Surviving the Cure: Late Effects after a Transplant Using Donor Cells (Allogeneic Transplant)

Celebrating a Second Chance at Life
Survivorship Symposium

April 27 – May 3, 2024

Betty Ky Hamilton MD
Associate Professor of Medicine,
Cleveland Clinic
Overview

• Overview of Survivorship and Late Effects after Transplant

• Recognizing the Burden of Late effects and Patient-Centered Outcomes

• Understanding Late Effects and Need for Survivorship Care and Research

• Approach to survivorship- establishing a long-term care plan
Survivorship after Allogeneic HCT

- By 2030, the number of survivors is estimated to be >500,000


2024 SURVIVORSHIP SYMPOSIUM
Survivorship after Allogeneic HCT- Older Survivors

- The age of transplant recipients continue to increase
- Older patients have more co-morbid health issues, complicating transplant and long-term late effects


2024 SURVIVORSHIP SYMPOSIUM
Late Effects after Transplant

- 66% of survivors report at least one chronic health condition compared to 39% of health siblings
- Life expectancy among 5-year survivors 30% lower compared to the general population (cohort from 1970-2002)

Sun et al. Blood 2010; 116 (17): 3129-3139

2024 SURVIVORSHIP SYMPOSIUM
## Late Effects after HCT

<table>
<thead>
<tr>
<th>Grade 3 or 4 chronic health condition</th>
<th>All survivors, %</th>
<th>Siblings, %</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>6.8</td>
<td>2.6</td>
<td>2.85 (1.37-5.90)</td>
</tr>
<tr>
<td>Auditory/visual impairment</td>
<td>2.8</td>
<td>1.0</td>
<td>2.89 (0.88-9.47)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>2.9</td>
<td>0.7</td>
<td>4.33 (1.03-18.13)</td>
</tr>
<tr>
<td>Endocrine</td>
<td>2.4</td>
<td>1.0</td>
<td>2.36 (0.73-7.61)</td>
</tr>
<tr>
<td>Musculoskeletal problems</td>
<td>3.4</td>
<td>0.7</td>
<td>5.08 (1.23-21.10)</td>
</tr>
</tbody>
</table>
## Late Effects after HCT and Impact of GVHD

<table>
<thead>
<tr>
<th>Grade 3 or 4 chronic health condition</th>
<th>All survivors, %</th>
<th>Siblings, %</th>
<th>RR (95% CI)</th>
<th>Survivors with chronic GVHD (RR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>6.8</td>
<td>2.6</td>
<td>2.85 (1.37-5.90)</td>
<td>2.99 (1.33-6.77)</td>
</tr>
<tr>
<td>Auditory/visual impairment</td>
<td>2.8</td>
<td>1.0</td>
<td>2.89 (0.88-9.47)</td>
<td>3.81 (1.07-13.53)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>2.9</td>
<td>0.7</td>
<td>4.33 (1.03-18.13)</td>
<td>7.70 (1.73-34.28)</td>
</tr>
<tr>
<td>Endocrine</td>
<td>2.4</td>
<td>1.0</td>
<td>2.36 (0.73-7.61)</td>
<td>3.40 (0.94-12.22)</td>
</tr>
<tr>
<td>Musculoskeletal problems</td>
<td>3.4</td>
<td>0.7</td>
<td>5.08 (1.23-21.10)</td>
<td>10.87 (2.47-47.95)</td>
</tr>
</tbody>
</table>
Late Effects after Allogeneic HCT

Years

1 3 5 10 15 20 30+

Transplant

- Acute GVHD
- Chronic GVHD
- Infections
- Disease relapse
- Pulmonary dysfunction
- Cataracts
- Thyroid Dysfunction
- Bone loss
- Cardiovascular Disease
- New malignancies

2024 SURVIVORSHIP SYMPOSIUM

BMT infonet.org
Patient Centered Outcomes and Late Effects

- NIH Late Effects Initiative: Patient Centered Outcomes Working Group

<table>
<thead>
<tr>
<th>Health-Related Quality of Life (HRQOL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Symptoms and Functioning</td>
</tr>
<tr>
<td>Psychological Symptoms and Cognitive Functioning</td>
</tr>
<tr>
<td>Social Functioning and Environmental Domains</td>
</tr>
</tbody>
</table>

