

ADVANCES IN HEMATOLOGY

Current Developments in the Management of Hematologic Disorders

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Risk Factors of Cardiovascular Disease After Hematopoietic Cell Transplantation



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H&O What kinds of morbidity have been seen in long-term survivors of hematopoietic cell transplantation (HCT)?

SA HCT has been increasingly used over the past few decades as a curative option for many hematologic malignancies. Advances in transplant strategies and supportive care have substantially improved overall survival after transplantation. Among long-term survivors of transplantation (10 years post-HCT), nearly two-thirds will have a chronic health condition. In one third of patients, these conditions will be severe or life-threatening, and can include secondary cancer, pulmonary disorders, endocrine problems, thyroid disorders, and premature menopause. Cardiovascular problems include stroke, heart attack, and congestive heart failure. These complications, especially the cardiovascular conditions, appear to develop much earlier than they do in the general population. They are unusually lethal. For example, among post-transplant patients who develop congestive heart failure, the overall survival is less than 50% by 5 years after diagnosis.

H&O What have previous data shown about cardiovascular risk after HCT?

SA In a 2011 study, we looked at what drives the risk of cardiovascular disease post-transplant. We examined factors such as pretransplant chemotherapy, irradiation exposure, and transplant-related conditioning. We

also looked at the role of post-transplant chronic health conditions—the new conditions that develop after transplant. We aimed to determine how these new conditions modify the risk of heart failure and other cardiovascular outcomes. We found that risk factors such as hypertension and diabetes were important modifiers of risk in this population, especially in the context of previous exposure to cardiotoxic therapy, chemotherapy, or irradiation.

H&O Could you please describe your recent study on the role of cardiovascular risk factors in cardiovascular disease post-HCT?

SA It was a retrospective cohort study of autologous and allogeneic transplant survivors that aimed to quantify the overall incidence of cardiovascular risk factors, such as hypertension, diabetes, and dyslipidemia, as well as identify how these conditions shape the subsequent risk of cardiovascular outcomes. All patients had undergone transplantation from 1995 through 2004, and had survived for at least 1 year after transplantation. Assessments were made at 1 year, 5 years, and 10 years after transplantation.

Five years after transplantation, approximately 33% of patients had hypertension, 40% had dyslipidemia or abnormal cholesterol levels, and 15% had diabetes. Nearly 25% had multiple cardiovascular risk factors. Ten years after transplantation, hypertension, diabetes, dyslipidemia, and the presence of 2 or more cardiovascular risk factors were found in 37.7%, 18.1%, 46.7%, and 31.4%

of patients, respectively. These rates are much higher than those found in the general population.

We found that the subgroup of patients at highest risk of having hypertension, diabetes, dyslipidemia, or multiple cardiovascular risk factors consisted of those who had undergone allogeneic transplant. These patients were at especially high risk of developing these conditions at a much greater magnitude as compared with control patients in the general population matched for characteristics such as age and sex.

The second part of our study was to identify the transplant-specific predictors that increase the risk of cardiovascular events. We found that specific treatments could substantially increase the risk. For example, many transplant patients receive a conditioning regimen consisting of either high-dose chemotherapy or high-dose chemotherapy plus total body irradiation. Patients who received total body irradiation plus chemotherapy had a 40–50% higher risk of developing diabetes or abnormal cholesterol levels compared to patients who received high-dose chemotherapy alone. Patients who developed graft-versus-host disease during the immediate post-transplant period had a substantially higher risk of hypertension, diabetes, and dyslipidemia. These factors have emerged as independent predictors of risk after adjusting for age, sex, race/ethnicity, weight, body size, and type of conditioning chemotherapy.

H&O How can the study findings be used in clinical care?

SA A growing number of long-term transplant survivors are being seen in private clinics or hospital settings, and many of them are at risk of developing cardiovascular risk factors. These risk factors may not be preventable, but there are several interventions that can improve quality of life. Risk-based screening for diabetes, cholesterol problems, or

high blood pressure will help set the stage for early interventions such as lifestyle modification or pharmacologic therapy to control some of these issues. In addition, our study showed that patients who have multiple cardiovascular risk factors are at a substantially increased risk of developing heart failure, heart attacks, and strokes at a very young age. In certain subgroups, such as those who received cardiotoxic chemotherapy prior to HCT, up to 20% of patients developed cardiovascular complications such as heart failure, stroke, and heart attacks. Patients who have not developed cardiovascular complications but are at increased risk due to the presence of these cardiovascular risk factors could be monitored closely using novel cardiac imaging techniques. Importantly, these patients may benefit from aggressive management of cardiovascular risk factors in order to avert life-threatening complications.

We are now able to consider the health and long-term quality of life of transplant survivors and initiate early interventions. Studies such as this one can help identify high-risk patients and set the stage for targeted, focused future clinical studies to improve patient outcomes.

Suggested Readings

Tichelli A, Bucher C, Rovó A, et al. Premature cardiovascular disease after allogeneic hematopoietic stem-cell transplantation. *Blood*. 2007;110:3463-3471.

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