Hematopoietic Cell Transplantation (HCT) & Palliative Care: An Oxymoron?

Kelly Wu, MD
Senior Associate Consultant
Division of General Internal Medicine
Section of Palliative Medicine

Mark R. Litzow, MD
Professor of Medicine
Division of Hematology
Section of Palliative Medicine

Mayo Clinic, Rochester, MN
Oxymoron

- a combination of contradictory or incongruous words
Disclosures

• Nothing to disclose
• No discussion of off-label uses for medications
Grim Reaper?
Objectives

• Define Palliative Medicine

• Discuss the benefits of early integration of Palliative Medicine
Palliative care is specialized medical care for people with serious illnesses. This type of care is focused on providing patients with relief from the symptoms, pain, and stress of a serious illness - whatever the diagnosis. The goal is to improve quality of life for both the patient and the family.
Palliative care is provided by a team of doctors, nurses, and other specialists who work with a patient's other doctors to provide an extra layer of support. Palliative care is appropriate at any age and at any stage in a serious illness, and can be provided together with curative treatment.
Palliative Medicine Definition

- Diagnosis
- Disease Directed Therapy
- Palliative Medicine
- Bereavement Care
- Hospice Benefit
- Death
Palliative Medicine Definition

- Symptom management
- Support
- Start early
Benefits of Early Palliative Care

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early Palliative Care for Patients with Metastatic Non–Small-Cell Lung Cancer


Benefits of Early Palliative Care

• Improved quality of life

• Improved mood

• Prolongation of survival by about 2 months
In Summary

• Palliative Care Provides:
  • Symptom management and Support

• Starting Palliative Care Early:
  • Improved QOL, mood and prolonged survival
How transplanters get through the winter in Minnesota!
Palliative care and SCT together? Really?

- Improvements in high-dose therapies, and increasing success rate
- Better supportive care $\rightarrow$ Better Outcomes
- Though mortality improved, risk still exists
  - Impacted by age, comorbidities, disease genetics
- QOL remains a consideration regardless of outcomes

Objectives

• Define the scope of HCT* & Palliative Care

• Recognize three common post-HCT care trajectories

• Describe how palliative care principles and practices can be incorporated into the practice of hematopoietic cell transplantation

• *I will use the terms HCT and BMT interchangably.
Trends in Transplants by Transplant Type and Recipient Age*
“Transplanters”
- “Here comes the Death Squad.”
- “The palliative care people say ‘In fact, there IS something we can do.’ It’s just not what my patient came here for—to be cured.”
- “A 6% chance is cure is better than a 0% chance for cure.”

“Palliative Care Types”
- “It sure would be nice to see these patients earlier. Like when they could talk. Hard to plan a life review when she’s comatose and has 48 h to live.”
- “Well, what about the 94% who go through living hell in order to benefit that 6%? Shouldn’t they know the odds, and what they’re getting into, because I think some of them would choose differently.”
- “Every transplant program already has a palliative care unit where people go to die. The MICU.”

Appreciating the Survival Statistics
Significant and Rapid Improvement in Survival After Unrelated Donor Hematopoietic Cell Transplantation: Analysis of National Marrow Donor Program Facilitated Transplants from 2000 to 2009

Navneet S Majhail, MD, MS

Medical Director, Health Services Research, National Marrow Donor Program, Minneapolis, MN

Adjunct Associate Professor of Medicine, University of Minnesota, Minneapolis, MN
Study Population

- 15,040 unrelated donor HCT recipients
- Analyses stratified by age and diagnosis

<table>
<thead>
<tr>
<th>Cohort</th>
<th>2000-2004 N</th>
<th>2005-2009 N</th>
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<tr>
<td>Malignant diseases, age &lt;18 yrs</td>
<td>906</td>
<td>1017</td>
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<tr>
<td>Malignant diseases, age 18-59 yrs</td>
<td>3808</td>
<td>5745</td>
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<tr>
<td>Malignant diseases, age ≥60 yrs</td>
<td>412</td>
<td>1783</td>
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<tr>
<td>Non-malignant diseases</td>
<td>476</td>
<td>893</td>
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</table>
Overall Survival, 3-year

- **Malignant diseases, age <18 yrs**
  - 55 (52-58)%
  - 45 (42-48)%
  - P<0.001