- Limited interventions to improve outcomes in long-term survivors
- Lack of consistency in selection of patient-centered outcomes
- Recommend integration of patient-centered outcomes in survivorship care
Patient Centered Outcomes after Allogeneic HCT

• Despite positive perception of quality of life recovery in HCT, many long-term survivors report residual deficits

Survivors with ≥ 3 late effects had lower physical functioning, lower likelihood of full-time work or study, and higher likelihood of limitations on usual activities.
Patient Centered Outcomes and GVHD

• Quality of Life and Graft-versus-Host Disease
  • Depression associated with survival, hospital stay, acute GVHD, chronic GVHD symptoms
  • Chronic GVHD associated with significant symptom burden and quality of life impairments; PROs are predictors of survival

Acute GVHD

Chronic GVHD Symptoms

29.99
P < 0.01

19.75

Depressed
Not depressed

El-Jawahri et al. BBMT 2018; 24: 2285-2292
Impact of GVHD: Living with Chronic GVHD Survey

- Of 137 respondents of a survey who were identified to be potentially employable in the general workforce:

  **Cognitive Disability (score 7-10 “severe”)**
  - Managing personal finances
  - Using a computer
  - Interacting socially with friends/family
  
  **Physical Disability (score 7-10 “severe”)**
  - Personal hygiene
  - Dressing
  - Eating
  - Ability to use restroom
  - Ability to move around house
  - Ability to get around outside of house
  - Preparing meals
  - Shopping
  - Housework

  **47% respondents**

  **Work Disability**
  - Ever taken disability leave because of chronic GVHD
  - Ever left a job because of chronic GVHD

  **62.8% respondents**

  **67.4% respondents**

Hamilton et al. ASH 2021 abstract
Understanding Mechanisms of Late Effects after HCT

PATIENT
Age, Sex, Race/Ethnicity, family history, Lifestyle/health behaviors, genetic susceptibility

Primary disease

Chemo radiation
Conditioning

HCT

GVHD
Immunosuppressive therapy

Immunodeficiency infections (viral)

LATE EFFECTS:
• CV disease
• Subsequent malignancies
• Bone Health
• Renal/Liver
• Sexual Health
• Neurocog
• Psychosocial

Hormonal dysfunction
De novo CV risk factors
Endothelial injury

Accelerated processes
Survivorship Screening and Preventative Practices

Survivorship

International Recommendations for Screening and Preventative Practices for Long-Term Survivors of Transplantation and Cellular Therapy: A 2023 Update

Seth J. Rotz¹,²,* #, Neel S. Bhatt³,* Betty K. Hamilton⁴, Christine Duncan⁴, Mahmoud Aljuri⁵, Yoshiko Atsuta⁶, Kristen Beebe⁷, David Buchbinder⁸, Peggy Burkhardt⁹, Paul A. Carpenter⁷, Naeem Chaudhri¹⁰, Mohamed Elemuarry¹¹, Mahmoud Elsawy¹², Gregory MT Guilcher¹³, Nada Hamad¹⁴, Amado Karduss¹⁵, Zinaida Peric¹⁶, Duncan Purtill¹⁷, Douglas Rizzo¹⁸,¹⁹, Morgani Rodrigues²⁰, Maria Belén Rosales Ostriz²¹, Nina Salooja²², Helene Schoemans²³, Adriana Seber²⁴, Akshay Sharma²⁵, Alok Srivastava²⁶, Susan K Stewart²⁷, K. Scott Baker³, Noreen S Malik²⁸, Richard Ilbueck³⁹

Rotz et al. Transplant Cell Ther. 2024
Survivorship after Allogeneic HCT

ORGAN FUNCTION:
- Cardiovascular disease
- Pulmonary
- Renal/GU
- Gastrointestinal/liver
- Endocrine
- Vision/hearing
- CNS/PNS
- Musculoskeletal
- Sexual health

