

# Clinical practice pattern of management of plasma cell dyscrasia for kidney transplant candidates and recipients in the United States

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## Abstract

**Background:** Plasma cell dyscrasia (PCD) is a rare but important cause of end stage kidney disease (ESKD). Kidney transplant is the treatment of choice in patients with ESKD. However, the complexity of PCD care and risk of disease recurrence poses challenges to kidney transplant candidacy and outcomes. We examined the current clinical practice patterns of clinicians who care for patients with PCD and identified barriers to kidney transplantation for patients with PCD.

**Methods:** A web-based survey was developed and distributed from January to July 2024 to kidney transplant clinicians (American Society of Transplant (AST) members), hematologists (PCD experts), and onco-nephrologists.

**Results:** Seventy clinicians (50 transplant nephrologists, 18 hematologists, and two surgeons) from 42 transplant centers in the US participated in the survey. Clinical practice patterns pre and post kidney transplant for patients with PCD are highly variable among institutions, and only 36% reported having a protocol for pre- and post-transplant management for patients with PCD. Particularly, the requirement for pre-transplant hematologic remission criteria, induction and maintenance immunosuppression regimens and protocols for prophylaxis and screening for opportunistic infection are areas of future study. Clinicians listed lack of data and practice guidance as well as communication challenges among multiple specialties especially hematology and kidney transplant clinicians as notable barriers.

**Conclusions:** Our study identified the highly variable current practice patterns when evaluating and managing patients with PCD for kidney transplant. Our findings emphasize the need for collecting and sharing clinical data to support standardized practices and serve as a basis for the upcoming multi-societal management recommendation for kidney transplant for patients with PCD.

## Keywords

Kidney transplant, plasma cell dyscrasia, multiple myeloma, AL amyloidosis, practice pattern

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## Introduction

Plasma cell dyscrasias (PCD) represent a group of disorders characterized by monoclonal protein produced by plasma cell clones, such as multiple myeloma, AL amyloidosis, and monoclonal gammopathy of renal significance (MGRS). PCD frequently leads to renal complications and end-stage kidney disease (ESKD). Nearly 10% of patients with newly diagnosed multiple myeloma requires dialysis at presentation and 50% of patients with multiple myeloma can develop kidney disease after diagnosis. Kidney involvement in AL amyloidosis occurs in up to 80% of cases, and is most often characterized by nephrotic range proteinuria,<sup>1–3</sup> and reduced kidney function in cases of vascular-predominant amyloidosis. MGRS is diagnosed by kidney biopsy, and 10%–20% of the cases can progress to ESKD.<sup>4</sup>

Despite a high frequency of kidney involvement, patients with PCD are disproportionately excluded from the process of kidney transplant evaluation. While multiple myeloma represents 1.2–1.6% of dialysis population,<sup>5,6</sup> they rarely undergo kidney transplantation. According to United Network for Organ Sharing (UNOS), only 8–16 kidney transplants were performed yearly for patients with history of multiple myeloma (2011–2018), accounting for only 0.05% of total kidney transplants in this time frame. Similarly, 40–45 kidney transplants (0.2%) were done yearly for AL amyloidosis.<sup>7</sup> More recent data on patients' survival after kidney transplantation for multiple myeloma<sup>8–10</sup> and AL amyloidosis<sup>11–13</sup> suggest similar allograft and patient survivals compared to those with diabetes. However, the management of patients with PCD poses unique challenges in the kidney transplant setting due to lack of standardized approaches to evaluating the kidney transplant candidacy, the risk of recurrence and complications associated with immunosuppression. Current American Society of Transplantation (AST) guidelines for transplant evaluation for patients with hematological malignancies have limited guidance on these specific topics.<sup>14</sup>

This study aims to investigate the clinical practice patterns of kidney transplantation in patients with PCD, focusing on pre-transplant evaluation, disease management, and strategies to mitigate recurrence through a national survey of kidney transplant clinicians and hematologists who specialize in PCD in the US. This manuscript is a work product of the AST Kidney Pancreas Community of Practice (KPCOP), Transplant Onconephrology workgroup.

## Methods

### Survey design and distribution

We developed the survey instrument by multi-disciplinary discussion among the workgroup members. Transplant Onconephrology workgroup of AST KPCOP, a multidisciplinary team consisting of nephrologists (12), hematologists (4), and renal pathologist (1), developed the survey

items to ensure their readability, interpretability, and applicability to the kidney transplant setting. We asked about kidney transplant listing criteria and pre- and post-kidney transplant management of immunosuppression and PCD. The survey instrument is included in the supplement materials (Supplemental Document).