- **Malignant diseases, age 18-59 yrs**
  - 42 (41-44)%
  - 35 (33-37)%
  - P<0.001

- **Malignant diseases, age ≥ 60 yrs**
  - 35 (33-37)%
  - 25 (21-30)%
  - P<0.001

- **Non-malignant diseases**
  - 69 (66-72)%
  - 60 (55-64)%
  - P<0.001

Years:
- 2000-2004
- 2005-2009
Treatment Related Mortality, 3-year

Malignant diseases, age <18 yrs

- 2000-2004: 28 (25-31)%
- 2005-2009: 21 (18-23)%

Malignant diseases, age ≥ 60 yrs

- 2000-2004: 34 (30-39)%
- 2005-2009: 31 (29-33)%

Malignant diseases, age 18-59 yrs

- 2000-2004: 37 (35-38)%
- 2005-2009: 28 (27-29)%

P-values:
- Malignant diseases, age <18 yrs: P<0.001
- Malignant diseases, age ≥ 60 yrs: P=0.20
- Malignant diseases, age 18-59 yrs: P<0.001
Relapse, 3-year

Malignant diseases, age <18 yrs

P=0.01

32 (29-36)%

27 (24-30)%

0 6 12 18 24 30 36
Months after transplant

Probability, %

Malignant diseases, age 18-59 yrs

P=0.03

35 (33-36)%

32 (31-34)%

0 6 12 18 24 30 36
Months after transplant

Probability, %

Malignant diseases, age ≥ 60 yrs

P=0.01

46 (41-51)%

39 (37-41)%

0 6 12 18 24 30 36
Months after transplant

Probability, %

2000-2004

2005-2009

25 Years
50,000 Transplants
Projected number of HCT transplant survivors in the United States by year 2030

100-day Mortality after Unrelated Donor Transplants, 2010-2011

- Early Disease
- Advanced Disease
- Accelerated Phase
- Other

- Intermediate Disease
- Chronic Phase
- Blast Phase

Mortality, %

AML | ALL | CML | MDS/MPS | Aplastic Anemia | Immune Deficiency
---|---|---|---|---|---
15 | 10 | 20 | 10 | 10 | 10

CIBMTR
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH
Causes of Death after Transplants Done in 2009-2010

**Unrelated Donor**
- Primary Disease: 37%
- New Malignancy: 1%
- GVHD: 18%
- Infection: 18%
- Other: 18%
- Organ Failure: 8%

**HLA-identical Sibling**
- Primary Disease: 49%
- GVHD: 16%
- Infection: 13%
- Other: 16%
- Organ Failure: 5%
- New Malignancy: 1%

**Autologous**
- Primary Disease: 72%
- New Malignancy: 1%
- Infection: 7%
- Organ Failure: 3%
- Other: 17%
Left Ventricular Assist Device (LVAD)

- Patients can be fully mobile
- Left ventricular assist device (LVAD) connected to heart
- Battery
- A cable connects the external control unit and internal LVAD through a small hole in the abdomen
- Control unit

LVAD pumps blood into the aorta (to the body)

Blood from the left ventricle enters the LVAD

LVAD Cable connecting to control unit

Heart is shown in cross-section
QOL trajectory in LVAD-DT patients—a useful paradigm comparing post BMT outcomes?
Subsequent causes of death for adult (A) allogeneic & (B) autologous SCT recipients who survived w/o recurrent malignancy at least 5 yrs

Syrjala K L et al. JCO 2012;30:3746-3751
Courses “A” and “B”
When things don’t go well or don’t get better after “BMT”

DAY +0
Early Complications (1st month or two)—Curve “A>B”

- Mucositis
- Hemorrhagic cystitis
- Sinusoidal Obstruction Syndrome
- Acute/subacute GVHD
- Renal failure
- Cardiomyopathy and arrhythmia
- Delayed engraftment
  - Transfusion dependence
  - Infection
Clinical grading of acute GVHD

