

Cardiac complications after bone marrow transplantation: incidence of disease and associated risk factors

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Objectives:

The number of patients that have undergone bone marrow transplantation has continued to rise with the cumulative number of transplant recipients in the United States reaching 340,000 in 2014. Of importance is the fact that these transplant survivors have a 3 fold increased risk of cardiovascular disease when compared to their peers. With this increasing population it is becoming more and more important to understand the cardiac complications that develop after bone marrow transplantation and to establish ways to prevent these adverse events. The objective of our study was to establish the incidence of cardiovascular disease after bone marrow transplantation in the modern era, identify pre-transplantation cardiovascular risk factors and chemotherapeutic exposures as a potential contributor to disease, and to spark further research in this field.

Methods:

De-identified medical records of patients that underwent hematopoietic stem cell transplantations at VCU Medical Center between January 2013 and January 2016 and were referred to the Cardio-Oncology clinic were reviewed. The data analyzed included demographic data, underlying hematologic malignancy, previous chemotherapeutic exposure, date and type of HSCT, pre-transplant cardiovascular risk factors (hypertension, hyperlipidemia, or diabetes), cardiovascular disease established before transplantation, cardiovascular disease diagnosed after transplantation, ECG findings, time from transplantation to the onset of arrhythmia, ejection fraction as measured by transthoracic echocardiogram or myocardial perfusion imaging, and patient deaths. Each patient was assessed by a board certified Cardiologist with experience in the field of Cardio-Oncology.

Results:

508 patients underwent hematopoietic stem cell transplantation (292 Autologous, 216 Allogenic). Of those patients 89 were referred to our Cardio-Oncology clinic for cardiovascular disease. The most common disease observed was

arrhythmia with 31 cases (6% of all transplants, 35% of cardiovascular cases). Of these arrhythmias atrial fibrillation was the most common with 27 cases observed (5% of all transplants, 30% of cardiovascular cases). The time from transplantation to the onset of atrial fibrillation had two peaks with 15 cases observed within the first 10 days after transplantation and a second peak between 200-300 days after transplantation with 5 cases observed. Surprisingly the second most common cardiovascular disease observed was dysautonomia with 20 cases accounting for 4% of all transplanted patients and 22% of all cardiovascular disease. Refractory hypertension was also relatively common with 17 cases observed (3% of all transplants, 19% of all cardiovascular cases). There were 9 cases of coronary artery disease (2% of all transplants, 10% of cardiovascular disease), and 7 cases of heart failure (1% of all transplants, 8% of cardiovascular disease). While atrial fibrillation was the most commonly observed, 46% of these patients had a pre-transplant diagnosis of afib. On the other hand 0% of patients diagnosed with dysautonomia had this disease before transplantation. About 50% of patients that developed cardiovascular complications had pre-transplant cardiovascular risk factors.

Conclusions:

Several studies have identified atrial fibrillation as a common complication after transplantation, which is consistent with our findings. These studies have shown that the majority of atrial fibrillation occurs within the first 10 days after transplantation. Our study supported this finding with 15/27 cases occurring within the first 10 days. Of interest is our discovery of a second peak of atrial fibrillation onset 200-300 days after transplantation. To our knowledge this has not been previously described, and is likely due to the fact that many previous studies did not follow patients beyond the first 100 days after transplantation. Of interest is our finding that dysautonomia is almost just as common, which has not previously been identified. Furthermore while almost half of the patients that were referred to our clinic for afib had a pre-existing history of afib, none of the cases of dysautonomia had a preceding history of this disease. There is evidence that autonomic dysfunction also plays a role in the development of atrial fibrillation, and given the fact that these were the two most common diseases observed this suggests that the interplay between the autonomic nervous system and the cardiovascular system after bone marrow transplantation is an important relationship that warrants further study. Lastly, our study showed that almost half of our patients had cardiovascular risk factors before transplantation. It is likely that aggressive prevention and treatment of cardiovascular risk factors before bone marrow transplantation may help prevent post-transplantation complications.