Review Article

Renal Transplantation in Antineutrophil Cytoplasmic Antibody-Associated Vasculitis: Current Perspectives

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Keywords

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Abstract

Background: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is the leading cause of rapidly progressive glomerulonephritis, which may follow an unfavorable disease course. Despite therapeutic advances, a number of patients with AAV will eventually develop end-stage renal disease (ESRD). Renal transplantation (RTx) is associated with a survival benefit and improves quality of life in patients with ESRD. **Summary:** In recent years, RTx has been increasingly used also in patients with vasculitis. The posttransplant patient- and graft-survival rates in AAV were at least comparable to other diagnoses in most studies. Prior to transplantation, patients should be in stable remission for 12 months. Persistent ANCA positivity does not exclude patients from the waiting list. Even though the recurrence risk is generally low with modern posttransplant immunosuppression, including mycophenolate mofetil and tacrolimus, patients with AAV, particularly those with positive antiproteinase-3 ANCA who may have increased risk of relapse or recurrence of the disease, require constant surveillance. Similar to treatment of relapsing disease in the nontransplant setting, rituximab may become treatment of choice for posttransplant recurrences. **Key Messages:** RTx is the preferred renal replacement therapy of choice for AAV patients with ESRD. It is recommended that patients should be in remission for about 12 months prior to proceeding with RTx. ANCA positivity alone is not a contraindication for transplantation. The risk of relapse posttransplantation is minimal with currently used posttransplant immunosuppressive regimen.

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Introduction

Antineutrophil cytoplasmic antibodies (ANCA)-associated vasculitides (AAV) are a group of systemic autoimmune diseases characterized by necrotizing inflammation of (predominantly) small blood vessels. The group includes granulomatosis with polyangiitis (GPA, formerly Wegener's), microscopic polyangiitis (MPA), and eosinophilic GPA (formerly Churg-Strauss disease) [1]. As the name suggests, the diseases (particularly GPA and MPA) are closely associated with the presence of circulating Anti-ANCA that are frequently used as a diagnostic tool and are directed either against proteinase 3 (PR3-ANCA, more common in GPA) or myeloperoxidase (MPO-ANCA, more common in MPA) [1].

The diseases can afflict almost any organ in human body, but the classical triad described especially in GPA includes the involvement of ear-nose-throat organs, lungs, and the kidney. A “pauci-immune” (with few or no immune deposits) necrotizing crescentic rapidly progressive glomerulonephritis (RPGN) is the hallmark of renal disease in AAV, and AAV has been recognized as the most frequent cause of rapidly RPGN [2]. Renal disease in AAV is common, occurring in over 80% of patients during the disease course and may lead to end-stage renal disease (ESRD), either as a direct consequence of RPGN, chronic smoldering renal disease, or hemodynamically mediated progression not related to the activity of the disease [3, 4].

In the past, generalized AAV followed an unfavorable disease course with 1-year mortality as high as 80–90%. Treatment advances based on randomized controlled trials have improved the outcomes of AAV, but the overall mortality remains higher compared to general age-matched population [5, 6]. Moreover, the quality of life is impaired in AAV, and the patients frequently accrue significant damage, stemming from the vasculitis process itself (e.g., lung fibrosis, ESRD), side effects of administered treatment (e.g., infections, osteoporosis), and worsening of preexisting comorbidities (e.g., hypertension, obesity) [7, 8]. The disease course is further negatively influenced by frequent relapses, observed particularly in PR3-ANCA-positive patients [9] and leading to increased burden of immunosuppression.

ESRD remains a significant problem in the management of AAV, negatively influencing patient's outcome, with about 20–25% of patients with AAV reaching ESRD within a few years after diagnosis [3]. This review aims to provide an up-to-date overview of the current perspectives on the treatment and outcomes of patients with AAV reaching ESRD and focuses on the aspects of renal transplantation (RTx) in this disease.

Outcome of Patients with AAV after Kidney Transplantation

ESRD in patients with AAV has uniformly accounted for about 1% of all cases of ESRD in 3 recent reports from large registries from different parts of the world [10–12], but the number is estimated to be higher as some patients with AAV requiring dialysis are likely to remain undiagnosed, particularly those with renal-limited disease [13]. The overall mortality of AAV patients requiring dialysis has been reported to be generally similar to nondiabetic dialysis population in most retrospective as well as registry-based studies [2, 10–12, 14–16].

