Kidney transplantation outcomes among patients with multiple myeloma - systematic review of case reports and case series

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Introduction

- Patients with multiple myeloma (MM) and end stage kidney disease (ESKD) experienced unfavourable outcomes with kidney replacement therapy[1,2].
- Kidney transplantation (KT) is rarely performed for patients with MM and ESKD due to concerns for poor kidney outcomes, disease recurrence and heightened infection risk[3].
- Registry data has limitations and does not provide sufficient granularity to answer the questions on appropriate waiting time after ASCT before KT, acceptable MM treatment response prior to KT, risk of MM relapses after KT, and risk of other KT complications in the context of MM or the treatment for MM, amongst others, that would guide clinical decision making for each case consideration.

Aim

a. To describe the clinical characteristics of patients with MM who have undergone KT.

b. To document the KT outcomes, including graft function, complications, rejection episodes if any, PFS and OS with regards to MM.

c. To identify patient and MM characteristics that would inform risk of MM relapse after KT, including depth of MM response and wait time to KT.

Methodology

- Comprehensive search on electronic databases (MEDLINE, PubMed and EMBASE) from inception to March 19, 2024 were carried out using appropriate keywords and Medical Subject Headings (MeSH) terms.
- Case reports and case series of individuals fulfilling diagnosis of MM and received treatment with or without autologous stem cell transplant (ASCT) before KT were included
- We excluded case series on
  - individuals with monoclonal gammopathy of renal significance;
  - individuals with a diagnosis of MM after KT;
  - case reports/ case series of allogenic stem cell transplant; and
  - conference abstracts without full text.
- Two reviewers performed full-text screening independently, and a third reviewer arbitrated disagreements between the two reviewers.
- Systematic review is registered with PROSPERO [CRD42024513832].
- 8 patients of our own experience were included into data analysis

Methodology

- Continuous variables were presented as median and interquartile range. Categorical variables were presented as count number and percentage.
- Kaplan Meier survival analysis was used to determine 1, 3 and 5 year for:
  - overall survival;
  - MM-progression free survival; and
  - kidney graft survival.
- Comparisons of the outcomes between were made using log rank test ($p < 0.05$ defines statistical significance) for the following independent variables:
  - Wait-time 2 years or less vs wait-time more than 2 years
  - Depth of remission (strict complete remission (SCR)/ complete remission (CR) vs very good partial remission (VGPR) /partial remission (PR))
- Data analysis was carried out using IBM SPSS Statistics version 26.

Results

- Total of 15 articles and 63 KTs were included in the analysis.
- 3 (4.8%) patients had smoldering MM and did not receive treatment prior to KT. MM treatment characteristics prior to KT are illustrated in table 1.
- Native kidney biopsy results were reported for 41 (65.1%) patients, not performed in 9 (14.3%) patients, and information was not available in 13 (20.6%) patients (see Figure 1).
- 49 (77.8%) had ASCT prior to KT. Out of these, 1 patient had relapse of MM prior to KT and received second ASCT prior to KT.
- 27 (42.8%) patients received bortezomib based chemotherapy
- 2 patients received ASCT after kidney transplant – 1 patient proceeded with simultaneous liver-kidney transplantation prior to ASCT because of severe liver injury from chemotherapy, 1 had ASCT 4 months after KT because of early MM relapse
- 17 (27.0%) received maintenance therapy after ASCT – 8 were immunomodulatory drugs (IMiDs), 2 were proteasome inhibitors, 2 were daratumumab and 1 was carfilzomib/ pomalidomide/ dexamethasone given for progressive disease to achieve complete response (CR) prior to KT.