The survey was developed and distributed to kidney transplant clinicians, hematologists (plasma cell dyscrasia (PCD) experts), and onconephrologists. The survey was distributed from January to July 2024 via AST eNews (AST membership email listserv) and Hubs (AST online forum), the transplant nephrology WhatsApp group, the Plasma Cell Disorder Working Group (PCDWG) of Center for International Blood and Marrow Transplant Research (CIBMTR), and Twitter/X. The responses were obtained through Research Electronic Data Capture (REDCap) anonymously. We sent reminder emails to the email listserv 2 and 4 weeks after the first post. Personal emails were also sent to the AST members and PCDWG of CIBMTR to enhance the response rate. The study was approved by the institutional review boards of Mass General Brigham (IRB 2023P002018). We did not offer remuneration for study participation.

## Results

### Characteristics of survey participants

Table 1 summarizes the characteristics of the survey participants. Seventy clinicians (50 transplant nephrologists, 18 Hematologists, and two surgeons) from 42 different transplant centers in the US (21% of total 200 centers) and other non-UNOS member institutions participated in the survey (Table 1). We received a median of 1 response per center (IQR, 1–1, range 1–3). Fifty percent reported no existing protocol, while 36% reported an existing protocol for kidney transplant for patients with PCD, and the remaining 14% being unsure. The institutions that have an existing protocol developed one using internal hematology experts (76%), literature review (68%), or external institutions with expertise in care for PCD experts (28%). When respondents were asked if they were aware of the ASTs current guidelines on patients with paraprotein disease, only 37% responded yes, while the remaining 63% were unaware.<sup>14</sup>

### Evaluation of kidney transplant candidates with history of PCD

To understand the volume of kidney transplant evaluations and actual transplants for patients with PCD, we asked the clinicians about their practice. Regarding kidney transplant evaluations for patients with PCD, 1.4% ( $n=1$ ) reported none / year, 44% ( $n=31$ ) respondents reported evaluating 1–5 cases/year, 26% ( $n=18$ ) evaluated 5–10 cases/year, 14% ( $n=10$ ) evaluated >10 cases/year, while

**Table 1.** Demographic of survey participants.

Variables	N (total n=70) (%)
Role in the transplant team	
Nephrologist	50 (71)
Hematologist	18 (26)
Surgeon	2 (2.9)
Transplant center size (cases/year)	
1–100	9 (12.8)
101–200	20 (29)
201–300	14 (20)
301 and more	10 (14)
Unknown or non-UNOS center	17 (24)
Transplant evaluation for patients with PCD (cases/year)	
None	1 (1.4)
1–5	31 (44)
5–10	18 (26)
>10	10 (14)
Not sure	10 (14)
Transplant for patients with PCD (cases/year)	
None (policy to not transplant patients with PCD)	3 (4.3)
None	6 (8.6)
1–5	41 (59)
5–10	4 (5.7)
>10	4 (5.7)
Not sure	12 (17)
Resources used to develop policies for transplanting PCD (multiple answers allowed)	
Literature review	17 (68)
Collaboration with hematologists specialized in PCD	19 (76)
Collaboration with other institutes	7 (28)
Duration of remission requirement	
None	10 (14)
<1 year	4 (5.7)
>1 year	22 (31)
>3 years	13 (19)
>5 years	7 (10)
Other (e.g. case-by-case, depending on diseases)	14 (20)

14% ( $n=10$ ) were not sure (Table 1). In contrast, regarding kidney transplantation, 59% ( $n=41$ ) reported 1–5 cases transplanted per year, 5.7% ( $n=4$ ) reported 5–10 cases transplanted per year or more than 10 cases transplanted per year. Notably, 8.6% ( $n=6$ ) reported they don't transplant patients with PCD, and 4.3% ( $n=3$ ) reported they have a policy not to transplant patients with PCD (Table 1). These findings highlight the gap between the number of patients evaluated and those who get transplanted.