RTx is the preferred renal replacement therapy of choice for patients with ESRD as it improves quality of life and provides survival benefit and should be regarded as such also in patients with AAV. The survival benefit of RTx in AAV was demonstrated relatively long ago [15], even though the transplanted patients are usually younger and “healthier” than those remaining on dialysis, and direct comparison is therefore difficult. In a more recent study, including only wait-listed patients with GPA, receiving a kidney transplant was shown to largely reduce the risk of death, in particular due to cardiovascular disease [17]. Similarly,

while survival on renal replacement therapy did not differ between patients with AAV and age and sex-matched group of patients with nondiabetic cause of renal failure in a report from the ERA-EDTA Registry, patient- and graft survival of patients after transplantation was better in AAV than in other nondiabetic diagnoses [12].

The outcomes after RTx in AAV patients have been reported in a number of single-center and multicenter cohorts and register-based studies, each including 20–127 patients [10, 15, 18–25]. The studies have been reviewed in detail before [13, 26]. In brief, both patient- and graft-survival rates in AAV were at least as good as those of the control populations of nondiabetic patients and comparable with the data on survival available in large transplant registries. Only Tang et al. [10] reported on a worse patient- and graft survival in MPA patients compared to non-AAV patients in a study from the Australian and New Zealand Dialysis and Transplant Registry, but the reasons for this observation are not clear. The 5-year patient survival after transplantation ranged between 77 and 96%, and the 5-year graft survival between 60 and 100%, with an increasing trend observed in the most recent reports. Interestingly, among transplanted patients with different types of glomerulonephritis, vasculitis was shown to have the lowest graft failure rates [27]. Taken together, the outcome data support the use of RTx in AAV.

Timing of RTx in AAV

Case Description

AB is a 28-year-old female who was referred to transplant clinic for evaluation of renal transplant candidacy. AB presented at age 26 with myalgias, arthralgias, and hemoptysis over a 1-week period. Admission laboratory data revealed acute kidney injury with serum creatinine of 5.0 mg/dL with proteinuria and hematuria on urinalysis. Her chest CT revealed ground glass infiltrates bilaterally and her bronchoscopy confirmed alveolar hemorrhage. Serologic work up revealed positive MPO-ANCA at a titer of 98 units, negative antglomerular basement membrane antibody and negative ANA. Renal biopsy demonstrated pauci-immune necrotizing and crescentic glomerulonephritis. A diagnosis of MPO-ANCA-positive MPA was made.

She received induction therapy with oral cyclophosphamide and prednisone for 6 months and then was started on azathioprine for remission maintenance. Her renal function continued to progress and her repeat renal biopsy did not show active renal vasculitis. She reached ESRD and was started on hemodialysis. She is clinically in remission and completed 18 months of azathioprine for remission maintenance. Her MPO ANCA is negative.

Is this an Appropriate Time for Renal Transplant?

In our patient, the answer would be Yes.

The optimal timing of RTx in AAV is an important point to consider. Most authors agree that the disease should be quiescent for some time before RTx is performed. Both KDIGO Guidelines for Glomerulonephritis [28] and the Canadian Society of Transplantation [29] recommend that AAV patients should be in remission for 1 year prior to performing RTx. This stems mainly from the observation made by Little et al. [21], who demonstrated that patients transplanted <1 year postremission had the highest risk of death with a hazard ratio of 2.3. Even though this recommendation seems easy to be followed, the definition and recognition of vasculitis remission on dialysis may not be that easy, and in clinical practice, (minor) relapses may be difficult to discern from infectious complications common in dialysis population. Furthermore, a follow-up in expert vasculitis center may be recommended even after dialysis is started, to distinguish remaining disease activity from damage (e.g., in the cases of

persisting pathological imaging on chest CT) and to assist in preparing the patient for transplantation.