IMMUNITY/INFECTIONS

SUBSEQUENT MALIGNANT NEOPLASMS

PSYCHOSOCIAL:
- Neurocognitive
- Anxiety
- Depression
- Social isolation
- Return to work
- Financial toxicity

MULTI-DISCIPLINARY COLLABORATION

CHRONIC GHVD

Majhail et al. BBMT 2012: 18(30: 348-371
Rotz et al. Transplant Cell Ther. 2024 Feb 26: S2666-6367.
Sessions Pertaining to Specific Late Effects

• **How to Protect your Skin After Transplant**, Silvina Pugliese MD, *Stanford University*, Saturday April 27, 2:45-3:45 pm

• **New Cancers after Transplants**: *Steps you Can Take to Reduce Your Risk*, Saro Armenian DO, MPH, *City of Hope*, Sunday April 28, 11:00-12:00 pm

• **Protect Your Bones after Transplant or CAR T-cell Therapy**, Sarah Keller MD, *Cleveland Clinic*, Sunday April 28, 2:45-3:45 pm

• **Women’s Sexual Health after Transplant and CAR T-cell Therapy**, Jennifer Vencill, PhD, ABPP, CST, *Mayo Clinic*, Monday April 29, 11:00-12:00 pm

• **Riding the Emotional Roller Coaster of Survival**, Patricia Fank, PsyD and Mooney-Melvin LCSW, *Rush University*, Tuesday April 30, 1:30-2:30 pm

• **Don’t Count Sheep! Learn How to Fall and Stay Asleep**, Rini Fox PhD, MPH, *University of Arizona College of Nursing*, Monday April 29, 1:30-2:30 pm

• **Addressing Cognitive Challenges after Transplant and CAR T-cell Therapy**, Thomas Bergquist PhD, LP, ABPP, *Mayo clinic*, Thursday May 2, 11:00-12:00 pm

• **Living Well after Treatment: Coping with Fatigue**, Erin Costanzo PhD, *UW Health Carbone Cancer Center*, Friday May 3, 11:00-12:00 pm

• **Managing Infections after Transplant and CAR T-cell Therapy**, Erik Dubberke Md, MSPH, *Washington University*, Friday May 3, 11:00-12:00 pm
Survivorship after Allogeneic HCT

ORGAN FUNCTION:
- Cardiovascular disease
- Pulmonary
- Renal/GU
- Gastrointestinal/liver
- Endocrine
- Vision/hearing
- CNS/PNS
- Musculoskeletal
- Sexual health

SUBSEQUENT MALIGNANT NEOPLASMS

PSYCHOSOCIAL:
- Neurocognitive
- Anxiety
- Depression
- Social isolation
- Return to work
- Financial toxicity
- QOL

CHRONIC GHVD

Majhail et al. BBMT 2012: 18(30: 348-371
Rotz et al. Transplant Cell Ther. 2024 Feb 26: S2666-6367.
Cardiovascular Disease and Metabolic Syndrome

• Risk of cardiovascular-related events post transplant increased 2.3-3.7 fold compared to general population

• Metabolic syndrome 31-49% post HCT
  • Obesity
  • Dyslipidemia
  • Insulin resistance/diabetes
  • Hypertension
Risk of Coronary Heart Disease in HCT Survivors

- Allogeneic transplant survivors were at 2.07-fold higher odds of coronary heart disease compared to siblings
- Cardiovascular risk factors (CVRF): diabetes, HTN, dyslipidemia
Other factors important in HCT patients

- Prior exposure to anthracycline chemotherapy
- Chest radiation
- GVHD?
Cardiovascular Disease and Metabolic Syndrome