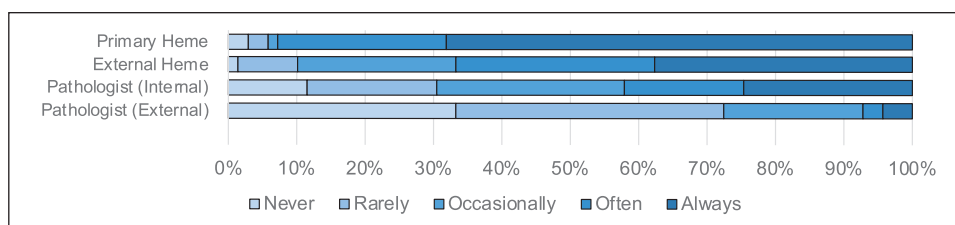
Evaluating patients with a history of PCD for kidney transplant requires coordination between multiple specialties. We asked our participants how often specialists were involved when evaluating kidney transplant candidates. Most (68%,  $n=47$ ) of the respondents always consulted candidate's primary hematologist (Figure 1). On the other hand, when the survey respondents were asked if they would consult other hematologists with expertise in PCD and kidney transplant, 38% ( $n=26$ ) responded always, and 29% ( $n=20$ ) responded often. In comparison, 23% ( $n=16$ ) occasionally referred to physicians with expertise in PCD and kidney transplants. We also evaluated the role of pathologists in kidney transplant evaluation. We compared the role of in-house pathologist vs pathologists at other centers. 28% ( $n=19$ ) occasionally consulted pathologists, 25% ( $n=17$ ) always consulted, 17% ( $n=12$ ) responded often while 12% ( $n=8$ ) responded never (Figure 1).

### Factors affecting candidacy for kidney transplant

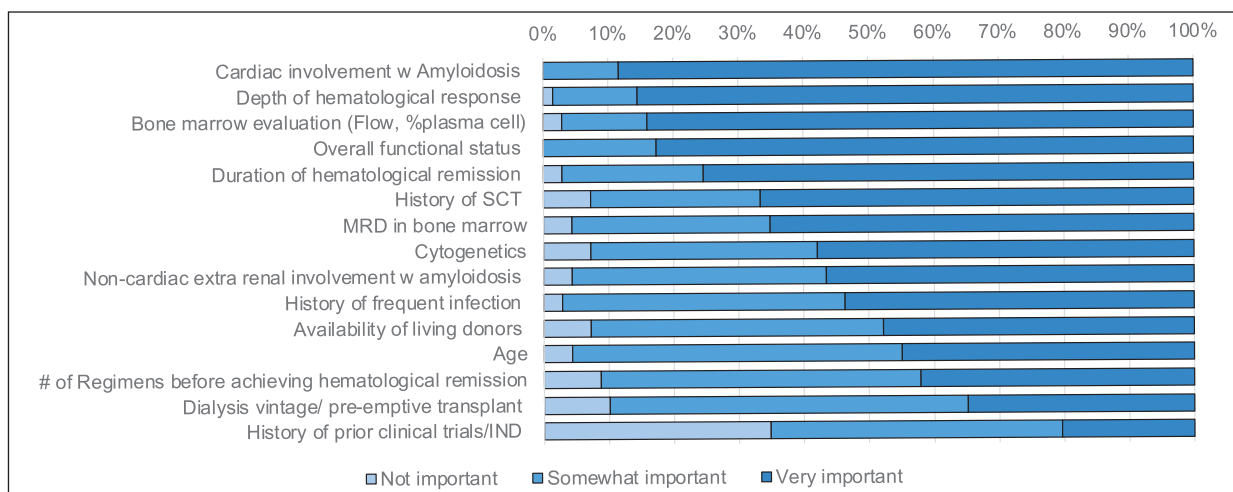
For patients with a history of PCD, candidacy for kidney transplantation is complex and involves a nuanced assessment based on various clinical variables (Figure 2). As per the respondents, some of the key factors included cardiac involvement with amyloidosis, duration and depth of hematological response, bone marrow evaluation (flow cytometry assessment, percentage of plasma cells in bone marrow), and overall functional status. Required duration of hematological remission prior to listing for a kidney transplant is highly variable (Table 1). Many required >1-year duration of remission, while some institutions (14%) had no requirements or the requirement was decided on a case-by-cases (20%). (N.B. the definition of hematological remission is at the discretion of respondents, as we didn't distinguish each PCD subtype in the survey.) Both nephrologists and hematologists reported concordant perspectives on the importance of patient's functional status, depth and duration of hematological response, and cardiac involvement with PCD. Nephrologists reported patient's age, hematological parameters (e.g. cytogenetics, bone marrow evaluation, minimal residual disease status, and history of hematopoietic stem cell transplant) and availability of living donors as more important factors, compared to hematologists. (Figure S1).

### Post-kidney transplant monitoring and management of PCD

Post-kidney transplant monitoring of recurrence in patients with a history of PCD is critical. As per the survey results, 68% and 28% of respondents believed hematologists and transplant nephrologists should be monitoring clinical biomarkers of PCD, respectively, while 1.4% reported ( $n=1$ )



**Figure 1.** The roles of various specialties in evaluating kidney transplant candidates. Participants were asked how often they would consult each specialty by 4-point Likert scale: never, rarely/occasionally, often, and always. Heme: hematology.



