIM Scores

- Tracheostomy with speaking and swallowing valve for several hours a day
- Regular diet PO
- Ambulating <50 with RW
- Median self care FIM score = 3.8

<table>
<thead>
<tr>
<th>Activity</th>
<th>FIM Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eating</td>
<td>5</td>
</tr>
<tr>
<td>Grooming</td>
<td>4</td>
</tr>
<tr>
<td>Bathing</td>
<td>2</td>
</tr>
<tr>
<td>Dressing: Upper Body / Lower Body</td>
<td>5 / 4</td>
</tr>
<tr>
<td>Toileting</td>
<td>3</td>
</tr>
<tr>
<td>Bed, chair, WC Transfers</td>
<td>4</td>
</tr>
<tr>
<td>Toilet Transfers</td>
<td>4</td>
</tr>
<tr>
<td>Tub, Shower Transfers</td>
<td>NA- UNSAFE</td>
</tr>
<tr>
<td>Ambulation RW</td>
<td>1</td>
</tr>
<tr>
<td>Stairs</td>
<td>NA- UNSAFE</td>
</tr>
<tr>
<td>Problem Solving</td>
<td>5</td>
</tr>
<tr>
<td>Memory</td>
<td>4</td>
</tr>
<tr>
<td>Comprehension</td>
<td>5</td>
</tr>
<tr>
<td>Expression</td>
<td>5</td>
</tr>
<tr>
<td><strong>Total FIM</strong></td>
<td><strong>70</strong></td>
</tr>
</tbody>
</table>
Rehabilitation Assessments

Aerobic testing
- Cardiopulmonary Exercise (treadmill/cycle)
- 6MWT
- Upper Extremity Endurance

Muscle function
- MMT, Handgrip force
- 1-rep Maximum

Mobility testing
- Gait Speed
- Sit-Stand test
- Timed up and Go
- Balance tests

Assessment of physical activity
- Pedometer/Accelerometers
- Physical Activity Questionnaires (PASE, IPAQ, DASI)
Proposed Protocols

- Progressive mobility/ambulation program
- Stair climbing and Resistance training: Up to 5 lbs.
- Education re: Lifting restrictions, Caretaker Training
- Postural correction/reeducation of ADLs
- Management of Comorbidities, Prevention of Complications
Rehabilitation Course
LOS: 12/21/16 – 1/2/17 = 13 days

- Tracheostomy tube was progressively weaned and removed.
- Sternotomy wound improved but continued to require negative-pressure wound therapy however he was able to assist in dressing changes.
- Self-care associated FIM scores increased were to the level of supervision for dressing and bathing but otherwise modified independent or better.
- Able to ambulate over 300 feet with a rolling walker at the supervision level.
### Discharge FIM Scores

<table>
<thead>
<tr>
<th>Activity</th>
<th>FIM Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eating</td>
<td>7</td>
</tr>
<tr>
<td>Grooming</td>
<td>6</td>
</tr>
<tr>
<td>Bathing</td>
<td>5</td>
</tr>
<tr>
<td>Dressing Upper Body / Lower Body</td>
<td>5 / 5</td>
</tr>
<tr>
<td>Toileting</td>
<td>6</td>
</tr>
<tr>
<td>Bed, chair, WC Transfers</td>
<td>5</td>
</tr>
<tr>
<td>Toilet Transfers</td>
<td>5</td>
</tr>
<tr>
<td>Tub, Shower Transfers</td>
<td>5</td>
</tr>
<tr>
<td>Ambulation WC / W</td>
<td>3 / 3</td>
</tr>
<tr>
<td>Stairs</td>
<td>4</td>
</tr>
<tr>
<td>Problem Solving</td>
<td>6</td>
</tr>
<tr>
<td>Memory</td>
<td>5</td>
</tr>
<tr>
<td>Comprehension</td>
<td>6</td>
</tr>
<tr>
<td>Expression</td>
<td>6</td>
</tr>
<tr>
<td><strong>Total FIM</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>
Rehabilitation in Renal Transplant
Patient is a 79 year old man with a PMH of ESRD secondary to longstanding, poorly controlled HTN that is s/p Living Relative Kidney Transplant from his daughter that was complicated by multi drug resistant Klebsiella pneumonia, enterococcus faecalis bacteremia secondary to urinary tract infection, pseudomonas bacteremia secondary to urinary tract infection, and aspergillus pneumonia admitted to inpatient rehabilitation for debility and optimization prior to home.