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>NCEP ATP III Definition for Metabolic Syndrome (≥3 risk factors)</th>
<th>Screening Guidelines</th>
<th>Preventative practice and treatment guidelines</th>
</tr>
</thead>
</table>
| **Weight, height, BMI**      | Waist circumference:                                             | Weight, height and BMI assessment at every clinic visit (at least yearly)            | BMI≥30kg/m², waist circum >40 men or >35 women
|                              | Men: >102 cm (>40 inches)                                       | Waist circumference measurement yearly                                               | Discuss interventions to maintain healthy weight by reducing caloric intake and increasing physical activity.   |
|                              | Women: >88 cm (>35 in)                                          |                                                                                      | -Nutrition consult                                                                                           |
|                              |                                                                  |                                                                                      | -Assess access to facilities for physical activity                                                          |
| **Abnormal cholesterol**     | ≥150 mg/dL or on treatment for elevated levels                   | Lipid profile                                                                        |                                                                                                               |
| **Triglycerides**            |                                                                   | -For high risk patients: (ongoing risk factors: sirolimus, CNI, corticosteroids)      |                                                                                                               |
|                              | Men: <40 mg/dL or on treatment                                   | -repeat evaluation every 3-6 months.                                                 |                                                                                                               |
|                              | Women: <50mg/dL or on treatment                                  | -For patients with elevated cholesterol but not warranting therapy, and/or other risk factors (personal history, family history, history of TBI, hx or current GVHD, use of steroids, repeat evaluation at 6 months, 1 year, and yearly thereafter. |
|                              |                                                                  | -For patients with no risk factors lipid profile every 5 years.                      |                                                                                                               |
| **HDL cholesterol**          |                                                                  |                                                                                      |                                                                                                               |
|                              |                                                                  | -Assess overall cardiovascular risk                                                  | -Statin therapy is first-line treatment for primary prevention of CVD in patients with elevated LDL (≥190mg/dL), those with DM, who are 40-75 years of age, and those at sufficient CV risk; with the goal of achieving reductions in LDL. |
|                              |                                                                  | http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/ according to age group | -Use of fibrate should be considered for TG>500                                                             |

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>NCEP ATP III Definition for Metabolic Syndrome (≥3 risk factors)</th>
<th>Screening Guidelines</th>
<th>Preventative practice and treatment guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure</td>
<td>≥130/≥85 mmHg or on treatment for HTN</td>
<td>BP assessment at every clinic visit</td>
<td>- Elevated BP (120-129/&lt;80 mmHg): Non-pharmacologic treatments</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- at least yearly for patients with normal BP (&lt;120/80 mmHg)</td>
<td>- Stage 1 HTN (BP 130-139/80-89 mmHg): non-pharmacologic therapy, OR if estimated 10-y CVD risk ≥10%, consider BP</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- every 3-6 months for elevated blood pressure (120-129/&lt;80 mmHg)</td>
<td>lowering medication</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Stage 2 HTN (BP ≥140/90 mmHg), pharmacologic therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(thiazide or ACE/ARB if CKD/DM is indicated</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>≥100mg/dL fasting or on treatment for DM</td>
<td>Screening for fasting glucose or HgbA1c</td>
<td>For impaired fasting glucose (glucose 100-126), encourage weight loss and increased physical activity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Repeat evaluation every 3-6 months for patients with abnormal levels or those on</td>
<td>For DM, defined by fasting glucose of ≥126mg/dL, HgbA1c ≥6.5% or random glucose ≥ 200mg/dL; encourage lifestyle</td>
</tr>
<tr>
<td></td>
<td></td>
<td>steroids. For standard risk patients, screen for fasting glucose or HgbA1C every 3</td>
<td>modification as above, and pharmacotherapy (first line metformin, consider SGLT-2 inhibit or GLP-1R), as needed,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>years.</td>
<td>to achieve HgbA1C &lt;7%.</td>
</tr>
</tbody>
</table>

Gaps and Emerging Cardiovascular Research in Cancer Survivorship

- 79 allogeneic HCT survivors
- Coronary heart disease detected in 42% of subjects
- Framingham risk score was less predictive than calcium scores

243 autologous HCT survivors: coronary artery calcium scores predict coronary heart disease and survival

Wu et al. Cancer 2024 Feb 15
Emerging Cardiovascular Research in Cancer Survivorship

Pharmacologic interventions in cancer survivors

Avula et al. JACC Heart Fail 2024 Jan; 12(1): 67-78
Neilan et al. JAMA 2023 Aug 8; 330(6): 528-536
Song et al. BMC Cancer 2022 Jul 19; 22(1):795
Late Effects/Second Cancers after HCT