The question of ANCA positivity at the time of RTx is another important aspect that needs to be assessed prior to transplantation. In general population of patients with AAV, ANCA positivity per se is not always associated with disease activity, and it was shown that changes in ANCA levels may be associated with the reduction of immunosuppression rather than disease activity [30]. On the other hand, persistent ANCA positivity is a known risk factor for relapse in AAV, especially in patients with PR3-ANCA positivity. While some authors did not detect any relationship between ANCA status and relapse after RTx [18], in other studies, the association of ANCA positivity at the time of RTx with an increased risk of relapse reached borderline significance ($p = 0.05$) [22] or ANCA positive recipients were not more likely to relapse but were more likely to develop severe vasculopathy in the graft [21]. Marco et al. [23] found a significant difference ($p = 0.008$) in relapse rates between patients with and without ANCA positivity at the time of RTx, and Geetha et al. [31] recently described that patients with PR3-ANCA were twice as likely to relapse after transplantation than MPO-ANCA positive patients.

To sum up, the KDIGO Guidelines [28] do not recommend delaying RTx because of ANCA positivity if the patient is in clinical remission, but individual approach to each patient is required and routine monitoring of ANCA levels should undoubtedly be a standard of both pre- and posttransplantation care in AAV patients. Patients with particularly increasing ANCA levels may require more frequent visits and close monitoring for signs of disease relapse/recurrence is warranted.

Except for assessing the vasculitis activity, the evaluation of patients with AAV before enlisting them on the wait list does not differ from other non-AAV patients with ESRD. Despite the positive posttransplant outcomes reported above, the rate of wait-listing was lowest in vasculitis among all glomerulonephritides in a report from the United Network for Organ Sharing registry data, and patients with vasculitis also had lower rates of deceased donor kidney transplantation after wait-listing [32]. Similarly, in the ERA-EDTA Registry [12], the time spent on dialysis prior to transplantation was longer in AAV than in other nondiabetes patients. While some waiting prior to transplantation in AAV may be appropriate, disease-specific barriers to transplantation should be removed.

Relapses and Disease Recurrences after Transplantation

Case Description – Continued

AB underwent a living related renal transplant in 2007. She had immediate graft function and was maintained on prednisone, mycophenolate mofetil, and tacrolimus. Her allograft function remained stable with a serum creatinine of 1.0 mg/dL, and she had no episodes of allograft rejection or recurrence of vasculitis until 2014.

What Is the Optimal Posttransplant Immunosuppression?

Posttransplant immunosuppression in AAV patients should be geared to prevent allograft rejection as well as recurrence of vasculitis. There is no consensus on the choice of induction therapy for renal transplant. Both interleukin-2 receptor antagonists and antithymocyte globulin have been used. Given increased risk of posttransplant malignancy with antithymocyte globulin, we suggest that cautious use in patients with history of malignancy and higher cumulative cyclophosphamide exposure. In the pooled analysis of transplanted AAV patients by Nachman et al. [18], cyclosporine-based regimen did not have a protective effect compared to azathioprine and corticosteroid regimens. Observational studies have shown

that the combination of mycophenolate mofetil, prednisone, and tacrolimus has decreased vasculitis relapse rates posttransplant to 5–10% with very few recurrences in the allograft [20, 22]. This, together with the established efficacy of this regimen for prevention of allograft rejection made mycophenolate-based treatment the preferred regimen for posttransplant immunosuppression in AAV patients. Although azathioprine was superior to mycophenolate mofetil as a maintenance agent in nontransplant AAV patients in a randomized trial [33], use of azathioprine in transplant patients is associated with higher risk of allograft rejection and skin cancers compared to mycophenolate mofetil making it a less favorable agent for post-transplant immunosuppressive therapy.

What Is the Risk of Recurrence in our Patient?

As mentioned above, with modern antirejection immunosuppressive regimens, the risk of both extrarenal disease flares and disease recurrence in the graft is low in patients with AAV. While the risk of relapse is already relatively low on dialysis, it was shown that it can be further decreased after transplantation [15]. Overall, the relapse rates described in previous studies ranged from 0.006 to 0.1 per patient per year, and there seems to be a decreasing trend in relapse rates in the most recent studies [13]. Disease recurrence in the graft is a rare cause of graft loss, but it was shown that AAV recurrence is independently associated with graft loss [25].

There seems to be heterogeneity in the time to relapse after RTx (ranging from only 5 days to >13 years [23], and a mean time being 31 months [18]), severity, and location of relapses. In the study by Marco et al. [23], 38% of relapsing patient had renal involvement, 48% extrarenal involvement, and the remaining patients displayed signs of both renal and extra renal involvement. The type of involvement differed between PR3- and MPO-ANCA-associated disease, with extrarenal involvement (particularly of upper and/or lower respiratory tract) being more common in patients with PR3-ANCA.