<table>
<thead>
<tr>
<th>Grade</th>
<th>Skin (area affected)</th>
<th>GI (diarrhea L/d)</th>
<th>Liver (bilirubin mg/dL)</th>
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<tbody>
<tr>
<td>I</td>
<td>&lt;25%</td>
<td>&lt;0.5</td>
<td>&lt;3</td>
</tr>
<tr>
<td>II</td>
<td>25%–50%</td>
<td>&lt;1.0</td>
<td>3–6</td>
</tr>
<tr>
<td>III</td>
<td>&gt;50%</td>
<td>&lt;1.5</td>
<td>6–15</td>
</tr>
<tr>
<td>IV</td>
<td>Desquamated bullae, blood loss</td>
<td>Illus, bloody diarrhea</td>
<td>&gt;15 or increased ALT/AST</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Overall grading</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade</td>
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<tr>
<td>-------</td>
</tr>
<tr>
<td>I</td>
</tr>
<tr>
<td>II</td>
</tr>
<tr>
<td>III</td>
</tr>
<tr>
<td>IV</td>
</tr>
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</table>
Effect of acute GVHD on survival after BMT

N=463
LATE COMPLICATIONS (months to years)—Curve “C>B”

- Chronic graft vs host disease
- Endocrine dysfunction (retarded growth, sterility, hypothyroidism)
- Cataracts
- Infections
- Joint damage (aseptic necrosis of bone)
- Dental caries
- Second malignancies
- Psychosocial problems
NIH consensus criteria for chronic GVHD

- cGVHD includes:
  - (1) classic cGVHD (without features of aGVHD)
  - (2) Overlap Syndrome = features of cGVHD & aGVHD appear together
- Other possible diagnoses for clinical sx excluded
- No time limit is set for the diagnosis of chronic GVHD
- ≥ 1 diagnostic clinical sign of cGVHD (morphea) or 1 distinctive (dry eyes) confirmed by Bx or tests (PFT’s)

Filipovich et al. BBMT 2005 Dec;11(12):945-56.
NIH Consensus Conference Revision

- Acute
- Late Acute (15-40%)
- Overlap (20-30%)
- Chronic (40-60%)

Day 0 - Day 100

Stephanie Lee ASH 2008
Jagasia 2007
Cho 2008
Arora 2008
Chronic GVHD

- Major cause of post transplant morbidity and mortality

- Affects 30-70% of allogeneic recipients
  - (Lower risk in related, UCD, children, T cell depleted)

- Median onset 4-6 months, 5-10% diagnosed > 1 year

- Leading cause of non relapse mortality
  - Infection 60-85% deaths

- Major impact on quality of life
Chronic GVHD Clinical Manifestations

- Skin
- Liver
- Gastrointestinal tract
- Lungs
- Vaginal stenosis, thrombocytopenia, sicca syndrome, polymyositis, myasthenia gravis, nephrotic syndrome
<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>AML (N=214)</th>
<th>ALL (N=167)</th>
<th>CML (N=238)</th>
<th>Aplastic Anemia (N=60)</th>
<th>Total (N=679)</th>
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<tbody>
<tr>
<td>Relapse</td>
<td>117 (56)</td>
<td>79 (48)</td>
<td>108 (47)</td>
<td>0</td>
<td>304 (46)</td>
</tr>
<tr>
<td>GVHD</td>
<td>47 (23)</td>
<td>38 (23)</td>
<td>81 (36)</td>
<td>38 (66)</td>
<td>204 (31)</td>
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<tr>
<td>Infection without GVHD</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Bacterial</td>
<td>5</td>
<td>2</td>
<td>5</td>
<td>3</td>
<td>15</td>
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<tr>
<td>Viral</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>8</td>
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<tr>
<td>Fungal</td>
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<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Protozoal</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
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<tr>
<td>Infectious pneumonia†</td>
<td>2</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>7</td>
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<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>New cancer</td>
<td>15 (7)</td>
<td>16 (10)</td>
<td>8 (4)</td>
<td>1 (2)</td>
<td>40 (6)</td>
</tr>
<tr>
<td>Organ failure</td>
<td>11 (5)</td>
<td>14 (9)</td>
<td>10 (4)</td>
<td>5 (9)</td>
<td>40 (6)</td>
</tr>
<tr>
<td>Other‡</td>
<td>7 (3)</td>
<td>10 (6)</td>
<td>7 (3)</td>
<td>7 (12)</td>
<td>31 (5)</td>
</tr>
<tr>
<td>Unknown</td>
<td>6</td>
<td>3</td>
<td>10</td>
<td>2</td>
<td>21</td>
</tr>
</tbody>
</table>
Skin

