

Hematopoietic Stem Cell Treatment Survivorship:

Assessing Functional Outcomes

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No Disclosures

Topics:

State of the science for assessing functional impairments after transplant:

- What functions impact disability
- What to assess for which functional outcomes

Transplant Survivorship Challenges

Organ Function

Cardiac
Endocrine
Musculoskeletal
Genitourinary
GI/Hepatic
Neurologic
Pulmonary



Subsequent Malignancies

Recurrent cancer
New cancers

Sexuality & Reproduction

Fertility
Health of offspring
Sexual functioning

Physical & Psychosocial Function

Physical/health limitations
Mental health
Employment
Education
Social network/support
Chronic symptoms:
 Fatigue, Cognition,
 Insomnia, Neuropathy
Lifestyle

Environment & Finances

Family / Caregiver function
Access to health & resources
Insurance
Financial toxicity

Impaired Long-Term Functional Outcomes

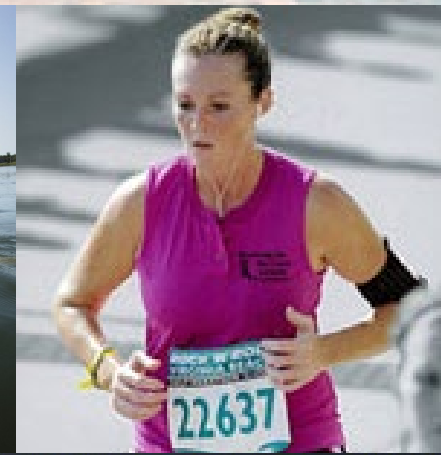
Bevans, *BBMT*, 2017, 23:538

High rates and impacts (but no practice standards in transplant) *

** % represents maximum prevalence across multiple studies*

- Physical dysfunction 35%
 - Physical inactivity 85%
- Sleep disruption 51%
- Emotional distress (anxiety, depression, PTSD symptoms) 43%
- Fatigue 42%
- Cognitive dysfunction 40%
- No Return to Work 40%
- Positive Change: Resilience, Personal Growth 85%

Bishop, *Psycho-Onc*, 2011, 20:926



Survivorship

Is INDIVIDUAL:
Where are the problems,
the pace of recovery,
recovery goals



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Functional Outcomes: What impacts disability

1. Return to Work

- Full return to work takes up to 3 years

Kirchhoff, *J Cancer Surviv.* 2010, 4(1):33; Bhatt, *Transplant Cell Ther.* 2021, 27(8):679

2. Physical Function

- Recovery to pre-transplant takes a year; At 10 years adults remain with lower function than controls

Syrjala, *JAMA*, 2004, 291(19):2335; Syrjala, *J Clin Oncol* 2005, 23(27):6596

3. Cognitive Function

- Recovery to pretransplant can take 2-5 years
- More subtle 'real-world' function more difficult to measure (multitasking, distractibility)

Syrjala, *J Clin Oncol.* 2011, 29(17):2397

4. Emotional Function

- Recovery takes 2 years; At 10 years, continue poorer mental health and greater use of psych meds than controls

Syrjala, *JAMA*, 2004, 291:2335; Syrjala, *J Clin Oncol* 2005, 23:6596

5. Support Network, Social Support

- Social support or isolation is associated with health outcomes

Nørskov, *J Cancer Surviv.* 2021, 15(6):866-875; Amonoo, *Cancer.* 2021, 127(8):1260-1265

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What to Assess: Types of measures

Sources of information

1. Patient Reported Outcomes (PRO)
2. Physical Performance functional tests
3. Lab-based tests, exams
4. Medical records
 - Question reliability, validity: Who is entering the information, What is their focus/priority?

Types of measures: PRO

Patient Reported Outcomes Need to Be: widely used, reliable, validated in survivors, sensitive, specific, with norms & cut points

➤ Online assessments can be completed successfully by 90%+ of HCT survivors

Shaw, *Cancer*, 2017, 123(23):4687

Wood, *BBMT*, 2013, 19(3):450

Global physical function and mental function

PROMIS system, 10 items (NIH developed, free)

Shaw BE. *Cancer*, 2018, 15:124(4):841

SF-12, 12 items (early version free, now has fee)

Health-related quality of life: Measuring multiple functions and symptoms

PROMIS: separate scales such as physical function

PRO CTCAE: developed at NIH as companion to the MD rated CTCAE toxicity ratings

SF-36

EORTC QLQ-C30

FACT (FACIT.org)