It should be stressed that diagnosis of AAV flare after transplantation may be difficult as the relapses may mimic infections and other complications of immunosuppressive therapy used after RTx. Disease recurrence in the allograft should be considered in differential diagnosis of sudden worsening of renal function and needs to be confirmed by renal biopsy. It is therefore recommended that continuous vigilance in all AAV transplant recipients is required for early detection of relapses.

Posttransplant Management

Case Description – Continued

In 2014, AB stopped her prednisone abruptly and started experiencing arthralgias and presented to hospital with hemoptysis. Her laboratory data were notable for serum creatinine of 2.1 mg/dL, ESR 90, CRP 12 (normal <0.5), urinalysis demonstrated proteinuria and hematuria and her MPO ANCA was positive at a titer of 110 units. Her tacrolimus level was undetectable confirming nonadherence to immunosuppressive medications. Chest CT revealed ground glass infiltrates bilaterally and her bronchoscopy confirmed alveolar hemorrhage. Allograft renal biopsy demonstrated pauci-immune necrotizing and crescentic glomerulonephritis. She received induction therapy with rituximab 375 mg/m² once a week for 4 weeks and methylprednisone 1,000 mg daily for 3 days followed by oral prednisone. She was continued on tacrolimus and mycophenolate mofetil. Her serum creatinine improved to 1.0 mg/dL by week 4 and her vasculitis was in remission by week 10. Her prednisone was tapered to 5 mg over a 5-month period. Her allograft function in 2019 remains stable with a serum creatinine of 1.1 g/dL and benign urinalysis. Her MPO-ANCA remains negative.

How do you Monitor a Posttransplant Patient with AAV?

There are no standardized monitoring protocols that are specific for transplanted AAV patients. Posttransplant surveillance in AAV patients should focus on relapse detection in addition to monitoring for rejection, drug-induced adverse events, and opportunistic infections. Infection prophylaxis and vaccination recommendations do not differ from non-AAV transplant population, and even though infection has not been a major problem in recent series on posttransplant AAV patients, previous high doses of immunosuppression may make some AAV patients more fragile. In AAV patients, a pretransplant cyclophosphamide cumulative dose of >36 g has been shown to increase the risk of malignancy particularly, bladder cancer and lymphoma. Postrenal transplant urine cytology monitoring of urine cytology is suggested in patients who have had exposure to high cumulative cyclophosphamide [34]. Regimens employing lower cumulative cyclophosphamide dosing are associated with 2-fold risk of increased cancer in AAV patients compared to general population with most cancers accounted by nonmelanomatous skin cancer [35]. In this context, it is important to remember that azathioprine is associated with increased risk of nonmelanomatous skin cancer and should be discontinued or switched to alternate antimetabolite. In a report from United Network for Organ Sharing registry data patients with small-vessel vasculitis after transplantation had a higher risk of developing posttransplant solid organ malignancies (11.3 vs. 9.3%, $p = 0.006$) and lymphoproliferative disorder (1.3 vs. 0.8%, $p = 0.026$) [36].

As in nontransplant AAV setting, vasculitis activity should be monitored every 3–6 months clinically and by measurement of serum creatinine and urinalysis. Microscopic hematuria can be an early indicator of vasculitis relapse before a rise in serum creatinine becomes evident, and it is prudent to examine the urine for dysmorphic red blood cells and red blood cell casts and check inflammatory markers and ANCA in patients with new onset hematuria. The utility of serial ANCA measurements in transplanted AAV patients has not been studied. It is reasonable to extrapolate that similar to the nontransplant setting, persistent positivity for ANCA or rise in ANCA titer are not reliable predictors of relapse, but these patients require vigilance for relapse, and special attention needs to be paid to patients with ANCA conversion from negative to positive.

How to Treat Posttransplant Disease Relapse?