Cumulative Incidence (95% CI) at 20 years post-HCT:

- > 50 years old: 23.6% (18.4%, 28.8%)
- 20-50 years old: 13.5% (11.8%, 15.2%)
- < 20 years old: 8.1% (6.1%, 10.1%)

No. at risk

- > 50 years old: 1059 500 216 85 28 5
- 20-50 years old: 2684 1784 1330 888 509 211 58 7
- < 20 years old: 1162 753 575 449 352 201 98 29


2024 SURVIVORSHIP SYMPOSIUM
Subsequent Malignancies after Allogeneic HCT

INCIDENCE AFTER HCT:
- Skin cancer
  - Any skin SIR 7.2
  - Melanoma SIR 1.4-8.3
- Oral cavity cancer SIR 7.3-17
- Thyroid cancer SIR 5.8-6.6
- Esophageal cancer SIR 8.5-11
- Liver cancer SIR 6.3-28

## Subsequent Malignancies after Allogeneic HCT

<table>
<thead>
<tr>
<th>Site</th>
<th>Risk Factors</th>
<th>Screening and Prevention Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin (SCC and BCC, melanoma)</td>
<td>Acute and Chronic GVHD, Myeloablative TBI, HCT at age &lt;18, White, T-cell depletion</td>
<td>Routine skin examination (at least annually), dermatology consult for suspicious lesions, Sunscreen use</td>
</tr>
<tr>
<td>Thyroid</td>
<td>TBI, female, HCT at age &lt;20, chronic GVHD</td>
<td>Annual exam</td>
</tr>
</tbody>
</table>
| Oropharyngeal             | Chronic GVHD, prolonged immunosuppressive therapy (>24 mos), history of localized field irradiation, HCT at age <10, male, tobacco use, HPV status | **Screening every 6-12 months** depending on risk factors  
**Dental exam every 6 months.**  
Cessation of tobacco product use  
**HPV vaccination as indicated** |
| Esophageal                | Chronic GVHD, prolonged immunosuppressive therapy (>24 mos)                                            | No specific guidelines for screening, but symptom based: upper GI endoscopy for patients with persistent GERD or dysphagia symptoms. |
| Liver                     | TBI, HCT at younger age (<34 years), liver cirrhosis, chronic hepatitis C infection                     | No specific guidelines for screening those at low risk.  
For those with cirrhosis or chronic hepatitis, consider AFP and U/S every 6-12 months |

# Subsequent Malignancies after Allogeneic HCT

<table>
<thead>
<tr>
<th>Site</th>
<th>Risk Factors</th>
<th>Screening and Prevention Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>Tobacco use</td>
<td>Screening with low-dose CT considered for high risk groups only:</td>
</tr>
<tr>
<td></td>
<td>- &gt;55 years and ≥30 pack-year smoking history (excluding those who quit smoking &gt;15 years ago)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- ≥50 and ≥20 pack-year smoking history with additional risk factor (asbestos, family history, second hand smoke)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Encourage smoking cessation</td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>TBI, HCT at age &lt;18, localized field radiation, use of growth factors, ATG, family history</td>
<td>Age 20-40: annual breast exam</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Age &gt;40: annual breast exam and annual mammography</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Age 25 or 8 years after XRT (whichever first): annual breast exam, annual mammogram, annual breast MRI</td>
</tr>
<tr>
<td>Cervical</td>
<td>Chronic GVHD, prolonged systemic immunosuppressive therapy, age &gt;34 years</td>
<td>HPV vaccination as indicated</td>
</tr>
<tr>
<td>Gastrointestinal (stomach/colorectal)</td>
<td>None reported</td>
<td>Stomach- no specific guidelines but symptom based: upper GI endoscopy for symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Colorectal-Starting at ≥50 years of age (average risk)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sigmoidoscopy: every 5 years +/- stool testing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Colonoscopy: every 10 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Guiac-based: annually or Cologuard: every 3 years</td>
</tr>
</tbody>
</table>

**New Cancers after Transplants: Steps you Can Take to Reduce Your Risk**, Saro Armenian DO, MPH, *City of Hope*, Sunday April 28, 11:00-12:00 pm
Immunity and Late Infections after Allogeneic HCT

• In a study of 72 patients surviving 20-30 years after HCT, similar levels of antibodies. Overall, immunity in long-term survivors normal/near normal.

