DR TAREK ALHAMAD (Orcid ID : 0000-0003-4289-0817)

DR MICHELLE LUBETZKY (Orcid ID : 0000-0003-1076-7953)

DR KRISTA L. LENTINE (Orcid ID : 0000-0002-9423-4849)

DR RONALD F. PARSONS (Orcid ID : 0000-0002-9243-1582)

DR KENNETH J WOODSIDE (Orcid ID : 0000-0002-7495-3758)

DR CHRISTOPHER BLOSSER (Orcid ID : 0000-0001-8368-6682)

DR ALEXANDER CLARK WISEMAN (Orcid ID : 0000-0002-8619-0938)

DR NEERAJ SINGH (Orcid ID : 0000-0002-0141-3371)

DR SU-HSIN CHANG (Orcid ID : 0000-0001-5872-9556)

DR GAURAV GUPTA (Orcid ID : 0000-0003-1919-1970)

DR MIKLOS ZSOLT MOLNAR (Orcid ID : 0000-0002-9665-330X)

DR ARPITA BASU (Orcid ID : 0000-0002-0533-4582)

DR EKAMOL TANTISATTAMO (Orcid ID : 0000-0003-0883-6892)

DR LEONARDO V RIELLA (Orcid ID : 0000-0002-7636-3196)

DR DARSHANA M DADHANIA (Orcid ID : 0000-0002-7973-1521)

Article type : O - Original Article

Kidney Recipients with Allograft Failure, Transition of Kidney Care (KRAFT): A Survey of Contemporary Practices of Transplant Providers

Authors: Tarek Alhamad (000-0003-4289-0817)[1], Michelle Lubetzky[2], Krista L. Lentine[3], Emmanuel Edusei[2], R. Parsons[4], M. Pavlakis[5], Kenneth J. Woodside[6], D. Adey[7], Christopher D Blosser[8], Beatrice P. Concepcion[9], J. friedewald[10], A. Wiseman[11], Neeraj Singh[12], S-H. Chang[1], Gaurav Gupta[13], Miklos Z. Molnar[14], Arpita Basu[4], Edward Kraus[15], Song Ong[16], Arman Faravardeh[17], Ekamol Tantisattamo[18], Leonardo Riella[19], Jim Rice[20], Darshana M. Dadhania (ORCID 0000-0002-7973-1521)[2]

[1] Washington University in St. Louis, Saint Louis, MO

[2] New York Presbyterian Hospital- Weill Cornell Medicine, New York, NY

[3] Saint Louis University, Saint Louis, MO

[4] Emory University, Atlanta, GA,

[5] Beth Israel Deaconess, Boston, MA

[6] University of Michigan, Ann Arbor, MI

[7] University of California San Francisco, San Francisco, CA,

[8] University of Washington and Seattle Children's Hospital, Seattle, WA

[9] Vanderbilt University Medical Center, Nashville, TN,

[10] Northwestern University, Chicago, IL,

[11] University of Colorado, Denver, CO,

[12] Willis Knighton Health System, Shreveport, LA

[13] Virginia Commonwealth University, Richmond, VA,

[14] University of Tennessee Health Science Center, Memphis, TN

[15] Johns Hopkins, Baltimore, MD,

[16] University of Alabama at Birmingham, Birmingham, AL,

[17] Balboa Nephrology, San Diego, CA,

[18] University of California Irvine, Orange, CA,

[19] Brigham and Women, Boston, CA,

[20] Scripps Heath, San Diego, CA

†Corresponding author:
Tarek Alhamad
talhamad@wustl.edu

ABBREVIATIONS:

AST-KPCOP; American Society of Transplantation Kidney Pancreas Community of Practice, CNI; calcineurin inhibitor, KDIGO; Kidney Disease Improving Global Outcomes, KRAFT; Kidney Recipients with Allograft Failure - Transition of Care, PRA; panel reactive antibodies, SRTR; Scientific Registry of Transplant Recipients

Abstract

Kidney allograft failure and return to dialysis carries a high risk of morbidity. A practice survey was developed by the AST Kidney Pancreas Community of Practice workgroup and distributed electronically to the AST members. There were 104 responders that represented 92 kidney transplant centers. Most survey respondents were transplant nephrologists at academic centers. The most common approach to immunosuppression management was to withdraw the anti-metabolite first (73%), while 12% responded they would withdraw calcineurin inhibitor first. More than 60% reported that the availability of a living donor is the most important factor in the decision to taper immunosuppression, followed by the risk of infection, risk of sensitization, frailty, and side effects of medications. More than half of respondents reported that embolization was either not available or offered to less than 10% as an option for surgical intervention. More than half reported that ≤50% of failed allograft patients were re-listed before dialysis, and less than a quarter of transplant nephrologists perform frequent follow-ups with their failed allograft patients after dialysis. This survey demonstrates a heterogeneity in the care of patients with a failing allograft and the need for more evidence to guide improvements in clinical practice related to transition of care.

Introduction

Despite the improvement of long-term kidney allograft survival, allograft failure with return to dialysis is common. It is estimated that 12% of the patients on the current kidney transplant waiting list have had a previous failed transplant.[1] Returning to dialysis remains a major challenge for patients and providers.

Patients face a higher risk of morbidity and mortality in addition to depression and social challenges in a transition period that is often not well monitored or managed by the transplant providers.[2] The estimated mortality rate in patients with failed allograft is 16% in the first year with persistently increased risk compared to those starting dialysis without a prior failed transplant. [3, 4]

The major cause of mortality after returning to dialysis is thought to be related to infections and cardiovascular disease.[4] Continuing immunosuppressive medications exacerbates the risk of infections. In a study by Gregoor et al, patients with failed allograft who continued on low-dose immunosuppression had an increased risk of infections and mortality compared to patients in whom immunosuppression medications were discontinued.[5] Conversely, weaning off immunosuppression medications carries a higher risk of sensitization of the failed allograft which may reduce opportunities for second kidney transplant, increase dialysis time in between transplants and necessitate more complex immunosuppressive treatment in the future due to positive crossmatch or rejection. [6]

Additionally, a failed allograft can cause a chronic inflammatory state that can lead to erythropoietin-resistant anemia, hypertension, chronic pain, hematuria, and even allograft rupture.[7-10] Options for medical management in symptomatic rejection of the failed allograft are limited, and the number of cycles of pulse steroids that should be attempted prior to proceeding with a surgical intervention is not well defined.