Table 1: MM treatment characteristics before KT

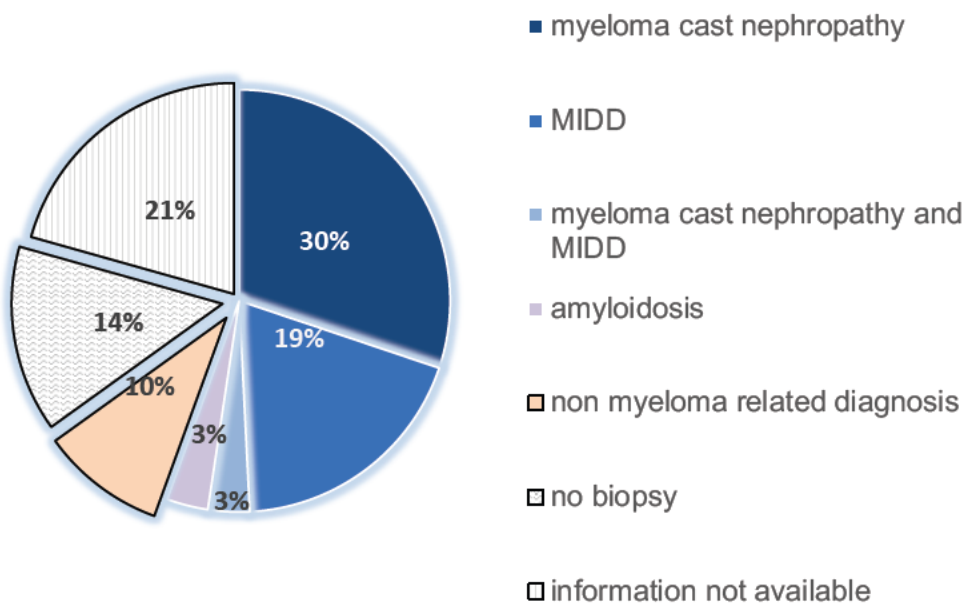
ASCT performed	
Before KT, n (%)	49 (77.8)
After KT, n (%)	2 (3.2)
Not done, n (%)	12 (19.0)
Wait time	
Median waiting time, months (IQR)	36 (33)
Wait-time 2 years or less, n (%)	17 (27.0)
Wait-time more than 2 years, n (%)	38 (60.3)
Information not available, n (%)	8 (12.7)
Depth of MM response	
Stringent complete response (SCR)/ complete response (CR), n (%)	38 (60.3)
Very good partial response (VGPR), n(%)	13 (20.6)
Partial response (PR), n (%)	4 (6.3)

Results

Kidney transplant characteristics

- Excluding 1 patient who developed ESKD 19 years after MM diagnosis, 1 patient who had preemptive kidney transplant at 42 months after ASCT because of CKD progression, 3 smoldering MM cases and 2 ASCT after KT (as above), waiting time to KT was available for 55 (87.3%) patients and depth of MM response prior to KT was available for 58 (92.1%) patients. The aggregate results are shown in table 1.
- 35 (55.6%) received living kidney donation, including 3 ABO incompatible KT.
- Basiliximab and anti-thymocyte globublin were used in 38 (60.3%) and 11 (17.5%) respectively.
- The 3 patients who underwent ABOi KT also received rituximab and plasma exchange.