**Figure 2.** Factors considered to evaluate candidacy for kidney transplant. Respondents ranked the significance of these factors on a 3-point Likert scale: very, somewhat, or not important.

that general nephrologists should monitor these markers (Table 1).

Figure 3 represents various biomarkers to be monitored after kidney transplant. Most reported monitoring proteinuria, serum free light chain (FLC), urinary protein electrophoresis (UPEP) with immunofixation, and serum protein electrophoresis (SPEP) with immunofixation every 3 months. Kidney biopsy and minimal residual disease (MRD) monitoring through bone marrow biopsy would be only performed when clinically indicated.

Maintenance therapies for PCD after kidney transplant were also variable. While 19% indicated that they would prefer no maintenance therapy for PCD post-kidney transplant, 28% and 12% indicated use daratumumab or proteasome inhibitors, respectively. A small number of participants (4.3%) reported the use of immunomodulatory drugs (IMiD), such as lenalidomide.

### Immunosuppression management peri- and post-kidney transplant

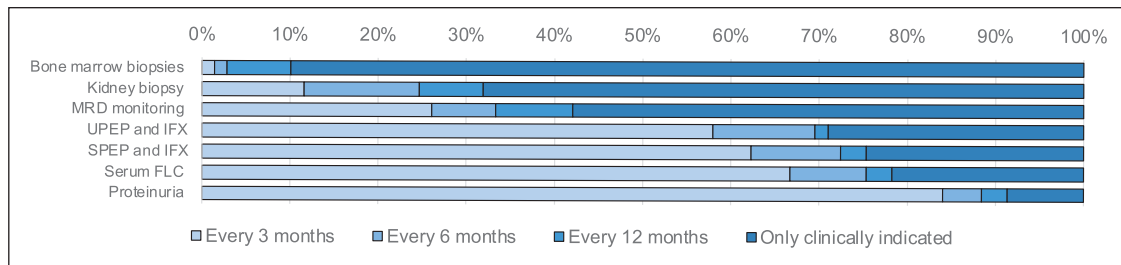
Immunosuppression is key in avoiding transplant rejection. However, because patients with PCD are typically treated

with various myelosuppressive chemo- and targeted therapies, and are at higher risk of infection, transplant clinicians may consider modifying immunosuppression to avoid over-immunosuppression. For induction regimens (multiple answers allowed), 52% would use basiliximab, while 45% would use thymoglobulin, 32% reported to use glucocorticoids. For maintenance immunosuppression regimen, clinicians reported using agents such as steroids ( $n=41$ , 59%), tacrolimus ( $n=54$ , 78%), mammalian target of rapamycin (mTOR) inhibitors ( $n=11$ , 16%), mycophenolate (MPA,  $n=52$ , 74%), azathioprine (AZA,  $n=4$ , 6%), and belatacept ( $n=7$ , 10%) for maintenance therapy. Clinicians also reported that reduced doses of AZA and MPA are more likely to be adapted compared to standard doses. 40% ( $n=28$ ) responded using reduced doses of MPA compared to 34% ( $n=24$ ) using standard dose. Similarly, out of the four respondents that picked AZA as the agent for maintenance, three reported using reduced doses.

### Post-kidney transplant infection prophylaxis

Post-kidney transplant patients are at high risk for viral and bacterial infections due to immunosuppression and it





**Figure 3.** Factors used to monitor clinical biomarkers for PCD post kidney transplant. Monitoring frequency was divided into every 3 months, 6 months, 12 months and upon clinical indication post kidney transplant.

is a common practice to use prophylactic agents post-kidney transplant. Clinicians were asked if they believed duration of infectious prophylaxis and viral load monitoring should be changed in transplant populations with PCD. 71% ( $n=50$ ) opted for regular prophylaxis as compared to 20% ( $n=14$ ) who opted for extended prophylaxis. Similarly, 45% ( $n=31$ ) clinicians monitor viral load regularly, as for other patients without PCD, compared to 13% ( $n=9$ ) of clinicians who reported monitoring more frequently in patients with PCD.