Timely referral of the patients with failed allograft for re-transplantation is crucial, as the median wait time for sensitized patients with a failed allograft is increased. Failing allograft clinics that have been established by some transplant centers facilitate renal replacement counseling, transition of care, dialysis access placement, and the management of immunosuppression medication after starting dialysis.[11]

The purpose of this study was to survey transplant providers and understand the current practice related to reduction of immunosuppression, perceived risks associated with continuing immunosuppression, and management of patient with failing allograft including the transition of care to general nephrologists.

Methods

Survey Design:

In 2017, the American Society of Transplantation Kidney Pancreas Community of Practice (AST-KPCOP) established a workgroup to study Kidney Recipients with Allograft Failure – Transition of Care (KRAFT) to understand the current data and practice patterns related to the management of recipients with a failing allograft. The workgroup developed the questions collaboratively and the survey was piloted with the KPCOP workgroup members. Where needed, the wording of the questions was adjusted for clarity. The final survey consists of 25 questions; 4 questions related to the approach for tapering immunosuppression, 10 related to perceived risks associated with tapering immunosuppression, 6 questions related to monitoring a patient with a failing allograft, 3 related to management of rejection in a patient with a failed allograft and 3 related to program description which included provider role, practice type, and transplant hospital name or United Network for Organ Sharing (UNOS) Center ID. Centers were asked in their opinion, how important FRAILTY was to the decision to taper off immunosuppression. Responses were anonymous, but UNOS ID / hospital name was used for tracking and to identify one representative response per program.

Survey Administration and Participants:

The survey was approved by the Weill Cornell Medicine Institutional Review Board (submission number 1805019273) on May 18, 2018 and approved by the Education Committee of AST for distribution. The survey was built into the REDCap® Survey tool and distributed via electronic link on the KPCOP Hub in December 2018 followed by individual email distribution to the transplant program medical directors on February 2019, March 2019 and April 2019. We received 53 responses by end of February, 35 by end of March and the remaining 30 thereafter. The survey was open until August 9, 2019. Each workgroup member actively encouraged their colleagues to complete the survey. We registered total of 118 responses and 10 of those responses were from individuals who had already completed the survey once and therefore were not allowed to proceed to complete the survey.

Of 108 responses, 2 were excluded due to incomplete responses to the survey. Of the 106 remaining responses, 12 responses were from providers outside the United States. Of the 94 U.S. responses, 14 represented multiple responses from the same centers resulting in a total of 80 unique responses, 77 adult and 3 children. We included the first complete response from each of the 80 U.S. programs and included the 12 additional responses from outside of the United States. Out of these 12 non-US responses, 3 were from Canada, 3 from the Middle East, and 6 did not identify their country.

Participating Programs:

To compare the characteristics of the transplant programs that provided a response compared to those who did not, we identified 77 unique U.S. adult transplant programs that perform more than 10 transplants per year. Based on the Scientific Registry of Transplant Recipients (SRTR) and UNOS ID, we identified 119 U.S adult transplant programs that did not respond to the survey and performed at least 10 transplants per year. We extracted the following program characteristics from the SRTR data for transplants occurring between 7/1/17 and 6/30/18: adult kidney transplant volume, age, gender, race, previous transplants, panel reactive antibodies (PRA), and cause of end stage renal disease.

Statistical Analysis:

Each kidney transplant center was represented only once in the analysis. For programs with multiple respondents, we selected the first complete response to represent the center consistent with previous surveys.[12-14] Responses to each survey question were described with percentages or frequencies, as appropriate, using the number of respondents to a given item as the denominator.

To compare the characteristics of kidney transplant centers that responded to the centers that did not respond, Chi-square tests were conducted to compare percentages for categorical variables and t-tests were used to compare frequencies or means for continuous variables. All tests were two-sided. Statistical significance was determined by an alpha level of 0.05. All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC).

Results

Survey Participants

There were 92 unique responses used to perform the analysis and generate all the figures excluding Table 1 which was generated using SRTR data. Majority of the respondents, 84%, were transplant nephrologist, 12% were transplant surgeons and 4% were other providers, and 87% of the participants had an academic affiliation.

Participating Program Characteristics

Of the 196 adult kidney transplant programs with more than 10 transplants, we received a response from 41% (n=77), representing approximately 49% of all adult kidney transplant volume recorded between 7/1/17 and 6/30/18. Compared to adult transplant programs that did not respond, participating centers had higher volume of living and deceased donor kidney transplants and female transplant patients (**Table 1**). There was no statistically significant difference in patient age, race,

percentages of repeat transplants, sensitized patients, or cause of end stage kidney disease between responding centers and non-responding centers.

Approach for Immunosuppression Reduction

Among the 92 participating kidney transplant centers, 61% reported that there was a need to standardize reduction of immunosuppression in patients with a failing kidney allografts. Centers were asked about which immunosuppressive medications should be stopped first. The majority stated that antimetabolite should be stopped first, with 73% of providers reporting that they stopped the anti-metabolite first. Only 12% of providers reported that they stopped calcineurin inhibitors (CNI) first and 2% of providers reporting stopping steroids first. An additional 13% reported that there is no unified protocol on which medication would be stopped first (**Figure 1a**)

When asked about their approach to immunosuppression management if the expected waiting time for a second kidney was more than 3 years, 30% respondents said they tapered medications over 2 to 3 months, while 20% continued low doses of immunosuppression medications until the patient received the next kidney transplant. Other respondents tapered according to urine output: 21% tapering if the urine output was less than 0.5 liter and 4% tapering if the urine output is less than 1 liter. About one fifth (21%) of responders said they had no unified protocol.