Figure 1: Native kidney biopsy diagnosis at time of myeloma diagnosis

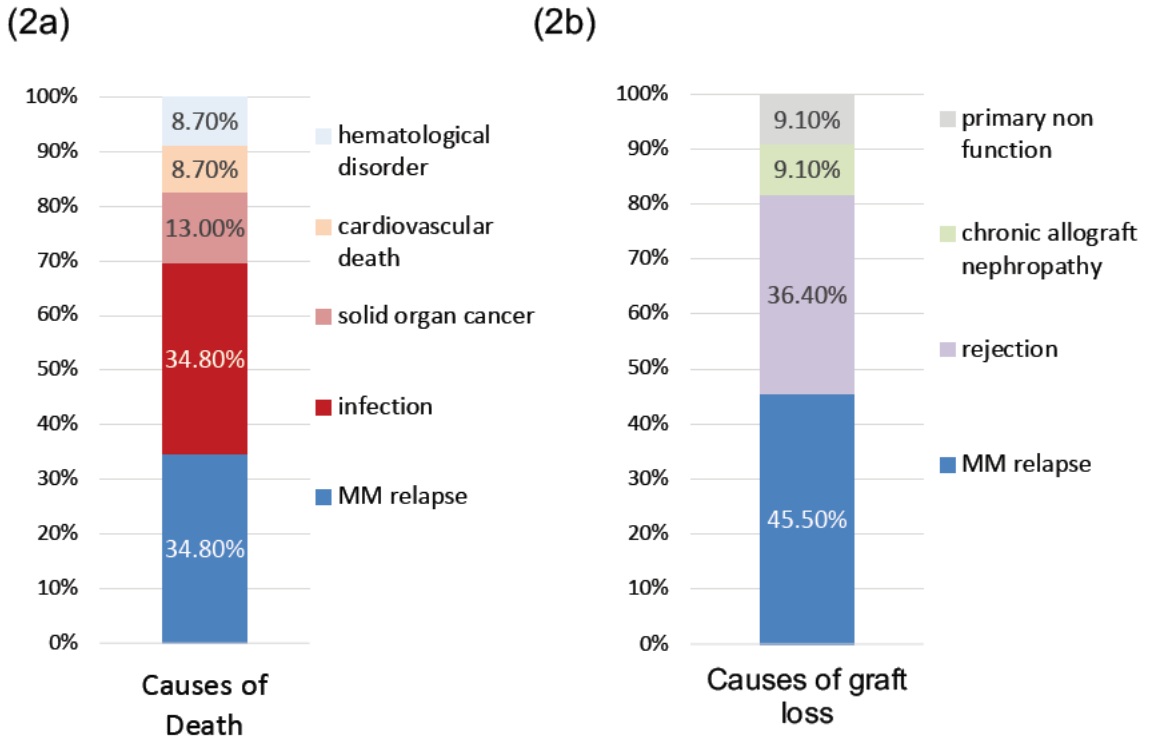


Results

- 1 patient (1.6%) had primary non function.
- Median follow up duration after KT reported was 41 (IQR 41) months.
- Overall survival at 1, 3, and.5 years are 96.7%, 71.0% and 62.3% respectively.
- MM progression-free survival at 1, 3, and 5 years were 75.9%, 54.1%, and 48.8% respectively.
- Death-censored graft survival at 1, 3 and 5 years were 93.5%, 87.8%, and 78.8% respectively.
- The main causes of death were shown in Figure 2a. Causes of graft loss were shown in Figure 2b. MM relapse is the predominant cause for both graft loss and death.
- Solid organ cancers developed in 4 (6.3%) patients with mortality of 75%. 1 (1.6%) developed myeloid neoplasm.
- Rejection developed in 16 (25.3%) patients. Out of these 16, rejection episodes in 3 (18.8%) patients were reported to have temporal relationship with usage of IMiDs and anti-CD38.
- Use of proteasome inhibitor and KT wait time did not affect patient survival, MM relapse nor KT graft survival.
- Depth of MM remission did not affect patient survival nor KT graft survival. There was a trend towards better MM-progression free survival in patients with SCR/CR but did not achieve statistical significance ($p = 0.119$) (Figure 3).

