Transplantation in Older Adults: Who is a Good Candidate

Celebrating a Second Chance at Life Survivorship Symposium

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The University of Texas
MD Anderson Cancer Center

Stem Cell Transplantation in Older Patients

Uday Popat MD MBA
BMT Infonet Survivorship Symposium
May 3, 2022
Key Points

Older patients are most in need of, and are increasingly undergoing stem cell transplantation (SCT)

• but outcomes need to be improved

Factors predicting likelihood of success (Prognostic Factors)

• Other health concerns at time of transplant (comorbidities)
• Geriatric assessment:
  • ability to plan and do daily activities independently
  • Cognitive status (ability to process information)

Key Points cont’d

• How do you improve outcomes in older patients?
  • Better conditioning regimen:
    • fractionated busulfan regimen
  • Better supportive care:
    • Enhanced recovery in stem cell transplantation program (ER-SCT) to
      • maintain patient’s ability to physically recover from treatment (physiological reserve) despite older age
      • reduce non-relapse mortality

How old is “old” for transplant?

• It changes as I get older?
  • >60
    • When prognosis is poor
    • When you use reduced intensity regimen
  • >65
    • Medicare

• Median age of all blood cancers except ALL is around 68-70
• Transplant can be curative in substantial number of patients
Increasing age of patients undergoing allogeneic transplantation

CIBMTR Data

MD Anderson data ≥ 65 Years

Number of Transplants

Transplantation Year

Overall Survival by Age after Transplant with Matched Donors 2010-2015

AGD at SCT
- <40
- 40-60
- ≥70
- ≥70-pancreatic
- ≥70-lung-cancer
- >70-lung-cancer

68%
59%
48%

43%
42%
52%

(totals number =1,545)
**Key Points**

Older patients are most in need, and are increasingly undergoing stem cell transplantation (SCT)

- But Outcomes Need to be Improved

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**When? What determines likelihood of success?**

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-term disease-free survival</td>
<td>Treatment related mortality and morbidity (like chronic GVHD)</td>
</tr>
</tbody>
</table>
Benign or Risk

- Long-term disease-free survival
- Treatment-related mortality and morbidity (like chronic GVHD)

Mortality
Patient Views
Age & Comorbidities
Prognosis
Morbidity
Alternatives

To transplant or not

Benefit
Risk

Other health issues predict for transplant-related mortality

Sorror et al Blood. 2004; 104:961-968

Uday Popat MD
Geriatric Assessment: Predicts for Transplant-Related Mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Population</th>
<th>50-59 Years</th>
<th>60+ Years</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
<td>P</td>
</tr>
<tr>
<td>GA Variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IADL Impairment</td>
<td>2.4</td>
<td>1.6-3.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Slow Walk Speed</td>
<td>1.8</td>
<td>1.1-2.8</td>
<td>.01</td>
</tr>
<tr>
<td>Low Mental Health</td>
<td>1.7</td>
<td>1.1-2.5</td>
<td>.01</td>
</tr>
<tr>
<td>Low Albumin</td>
<td>1.5</td>
<td>.9-2.5</td>
<td>.09</td>
</tr>
<tr>
<td>High CRP</td>
<td>2.6</td>
<td>1.6-4.2</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

IADL = Instrumental activities of daily living  
HR = hazard ratio  
CI = Confidence Interval  
P = P-value  

Muffly L, Haematologica, 2014

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• But Outcomes need to be improved

Factors predicting likelihood of success (prognostic factors)

• Other health concerns at time of transplant (comorbidities)

• Geriatric assessment:
  • ability to plan and do daily activities independently
  • cognitive status (ability to process information)
How do we improve outcomes in older patients?

How do you improve outcomes

Induction → Transplant → Maintenance

Conditioning
Supportive Care
Main Idea

You can reduce toxicity and related mortality of an intense conditioning regimen given before transplant by simply giving it over a longer period of time.

Fractionated* Busulfan (f-bu) Regimen

Even longer, intense, myeloablative schedule of busulfan to reduce toxicity, GVHD and mortality.

