Managing Cardiovascular Disease in the Hematopoietic Stem Cell Transplant Population

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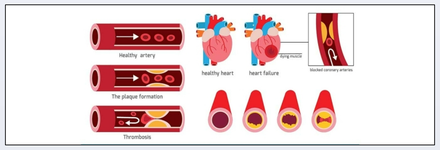
Introduction

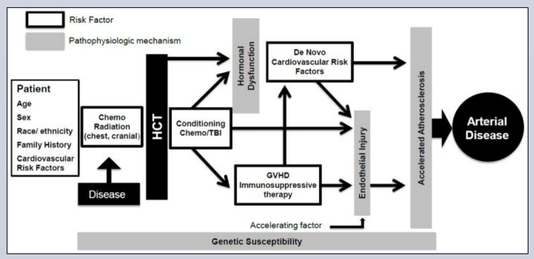
- Globally, cardiovascular disease can be responsible for 1 in every 3 deaths - more than all forms of cancer and lower respiratory disease combined.
- CVD has crippled national health care costs and is responsible for 14% of all health expenditures in The United States- more than any other disease category.
- There a modifiable and non-modifiable risk factors alike that contribute to CVD
- Risk stratification efforts have fallen short on the hematopoietic stem cell transplant population
- This population includes (but not limited to) the following diseases: lymphoma, leukemia, aplastic anemia, myelofibrosis, myelodysplastic syndrome and myeloma.



Cardiovascular Disease in the HCT Population

HCT recipients have a 2.3-4.0 fold increased risk of death by cardiovascular causes compared to the general population.

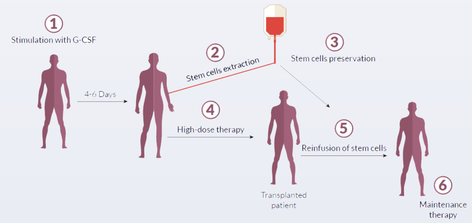
- CVD in HCT recipients comprise three categories: **cardiac dysfunction, cardiovascular risk factors, and arterial disease.**
- Arterial disease (coronary artery, cerebrovascular, and peripheral artery disease) currently poses a 2-fold higher risk in HCT recipients compared to the general population.
- HF contributed up to 9% of mortality of patients in the immediate post-HCT phase of transplant.
- Risk factors for early HF include reduced pre-HCT ejection fraction, conditioning with high-dose cyclophosphamide, and total body irradiation.
- Cardiovascular risk factors pre-transplant can also significantly impact/ accelerate post-transplant complications.
- Exposure to radiation and antineoplastic agents leads to both vascular and/or direct cardiac injury.
- High dose Cytarabine conditioning leaves patients with larger numbers of circulating endothelial cells post treatment leading to disruptions in the microvascular bed and subsequently, accelerating thrombus formations.
- Clinical factors associated with post-HCT dyslipidemia include family history, obesity, high-dose TBI, acute GVHD, chronic GVHD, and chronic liver disease.



The Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI)

The HCT-CI was originally developed by a team of clinical researchers at The Seattle Care Alliance/ Fred Hutchinson Cancer Research Center in Seattle, Washington. Together, they studied data from 1055 transplant patients between the years of 1999-2004 and used what they found to create the HCT-CI in hopes of helping providers choose the best chemotherapy conditioning regiment with the least amount of harmful side effects.