Types of measures: PRO

Depression

PHQ-9 (or PHQ-8 or PHQ-2): clinical cut point using diagnostic criteria, 9,8, or 2 items

PROMIS empirical testing rather than diagnostic symptom or theory-based

Others: HADS, Beck Depression Inventory (BDI), SCL-90-R, CESD

Anxiety

GAD-7 (Generalized Anxiety Disorder -7): clinical cut point using diagnostic criteria

PROMIS

Post-traumatic Stress Disorder

PCL-5, PCL-C: clinical cut point using diagnostic criteria, PCL-5 has 20 items

PC-PTSD-5: 5 item screener

uncertainty



On the edge

Loss of CONTROL

Fear of Recurrence

STRESS



WORRY

Types of measures: PRO

Distress

Distress Thermometer

Brief Symptom Inventory

Cancer and Treatment Distress (CTXD): Developed in HCT
6 subscales, sensitive for
clinical depression, anxiety, PTSD symptoms
Cut point for elevated distress
Value for associations with QOL and
functional outcomes

Syrjala, *Cancer* 2017, 123(8):1416-1423

Syrjala, *Psychoonc*, 2016, 25(5):529

McGregor, *Brain Behav Immun*. 2013, 30:S142

Kuba, *Psychoonc*, 2017 26(8):1164

Liang, *BBMT*, 2019, 25(1):145

Types of measures: PRO

Distress

Distress Thermometer

Brief Symptom Inventory

Cancer and Treatment Distress (CTXD):

- Uncertainty
Not knowing what the future will bring
Thinking about the possibility of recurrence.
- Health Burden
Not being able to do what I used to do
Feeling tired or worn out
- Family Strain
Wondering about the emotional toll on my family
Being a burden
- Identity / Appearance
Changes in my appearance
Changes in my sex life
- Managing Medical System
Dealing with the medical system
Getting information when I need it
- Finances
The cost of my health care
Wondering how to support myself and my family

Types of measures: PRO

Work, Disability – associated with physical & mental limitations, comorbidities, future illness (but no data in HCT)

1. Work Productivity and Activity Impairment Questionnaire (WPAI)
2. Work Limitations Questionnaire (WLQ)
3. WHO Health and Performance Questionnaire (HPQ)

Assess:

- Absenteeism
- Presenteeism (being at work but not productive)
- Physical and mental impairment
- Activity limitations
- Participation restrictions

Kamal, *J Manag Care Spec Pharm.* 2017, 23(2):136

Prasad, *PharmacoEconomics*, 2004, 22, 225

Ah, *J Cancer Surviv*, 2018, 12(2):246

<https://www.cdc.gov/ncbddd/disabilityandhealth/disability.html>

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Types of measures: Physical Function Testing

Physical Performance tests

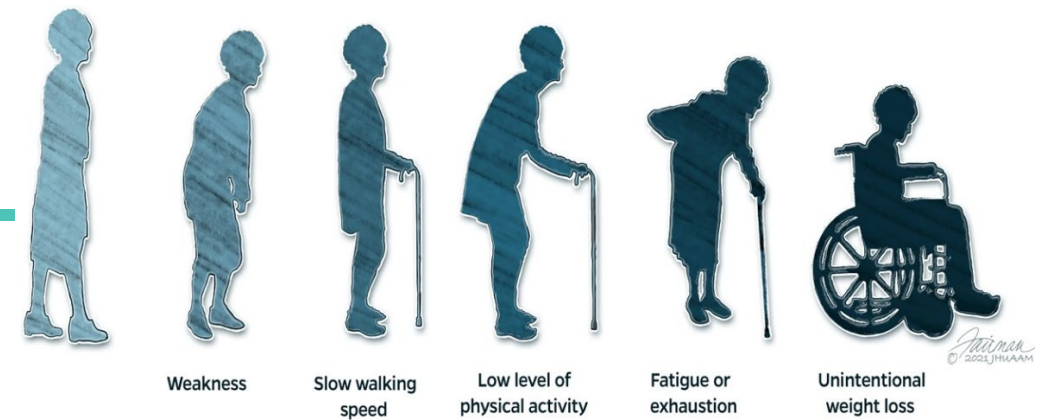
- 6 Minute Walk (or self-report of slow walking)
- 1 Rep Max strength test
- Hand dynamometer (grip strength) or self-report of weakness
- Treadmill stress testing with VO_{2max} (aerobic capacity)