Clinicians were also asked about their specific immunosuppression management if there was no living donor and the waiting time for the next kidney transplant was more than 3 years. In this scenario, 47% tapered all immunosuppression medications within 2 to 6 months, 21% kept prednisone and tapered the rest, 10% kept low dose CNI and tapered the rest, 5% kept CNI and prednisone and tapered the antimetabolite, 3% kept low doses of all immunosuppression medications, and 2% kept a low dose of antimetabolite and tapered the rest.

When asked about the management of immunosuppression in patients with failing allograft who had a possible living donor, 38% of respondents said they continued CNI and prednisone, and stopped antimetabolite; 32% kept low doses of all immunosuppression medications; 21% kept all immunosuppression medications without reduction; and 10% reported no unified protocol (**Figure 1b**).

Factors in the decision to taper off immunosuppression medications

The survey inquired about the factors influencing their decision for tapering immunosuppression. When asked about the most important factors in the decision to taper immunosuppression, 15% reported that

continuing immunosuppression medications after dialysis was not a risk factor for adverse events and mortality, 14% were not sure, and 71% reported it is a risk factor. We examined the essential components of factors that would drive the providers' decision toward tapering off immunosuppression. Each factor was graded as three levels; very important, intermediate important, and not very important (**Figure 2**).

More than 60% reported that the availability of a living donor is the most important factor in the decision to taper off immunosuppression, followed by risk of infection, risk of sensitization, frailty, and side effects of medication. The least important factors were reported urine volume (33%), followed by age of the patient (26%), and comorbidities (20%).

Medical and surgical management of the side effects of failed allograft

When asked about the initial approach for managing signs and symptoms of a failing allograft (multiple choice question), 85% responded that they treated with high dose steroids while 35% of the respondents referred patients for an allograft nephrectomy as the initial management. Less than 6% made other immunosuppression adjustments and/or interventions including increasing the dose of CNI, increasing the dose of antimetabolite, or referring for coil embolization.

To be more specific, we asked about the timing of referral for allograft nephrectomy (multiple choice question). We found that 79% referred patients for nephrectomy if there were persistent signs and symptoms of rejection, 55% referred patients when patients first started to have symptoms, 36% referred patients if patients had anemia with limited response to erythrocyte stimulating agents, and 8% responded that there was no unified protocol.

If a patient was scheduled for a nephrectomy, 33% of respondents continued prednisone for some time after the procedure, 33% stopped all medications immediately after the surgery, 30% stopped all medications within a week or two after the surgery and 2% stopped before the surgery.

Coil embolization was not commonly performed. The majority (60%) of the respondents reported less than 10% of their patients underwent embolization for failed allograft and 32% reported that embolization was not available at their center.

Preparing for the next kidney transplant

In terms of listing for the next kidney transplant, 32% of respondents reported that 25-50% of the patients were listed for transplant before starting dialysis, 28% reported less than a quarter were

preemptively listed, 22% reported that majority, 50% to 80%, were preemptively listed, while only 6% reported more than 80% were listed before dialysis initiation. Twelve percent were unsure (**Figure 3a**).

There was a variation in how and when panel reactive antibodies (PRA) were checked in patients with failed allografts. Majority, 76%, of centers responded they would check PRA only if the patient was listed for another kidney transplant, 15% would check PRA every 3 months, 2% every 6 months, and 2% every year. Four percent did not know how often PRAs were checked.

Communications and transition of care

After starting dialysis, 36% of transplant nephrologists responded that they did not have a unified protocol of follow up, 21% did follow up visits every 3 to 6 months until patients were off immunosuppression medications, 17% did only 1 visit, and 11% never saw their patients after starting dialysis (**Figure 3b**). As for frequency of communications with the general nephrologist to discuss transition of care, 49% reported always, 28% sometimes, 7% rarely, and 2% never, while 14% did not provide an answer (**Figure 3c**).

Centers with multiple responses

There were 14 duplicates from 13 centers that were excluded from the analysis. Side by side comparison of the responses using one response per center versus inclusion of all responses demonstrates that there was less than 5% difference for each of the responses.

Discussion

This contemporary survey of predominantly U.S. transplant practitioners characterizes current practice patterns for the management of immunosuppression and the care of the recipient with a failing kidney allograft. Our data comes from transplant providers who care for approximately 49% of adult transplant centers across the United States and demonstrates not only heterogeneity in the management of the failed kidney allograft but also the need for more data to guide management. Our data demonstrate that (1) majority of the providers feel that there is need to standardize immunosuppressive management in a patient with a failed kidney allograft with the goal of improving patient outcomes, (2) the possibility of a living donor was the most important factor in the decision to wean or not wean off immunosuppressive therapies, (3) less than 30% of the programs responded that majority of the patients with a failing kidney allograft are relisted prior to starting dialysis, and (4) less than 30% followed the patients at a regular interval after kidney allograft failure.

These contemporary survey responses suggest a change in attitudes over time in terms of immunosuppression management and withdrawal. More than two thirds of the respondents reported that the first medication that they stopped in a failed allograft was antimetabolites whereas 12% stopped CNI first. This represents a change from a 2012 survey, wherein 58% of respondents stopped antimetabolites first and 38% tapered CNI first.[15] Findings from a few studies may have led to this change in practice. A retrospective single center study published in 2014 examined the impact of weaning of immunosuppression and reported that 0 out of 24 patients who were maintained on CNIs required transplant nephrectomy, compared to 41% of patients who were weaned of immunosuppression.[6]

At the present time, there is paucity of prospective data identifying the best approach for managing immunosuppression after a failed kidney transplant. Based on review of the literature, Pham and colleagues suggest continuing immunosuppression in those with a potential living donor or with some residual renal function and suggest discontinuing antimetabolite/mTOR inhibitors at start of dialysis and tapering the CNI over the next 4 to 6 weeks followed by slow tapering of prednisone.[16] Similarly, the British Transplantation Society suggests (Grade 2C), despite low evidence, to taper immunosuppression after allograft failure but also consideration maintaining immunosuppression in those who may be re-transplanted within one year.[17] Our survey demonstrates that stopping the antimetabolite first and then taper CNIs is common in contemporary practice. However, our survey also demonstrates that there is great heterogeneity in the approach with only 46% of responding providers tapering off all immunosuppressive therapies over 2 to 6 months period if there is no opportunity of transplant in the near future. Consistent with published general guidelines, the survey respondents felt having the possibility of a living donor for repeat transplant was the most important factor they considered when deciding to wean immunosuppression. However, despite this agreement, the approach to immunosuppression reduction varied significantly.