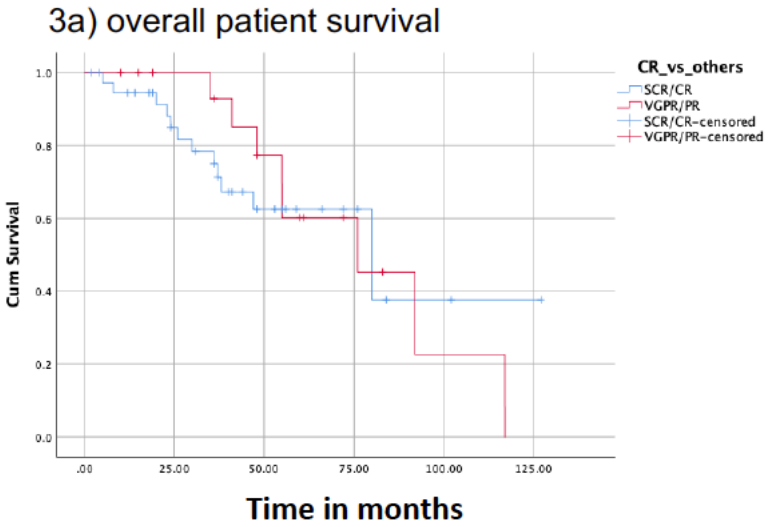
Results

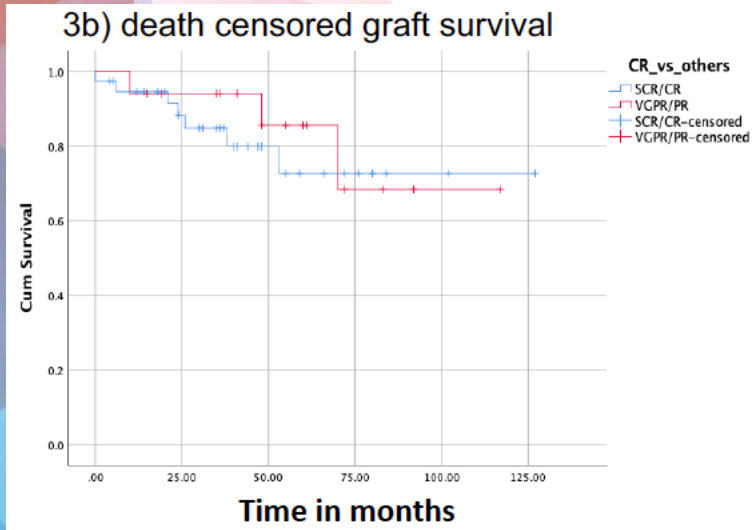
Figure 2: Causes of death (2a) and graft loss (2b) among MM patients who received KT

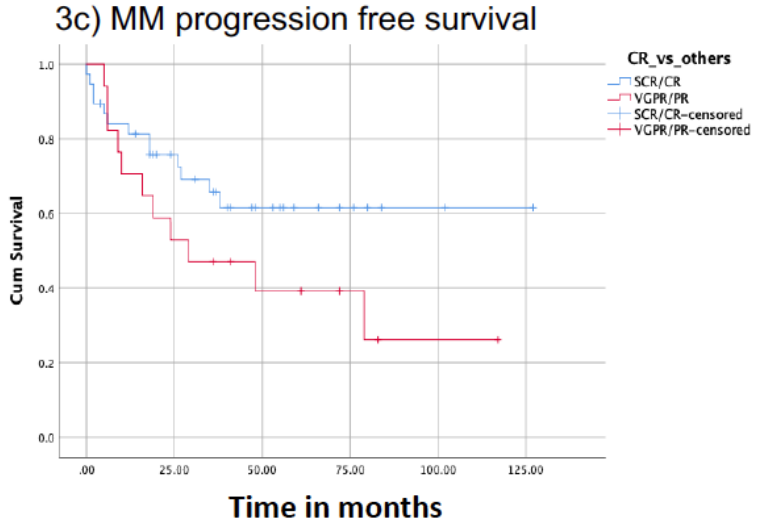


Results

Figure 3: Kaplan Meier survival analysis for overall patient survival (3a), death censored graft survival (3b) and MM progression free survival (3c) analysed by depth of MM response prior to KT







Conclusion

- Outcome of MM patients receiving KT are acceptable but significant morbidity remains.
- Shorter wait time to KT after MM treatment is not associated with poorer outcome and may be considered.
- MM relapse is the main determinant of death and graft loss.

References

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