Metabolic Syndrome and Cardiovascular Risk in Long-Term Cancer Survivors

Samantha Burns Artherholt1,2
Karen L. Syrjala2,3, Jean C. Yi2,
Mary E.D. Flowers2,4, Paul J. Martin2,4

1School of Public Health and Community Medicine, University of Washington
2Clinical Research Division, Fred Hutchinson Cancer Research Center
3Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine
4Department of Medicine, University of Washington School of Medicine
Acknowledgements

- Supported by grants from
  - National Cancer Institute (CA112361 and CA092408)
  - National Cancer Institute/National Institute on Aging P20 (CA103728)
- Dr. Karen Syrjala
- Survivors who participated in this research
- All contributors
Background

• Late medical effects after systemic treatment vary widely, as documented in cross-sectional surveys of cancer survivors.

• Little research has investigated the prevalence or characteristics of late cardiovascular effects of high dose chemotherapy and hematopoietic stem cell transplantation (HSCT) for malignancies using standardized, objective tests.
Metabolic Syndrome

- A constellation of risk variables
  - Hypertension (BP ≥ 130/85 mm Hg)
  - Hyperlipidemia (HDL < 40 or 50 mg/dL, triglycerides ≥ 150 mg/dL)
  - Abdominal obesity (waist circumference > 102 or 88 cm)
  - Insulin resistance (fasting glucose ≥ 100 mg/dL)
- Metabolic syndrome increases risk of cardiovascular disease and diabetes
- Prevalence typically increases with age
- Rates of metabolic syndrome in long-term cancer survivors are not well-defined
Method: Participants

- All locally residing HSCT survivors who met eligibility criteria for screening were approached and screened by phone
- Eligible survivors completed on-site physiological testing at the Hutchinson Center
Participants

• Inclusion criteria
  – 5-20 years post-transplant for hematologic malignancy
  – Current age 18-49
  – Able to travel to the Hutchinson Center
  – Able to walk without assistance or aids

• Exclusion criteria
  – Relapse of cancer post-transplant or second cancer
  – Hepatitis C, HIV or AIDS
  – Pulmonary disease or emphysema
  – Arthritis, muscle, joint, or nerve disease
  – Autoimmune disease
  – On immunosuppressive medications
  – Diabetes requiring insulin
  – Uncontrolled cardiovascular disease or cardiac problems
  – Thyroid or electrolyte imbalance not controlled with medication
  – Smoking, alcohol >2/day, or recreational drug use
  – Physician advice not to exercise
  – Unable to read and understand English
Flow Diagram

190 Met initial eligibility criteria and contacted

162 Completed Screening

28 Active or passive refusal

18 Ineligible

57 Enrolled in onsite testing and patient reported outcomes (PRO)

87 Ineligible for onsite testing, enrolled in PRO only
Method: Procedure

• **Physiological tests** included:
  – Blood pressure
  – Lipid panel
  – Waist circumference
  – Blood glucose level
  – C-reactive protein (CRP)
  – DXA scan for body fat percent

• Participants paid $100
### Demographic Characteristics of Survivors (N=57)

<table>
<thead>
<tr>
<th>Category</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, M ± SD</td>
<td>39.6 ± 9.2</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>31 (54%)</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
</tr>
<tr>
<td>Not Hispanic or Latino</td>
<td>53 (93%)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>49 (85%)</td>
</tr>
<tr>
<td>Educational status, n (%)</td>
<td></td>
</tr>
<tr>
<td>High school degree/GED only</td>
<td>7 (9%)</td>
</tr>
<tr>
<td>Family income, n (%)</td>
<td></td>
</tr>
<tr>
<td>&lt;$40,000</td>
<td>13 (23%)</td>
</tr>
<tr>
<td>&gt;$80,000</td>
<td>31 (54%)</td>
</tr>
<tr>
<td>Marital status, n (%)</td>
<td></td>
</tr>
<tr>
<td>Married/living with a partner</td>
<td>38 (67%)</td>
</tr>
</tbody>
</table>
Clinical Characteristics of Survivors (N=57)

Diagnosis, n (%)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Myeloid Leukemia</td>
<td>19</td>
<td>33%</td>
</tr>
<tr>
<td>Acute Lymphocytic Leukemia</td>
<td>7</td>
<td>12%</td>
</tr>
<tr>
<td>Acute Myeloid Leukemia</td>
<td>6</td>
<td>11%</td>
</tr>
<tr>
<td>Hodgkin Disease</td>
<td>6</td>
<td>11%</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>5</td>
<td>9%</td>
</tr>
<tr>
<td>Myelodysplastic Syndrome</td>
<td>5</td>
<td>9%</td>
</tr>
<tr>
<td>Other</td>
<td>9</td>
<td>15%</td>
</tr>
</tbody>
</table>

Type of transplant, n (%)

<table>
<thead>
<tr>
<th>Type of transplant</th>
<th>n</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allogeneic</td>
<td>45</td>
<td>79%</td>
</tr>
<tr>
<td>Autologous</td>
<td>12</td>
<td>21%</td>
</tr>
</tbody>
</table>

Age at transplant, M ± SD

<table>
<thead>
<tr>
<th>Age at transplant</th>
<th>M ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>28.1</td>
<td>10.7</td>
</tr>
</tbody>
</table>

Years since transplant, M ± SD

<table>
<thead>
<tr>
<th>Years since transplant</th>
<th>M ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.5</td>
<td>4.2</td>
</tr>
</tbody>
</table>
Results
Survivors with high BP (systolic $\geq 130$, diastolic $\geq 85$)
Hyperlipidemia: HDL

Survivors with low HDL (<40 for males, <50 for females)

NHANES 26%

18%
Hyperlipidemia: Triglycerides

Survivors with high triglycerides (≥150)

NHANES 34%
Abdominal Obesity

Survivors with high waist circumference (>102 cm for males, >88 cm for females)

NHANES 46%
Insulin Resistance

Survivors with high fasting glucose (fasting glucose ≥100)

NHANES 18%
Metabolic Syndrome

Percent of healthy 18-50 year old survivors meeting criteria

NHANES 14%
C-Reactive Protein

- 78% with metabolic syndrome also had elevated CRP ($\chi^2=5.58$, $P=.02$).
Body Fat Percent

- When BFP was substituted for waist circumference as a cardiac risk factor, 26% of survivors met criteria for metabolic syndrome.
Limitations and Strengths

- **Limitations**
  - Small sample
  - Cross sectional study
  - Does not provide fully representative population-based cohort for determining prevalence

- **Strengths**
  - New information in HSCT survivor cohort
  - Standardized objective test results
Conclusions

- In these survivors cardiovascular risks were elevated despite young age and seemingly good health
  - 16% meet criteria for metabolic syndrome
  - 42% have elevated CRP
  - 62% are obese by body fat percent
- A significant number of survivors are at risk for developing later problems
  - 51% meet one or two of the criteria for metabolic syndrome
- These are underestimates of medical problems in HSCT survivor populations
Implications

- Primary care providers and patients need education
- Surveillance guidelines are needed
  - Expand list of recommended tests
  - Mandate routine testing at younger ages
- Behavioral methods to address cardiovascular risks, such as diet and exercise, are particularly important for these survivors
- Clinical trials need to target these complications