Patients with a failed allograft are also at higher risk of mortality after starting dialysis compared to those who were never transplanted. Previous papers suggest that this increased mortality is primarily due to cardiac (36%) or infections complications (17%).[3, 18] Maintaining full immunosuppression has been associated with increased risk of hospitalization and infection within 6 months of starting dialysis.[19] Risk of infection was the second most important factor in deciding to wean off immunosuppression in our survey, after availability of a living donor for repeat transplant. On the other hand, the presence of a failed allograft in ESKD patients who had completed withdrawal of immunosuppressive therapies is

associated with higher CRP levels, lower albumin and decreased muscle mass compared to those who were never transplanted,[8] parameters associated with frailty. These data suggest that both ends of the spectrum, continuing immunosuppressive therapies and withdrawing all immunosuppressive therapies, are associated with negative consequences for ESKD patient with a failed allograft, highlighting the need for more robust data and strategies to improve the management of these patients.

Avoidance of sensitization may be possible through slower tapering of immunosuppression and is also an important consideration when weighing the risk of infection that comes with continuing immunosuppression. .[20] This risk of sensitization is not fully appreciated in the early months post graft failure. Augustine and colleagues demonstrated that 56% of individuals were highly sensitized at 6-24 months post kidney graft failure.[6] Among individuals whose immunosuppression was weaned, sensitization increased from 21% at time of graft failure to 68% at 6-24 months post graft failure. In contrast, those who remained on immunosuppression had minimal risk of sensitization. Furthermore, transplant nephrectomy secondary to acute rejection was required in 41% of those who were weaned off immunosuppression while 0% of those who were still on immunosuppression required graft nephrectomy.

Urine output, which is a useful gauge of residual renal function, was ranked as the least important factor in our survey by respondents when deciding about weaning immunosuppression. A previous study suggested an association of continuing immunosuppression with survival benefit in patients with allograft loss, who returned to peritoneal dialysis and had some residual kidney function.[21] In a different question that we asked, 21% of the respondents would taper immunosuppression based on urine output of less than 0.5 liter and only 4% would tapper if urine output was less than 1 liter. While there are little data to support tapering of immunosuppression based upon urine output, Jassel et al. found mortality benefit in patients who remained on immunosuppression. This survival benefit was higher at higher levels of preserved GFR.[21]

Timely referral for another kidney transplant is vitally important, as the time to re-transplantation may be longer than for *de novo* transplant candidates due to sensitization. Our survey showed that 60% of the respondents reported that less than half of their patients with a failed kidney allograft were listed preemptively for another kidney transplant. More efforts are needed to improve referral rates. Such practice is consistent with a general recommendation of the 2020 Kidney Disease Improving Global Outcomes (KDIGO) transplant candidate guideline to refer potential kidney transplant candidates for

evaluation at least 6 to 12 months before anticipated dialysis initiation to facilitate identification and evaluation of living donors and plan for possible pre-emptive transplantation.[22]

Many general nephrologists may not be familiar with the management and goals of immunosuppression after allograft loss. Unfamiliarity with immunosuppression care and lack of follow up with transplant centers may lead to mismanagement and unfavorable outcomes. Our study showed that less than a quarter of transplant nephrologists perform frequent follow-ups with their failed allograft patients after starting dialysis. At the same time, around 75% of transplant nephrologists communicate always or sometimes with the nephrologists in the community regarding care of their patients with allograft failure.

For medical and surgical management, the majority of the respondents (85%) use high dose steroids for the management of the initial symptoms, and 79% refer for nephrectomy if there are persistent signs or symptoms of rejection. As for the management of medications around the time of nephrectomy, there is a clear disagreement among respondents, which is driven by the lack of data. Despite previous publications suggestions that embolization carries less mortality and less complications than surgical allograft nephrectomy,[23, 24] 32% of respondents reported that embolization was not available, and 60% reported that embolization compromised less than 10% of surgical nephrectomies.

Our study has several limitations. First, respondents' answers to the survey questions might not be entirely generalizable. We used the first response from each center and this may not reflect the overall practice patterns of a given transplant center. Second, not all transplant centers were represented in this survey; however, the centers in the US that responded represent 49% of the total yearly kidney transplant volume in the US. Furthermore, it should be noted that our study did not address the challenge associated with prescribing and monitoring maintenance immunosuppression following graft failure. Last, we did not examine the question of what percentage of patients would be eligible or be interested in a subsequent transplant.

In conclusion, this survey of kidney transplant centers highlights the heterogeneity in the practice of immunosuppression withdrawal in failing allografts. Clear areas of opportunity exist for formal studies to address how best to adjust of immunosuppression in the failing allograft to mitigate high rates of morbidity and mortality during this transition time period. Additionally, we identified opportunities for improvement in referral to re-listing before starting dialysis and gaps that exist in follow up care on patients after returning to dialysis. This study calls for the need for further data to support our practices

and the need for standardized protocols regarding the transition of care of patients with failed allografts.

Acknowledgements

This manuscript is a work product of the American Society of Transplantation's Kidney and Pancreas Community of Practice (KPCOP) Failing Allograft Workgroup. The authors thank survey respondents, including members of the AST Kidney-Pancreas COP. An abstract describing portions of this work was presented as an abstract at the 2019 American Society of Nephology Kidney Week, Washington, DC.

Disclosures/Conflicts of Interest:

The authors of this manuscript have no conflicts of interest to disclose as described by the American Journal of Transplantation.

Data Availability Statement

Data is available upon request and approval from authors.

FIGURE LEGENDS

Figure 1a. Initial approach toward reduction of immunosuppression medications in patients with failed allografts.

Figure 1b. Approach toward immunosuppression management in a failed allograft if living donor is available.

Figure 2. Perception of important factors in decision to taper immunosuppression.

