Impact of renal impairment on light chain amyloidosis outcomes after autologous hematopoietic stem cell transplantation

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Light chain amyloidosis (AL) is a rare clonal plasma cell neoplasm characterized by the deposition of amyloid fibrils derived from the aggregation of misfolded immunoglobulin light chains in vital organs such as heart and kidneys resulting in irreversible organ damage (1). The severity of organ damage is the most important determinant of outcome. Both cardiac and renal staging systems have been proposed and validated as predictors of outcome. Cardiac staging system, initially developed and then revised by the Mayo Group, utilizes cardiac biomarkers (NT-proBNP, troponin T and I) and serum free light chain levels to stratify the patients (2,3). Renal staging system, developed by the Pavia Group, depends on the degree of proteinuria and glomerular filtration rates (GFRs) (4). Cardiac stage in general is a predictor of non-relapse mortality and overall survival, while renal stage is a predictor of renal recovery and dialysis dependence (2-4). Renal involvement is seen in approximately 70% of patients with AL (5). However, there are limited data on the impact of baseline renal dysfunction on the outcomes of AL after autologous stem cell transplantation (ASCT).

Sidiqi and colleagues recently reported their long-term experience at the Mayo Clinic with ASCT for AL patients with impaired baseline renal function (6). A total of 655 patients undergoing ASCT between 1999 and 2017 were included in the study. Using a cutoff value of GFR of 45 mL/min, they defined renal impairment as any patient with GFR <45 mL/min. Patients were divided into two groups: normal renal function (NRF: N=568) and impaired renal function (IRF: N=87). The two groups were similar in age, gender, and cardiac involvement. However, patients with IRF had more advanced renal stage (100% with stage II or III *vs.* 37% with NRF), more patients with >2 organs involved (26% *vs.* 17%), and more patients who received reduced melphalan dose (<200 mg/m^2) for conditioning (70% *vs.* 21%).

In terms of outcome, they reported no difference in overall or complete hematologic response rates between the IRF and NRF cohorts. Overall, 6.7% patients required hemodialysis by day 100, with a higher proportion of IRF cohort requiring hemodialysis (16% *vs.* 6%). Furthermore, patients with IRF required more frequent hospitalization (80% *vs.* 70%), had longer hospital stay (15.5 *vs.* 12.1 days), and had higher rates of bacteremia (46% *vs.* 29%). IRF cohort had significantly higher 100-day mortality (14% compared to 5%). However, the median overall survival and progression-free survival were not significantly different between the two cohorts, albeit with a better overall survival tendency for patients with NRF (142 *vs.* 118 months, P=0.07) (6).

This report by Sidiqi *et al.* (6), is a significant contribution in enhancing our understanding of the role of renal impairment on the outcome of ASCT for AL. It underscores the importance of renal function in selecting patients for ASCT, as IRF is associated with higher early mortality and a greater need for dialysis by day 100, which may significantly impair the quality of life. Since the recent

improvement in the outcome of ASCT for AL is mainly due to better patient selection (7), we should seriously consider the degree of renal impairment when determining transplant eligibility for these patients. Although an elegant study, it failed to explain why patients with IRF had similar OS as patients with NRF despite a higher early mortality. They included patients with GFR of 45–59 in the NRF cohort, which is considered abnormal, and failed to show the impact of melphalan dose on survival.

In conclusion, the findings reported by Sidiqi *et al.* (6) are encouraging and support the feasibility of ASCT in AL amyloidosis patients with renal impairment, however with significant toxicity early after transplant. The use of reduced dose melphalan needs to be further explored in this setting, as it may potentially mitigate some of the early post-transplant toxicities. Also, given the rarity of AL, clinical trials through collaborative groups, such as Blood and Marrow Transplantation Clinical Trials Network (BMTCTN), are needed to better understand the role of ASCT in AL amyloidosis with renal impairment.

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Footnote

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