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ORAL ABSTRACTS

114.SICKLE CELL DISEASE, SICKLE CELL TRAIT AND OTHER HEMOGLOBINOPATHIES, EXCLUDING THALASSEMIAS: CLINICAL AND EPIDEMIOLOGICAL

SCD Dyslipidemia Normalizes Long-Term Following Nonmyeloablative Hematopoietic Cell Transplantation

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Dyslipidemia is common in patients with sickle cell disease (SCD). Individuals with SCD have a unique type of dyslipidemia. This SCD dyslipidemia (hypocholesterolemia subtype) is characterized by low total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), and high-density lipoprotein cholesterol (HDL-c), and normal triglycerides (TG). This SCD dyslipidemia state is theorized to be cardioprotective regarding atherosclerotic risk due to the hypolipidemic condition.
Hematopoietic cell transplantation (HCT) is a potentially curative therapy for SCD. Nonmyeloablative HCT has been employed at the National Institutes of Health (NIH) and internationally with good results. Long-term survivors of HCT, specifically for hematologic malignancies, are at increased risk for dyslipidemia (hypercholesterolemia subtype), thus increasing atherosclerotic risk long-term. There are no studies investigating the short or long-term effects of HCT on SCD dyslipidemia. Therefore, we report a novel study to characterize lipid profiles at baseline and after HCT for SCD.
This cohort study analyzes data from patients who received their first nonmyeloablative HLA-matched sibling or haploidentical HCT for SCD at the NIH from May 2009 to December 2021. All patients received sirolimus as GVHD prophylaxis. Total cholesterol, HDL-c, LDL-c, and triglycerides were collected pre-HCT, one-year post-HCT, and annually thereafter via a fasting serum-based lipid panel (median follow-up of 4 years). Data were analyzed using linear generalized estimating equation regression models to measure the influence of factors such as year of HCT, sirolimus use, gender, age, and graft failure on TC, LDL-c, HDL-c, and TG levels. A total of 116 patients were included in this analysis. There were 72 male and 44 female patients. The median age was 31 (range 10 to 64) years. 90% of the patients had Hb-SS, 3% Hb-SC, 5% Hb-Sβ^0, and 2% Hb-Sβ^+. Overall survival is 87%, and 19% experienced graft failure. The median time on sirolimus post-HCT was one year.
Baseline, one-year, and two-year mean (25th, 75th percentile) values, respectively, for the TC, LDL-c, HDL-c, and TG are as follows: TC [130.7 (107.0, 147.0), 183.2 (144.5, 220.0), 175.2 (144.5, 209.0)], LDL-c [72.5 (50.0, 87.0), 109 (73.5, 130), 104.2 (75.5, 128.0)], HDL-c [32.3 (23.8, 39.3), 49.4 (38.0, 55.5), 49.2 (41.5, 58.0)] and TG [127.3 (88.5, 156.5), 125.9 (87.0, 153.5), 112.6 (72.0, 133.5)]. Generally, the first-year post-HCT changes were maintained annually thereafter. (Figure 1).
According to linear regression modeling, the change in TC, LDL-c, HDL-c, and TG at one-year post-HCT was +50.3 mg/dL ($p<0.0001$), +36.4 mg/dL ($p<0.0001$), +20.4 mg/dL ($p<0.0001$) and -26.5 mg/dL ($p<0.0001$), respectively. For failed grafts, the estimated changes after one-year post-HCT in TC, LDL-c, HDL-c, and TG were +6.5 mg/dL ($p=0.45$), -2.1 mg/dL ($p=0.78$), +14.8 mg/dL ($p<0.0001$), and -28.0 ($p=0.03$), respectively. The use of sirolimus only resulted in a significant change in TG (+32.8 mg/dL ($p = 0.004$)). Age had statistically significant changes only on TC (+1.08 mg/dL for a one-year change in age, $p=0.005$) and LDL-c (+0.73 mg/dL for a one-year change in age, $p=0.03$). There were no significant differences in TC, LDL-c, HDL-c, and TG levels ($p>0.05$) based on gender and HCT type.
To summarize, HCT with sustained grafts led to significant rises in TC, LDL-c, and HDL-c and a decline in TG from baseline to one-year post-HCT, resulting in the normalization of lipid profiles. These changes were maintained annually thereafter. Graft failure most notably resulted in TC and LDL-c level declines back to pre-HCT baseline (Figure 2), while HDL-c and TG levels did not completely revert to baseline values. Sirolimus effects were significant on TG levels alone. These findings suggest that the mechanism underlying SCD dyslipidemia is corrected with the reversal of SCD. Long-term follow-up studies are indicated to assess patients' risk for atherosclerosis and adverse cardiac outcomes.

Disclosures No relevant conflicts of interest to declare.