Figure 3a. Re-listing for the next kidney transplant before starting dialysis

Figure 3b. Frequency of follow up with transplant nephrologists after starting dialysis

Figure 3c. Team discussion about transition of care for patients with failed allograft

Table 1. Characteristics of the Adult Kidney Transplant Programs Responding to the Survey

Program Characteristics	**Responded[a] (n=77)**	**Did Not Respond[a] (n=119)**	**P value**
Percentage of Adult Transplant Performed	49.2%	50.8%	
Kidney Transplant, median (Q1, Q3)	118 (67, 183)	64 (33,104)	**<0.0001**
Living Donor Transplants, median (Q1, Q3)	31 (13, 53)	17 (7, 30)	**0.008**
Deceased Donor Transplants, median (Q1, Q3)	84 (46, 119)	50 (24, 78)	**<0.0001**
Recipients age 65 and older, median percentage (Q1, Q3)	19% (16,23)	20% (15, 27)	0.29
Female, median percentage (Q1, Q3)	40% (36, 44)	39% (33, 44)	**0.04**
Race/Ethnicity, median percentage (Q1, Q3)			
Caucasian	44% (28,66)	48% (30, 65)	0.56
African American	22% (11, 37)	21% (11, 33)	0.62
Hispanic	9% (4, 27)	10% (5, 25)	0.68
Previous Transplant, median percentage (Q1, Q3)	13% (10, 17)	12% (9, 16)	0.15

Peak PRA >80, median percentage (Q1, Q3)	14% (11, 21)	14% (10, 19)	0.42
Cause of ESKD, median percentage, (Q1, Q3)			
Glomerular disease	25% (20, 29)	25% (19, 30)	0.52
Diabetes mellitus	24% (21, 30)	27% (20, 33)	0.12
Hypertension	22% (15, 29)	21% (15, 29)	0.99

[a]Adult Kidney transplant programs with less than 10 transplants during the 7/1/17 and 6/30/18 interval were not included in this table.

PRA, panel reactive antibodies; ESKD, end stage kidney disease.

Figure 1a. Initial approach toward reduction of immunosuppression medications in patients with failed allografts.

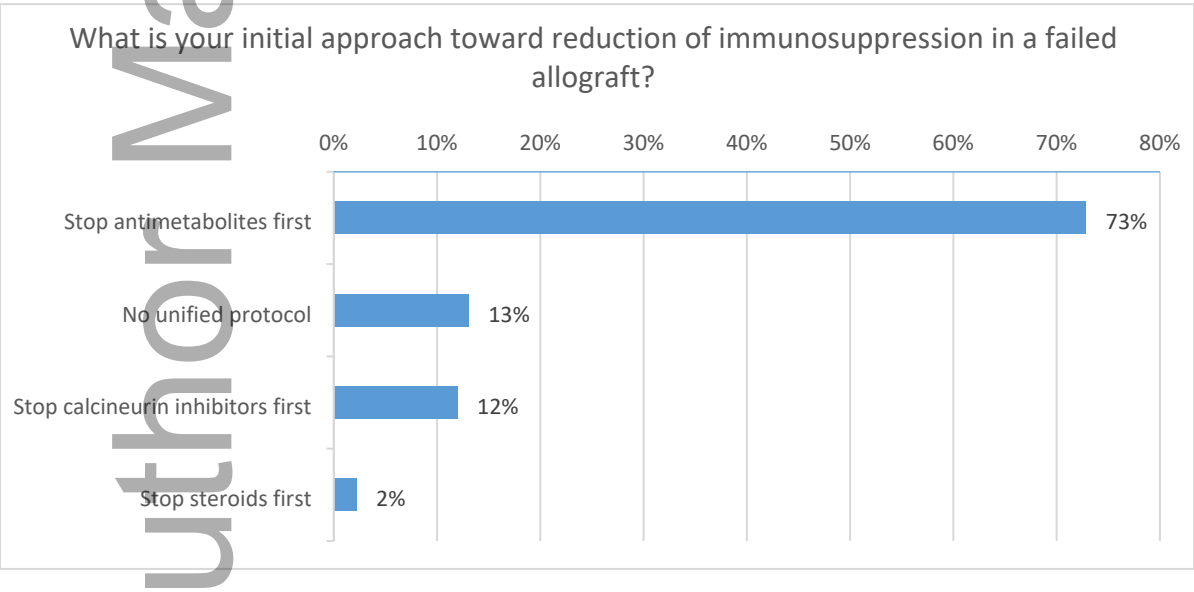


Figure 1b. Approach toward immunosuppression management in a failed allograft if living donor is available