### Challenges and barriers when caring for kidney transplant candidates or recipients with PCD

As part of the survey, we asked the participants to share the various barriers and challenges that clinicians face when pursuing kidney transplants for patients with PCD (Supplement Material). We noted several themes: (1) lack of large-scale data on pre-and post-transplant monitoring, immunosuppression and infection prophylaxis, (2) challenges in care coordination among multiple specialties (local nephrologists, transplant nephrologists, and hematologists), (3) Need for bidirectional learning and collaboration, and (4) call for clinical management guidelines. Overall, many concluded that despite growing opportunities for co-managing potential kidney transplant candidates with history of PCD, there remains a variation in clinical practice due to the lack of a comprehensive set of guidelines for evaluation and management.

## Discussion

In this multicenter survey, we aimed to understand the current practice pattern of kidney transplants for patients with a history of paraprotein-associated kidney diseases, focusing on pre-transplant evaluation, disease management, post-transplant outcomes, and strategies to prevent recurrence.

Evaluating potential candidates among patients with PCD hinges on achieving and maintaining adequate disease control. The survey results show a wide variation in practice across transplant institutions, from no formal policy to multiple kidney transplants per year. This area serves the shared interest among general nephrology, transplant nephrology, and hematology-oncology, and highlights the need for standardized protocols and

evidence-based guidelines tailored to this unique patient population. A multidisciplinary approach will be essential to construct a criterion to streamline the process of determining candidacy.

Managing immunosuppression post-kidney transplant in patients with PCD is particularly challenging. The risk of graft rejection and disease relapse requires careful balancing, but data are lacking to guide the therapies. Additionally, maintenance therapy for PCD after kidney transplant was highly variable. While IMiDs are highly effective maintenance regimen for PCD, transplant clinicians should be aware of the risk of acute rejection from IMiD.<sup>15–17</sup> Further investigation can also help analyze the role of maintenance therapies targeting the underlying plasma cell disease in the context of transplant.

Monitoring post-transplant includes serial measurements of plasma and urine biomarkers. Protocol allograft biopsies, which may allow for early identification of disease recurrence for timely initiation of therapies, were not favored likely due to the invasive nature of biopsy and limited benefit gained from the procedure.

Our study has several limitations. First, a small sample size, which covers only 21% of transplant institutions in the US, is a limitation. Additionally, our study respondents are mostly from medium- to large-volume transplant centers (Table 1). This may have skewed the clinical practice patterns in offering kidney transplant for high-risk populations (e.g., patients with PCD), as large-volume transplant centers may have higher risk tolerance to absorb undesirable outcomes (e.g., graft failure). Additionally, due to the voluntary nature of the survey, the responses are likely skewed from those who are already interested and involved in kidney transplant for patients with PCD. While the small sample size restricts the generalizability of our findings, it offers a focused perspective on the real-world approach to kidney transplant and provides insights into challenges and variability in managing kidney transplants in patients with PCD. Despite these limitations, the data provides a valuable starting point for discussing standardization of care. Second, the survey collected the data for PCD as a whole, and didn't ask the practice patterns in specific PCD, such as AL amyloidosis vs. MGRS.<sup>18</sup> Frequency and timing of disease recurrence post-kidney transplant, as well as hematological response criteria vary among each

PCD,<sup>19,20</sup> and thus, monitoring strategies should be tailored accordingly. In fact, 36% of respondent reported the duration of hematologic response would differ by different kinds of PCD diseases. Further detailed consideration to fit each clinical condition is warranted.

Acknowledging the need of clinical management guidance uncovered by the current survey, the AST KPCOP transplant onconeurology workgroup and International Kidney Monoclonal Gammopathy research group recently published a multi-societal, clinical management recommendations of kidney transplant patients with PCD.<sup>21</sup> This clinical management recommendations include available data on recurrence risk and timing, pre-and post-transplant disease monitoring, and immunosuppression management for each subtype of PCD.<sup>21</sup> Given the evolving therapies for PCD, the recommendations serve as a live guidance that requires timely updates.

In summary, the survey results call for developing interdisciplinary, evidence-based standardized clinical guidelines to improve kidney transplant practices in patients with PCD. Collaborative efforts across various specialties and transplant centers should enhance data collection and generate evidence to guide clinical care.

### Data availability

Data are available by reasonable request to the corresponding author.

### Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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### Ethical considerations

The study was approved by the institutional review boards of Mass General Brigham (IRB 2023P002018).

### Consent to participate

By answering the voluntary survey, the participants consent to participate to the study.

### Consent for publication

N/A

### Guarantor

NM

### Contributorship


Participated in research design: all authors.


Participated the writing of the paper: all authors.

Participated in the performance and data analysis, interpretation of the paper: all authors.

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### Supplemental material

Supplemental material for this article is available online.

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