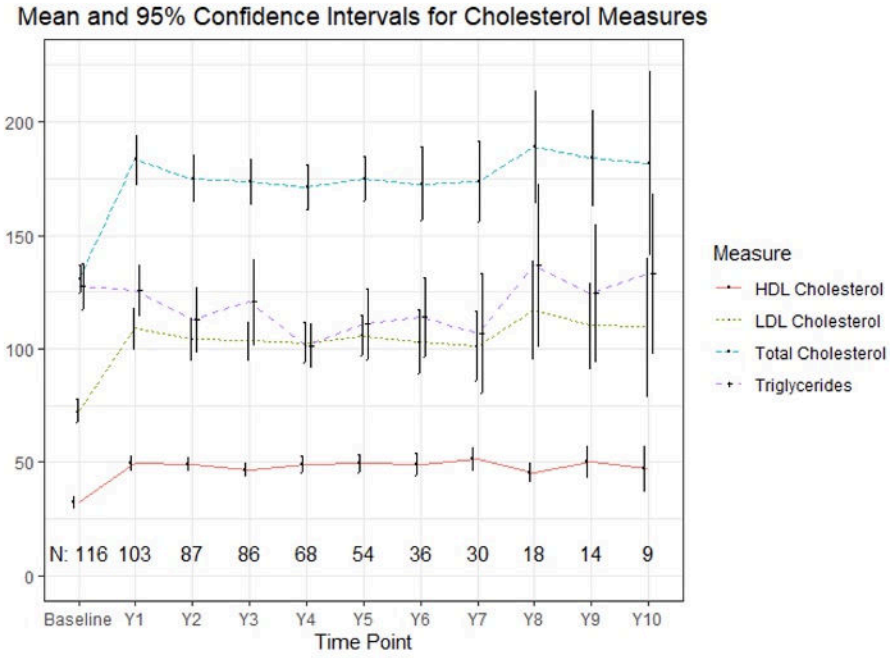

Figure 1. Mean lipid levels after nonmyeloablative hematopoietic cell transplant for sickle cell disease. The median time on sirolimus post-HCT was one year. The use of sirolimus resulted in a significant change in triglycerides.

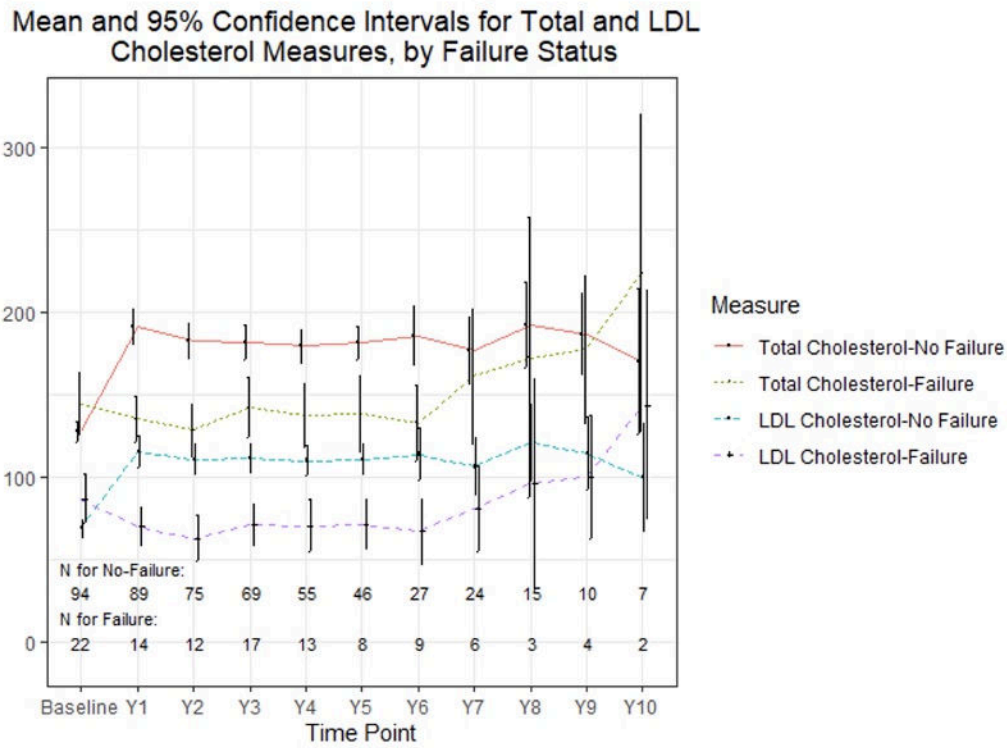

Figure 2. Mean total cholesterol and LDL-c measures post-transplant stratified by presence or absence of graft failure. Beyond seven years post-transplant, the increases in Total and LDL cholesterol in the graft failure group are based on very small sample sizes; they might not be replicated in larger samples.

Figure 1

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