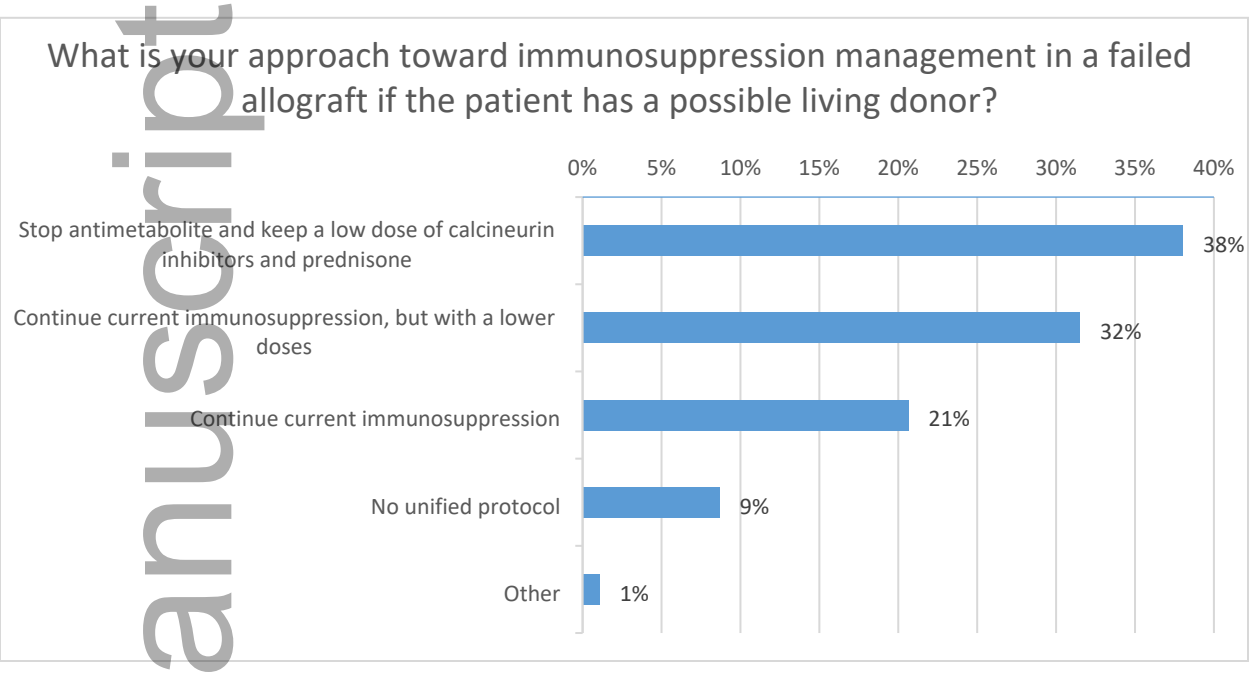


Figure 2. Perception of important factors in decision to taper immunosuppression.

