

## Bone marrow transplantation – how can we maximize cardiac status?

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The session 8 had three very important presentations beginning with an introductory overview of bone marrow transplantation, followed by a directed talk about arrhythmias and bone marrow transplantation and then an overview of the effects of cancer on cardiac and physical function and the beneficial effects of exercise training in cancer care.

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## IMPAIRMENTS IN CARDIOVASCULAR RESERVE CAPACITY AND EFFICACY OF EXERCISE COUNTERMEASURES IN CANCER PRESENTED BY LEE W. JONES, PHD (CARDIOLOGY SERVICE, MSKCC)

There is an impaired cardiovascular reserve capacity in cancer due to pre-diagnostic risk factors and indirect injury from cancer treatment (“Multiple Hit Hypothesis”) that can be measured with symptom limited cardiopulmonary exercise testing. The latter shows a reduction in peak oxygen consumption ( $V_{O2}$  peak) in cancer patients compared to matched control patients without cancer. Contributing factors include a reduction in pulmonary function (fibrosis or metastatic disease), cardiac systolic function, anemia, changes in sympathetic tone and peripheral effects of treatment (muscle atrophy, deconditioning and changes in energy utilization). Exercise training is the ultimate multi-targeted treatment and has been shown to reduce cardiovascular events in adult survivors of pediatric cancer and in women with breast cancer both during and after chemotherapy. There are limited data on efficacy of exercise training on cardiovascular risk and further studies are required [1–6].

## STEM CELL TRANSPLANT: CURRENT ROLE AND EMERGING STRATEGIES PRESENTED BY MADAN JAGASIA, MBBS, MS (VANDERBILT UNIVERSITY MEDICAL CENTER)

Stem cell transplant (SCT) is a critical tool in hematologic malignancies. Stem cells can be harvested from the patient (autologous) or from a donor (allogeneic). For the latter, the cell source is important with best outcomes with HLA-matched related donors compared with successively less favorable outcomes with matched unrelated donors and partially matched unrelated donors. For older patients and for patients with a high co-morbidity burden, lower intensity effective conditioning regimens have been developed.

Stem cell transplant can be done with curative intent (acute leukemia, myelodysplasia [MDS], chronic myelogenous leukemia [CML], chronic lymphocytic leukemia [CLL], relapsed germ cell tumors) and with non-curative attempt to prolong disease free survival (plasma cell disorders). The three most common indications for SCT today are plasma cell disorders, non-Hodgkin’s lymphoma

(NHL) and acute myelogenous leukemia (AML). A survival benefit has been demonstrated for HL, NHL and AML. Sickle cell anemia has been “cured” with SCT. In 2013, there are approximately 125,000 and 200,000 cumulative survivors of allogeneic and autologous SCTs.

A continuing problem with SCT, especially, but not limited to allogeneic transplant, is graft versus host disease (GVHD). GVHD is caused by T-cell activation and proliferation and can be acute or chronic. Post-transplant cyclophosphamide has been partially effective in reducing the incidence of GVHD and alternative donor sources such as cord blood and haplo-identical donor cells have also been associated with a reduction in GVHD [7–11].

## QT PROLONGATION AND OTHER ELECTROPHYSIOLOGIC CONSIDERATIONS IN CANCER PATIENTS UNDERGOING STEM CELL THERAPY PRESENTED BY MICHAEL FRADLEY, MD (DIVISION OF CARDIOVASCULAR MEDICINE, MORSANI COLLEGE OF MEDICINE, UNIVERSITY OF SOUTH FLORIDA)

As the field of cardio-oncology continues to expand, arrhythmias and other electrophysiologic phenomena are increasingly recognized as common cardiotoxicities of cancer therapy. Atrial fibrillation (AF) and other supraventricular arrhythmias as well as QT prolongation are particularly common, especially in patients considered for stem cell transplantation (SCT). Accurate QT measurement can be challenging, and in this population the Fridericia correction formula may be most appropriate (as opposed to the Bazett formula). Multiple chemotherapies including many of the tyrosine kinase inhibitors (TKI) are associated with QT prolongation, often via intracellular signaling pathways. Nonetheless, in the oncology population, multiple factors including polypharmacy and cancer-related complications also contribute to QT prolongation. Although patients undergoing SCT often demonstrate some degree of QT prolongation, this has not translated into excess risk. The 2-year non-relapse mortality was not statistically significant when comparing those patients with normal QT intervals as baseline to patients with QT prolongation. AF is frequently observed in cancer patients, even if they are not on therapy or do not have a life threatening malignancy. Both melphalan,

a common preconditioning chemotherapeutic for SCT, and ibrutinib, a TKI used to treat certain B-cell lymphomas are frequently associated with AF. Approximately 8–10% of patients undergoing SCT will develop AF or SVT. Risk factors for these arrhythmias include older age, prior cardiovascular disease, and exposure to melphalan, anthracyclines or mediastinal radiation. Median time to developing AF post SCT is 9 days and on average, patients that develop AF remain in the hospital 3 days longer than those without arrhythmias. In addition, patients that develop AF or SVT in the peri-SCT period are more likely to require ICU admission, and also demonstrate

significantly elevated 30 day and one year mortality rates. While significant questions remain about the appropriate management of these arrhythmias in SCT patients, it is clear that they must be taken seriously [12–18].

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