• However, in adult and pediatric HCT recipients surviving 2-years, post HCT late fatal infection contributed to one-third of all deaths
  • Older age
  • Chronic GVHD on immunosuppression
  • Unrelated donors

• Vaccine preventable infections occurred in 7% of patients

Norkin et al. BBMT 2019 Feb; 25(2):362-368
## Infection/Immunity: Vaccine Preventable Diseases after Allogeneic HCT

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>3 months</th>
<th>6 months</th>
<th>8 months</th>
<th>10 months</th>
<th>12 months</th>
<th>24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td></td>
<td></td>
<td></td>
<td>X (cGVHD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human Papilloma Virus (HPV)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X (&lt;26 yrs)</td>
<td></td>
</tr>
<tr>
<td>Hepatitis A and B</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polio</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetanus/diptheria</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningococcus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shingles (Shingrix)</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>MMR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X (off IS)</td>
</tr>
<tr>
<td>Varicella (Varivax)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X (off IS)</td>
</tr>
<tr>
<td>Influenza</td>
<td>X (annually)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COVID</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RSV</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Bone Health after Allogeneic HCT

- Osteoporosis or low bone mineral mass occurs in 50-75% of patients after HCT.
- Bone loss and fracture manifest as pain and loss of function and have a significant negative impact on quality of life.
- The majority of bone loss occurs within 3-6 months after transplant.
- Risk factors: age, female sex, hypogonadism, nutritional deficiencies, lack of physical activity, liver/kidney disease, glucocorticoid exposure.

Bar et al. BBMT 2020; 26: 1784-1802
Bone Health after Allogeneic HCT

Pre-HCT assessment of risk factors
- Prior/current steroid use
- Vitamin D/Ca levels
- DXA scan

Calcium/Vit D
Consider pharmacologic interventions?

Day 100

1 year+

Protect Your Bones after Transplant or CAR T-cell Therapy, Sarah Keller MD, Cleveland Clinic, Sunday April 28, 2:45-3:45 pm

Higher risk patients:
- History of fragility factor
- T score -1.0 to -2.5 & FRAX risk MOP ≥20%, hip >3%
- T score < -2.5 osteoporosis
- Use of glucocorticoids for GVHD

Therapy:
- Antiresorptives (Bisphosphonates/denosumab)
- Hormonal therapy
- Parathyroid hormone receptor

Ongoing evaluation (yearly)
DXA every 1-2 years

Adapted from Bar et al. BBMT 2020; 26: 1784-1802

2024 SURVIVORSHIP SYMPOSIUM
Adverse psychological outcomes after Allogeneic HCT

- Psychological health status was assessed among long-term HCT survivors and their siblings
- Exposure to prednisone was associated with psychological distress
- Low household income and self-reported poor health, active chronic GVHD associated with 2-fold increase of somatic distress

Sun et al. Blood 2011; 118(17): 4723-4731
<table>
<thead>
<tr>
<th>Late effect</th>
<th>Symptoms</th>
<th>Risk Factors</th>
<th>Screening</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothyroid</td>
<td>Fatigue, dry skin, weight gain, depression</td>
<td>Radiation, chemotherapy</td>
<td>Annual thyroid hormone levels (TSH, T4)</td>
<td>Thyroid hormone replacement</td>
</tr>
<tr>
<td>Hypogonadism</td>
<td>Low libido, fatigue, vaginal dryness/pain, erectile dysfunction, infertility</td>
<td>High dose radiation, chemotherapy</td>
<td>Estradiol, FSH, LH, testosterone</td>
<td>Hormone replacement (if safe), referral to gyn/urology</td>
</tr>
<tr>
<td>Iron overload</td>
<td>Abdominal pain, organ dysfunction, musculoskeletal pain</td>
<td>Frequent blood transfusions</td>
<td>Ferritin, transferritin saturation, MRI</td>
<td>Iron chelation, phlebotomy</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>Numbness, tingling, burning, cold/sensitivity</td>
<td>Chemotherapy, neurotoxic medications, diabetes</td>
<td>Clinical assessment, treatment of underlying disorders</td>
<td>Treatment of underlying disorders, (non)-pharmacologic therapies (gabapentin, “scrambler”)</td>
</tr>
</tbody>
</table>
### Other Late Effects after Allogeneic HCT

