Early Cardiotoxicity After Haploidentical Hematopoietic Stem Cell Transplantation with Post-Transplant Cyclophosphamide: Incidence, Severity, and Association with Cytokine Release Syndrome

OSES, LUCRECIA[1]; Ferini, Gonzalo[1]; Gimenez, Alberto[1]; Bendek, Georgina[1]; Arbelbide, Jorge[1]; Huespe, Ivan[1]

[1]*Hospital Italiano de Buenos Aires*

Background: Early cardiac toxicity (ECT) is an emerging complication after haploidentical hematopoietic cell transplantation (haplo-HCT) with post-transplant cyclophosphamide (PTCy). The relationship between cytokine release syndrome (CRS) and ECT remains unclear. We evaluated the incidence, clinical characteristics, and association between CRS severity and ECT after haplo-HCT with PTCy.

Methods: We performed a retrospective single-center study of 133 consecutive adults undergoing their first haplo-HCT with PTCy (2015–2025). ECT within 100 days post-transplant was graded per CTCAE criteria, including both symptomatic and biomarker-defined cardiac injury. Cumulative incidence of ECT by maximum CRS grade was estimated using crude and adjusted Fine & Gray competing-risk models.

Results: ECT occurred in 62.4% of patients (83/133; 95%CI 53.6–70.7). Among the 83 evaluable patients with biomarker data, ECT was symptomatic in 48.2% and biochemical in 51.8%. Grade 1 was most common (54.2%), grade 2 occurred in 15.7%, and grade ≥3 in 30.1%. Notably, when biomarker-based classification was excluded, symptomatic ECT alone accounted for only 30.1% of the total cohort — substantially lower than the overall ECT incidence (62.4%), underscoring that biomarker screening detects a large proportion of otherwise unrecognized cardiotoxicity. The most frequent specific event was congestive heart failure (21.1%), followed by pericardial complications (7.5%), arrhythmia (3.8%), and acute pulmonary edema (3.8%). Symptomatic ECT patients were significantly older (54.9 vs 47.1 years, p=0.02) and had higher rates of hypertension (p=0.03). Higher maximum CRS grade was significantly associated with increased cumulative incidence of ECT (crude SHR 1.26, 95%CI 1.06–1.50, p=0.01; adjusted SHR 1.35, 95%CI 1.13–1.63, p<0.001), with most events occurring within 20–30 days post-transplant.

Conclusions: ECT is common after haplo-HCT with PTCy when systematic biomarker surveillance is incorporated. Increasing CRS severity independently predicts ECT, supporting a mechanistic link between inflammatory toxicity and cardiac injury. Early cardiovascular surveillance and preventive strategies should be considered, particularly in patients developing higher-grade CRS.