*Fractionated means dividing total dosage given to patient into several separate dosages.
## Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>N=78</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range)</td>
<td>61</td>
<td>(39-70)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AML(CR/Cri/Not CR)</td>
<td>19(10/3/6)</td>
<td>24%</td>
</tr>
<tr>
<td>MDS(R-IPSS high/V.High)</td>
<td>21(14)</td>
<td>27%</td>
</tr>
<tr>
<td>MPD (DIPSS Plus Int 2/High)</td>
<td>31(14/11)</td>
<td>40%</td>
</tr>
<tr>
<td>Myeloma/CML/ALL</td>
<td>1/3/3</td>
<td>9%</td>
</tr>
<tr>
<td>Disease Risk Index</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High or Very high</td>
<td>18</td>
<td>23%</td>
</tr>
<tr>
<td>Low/Intermediate</td>
<td>60</td>
<td>77%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>N=78</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Donor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Matched Related</td>
<td>29</td>
<td>37%</td>
</tr>
<tr>
<td>Matched Unrelated</td>
<td>49</td>
<td>63%</td>
</tr>
<tr>
<td>Comorbidity Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>11</td>
<td>14%</td>
</tr>
<tr>
<td>1-2</td>
<td>34</td>
<td>44%</td>
</tr>
<tr>
<td>3 or more</td>
<td>33</td>
<td>42%</td>
</tr>
<tr>
<td>Cell source</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral blood</td>
<td>73</td>
<td>94%</td>
</tr>
</tbody>
</table>

Overall and Progression-Free Survival

1 yr OS 85%, 95% CI: (76%, 94%)
1 yr PFS 81%, 95% CI: (73%, 91%)

Non-Relapse Mortality (NRM) and Relapse

100 day NRM = 4%, 95% CI: (0%, 8%)
1 yr NRM = 8%, 95% CI: (2%, 14%)
1 yr Relapse = 11%, 95% CI: (4%, 19%)
Non-Relapse Mortality by Age

- Age ≤60: 84%, 95% CI: (73%, 96%)
- Age >60: 9.1%, 95% CI: (0.0%, 18.1%)

Overall Survival by Age

- Age ≤60: 85%, 95% CI: (71%, 100%)
- Age >60: 84%, 95% CI: (73%, 96%)

Overall Survival by Comorbidity Score

- Comorbidity Score 0-2: 87%, 95% CI: (77%, 99%)
- Comorbidity Score 3+: 81%, 95% CI: (68%, 96%)

Non-Relapse Mortality by Comorbidity Score

- Comorbidity Score 0-2: 9%, 95% CI: (0%, 19%)
- Comorbidity Score 3+: 7%, 95% CI: (0%, 14%)

P-values:
- Overall Survival by Age: P=0.49
- Non-Relapse Mortality by Age: P=0.61
- Overall Survival by Comorbidity Score: P=0.53
- Non-Relapse Mortality by Comorbidity Score: P=0.71
**Key Points**

Older patients are most in need and are increasingly undergoing SCT
- But Outcomes are inferior

Current standard of Care for Older Patients
- Flu/Mel compared to Flu/Bu
- Low relapse but high NRM with Flu/Mel

Prognostic Factors
- Comorbidity Index
- Geriatric assessment: IADL, Impaired cognition

**How do you improve outcomes in older patients?**
- Better conditioning regimen:
  - ? fractionated busulfan regimen

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**How do you improve Outcomes**

- Induction
- Transplant
- ?Maintenance

- Conditioning
- Supportive Care
How do we further improve outcomes?

Can we redesign a transplant program for older patients, rather than modify what we do for younger patients?

Should We Consider Problems Of Aging?

FIGURE 1 | Relationship among sarcopenia, frailty, and physical function impairment.

Popat et al TCT20 abstract # 65
Enhanced Recovery after Surgery (ERAS) is a multimodal, evidence-based perioperative care pathway developed to improve recovery for patients undergoing major surgery.

**Definition of ERAS**

- **Enhanced Recovery after Surgery (ERAS):** A structured perioperative regimen aimed at improving outcomes and reducing hospital stay.
- **Components of ERAS:**
  - Early nutrition
  - Early mobilization
  - Early pain management
  - Early oral intake
  - Early discharge

**Benefits of ERAS:**

- Reduced length of stay
- Decreased complications
- Improved patient satisfaction

**Challenges of ERAS:**

- Implementation requires a multidisciplinary approach
- Requires significant staff training
- Initial costs

**Conclusion:** ERAS is a comprehensive strategy that has been shown to improve patient outcomes and reduce hospital stay, making it a valuable tool in modern surgery practice.
### Enhanced Recovery Stem Cell Transplant (ER-SCT)

**Goals:**
- Initiate multimodal care early in patients who are 65 or older to
  - Improve physiological reserve
  - Empower patients to participate in their care and well-being
  - Diagnose and optimize chronic medical conditions
  - Improve transplant outcomes

**Program roll-out October 1, 2017 after a year of planning**

**Multidisciplinary Effort**
- Physical Medicine & Rehabilitation physicians, Physical Therapy, Occupational Therapy
- Dietician
- Clinical Pharmacists
- Stem cell transplant advanced practice providers
- Stem cell transplant registered nurses
- Geriatrician
Enhanced Recovery Stem Cell Transplant

Stem Cell Transplant Team

- **Prehabilitation**
  - PM&R/PT/OT
  - Manage mobility concerns/barriers
  - Optimize physical function,
  - Cognition, routines, sleep and fatigue