Treatment of AAV relapse posttransplant is similar to the nontransplant setting [37]. Nonsevere relapses are often treated with increase in glucocorticoid dosing. For treatment of severe relapses, both cyclophosphamide and rituximab [18, 38] are effective for remission induction. Even though the experience with rituximab has been gained in the last decade only, it has been increasingly used. Sagmeister et al. [39] recently described a case of de novo ANCA-AAV after RTx performed for ESRD due to polycystic kidney disease, who was also successfully treated with rituximab (and plasma exchange). There are no studies addressing the comparative effectiveness of cyclophosphamide and rituximab for treatment of recurrent disease. Similar to nontransplant setting, rituximab may be preferred for remission induction in AAV patients who are in reproductive age group, those with history of malignancy and history of relapsing vasculitis and higher cumulative cyclophosphamide exposure prior to transplant. When cyclophosphamide is used for remission induction, we would recommend stopping mycophenolate mofetil and resuming once remission is achieved. When using rituximab for remission induction, our practice is to mycophenolate is continued with monitoring of blood count. In conclusion, the choice of induction therapy should be individualized based on patient age, disease severity, prior exposure to cyclophosphamide, and ANCA type.

Conclusions

RTx should be the preferred treatment in patients with AAV and ESRD. Posttransplant outcomes in AAV are at least as good as in other causes of ESRD. The rates of wait list are lower in AAV patients compared to other glomerular disease and efforts should focus on identifying factors that cause delay in wait listing. Prior to transplantation, patients should be in stable clinical remission for ≥ 12 months but ANCA negativity is not required. The risk of recurrence is low with modern immunosuppression. Posttransplant major vasculitis relapses may be treated with either cyclophosphamide or (increasingly used) rituximab.

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Statement of Ethics

The study protocol was approved by institutional review board.

Disclosure Statement

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Author Contributions

Z.H., V.T., and D.G.: review of literature and writing of the manuscript.

References

- 1 Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum*. 2013 Jan;65(1):1–11.
- 2 Moroni G, Ponticelli C. Rapidly progressive crescentic glomerulonephritis: early treatment is a must. *Autoimmun Rev*. 2014 Jul;13(7):723–9.
- 3 Moiseev S, Novikov P, Jayne D, Mukhin N. End-stage renal disease in ANCA-associated vasculitis. *Nephrol Dial Transplant*. 2017 Feb;32(2):248–53.
- 4 de Groot K, Pusey C. End-Stage Renal Disease and Vasculitis. In: Hoffman GS, Weyand CM, Langford CA, Goronzy JJ, editors. *Inflammatory Diseases of Blood Vessels*. 2nd ed. Oxford, UK: Wiley-Blackwell; 2012. pp. 534–43.
- 5 Tan JA, Dehghan N, Chen W, Xie H, Esdaile JM, Avina-Zubieta JA. Mortality in ANCA-associated vasculitis: ameta-analysis of observational studies. *Ann Rheum Dis*. 2017 Sep;76(9):1566–74.
- 6 Flossmann O, Berden A, de Groot K, Hagen C, Harper L, Heijl C, et al.; European Vasculitis Study Group. Long-term patient survival in ANCA-associated vasculitis. *Ann Rheum Dis*. 2011 Mar;70(3):488–94.
- 7 Basu N, Karabayas M, Pusey C. Prognosis and future developments in vasculitis. *Best Pract Res Clin Rheumatol*. 2018 Feb;32(1):148–65.