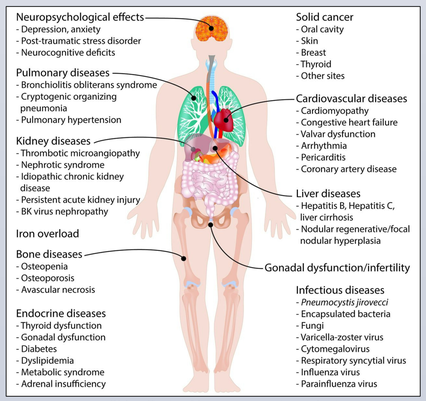
Comorbidities	Definitions of comorbidities included in the new HCT-CI	HCT-CI weighted scores
Arrythmia	Atrial fibrillation or flutter, sick sinus syndrome, and ventricular arrhythmias	1
Cardiac	*Coronary artery disease†, congestive heart failure, myocardial infarction, or EF ≤50%*	1
Inflammatory bowel disease	Crohn's disease or ulcerative colitis	1
Diabetes	Requiring treatment with insulin or oral hypoglycemics, but not diet alone	1
Cerebro-vascular disease	Transient ischemic attack or cerebro-vascular accident	1
Psychiatric disturbance	**Depression/anxiety requiring psychiatric consult or treatment**	1
Hepatic - mild	*Chronic hepatitis, Bilirubin >ULN- 1.5 X ULN, or AST/ALT >ULN-2.5XULN*	1
Obesity	**Patients with a body mass index >35 kg/m^2**	1
Infection	**Requiring continuation of anti-microbial treatment after day 0**	1
Rheumatologic	SLE, RA, polymyositis, mixed CTD, polymyalgia rheumatica	2
Peptic ulcer	Requiring treatment	2
Moderate/severe renal	*Serum creatinine >2 mg/dl, on dialysis, or prior renal transplantation*	2
Moderate pulmonary	*DLco and/or FEV_1 >65%-80% or Dyspnea on slight activity*	2
Prior solid tumor	*Treated at any time point in the patient's past history, excluding non-melanoma skin cancer*	3
Heart valve disease	Except mitral valve prolapse	3
Severe pulmonary	*DLco and/or FEV_1 ≤65% or Dyspnea at rest or requiring oxygen*	3
Moderate/severe hepatic	*Liver cirrhosis, Bilirubin >1.5 X ULN, or AST/ALT >2.5XULN*	3



- In 2004 Sorror and colleagues used the HCT-CI in the pre-transplantation phase to predict transplant outcomes during their study.
- They found that toxicity and non-relapse mortality risks increased in direct proportion to high HCT-CI scores in myeloablative/ non-myeloablative patients alike.
- The study implied that the HCT-CI could be used by referring Primary Care Physicians, Primary Oncologists and Hematologists when preparing for their patients' transplant.
- Sorror et al. conducted further research in 2007 to follow-up on their inclusion of the HCT-CI within their transplant work ups compared to other studies which relied solely on disease burden alone.
- They found that the incorporation of a patient-specific risk factor, such as comorbidities, resulted in refinement of risk stratification compared to other studies just assessing disease burden.

Conclusions

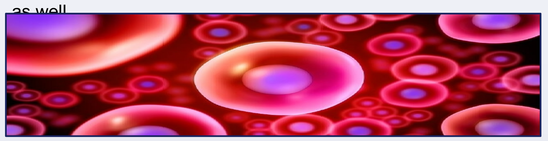
- Hematopoietic stem cell transplant patients are a very unique population with an equally unique set of risk factors pre-disposing them to cardiovascular disease.
- **HCT patients should be treated like the general population!**
- A study conducted at the Loyola University Medical Center analyzed forty-eight patients transplanted between 2012 and 2016 and found that **common CVD risk calculators (Framingham Risk, ASCVD, and QRISK) did not predict for atherosclerotic events nor cardiac events after transplant**.
- By utilizing the HCT-CI, and possibly even further expanding on to it, clinicians can ensure they are considering all of the data necessary in order to formulate the best and most-successful treatment plan for their patients.



Side effects of bone marrow transplants.

Recommendations

- Providers need to be cognizant of the socio-economic component that encompasses stem cell transplants
- Screening should also account for finances and disability benefits as many patients will not be able to work after transplant
- Patients should be assessed for caregiver support as they are not expected to manage their treatment alone
- Assessing the needs of caregivers *before* transplant will avoid burnout in the long-term
- Environmental factors should also be considered a risk- do patients have access to safe housing? Is their housing clean and free of mold, asbestos, lead and other environmental hazards?
- Ultimately, the HCT-CI is the best risk stratification tool to assess comorbidities and cardiovascular disease pre-transplant but there are other factors that should be accounted/ added on to the model as well



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Acknowledgements

Thank you to The Fred Hutchinson Cancer Research Center as well as The National Cancer Institute for their dedication to cancer research and innovation!