**Clinical features:**
- Maculopapular rash
- Lichen planus-like features
- Papulosquamous lesions or ichthyosis
- Hyperpigmentation
- Hypopigmentation
- Keratosis pilaris
- Erythema
- Erythroderma
- Poikiloderma
- Sclerotic features
- Pruritus
- Hair involvement
- Nail involvement

<table>
<thead>
<tr>
<th>% BSA involved</th>
<th>No Symptoms</th>
<th>&lt;18% BSA with disease signs but NO sclerotic features</th>
<th>19-50% BSA OR involvement with superficial sclerotic features “not hidebound” (able to pinch)</th>
<th>&gt;50% BSA OR deep sclerotic features “hidebound” (unable to pinch) OR impaired mobility, ulceration or severe pruritus</th>
</tr>
</thead>
</table>
Chronic GVHD
"I always wondered who got my transplant."
How and where does palliative care fit in?
Commonly encountered Palliative Care issues in BMT

- Symptom assessment and management
- Pain control
- Supportive care measures
  - Mucositis
  - Nutritional support
- Nausea, vomiting, and diarrhea
- Need for honest communication about medical prognosis
- Goals of care delineation
Palliative care and symptom palliation

How is palliative medicine practiced?

• Within context of patient’s values and goals
• Outcomes: comfort, QOL and dignity
• Continuous reassessment of patient’s goals
• No specific therapy is excluded
• Multidisciplinary
What does palliative medicine specifically offer?

- Medical decision-making
- Establish goals of care
- Coordinate care
- Manage symptoms
- Psychosocial and spiritual support
- Assure comfort, QOL and dignity

- Prognosis
- Ethics
- Technical assistance
- Active care of dying patients and loved ones
- Bereavement support
Long term care and QOL considerations in BMT patients

- Caregiver misperceptions
- Frequent clinic visits
- Insurance/financial
- Geographical limitations
- Limited local resources
  - Local medical community variably comfortable with post transplant

- Caregiver burnout
- EOL issues
  - Often arise, but when and how to address
  - Palliative care

These considerations emphasize the need for a “preparedness plan.”
80% of childhood cancer patients become long-term survivors

241 survivors at LTFU in S. Korea

The median FU was 7.8 years.

Late effects were identified in 59.8% of survivors and 23.2% had two or more late effects.

Most common late effects – endocrine (29.0%).

Chemotherapy (CTX), Stem cell transplantation (SCT) & radiotherapy (XRT) risk factors
Why establish LTFU for SCT survivors?

- 60,000 HSCT’s year
- Improved supportive care and mortality
- Guidelines Published

Majhail et al. BMT nature 47(3): 337–341; 2012
Late effects

- Cancers
- Cardiac complications
- Pulmonary complications
- Endocrine complications (XRT hypothyroid, DM, hypogonadism)
- Gynecologic complications
- Neurologic complications
- Psychologic complications
- Dyslipidemia (sirolimus)
- Iron overload
- Bone health /MSK (AVN’s, ROM issues)
- Eyes
- Infections
Modus Operandi

GVHD

Disease
Relapse

Functional
psychologic
social
domain
Why engage palliative care earlier?

- Patients may decline more aggressive BMT-based regimen
- Patients who choose BMT may benefit from a “preparedness plan”
  - Aggressive trial of therapy now, with emphasis on palliation later
- Treat symptoms including those associated with adverse events; pain
Barriers to Palliative Care

- “A major barrier to palliative care consultation is the belief that recommendations made by the PCCT may overlap with care that every physician should be able to provide for a patient. However, at this time, physicians with special training in palliative care possess the time, attitudes, knowledge and skills not yet shared by nor available to most physicians and therefore better equipped to handle the very time-consuming and complex interventions required by hospitalized patients with advanced illness.”

Palliative care and SCT together? Really?

- Improvements in high-dose therapies, and increasing success rate
- Better supportive care → Better Outcomes
- Though mortality improved, risk still exists
  - Impacted by age, comorbidities, disease genetics
- QOL remains a consideration regardless of outcomes

CONCLUSIONS

• Outcomes of BMT are improving
• Curative option of BMT available to greater numbers of patients
• Long-term survivors of BMT increasing in number
• Palliative care has much to offer BMT patients in areas of symptom management and preparedness planning
• Palliative care and BMT are not an oxymoron!!
THANK YOU

ANY