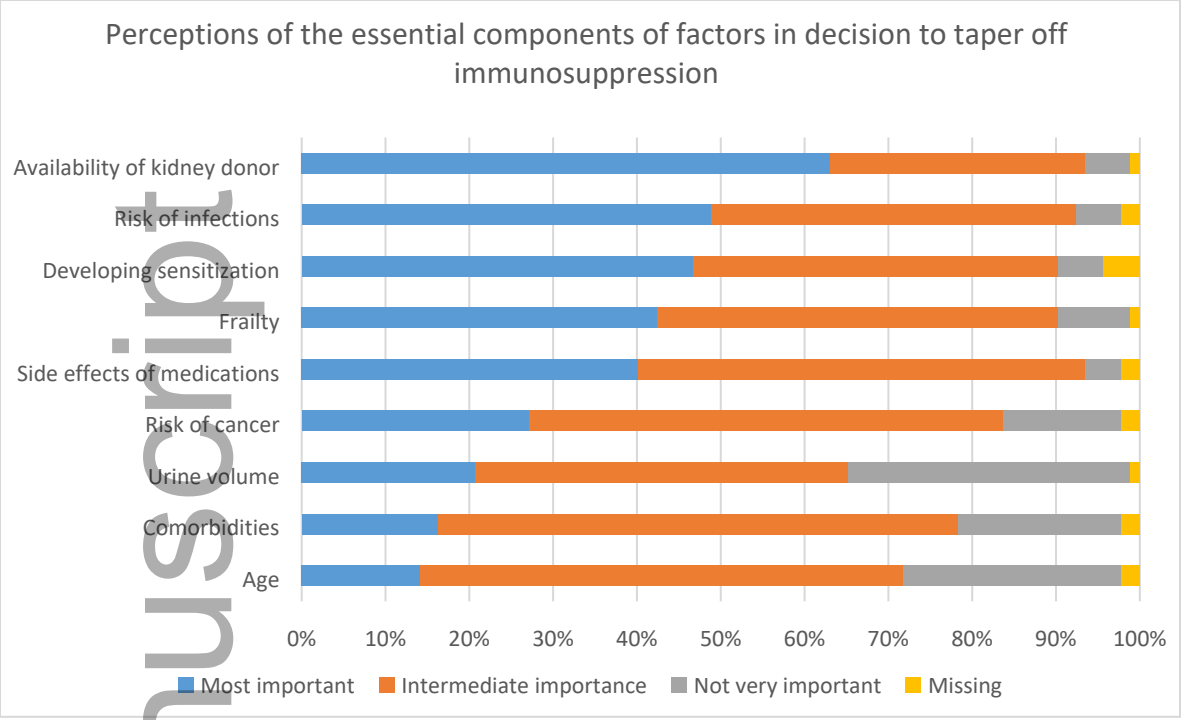


Figure 3a. Re-listing for the next kidney transplant before starting dialysis

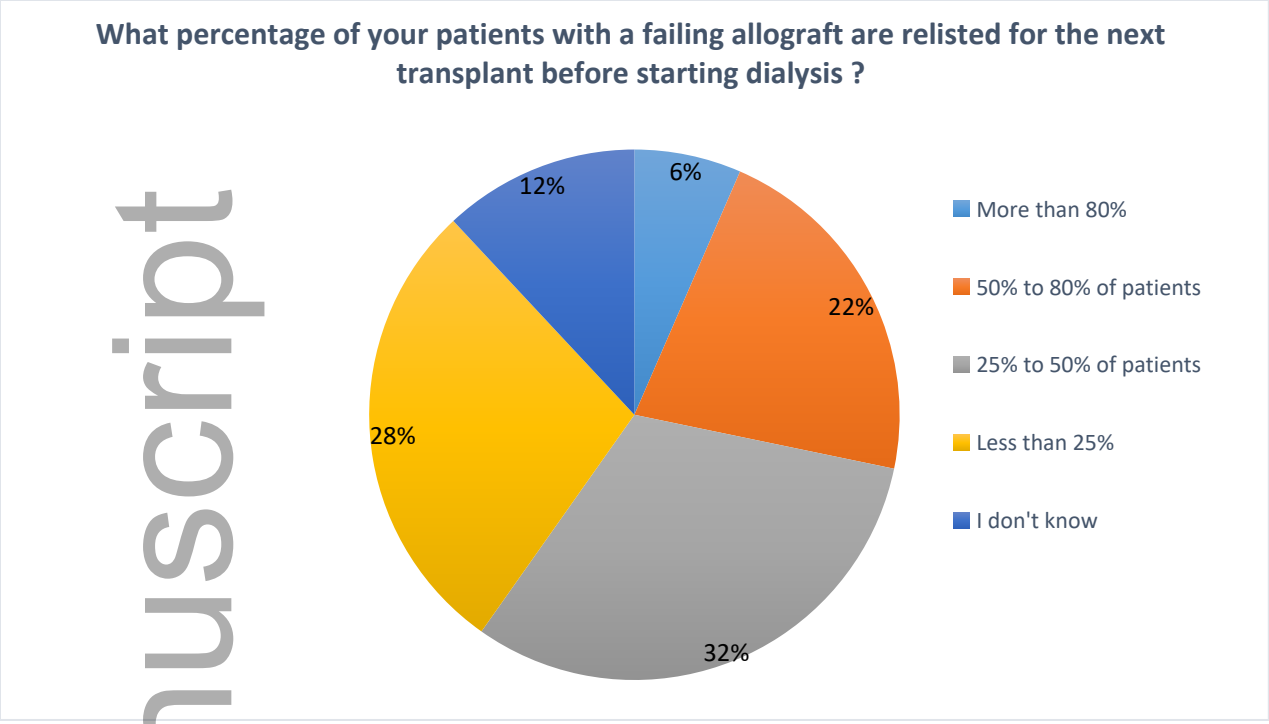


Figure 3b. Frequency of follow up with transplant nephrologists after starting dialysis

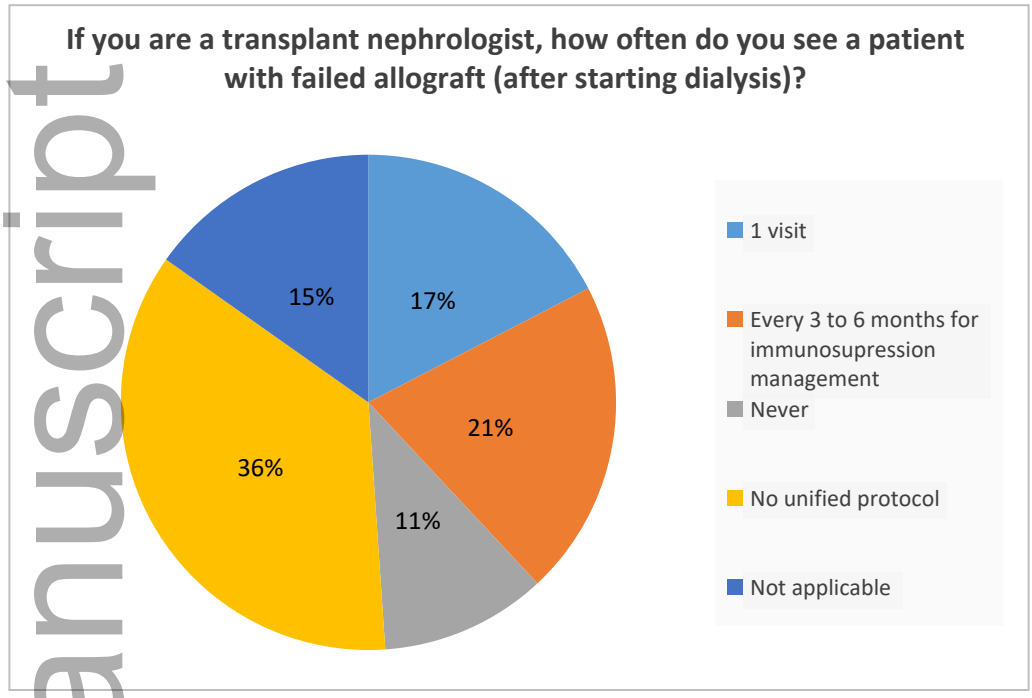
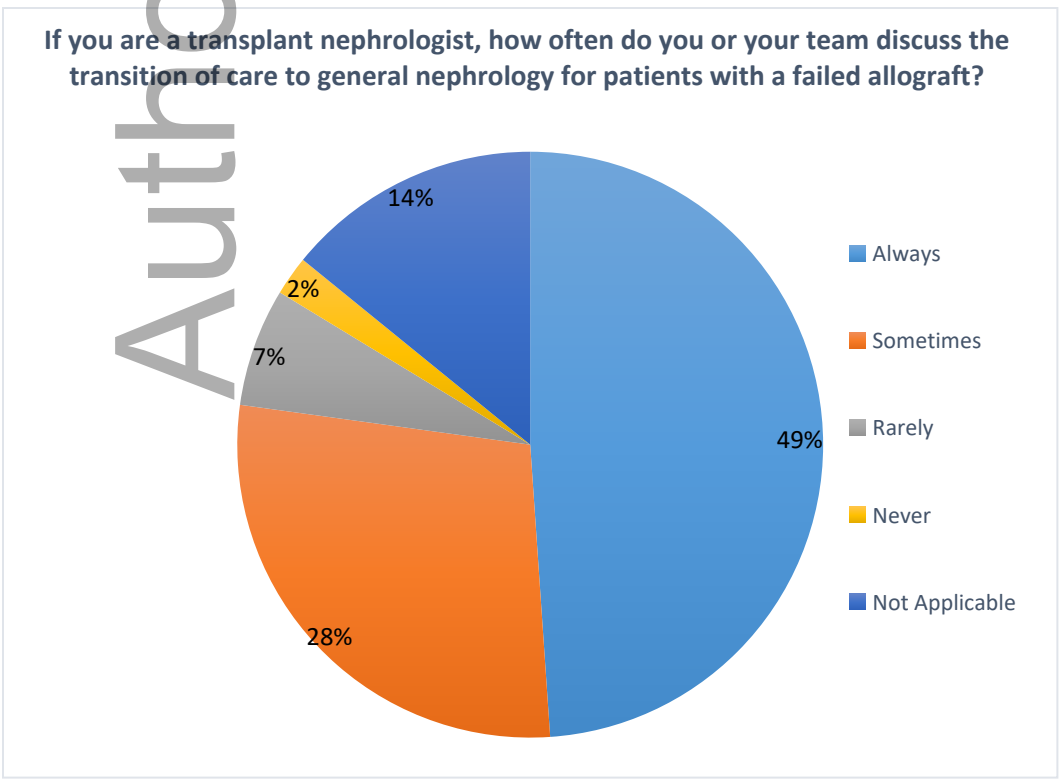


Figure 3c. Team discussion about transition of care for patients with failed allograft



References

1. Hart A, Smith J, Skeans M, et al. OPTN/SRTR 2018 Annual Data Report: Kidney. *American Journal of Transplantation*. 2020;20:20-130.

