Co-morbidity index for allogeneic hematopoietic cell transplant

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Background

- Comorbidities refer to additional clinical conditions that exist or occur during the clinical course of a patient with a primary (index) disease.
- An allogeneic hematopoietic cell transplant (HCT) is a transplant of stem cells between two individuals, related or unrelated.
- Myeloablative: a conditioning regimen using high dose chemotherapy and radiation
- Non-ablative: less rigorous conditioning regimen
Indications for Allogeneic Hematopoietic Stem Cell Transplants 2003 — Worldwide

- Unrelated donor (n = 4,900)
- Related donor (n = 8,800)

Transplants

AML | ALL | CML | Lymphoma | MDS/ MDS | Other leukemia | Other cancer | Aplastic | Other non-

AML: 4,900
ALL: 2,000
CML: 1,500
Lymphoma: 1,200
MDS: 1,100
Other leukemia: 500
Other cancer: 500
Aplastic: 500
Other non-malignant disease: 500

Total: 12,000
Survival after HLA-Identical Sibling Myeloablative Transplants for AML, 1996-2001 - by remission status and age
Survival After Myeloablative Transplants for Myelodysplastic Syndromes, 1996-2001, Age > 20 Years - by FAB Classification

Probability, %

YEARS

HLA-identical sibling, RA/RARS (N = 254)

Unrelated, RA/RARS (N = 92)

Unrelated, RAEB/RAEB-T/CMML (N = 257)

HLA-identical sibling, RAEB/RAEB-T/CMML (N = 648)

P = 0.0001
Background

- Impact of comorbidities on the outcome of the index disease
  - Impact therapeutic plans
  - More likely to impact non-relapse mortality than hematologic disease progression
  - HCT and older patient populations
    - Increased number of comorbidities
Trends in Allogeneic Transplants Recipient Age*, 1987-2004

* Transplants for AML, ALL, CML
Background

- Sorror et al. (Blood, 2005) developed HCT-specific comorbidity index
  - Adapted the Charlson Comorbidity Index
    - Added obesity, peritransplant infections, and psychiatric disturbances
    - Changed weight of arrhythmia, rheumatologic disease, and pulmonary dysfunction
  - Increased sensitivity for HCT specific disorders
  - Successfully predicted risks of non-relapse mortality
Figure 1. The HCT-CI compared with the CCI

Background

- Currently:
  - 30% of patients undergoing a myeloablative prep allogeneic transplant will not survive the first 100 days post-transplant
  - Transplant related mortality for a nonmyeloablative sibling transplant is 15-20%
  - Most common causes of post transplant mortality:
    - Severe GVHD
    - Infections
    - Organ toxicity
      - GI tract- Mucositis
      - Lungs- ARDS
      - Liver- VOD
  - But 40-50% of patients undergoing allogeneic stem cell transplant may have extended disease free survival
Rationale

Why develop a Comorbidity index?
- Create a tool that can be used to better assess clinical risk
- Improve pre-transplant counseling
- Validate Sorror’s results
Hypothesis

- High comorbidity index scores will be predictive of poor overall non-relapse mortality and survival.
Specific Aims

- Determine the prevalence and incidence of comorbidities in allogeneic HCT patients.
- Assess the predictive value of total comorbidity score on overall non-relapse mortality and survival.
- Examine the impact of individual comorbidity factors on overall survival.
Patients, materials, and methods

- **Patients**
  - n=112 (total set 224)
  - allogeneic stem cell transplant
  - 2000-2006
  - Conditioning regimens
    - Ablative
    - Non-ablative
  - Received standard treatments throughout clinical course
    - bacterial, viral, and yeast prophylaxis
    - Steroid treatment for GVHD
Patients, materials, and methods

- Data Collection and comorbidity variables
  - extracted from patient’s medical charts
  - active or requiring treatment at time of transplant
  - Comorbidity variables included:

  - Cardiac Function
  - Heart valve disease
  - Peptic Ulcer
  - BMI
  - Psych (depression or anxiety)
  - Infection
  - Renal
  - Prior Solid Tumor
  - Arrhythmias
  - GI
  - Diabetes
  - TIA or CVA
  - Hepatic Function
  - Rheumatologic
  - Pulmonary Function
Patients, materials, and methods

- Data check 10% of patients
- Missing data
  - PFT
  - Hepatic function (AST)
  - MUGA
  - What will we do
Results (pending!)

- Males n=59
- Females n=53
- Average age=46
- Comorbidity score
  - Range 0-11
  - Mean 2
Analysis

- Regression analysis and hazard ratio for each comorbid condition controlling for other comorbid conditions
- Look at overall score first, then each individual factor
- Ex for age:
  - Non-relapse mortality if <40 yrs / non-relapse mortality if >40 yrs risk ratio
- Cox adjusted multiple regression analysis to adjust for other variables
The future…..

- Additional Variables
  - Age, serology, disease stage, prophylactic regimen

- A different index
  - Change classification of PFT
  - MUGA
  - Hepatic lab values
What I’ve learned……

- Ask questions, then ask 100 more!
- Find a mentor who’s excited
- Learn the clinical base behind the data
- Get to know a patient
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