- 8 Robson J, Doll H, Suppiah R, Flossmann O, Harper L, Höglund P, et al. Damage in the anca-associated vasculitides: long-term data from the European vasculitis study group (EUVAS) therapeutic trials. *Ann Rheum Dis*. 2015 Jan;74(1):177–84.
- 9 Lionaki S, Blyth ER, Hogan SL, Hu Y, Senior BA, Jennette CE, et al. Classification of antineutrophil cytoplasmic autoantibody vasculitides: the role of antineutrophil cytoplasmic autoantibody specificity for myeloperoxidase or proteinase 3 in disease recognition and prognosis. *Arthritis Rheum*. 2012 Oct;64(10):3452–62.
- 10 Tang W, Bose B, McDonald SP, Hawley CM, Badve SV, Boudville N, et al. The outcomes of patients with ESRD and ANCA-associated vasculitis in Australia and New Zealand. *Clin J Am Soc Nephrol*. 2013 May;8(5):773–80.
- 11 Romeu M, Couchoud C, Delarozère JC, Burtsey S, Chiche L, Harlé JR, et al. Survival of patients with ANCA-associated vasculitis on chronic dialysis: data from the French REIN registry from 2002 to 2011. *QJM*. 2014 Jul;107(7):545–55.
- 12 Hruskova Z, Stel VS, Jayne D, Aasarød K, De Meester J, Ekstrand A, et al. Characteristics and Outcomes of Granulomatosis With Polyangiitis (Wegener) and Microscopic Polyangiitis Requiring Renal Replacement Therapy: Results From the European Renal Association-European Dialysis and Transplant Association Registry. *Am J Kidney Dis*. 2015 Oct;66(4):613–20.
- 13 Hruskova Z, Geetha D, Tesar V. Renal transplantation in anti-neutrophil cytoplasmic antibody-associated vasculitis. *Nephrol Dial Transplant*. 2015 Apr;30 Suppl 1:i159–63.
- 14 Weidanz F, Day CJ, Hewins P, Savage CO, Harper L. Recurrences and infections during continuous immunosuppressive therapy after beginning dialysis in ANCA-associated vasculitis. *Am J Kidney Dis*. 2007 Jul;50(1):36–46.
- 15 Allen A, Pusey C, Gaskin G. Outcome of renal replacement therapy in antineutrophil cytoplasmic antibody-associated systemic vasculitis. *J Am Soc Nephrol*. 1998 Jul;9(7):1258–63.
- 16 Haubitz M, Koch KM, Brunkhorst R. Survival and vasculitis activity in patients with end-stage renal disease due to Wegener's granulomatosis. *Nephrol Dial Transplant*. 1998 Jul;13(7):1713–8.
- 17 Wallace ZS, Wallwork R, Zhang Y, Lu N, Cortazar F, Niles JL, et al. Improved survival with renal transplantation for end-stage renal disease due to granulomatosis with polyangiitis: data from the United States Renal Data System. *Ann Rheum Dis*. 2018 Sep;77(9):1333–8.
- 18 Nachman PH, Segelmark M, Westman K, Hogan SL, Satterly KK, Jennette JC, et al. Recurrent ANCA-associated small vessel vasculitis after transplantation: A pooled analysis. *Kidney Int*. 1999 Oct;56(4):1544–50.
- 19 Deegens JK, Artz MA, Hoitsma AJ, Wetzels JF. Outcome of renal transplantation in patients with pauci-immune small vessel vasculitis or anti-GBM disease. *Clin Nephrol*. 2003 Jan;59(1):1–9.
- 20 Gera M, Griffin MD, Specks U, Leung N, Stegall MD, Fervenza FC. Recurrence of ANCA-associated vasculitis following renal transplantation in the modern era of immunosuppression. *Kidney Int*. 2007 Jun;71(12):1296–301.
- 21 Little MA, Hassan B, Jacques S, Game D, Salisbury E, Courtney AE, et al. Renal transplantation in systemic vasculitis: when is it safe? *Nephrol Dial Transplant*. 2009 Oct;24(10):3219–25.
- 22 Geetha D, Eirin A, True K, Valentina Irazabal M, Specks U, Seo P, et al. Renal transplantation in antineutrophil cytoplasmic antibody-associated vasculitis: a multicenter experience. *Transplantation*. 2011 Jun;91(12):1370–5.
- 23 Marco H, Mirapeix E, Arcos E, Comas J, Ara J, Gil-Vernet S, et al.; Catalan Study Group of Glomerular Diseases (GLOMCAT). Long-term outcome of antineutrophil cytoplasmic antibody-associated small vessel vasculitis after renal transplantation. *Clin Transplant*. 2013 May-Jun;27(3):338–47.
- 24 Schmitt WH, Opelz G, Van Der Woude FJ. Renal transplantation (RTx) is safe and successful in Wegener's granulomatosis (WG): data from the Collaborative Transplant Study [abstract]. *J Am Soc Nephrol*. 2002;13:564A–5A.
- 25 Göçeroğlu A, Rahmattulla C, Berden AE, Reinders ME, Wolterbeek R, Steenbergen EJ, et al. The Dutch Transplantation in Vasculitis (DUTRAVAS) Study: outcome of renal transplantation in antineutrophil cytoplasmic antibody-associated glomerulonephritis. *Transplantation*. 2016 Apr;100(4):916–24.
- 26 Geetha D, Kant S. Renal transplantation in anti-neutrophil cytoplasmic antibody vasculitis. *Expert Rev Clin Immunol*. 2018 Mar;14(3):235–40.
- 27 O'Shaughnessy MM, Liu S, Montez-Rath ME, Lenihan CR, Lafayette RA, Winkelmayer WC. Kidney transplantation outcomes across GN subtypes in the United States. *J Am Soc Nephrol*. 2017 Feb;28(2):632–44.
- 28 Kidney Disease: Improving Global Outcomes (KDIGO) Glomerulonephritis Working Group. KDIGO Clinical Practice Guideline for Glomerulonephritis. *Kidney Int Suppl*. 2012;2:139–274.
- 29 Knoll G, Cockfield S, Blydt-Hansen T, Baran D, Kiberd B, Landsberg D, et al.; Kidney Transplant Working Group of the Canadian Society of Transplantation. Canadian Society of Transplantation consensus guidelines on eligibility for kidney transplantation. *CMAJ*. 2005 Nov;173(10):1181–4.
- 30 Rasmussen N, Salmela A, Ekstrand A, de Groot K, Gregorini G, Cohen Tervaert JW, et al.; European Vasculitis Study Group (EUVAS). Changes in proteinase 3 anti-neutrophil cytoplasm autoantibody levels in early systemic granulomatosis with polyangiitis (Wegener's) may reflect treatment rather than disease activity. *Clin Exp Rheumatol*. 2013 Jan-Feb;31(1 Suppl 75):S38–44.
- 31 Geetha D, Lee SM, Shah S, Rahman HM. Relevance of ANCA positivity at the time of renal transplantation in ANCA associated vasculitis. *J Nephrol*. 2017 Feb;30(1):147–53.
- 32 O'Shaughnessy MM, Liu S, Montez-Rath ME, Lafayette RA, Winkelmayer WC. Kidney Transplantation Rates Across Glomerulonephritis Subtypes in the United States. *Transplantation*. 2017 Oct;101(10):2636–47.