Physical Activity and other health behaviors

- PRO reports
- Real-time measures:
Accelerometer, pedometer, other wearables and sensors



Frailty Phenotype



Frailty: 'Accelerated Aging'

1. Low muscle mass (sarcopenia by DXA or CT, low body mass index)
2. Low energy expenditure (inactivity)
3. Slow walking speed (6 min walk, difficulty with stair climb or walking a block)
4. Weakness (1 rep max or hand dynamometer grip strength)
5. "Exhaustion"

✓ Ideally assessed by physical performance testing but often done with PRO

➤ 8.4% of young adults, median of 8 years after HCT *Arora, JAMA Onc, 2016; 2: 1277*

7% in pediatric 10-year+ survivors *Eissa, Blood Adv, 2017; 1: 2243*

➤ After HCT, frail survivors have more chronic conditions, increase mortality risk

Ness, Transl Res. 2020, 221: 65

Ness, J Clin Oncol, 2013, 31(36):4496

Fried, Gerontol A Biol Sci Med Sci. 2001, 56(3):146

Arora, JAMA Oncol. 2016, 2(10): 1277

Arora, Cancer, 2021, 127(5):794

Types of measures: Cognition and Sleep Testing

Cognitive function

- MoCA (Montreal Cognitive Assessment) screening tool (not very sensitive)
- After 1 year: full or abbreviated neuropsychological testing
- PRO is more strongly associated with mental health tests rather than neuropsychological testing results

Sleep

- Pittsburgh Sleep Quality Index (PRO)
- Wearables (need evidence on how to interpret results: validity and reliability relative to impact of insomnia on function)

Hoogland, J Pain Symptom Manage, 2019, 57(5):952

- Sleep Study testing, including sleep apnea: Gold Standard

Types of measures: Lab or Exam

Lab-based tests or clinical exams

- Blood tests; can do home-based patient self-testing
- Lab or home-based portable testing devices: spirometry, blood pressure, glucose monitors, etc.
Turner, Transplant Cell Ther. 2021, 27(7);616; Chang, BBMT, 26(6):1233
- Bone density and body compositions: DXA (dual-energy x-ray absorptiometry) or CT scans for bone loss, muscle loss (sarcopenia), central adiposity/obesity



Types of measures: Lab or Exam



Aggregating tests can better indicate risk for mortality, physical disability, or cardiovascular events:

Metabolic Syndrome: elevated blood pressure, glucose, triglycerides, low HDL cholesterol, central adiposity (abdominal obesity)

- 38% in 2+ year survivors

- Predicts CARDIOVASCULAR EVENTS

Greenfield, *BMT*, 2021, 56(11):2820

Sarcopenic Obesity: low muscle body mass with large fat mass (component of frailty)

- After HCT, obesity based on fat mass often occurs without body mass index being overweight

- Pre-HCT sarcopenia seen in 34-55%, increases to 42-76% at 2.5 years

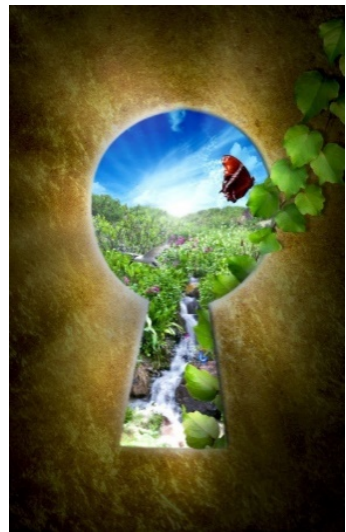
- Predicts SURVIVAL

Armenian, *JNCI*, 2019, 111:8,231; DeFillip, *BBMT*. 2018, 24(8):1741

KEY POINTS in Assessing Functional Outcomes



1. Functional outcomes measured by PRO, tests, scans or exams are closely tied to comorbidity syndromes of frailty, metabolic syndrome and sarcopenic obesity
2. Outcomes are interrelated: mental (emotional and cognitive) function predicts and is predicted by physical function outcomes
3. These outcomes impact work performance and disability
 - Flexibility and accommodation in work environment, can improve work success by removing barriers to function
4. Poor functional outcomes predict later illness, disability, mortality
Warrant our attention, routine assessment and intervention!



Thank You!
