ADVANCES IN LLM

Current Developments in the Management of Leukemia, Lymphoma, and Myeloma

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Assessing the Risk of Heart Failure in Patients With Acute Leukemia

Marielle Scherrer-Crosbie, MD, PhD
Professor of Medicine
Hospital of the University of Pennsylvania
Perelman School of Medicine
Philadelphia, Pennsylvania

H&O What is the risk of heart failure in patients with acute lymphoblastic leukemia or acute myeloid leukemia?

MSC Heart failure in patients with acute leukemia is not well studied. At my institution, we noticed that among populations of patients treated with anthracyclines—which are a backbone of treatment in acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML)—those with acute leukemia had an especially high rate of cardiovascular events, particularly heart failure. We assessed the rate of heart failure in a retrospective study of 450 patients with acute leukemia treated with anthracycline therapy. The rate of heart failure was 8.9%. Symptoms of heart failure developed approximately 4 months after treatment with anthracyclines. Not surprisingly, higher doses of 250 mg/m^2 or greater were more strongly associated with the risk of heart failure.

H&O How did you perform the retrospective study?

MSC The retrospective analysis of heart failure in ALL and AML originated as part of a larger study conducted at my former institution, Massachusetts General Hospital in Boston. The original study enrolled more than 5000 patients, including those with hematologic malignancies and breast cancer. All patients had received anthracyclines. The results were published in 2015. With a median follow-up duration of approximately 4 years, the risk of symptomatic heart failure and cardiac death was highest in patients with hematologic malignancies, at a rate of 4%. Among patients with breast cancer, the rate was 0.7%.

> The estimated 1-year cumulative incidence of heart failure is 1% for the low-risk group vs 35% for the high-risk group.

Further study of the patients with hematologic malignancies showed that those with acute leukemia had the highest rate of heart failure. This risk was not explained by their cardiovascular risk profile, which was better than that of patients with lymphoma. We were intrigued by this observation, but could not identify a clear explanation for it. There are a few possible reasons, however. Patients with acute leukemia receive high doses of anthracycline in a short period. They have large variations in their volume load. Echocardiography showed another interesting finding: patients with acute leukemia appear to have indices of cardiac function that may be slightly decreased compared with patients with other cancers, even before treatment and in the absence of cardiac risk factors. This susceptibility to heart failure might be caused by the cancer itself, the secretion of certain cytokines, a genetic predisposition, or some other factor.

Table. Variables Included in a Multivariable Fine and Gray Subdistribution Hazard Regression Model

	HR (95% CI)	β Coefficient Value	*P* Value	Score Points
Global longitudinal strain exceeding –15%	6.91 (3.27-14.59)	1.93	<.001	6
Pre-existing cardiovascular disease	3.74 (1.82-7.67)	1.32	<.001	4
Leukemia type (AML)	4.10 (1.90-8.85)	1.41	<.001	4
Ejection fraction <50%	3.50 (1.64-7.51)	1.25	<.001	4
Age >60 years	1.36 (0.76-2.44)	0.31	.300	1
Anthracycline dose ≥250 mg/m^2	1.96 (1.06-3.61)	0.67	.030	2

AML, acute myeloid leukemia; HR, hazard ratio.
Adapted from Kang Y et al. *JACC: CardioOncology*. 2019;1(2):208-217.

H&O How did you develop the risk score?

MSC Another objective of the retrospective study was to develop a risk score to help clinicians better evaluate whether their patients with acute leukemia are at high risk, medium risk, or low risk for developing heart failure. The risk score was based on univariate associations between clinical and echocardiographic baseline parameters and the development of symptomatic heart failure (Table). The parameters retained for the risk score were the most clinically relevant factors. We identified 5 parameters, and scored them as follows. Older age (>60 years) is 1 point. Preexisting cardiovascular disease is 4 points. The presence of AML, as opposed to ALL, is 4 points. An anthracycline dose of 250 mg/m^2 or higher is 2 points. The risk score incorporates 2 echocardiographic parameters. A left ventricular ejection fraction of less than 50% is 4 points. Another echocardiographic parameter is baseline global longitudinal strain, which is a measure of myocardial reformation and a strong indicator of cardiac systolic function. Impaired global longitudinal strain, as indicated by a baseline level exceeding –15%, is 6 points.

A score of 14 to 21 is considered high risk, a score of 7 to 13 is moderate risk, and a score of 0 to 6 is low risk.

H&O How can the risk score be used in clinical practice?

MSC This risk score must be validated in large studies. The best way to use it would be to identify those patients with a low score vs a high score. The estimated 1-year cumulative incidence of heart failure is 1% for the low-risk group vs 35% for the high-risk group. This information can help clinicians decide whether a patient might benefit from cardiology supervision. When possible, steps to modify or prevent risk factors are advisable for all patients, particularly those at high risk.

H&O Do you have any other recommendations for the management of heart failure in patients with ALL or AML?

MSC These patients are fragile and vulnerable, especially at the time of their diagnosis and throughout treatment. Referral to a cardiologist might be needed early in the disease course, even before any signs of heart failure. This kind of risk score can help the oncologist and the cardiologist collaborate more closely in the management of these patients, who have a high risk of heart failure.

Disclosure

Dr Scherrer-Crosbie has no real or apparent conflicts of interest to report.

Suggested Readings

Bergler-Klein J. Strain and left ventricular volumes for predicting cardiotoxicity: a life-saving approach in anthracycline cancer treatment? *Eur Heart J Cardiovasc Imaging*. 2015;16(9):968-969.

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