He was admitted to inpatient rehabilitation with the goals of improving functional mobility, self-care management and medical management of his multiple co-morbidities as well as family training and education.
### Initial FIM Scores

- Renal diet PO
- Ambulating <50 with RW
- Median self care FIM score = 3.3

<table>
<thead>
<tr>
<th>Activity</th>
<th>FIM Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eating</td>
<td>5</td>
</tr>
<tr>
<td>Grooming</td>
<td>4</td>
</tr>
<tr>
<td>Bathing</td>
<td>2</td>
</tr>
<tr>
<td>Dressing: Upper Body / Lower Body</td>
<td>2/1</td>
</tr>
<tr>
<td>Toileting</td>
<td>2</td>
</tr>
<tr>
<td>Bed, chair, WC Transfers</td>
<td>5</td>
</tr>
<tr>
<td>Toilet Transfers</td>
<td>3</td>
</tr>
<tr>
<td>Tub, Shower Transfers</td>
<td>5</td>
</tr>
<tr>
<td>Ambulation RW</td>
<td>5</td>
</tr>
<tr>
<td>Stairs</td>
<td>2</td>
</tr>
<tr>
<td>Problem Solving</td>
<td>5</td>
</tr>
<tr>
<td>Memory</td>
<td>4</td>
</tr>
<tr>
<td>Comprehension</td>
<td>5</td>
</tr>
<tr>
<td>Expression</td>
<td>5</td>
</tr>
<tr>
<td><strong>Total FIM</strong></td>
<td><strong>50</strong></td>
</tr>
</tbody>
</table>
Rehabilitation Goals PT/OT

- Patient/spouse will be modified independence with home exercise program upon discharge.
- Patient will be supervision assistance with car transfer and least restrictive assistive device.
- Caregiver will be modified independent in assisting patient safely upon discharge.
- Patient will demonstrate ability to perform energy conservation techniques 100% of the time when participating in ADLS/IADLS by discharge.
- Patient will demonstrate modified independence with UE HEP in order to increase independence with ADLS.
Proposed Protocols Specific For Post-Renal Transplant

- Cardiorespiratory Fitness, Using Branching Protocol
- Muscle Strength
- Body Composition
- Health Related Quality of Life
- Activity Participation and Exercise Intervention
- Patient remained off of dialysis throughout admission
- Patient no longer needing to use wheelchair, now with rolling walker with minimal assistance.
- Spouse and patient both demonstrated understanding of limitations and proper techniques for transfer and ADL care.
- On re-admission to acute inpatient for unrelated reason, “I do not need therapy because I can walk with no problem. I just finished doing inpatient rehab.”
<table>
<thead>
<tr>
<th>Activity</th>
<th>FIM Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eating</td>
<td>6</td>
</tr>
<tr>
<td>Grooming</td>
<td>6</td>
</tr>
<tr>
<td>Bathing</td>
<td>4</td>
</tr>
<tr>
<td>Dressing Upper Body / Lower Body</td>
<td>4 / 4</td>
</tr>
<tr>
<td>Toileting</td>
<td>4</td>
</tr>
<tr>
<td>Bed, chair, WC Transfers</td>
<td>3</td>
</tr>
<tr>
<td>Toilet Transfers</td>
<td>3</td>
</tr>
<tr>
<td>Tub, Shower Transfers</td>
<td>5</td>
</tr>
<tr>
<td>Ambulation walking 150 Feet</td>
<td>4</td>
</tr>
<tr>
<td>Walk 50 Feet with Two Turns</td>
<td>4</td>
</tr>
<tr>
<td>Problem Solving</td>
<td>6</td>
</tr>
<tr>
<td>Memory</td>
<td>6</td>
</tr>
<tr>
<td>Comprehension</td>
<td>6</td>
</tr>
<tr>
<td>Expression</td>
<td>6</td>
</tr>
<tr>
<td><strong>Total FIM</strong></td>
<td><strong>71</strong></td>
</tr>
</tbody>
</table>
References

- A randomized trial of exercise training after renal transplantation. Painter, Patricia Lynn¹ ⁴; Hector, Lisa¹; Ray, Karen¹; Lynes, Liliana¹; Dibble, Suzanne³; Paul, Steven M.¹; Tomlanovich, Stephen L.²; Ascher, Nancy L.²
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6478176/