- **Geriatrics**
  - Comprehensive geriatric assessment
  - Identify and manage Geriatric syndromes
  - Prognostic factors

- **Nutrition**
  - Diagnose & manage malnutrition
  - Maintain adequate nutrition during treatment

- **Pharmacological Management**
  - Clinical Pharmacist
  - Polypharmacy review
  - Optimize meds and fluids

- **Nursing**
  - Inpatient nursing team
  - Delirium Screen
  - Fall Risk
  - Encourage ambulation

Outcomes

- **Patient-Centered Outcomes**
  - Quality of Life
  - Function
  - Satisfaction

- **Survival**
  - Overall survival
  - Progression free survival

- **Clinical Outcomes**
  - Toxicities
  - Relapse
  - Non-relapse mortality

- **Healthcare Utilization**
  - ICU/Rehab unit usage
  - Length of Stay
  - Cost

Inpatient Management: Some interventions

- Motivate and encourage patients to
  - exercise
  - to perform
  - activities of daily living
  - instrumental activities of daily living
  - Initiative to prevent falls and monitor for delirium

- Reduce default fluid rate
- No premeds for blood products
- Curtail opioid use
- Separate order sets for elderly with age-appropriate meds and dose
- Allow regular diet

Popat et al TCT20 abstract # 65
Does it make a difference?  
What is the evidence?

Enhanced Recovery (ER-SCT)  
First Year Experience

Enhanced Recovery Group
- Between 10/1/2017 – 9/30/2018
- 64 patients were eligible
- Age ≥ 65 years
- 57 patients (89%) enrolled into ER-SCT
- All 64 included in this analysis

Control Group
- Between 1/1/15 – 9/30/17
- 140 patients were eligible
- Age ≥ 65 years
- All 140 included
**Patient Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>ER-SCT N=64</th>
<th>Controls N=140</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>26 (41)</td>
<td>53 (38)</td>
<td>0.7</td>
</tr>
<tr>
<td>Male</td>
<td>38 (59)</td>
<td>87 (62)</td>
<td></td>
</tr>
<tr>
<td><strong>Age:</strong> Median &gt;70</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ER-SCT</td>
<td>68 (65-74)</td>
<td>67 (65-79)</td>
<td>0.03</td>
</tr>
<tr>
<td>Controls</td>
<td>12 (19)</td>
<td>24 (17)</td>
<td></td>
</tr>
<tr>
<td><strong>Diagnosis:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AML/MDS</td>
<td>45 (70)</td>
<td>108 (77)</td>
<td>0.5</td>
</tr>
<tr>
<td>ALL</td>
<td>3 (5)</td>
<td>5 (4)</td>
<td></td>
</tr>
<tr>
<td>CML / MPD</td>
<td>10 (16)</td>
<td>16 (11)</td>
<td></td>
</tr>
<tr>
<td>CLL</td>
<td>4 (6)</td>
<td>3 (2)</td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td>2 (3)</td>
<td>4 (3)</td>
<td></td>
</tr>
<tr>
<td>Myeloma</td>
<td>0</td>
<td>2 (1)</td>
<td></td>
</tr>
<tr>
<td>Aplastic Anemia</td>
<td>0</td>
<td>2 (1)</td>
<td></td>
</tr>
</tbody>
</table>

**Prep & GVH prophylaxis**

<table>
<thead>
<tr>
<th>Prep &amp; GVH prophylaxis*</th>
<th>ER-SCT N=64</th>
<th>Controls N=140</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post Cyclophosphamide</td>
<td>17 (27)</td>
<td>18 (13)</td>
<td>0.01</td>
</tr>
<tr>
<td>Fractionated-Busulfan+Flu</td>
<td>28 (44)</td>
<td>17 (12)</td>
<td></td>
</tr>
<tr>
<td>Melphalan+Flu Tacrolimus/Methotrexate</td>
<td>9 (14)</td>
<td>24 (17)</td>
<td></td>
</tr>
<tr>
<td>Melphalan + Fludarabine Busulfan 4 or Other + Flu</td>
<td>9 (14)</td>
<td>80 (57)</td>
<td></td>
</tr>
</tbody>
</table>

*Conditioning Regimen and GVHD prophylaxis
1 additional patient had post-transplant cyclophosphamide and 4 days busulfan in each group

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**Overall Survival**

1 yr OS 74%, 95% CI (62-83)

1 yr OS 53%, 95% CI (45-61)

P = 0.007

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**Non-Relapse Mortality**

1 yr OS 26%, 95% CI (19-33)

1 yr NRM 13%, 95% CI (6-22)

P = 0.03

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Uday Popat MD
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Thank You

Questions?

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