2. Fuquay R, Teitelbaum I. Care of the patient after renal allograft failure: managing the present and planning for the future. *American journal of nephrology*. 2012;36(4):348-354.

3. Gill JS, Abichandani R, Kausz AT, Pereira BJ. Mortality after kidney transplant failure: the impact of non-immunologic factors. *Kidney international*. 2002;62(5):1875-1883.

4. Brar A, Markell M, Stefanov DG, et al. Mortality after renal allograft failure and return to dialysis. *American journal of nephrology*. 2017;45(2):180-186.

5. Smak Gregoor P, Zietse R, Van Saase J, et al. Immunosuppression should be stopped in patients with renal allograft failure. *Clinical transplantation*. 2001;15(6):397-401.

6. Augustine JJ, Woodside KJ, Padiyar A, Sanchez EQ, Hricik DE, Schulak JA. Independent of nephrectomy, weaning immunosuppression leads to late sensitization after kidney transplant failure. *Transplantation*. Oct 15 2012;94(7):738-43. doi:10.1097/TP.0b013e3182612921

7. Lopez-Gomez JM, Perez-Flores I, Jofre R, et al. Presence of a failed kidney transplant in patients who are on hemodialysis is associated with chronic inflammatory state and erythropoietin resistance. *J Am Soc Nephrol*. Sep 2004;15(9):2494-501. doi:10.1097/01.ASN.0000137879.97445.6E

8. Yelken BM, Gorgulu N, Caliskan Y, et al. Comparison of nutritional status in hemodialysis patients with and without failed renal allografts. *Clin Transplant*. Jul-Aug 2010;24(4):481-7. doi:10.1111/j.1399-0012.2009.01097.x

9. Zakir AH, Woodside KJ, Feliberti EC, Rajaraman S, Gugliuzza KK, Daller JA. Late renal allograft rupture in a patient with small vessel vasculitis following discontinuation of immunosuppression. *Transpl Int*. Oct 2003;16(10):761-4. doi:10.1007/s00147-003-0632-0

10. Ayus JC, Achinger SG. At the peril of dialysis patients: ignoring the failed transplant. *Semin Dial*. May-Jun 2005;18(3):180-4. doi:10.1111/j.1525-139X.2005.18304.x

11. Evans RDR, Bekele S, Campbell SM, et al. Assessment of a Dedicated Transplant Low Clearance Clinic and Patient Outcomes on Dialysis After Renal Allograft Loss at 2 UK Transplant Centers. *Transplant Direct*. Jun 2018;4(6):e352. doi:10.1097/TXD.0000000000000788

12. Lentine KL, Peipert JD, Alhamad T, et al. Survey of Clinician Opinions on Kidney Transplantation from Hepatitis-C Virus-Positive Donors: Identifying and Overcoming Barriers. *Kidney360*. 2020;

13. Lentine KL, Vest LS, Schnitzler MA, et al. Survey of US living kidney donation and transplantation practices in the COVID-19 era. *Kidney international reports*. 2020;5(11):1894-1905.

14. McAdams-DeMarco MA, Rasmussen SEVP, Chu NM, et al. Perceptions and practices regarding frailty in kidney transplantation: results of a national survey. *Transplantation*. 2020;104(2):349-356.

15. Bayliss GP, Gohh RY, Morrissey PE, Rodrigue JR, Mandelbrot DA. Immunosuppression after renal allograft failure: a survey of US practices. *Clinical transplantation*. 2013;27(6):895-900.

16. Pham PT, Everly M, Faravardeh A, Pham PC. Management of patients with a failed kidney transplant: Dialysis reinitiation, immunosuppression weaning, and transplantectomy. *World J Nephrol*. May 6 2015;4(2):148-59. doi:10.5527/wjn.v4.i2.148

17. Andrews PA, Standards Committee of the British Transplantation S. Summary of the British Transplantation Society Guidelines for Management of the Failing Kidney Transplant. *Transplantation*. Dec 15 2014;98(11):1130-3. doi:10.1097/TP.0000000000000426

18. Gill JS, Rose C, Pereira BJ, Tonelli M. The importance of transitions between dialysis and transplantation in the care of end-stage renal disease patients. *Kidney Int*. Mar 2007;71(5):442-7. doi:10.1038/sj.ki.5002072

19. Woodside KJ, Schirm ZW, Noon KA, et al. Fever, infection, and rejection after kidney transplant failure. *Transplantation*. Mar 27 2014;97(6):648-53. doi:10.1097/01.TP.0000437558.75574.9c

20. Casey MJ, Wen X, Kayler LK, Aiyer R, Scornik JC, Meier-Kriesche HU. Prolonged immunosuppression preserves nonsensitization status after kidney transplant failure. *Transplantation*. Aug 15 2014;98(3):306-11. doi:10.1097/TP.0000000000000057

21. Jassal SV, Lok CE, Walele A, Bargman JM. Continued transplant immunosuppression may prolong survival after return to peritoneal dialysis: results of a decision analysis. *Am J Kidney Dis*. Jul 2002;40(1):178-83. doi:10.1053/ajkd.2002.33927

22. Chadban SJ, Ahn C, Axelrod DA, et al. KDIGO Clinical Practice Guideline on the Evaluation and Management of Candidates for Kidney Transplantation. *Transplantation*. Apr 2020;104(4S1 Suppl 1):S11-S103. doi:10.1097/TP.0000000000003136

23. Cofan F, Real MI, Vilardell J, et al. Percutaneous renal artery embolisation of non-functioning renal allografts with clinical intolerance. *Transpl Int*. Apr 2002;15(4):149-55. doi:10.1007/s00147-002-0390-4

24. Lorenzo V, Diaz F, Perez L, et al. Ablation of irreversibly rejected renal allograft by embolization with absolute ethanol: a new clinical application. *Am J Kidney Dis*. Oct 1993;22(4):592-5. doi:10.1016/s0272-6386(12)80934-6