- 33 Hiemstra TF, Walsh M, Mahr A, Savage CO, de Groot K, Harper L, et al.; European Vasculitis Study Group (EUVAS). Mycophenolate mofetil vs azathioprine for remission maintenance in antineutrophil cytoplasmic antibody-associated vasculitis: a randomized controlled trial. [JAMA](#). 2010 Dec;304(21):2381–8.
- 34 Faurschou M, Sorensen IJ, Mellemkjaer L, Loft AG, Thomsen BS, Tvede N, et al. Malignancies in Wegener's granulomatosis: incidence and relation to cyclophosphamide therapy in a cohort of 293 patients. [J Rheumatol](#). 2008 Jan;35(1):100–5.
- 35 Heijl C, Harper L, Flossmann O, Stücker I, Scott DG, Watts RA, et al.; European Vasculitis Study Group (EUVAS). Incidence of malignancy in patients treated for antineutrophil cytoplasm antibody-associated vasculitis: follow-up data from European Vasculitis Study Group clinical trials. [Ann Rheum Dis](#). 2011 Aug;70(8):1415–21.
- 36 El-Husseini A, Saleh S, Hamad O, Mei X, Castellanos AL, Davenport DL, et al. Outcome of Patients With Small Vessel Vasculitis After Renal Transplantation: National Database Analysis. [Transplant Direct](#). 2018 Feb;4(3):e350.
- 37 Yates M, Watts RA, Bajema IM, Cid MC, Crestani B, Hauser T, et al. EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis. [Ann Rheum Dis](#). 2016 Sep;75(9):1583–94.
- 38 Murakami C, Manoharan P, Carter-Monroe N, Geetha D. Rituximab for remission induction in recurrent ANCA-associated glomerulonephritis postkidney transplant. [Transpl Int](#). 2013 Dec;26(12):1225–31.
- 39 Sagmeister MS, Weiss M, Eichhorn P, Habicht A, Habersetzer R, Fischereder M, et al. Case report: de novo ANCA-associated vasculitis after kidney transplantation treated with rituximab and plasma exchange. [BMC Nephrol](#). 2018 Oct;19(1):270.