<table>
<thead>
<tr>
<th>Late effect</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurocognitive dysfunction</td>
<td><strong>Women’s Sexual Health after Transplant and CAR T-cell Therapy</strong>, Jennifer Vencill, PhD, ABPP, CST, <em>Mayo Clinic</em>, Monday April 29, 11:00-12:00 pm</td>
</tr>
<tr>
<td></td>
<td><strong>Riding the Emotional Roller Coaster of Survival</strong>, Patricia Fank, PsyD and Mooney-Melvin LCSW, <em>Rush University</em>, Tuesday April 30, 1:30-2:30 pm</td>
</tr>
<tr>
<td>Muscle cramping</td>
<td><strong>Don’t Count Sheep! Learn How to Fall and Stay Asleep</strong>, Rini Fox PhD, MPH, <em>University of Arizona College of Nursing</em>, Monday April 29, 1:30-2:30 pm</td>
</tr>
<tr>
<td>Fatigue</td>
<td><strong>Addressing Cognitive Challenges after Transplant and CAR T-cell Therapy</strong>, Thomas Bergquist PhD, LP, ABPP, <em>Mayo clinic</em>, Thursday May 2, 11:00-12:00 pm</td>
</tr>
<tr>
<td></td>
<td><strong>Living Well after Treatment: Coping with Fatigue</strong>, Erin Costanzo PhD, <em>UW Health Carbone Cancer Center</em>, Friday May 3, 11:00-12:00 pm</td>
</tr>
<tr>
<td>Anxiety/Depression</td>
<td>Address reversible contributors (depression, poor sleep, medications), cognitive rehab, modafinil, methylphenidate</td>
</tr>
<tr>
<td></td>
<td>Hydration, treat electrolyte abnormalities, magnesium, stretching, quinine</td>
</tr>
<tr>
<td></td>
<td>Treat underlying abnormalities, exercise, referral to pall med/support onc</td>
</tr>
<tr>
<td></td>
<td>Referral to behavioral health, pharmacologic and non-pharmacologic intervention</td>
</tr>
</tbody>
</table>
Health care utilization after Allogeneic HCT

(A) Prevalence among BMT survivors

- Routine checkups
- BMT-related visits
- BMT/cancer center visits

(B) Prevalence among BMT survivors

- Emergency room visits
- Hospitalizations
- High health care utilization

Oliver et al. Cancer. 2024 mar 1; 130(5): 803-815
Health Maintenance after Allogeneic HCT

- Pre-HCT, 75-80% of patients had at least 1 annual visit with PCP
- By the 5th year post-HCT, 36% of survivors did not visit PCP
- Routine health screening rates are LOW

Fulcher et al. Transplant Cell Ther. 2023; 29:131. e1-e6
Risky Health Behaviors and Subsequent Late Mortality

Smoking and mortality risk

Heavy alcohol and mortality risk

Activity level and mortality risk

*Balas et al. Blood Adv 2023 Nov 28; 7(22):7028-2044*
Survivorship after Allogeneic HCT
Survivorship after Allogeneic HCT

Follow-up Care Plan

<table>
<thead>
<tr>
<th>Follow-Up Item</th>
<th>How Often</th>
<th>Who's Responsible</th>
<th>Due Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunizations</td>
<td>6 months, 8 months, 10 months, 12 months, 24 months post-allo-HCT</td>
<td>Infectious Disease or Primary Care Provider</td>
<td>12 month vaccines due ~11/25/23. MMR booster 10/2024. New mRNA COVID-19 vaccine.</td>
</tr>
<tr>
<td>Oral/Dental Care</td>
<td>Yearly</td>
<td>Ophthalmology</td>
<td>4/2024</td>
</tr>
<tr>
<td>Lung health-pulmonary function tests</td>
<td>Every 6 months</td>
<td>Local Dentist</td>
<td>Every 6 months</td>
</tr>
<tr>
<td>Bone health + bone density scan</td>
<td>Every 2 years</td>
<td>Primary Care Provider or BMT program</td>
<td>9/2025</td>
</tr>
<tr>
<td>Liver health</td>
<td>Each visit</td>
<td>BMT program</td>
<td>Each visit</td>
</tr>
<tr>
<td>Kidney health</td>
<td>Each visit</td>
<td>BMT program</td>
<td>Each visit</td>
</tr>
<tr>
<td>Endocrine health-TSH HgbA1c</td>
<td>Yearly</td>
<td>Primary Care Provider or BMT program</td>
<td>TSH- per primary care A1c 09/2023</td>
</tr>
<tr>
<td>Cardiovascular health-blood pressures, lipid panel, fasting glucose, height and weight, abdominal girth</td>
<td>Every 6-12 months</td>
<td>Primary Care Provider or BMT program</td>
<td>Fasting labs: 10/2024</td>
</tr>
</tbody>
</table>

- Physical function (2 min walk test, Get up and Go)
- Cognitive screen
- DXA scan, Ca, Vit D
- Height, weight, BMI

Pre-HCT “Survivorship” assessment

Day 100
Survivorship Assessment
Treatment Summary and Care plan

1 year
Survivorship Assessment
Treatment Summary and Care plan

2, 5, 10, 15 year
Every other year if GVHD

LATE EFFECTS
- ORGAN FXN
  - CV disease
  - Bone health
  - Renal/liver

SUBSEQUENT NEOPLASM

IMMUNODEFICIENCY

PSYCHOSOCIAL

Pre-transplant organ and psychosocial assessment

HCT
Resources: Return to Work/School

Returning to work:
- anthonynolan.org/patients-and-families/recovery-life/returning-work

Employment and Financial Health:
- bmtinfonet.org/transplant-article/employment-and-financial-health

Going back to school:
- bethematch.org/patients-and-families/transplant-for-children-and-teens-going-back-to-school/
- anthonynolan.org/patients-and-families/recovery-life/returning-education

Transition of Care
- gottransition.org

NMDP survivorship registry:
- bethematch.org/tcdirectory/search/advanced

Financial, psycho-social support, and evidence-based discussions on medical/health concerns in HCT patients:
- bmtinfonet.org
- my.bethematch.org
- stupidcancer.org
- hope4yawc.org
- cactuscancer.org
- blog.youngsurvival.org
- www.thesamfund.org
Resources for Patient/Partner Peer Support

Financial Toxicity:
• triagecancer.org/
• cancer.gov/about-cancer/managing-care/track-care-costs/financial-toxicity-pdq

Vocational support:
• cancerandcareers.org/en

Patient support from healthcare professional organizations:
• nccn.org/patientresources/patient-resources
• cancer.net/navigating-cancer-care

Peer support organizations:
• bmtinfonet.org/caring-connection
• nbmtlink.org/

Peer support podcasts:
• marrowmasters.simplecast.com/
Survivorship after Allogeneic HCT Summary

- The number of hematopoietic cell transplant survivors continues to increase.
- There is a significant burden of late effects, including organ dysfunction, second cancers, and a variety of psychosocial effects.
- Active research ongoing to better understand and intervene on late effects.
- Survivorship care begins early and should take a patient-centered approach.
Questions?

Betty Ky Hamilton MD
Associate Professor of Medicine,
Cleveland Clinic
Let Us Know How We Can Help You

Visit our website: bmtinfonet.org

Email us: help@bmtinfonet.org

Phone: 888-597-7674 or 847-433-3313

Find us on:

Facebook, facebook.com/bmtinfonet

X, twitter.com/BMTInfoNet