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LETTER TO THE EDITOR

Immunosuppressive regimens and outcomes of inflammatory bowel disease patients requiring kidney transplantation

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Abstract

Patients with inflammatory bowel disease (IBD) can develop extra-renal complications and as a result, suffer from end stage renal failure requiring kidney transplantation (KT). A brief review of available literature revealed that IBD patients undergoing KT have shorter overall survival rates compared to their controls. Literature reporting steroid regimens and survival outcomes specific to IBD and post kidney transplant are scarce and these studies have small sample sizes thus making it difficult to draw accurate conclusions. Further research is required in the form of a randomized controlled study to clarify the effect and mechanism of steroid immunosuppression on the prognosis of renal transplant recipients and explore new treatment schemes.

Key Words: Inflammatory bowel disease; Kidney transplantation; Steroids; Immunosuppression; Kidney failure; Ulcerative colitis; Crohn's disease

Core Tip: Patients with inflammatory bowel disease (IBD) can develop extra-renal complications and as a result, suffer from end stage renal failure requiring kidney transplantation (KT). A brief review of available literature revealed that IBD patients undergoing KT have shorter overall survival rates compared to their controls. We highlight through our paper, previously reported survival outcomes and immunosuppressive regimens used in this cohort of patients through a brief literature review.

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TO THE EDITOR

The recent systematic review published by Aref *et al*[1] titled 'Does steroid-free immunosuppression improve the outcome in kidney transplant recipients compared to conventional protocols?' provided thought provoking insight into the impact of steroid-free immunosuppression on the outcome of kidney transplant recipients. Further to the authors conclusions in their paper, we aim to highlight the effect of steroids and steroid free regimens on the outcomes of inflammatory bowel disease (IBD) patients who were kidney transplant receipts.

IBD is comprised of Crohn's disease (CD) and ulcerative colitis (UC). Patients with IBD can develop extra-intestinal manifestations. These include peripheral arthritis, oral aphthous ulcers, erythema nodosum, episcleritis, pyoderma gangrenosum, primary sclerosing cholangitis and uveitis[2]. Patients with IBD can develop renal manifestations of the disease, including nephrolithiasis, glomerulonephritis, tubulointerstitial nephritis, and secondary amyloidosis[3]. A study reported that the incidence of end stage renal disease (ESRD) in patients with CD was 5 times higher than cross matched controls[3]. Kidney injury can also result from dehydration, long term malnutrition and side effects of IBD medical therapy. These can all contribute to chronic kidney disease and eventually ESRD warranting kidney dialysis and transplantation[3].

Studies reporting IBD patients requiring kidney transplantation (KT) are scarce. However, existing literature discussing IBD, and post KT outcomes reports similar survival rates for IBD patients post transplantation. In a recent detailed study, in which 12 IBD patients (7 CD patients and 5 UC patients) underwent KT due to immunoglobulin A (IgA) nephropathy and polycystic kidney disease, the estimated survival of IBD patients was reported to be 80.8% *vs* 96.8% in patients without IBD (P = 0.001)[4]. Treatment with infliximab or a dalimumab resulted in stable disease or improvement in kidney transplant patients affected by mild to moderate IBD. Eleven out of 12 patients were on maintenance immunosuppression with low dose corticosteroids (5 mg prednisolone daily), calcineurin inhibitors (tacrolimus), and antimetabolite (mycophenolic acid in nine and mycophenolate mofetil in two); the twelfth patient was kept on low-dose corticosteroids and tacrolimus only. IBD course remained stable in the whole transplant group, but resulted in an increased risk of mortality and hospitalization, due to a higher infection rate[4].

Data on immunosuppression and steroid regimens specific to IBD and the post-KT period remains poorly reported. In a study, six patients (5 CD patients and 1 UC patient) out of 1537 patients with IBD, underwent KT for kidney failure secondary to amyloidosis, IgA nephropathy, oxalate nephropathy, haemolytic uraemic syndrome, and chronic kidney failure of unknown origin[5]. Five of the six patients received steroid therapy after transplantation, yet specific immunosuppressive regimens are not reported pre and post transplantation. The study discusses the outcomes of IBD patients post liver transplantation together with KT, hence it is not possible to comment on the post KT alone. However, the study does report an 84% survival rate during a total follow up of 103.0 mo and median follow up of 33 mo after solid organ transplantation. One male patient also developed papillary renal cell carcinoma in the transplanted kidney in this study. No graft rejection was reported[5]. In a different prospective cohort study that followed 26 patients with IBD and systemic ascorbic acid (AA) amyloidosis between 1989 and 2010, an 83% survival rate 15 years post transplantation was reported. In this study all patients had renal dysfunction as result of AA amyloidosis[6]. However, only six patients required renal transplantation due to ESRD. Four patients had deceased donor transplants and two patients had live-related transplants. There were five functioning grafts at census 0.8, 3.2, 4.2, 20.1 and 24.6 years after transplantation. One graft failure was reported at 14.5 years after renal transplantation due to recurrence of amyloidosis and sustained chronic inflammatory activity. The study notes that patients were provided with steroid regimens however does not provide specific details about whether these regimens were supplemented with other immunosuppressants[6]. Specific reporting regarding immunosuppressive regimens is warranted for IBD patients before and after KT.

In conclusion, IBD is an immunomediated disease that is associated with kidney disease and can cause ESRD in patients. From the available literature, it is suggested that patients with IBD that undergo KT have shorter overall survival rates compared to their controls. Reported data is scarce and inconclusive due to the small patient cohort sizes. Further research is required in the form of a randomized controlled study to clarify the effect and mechanism of steroid immunosuppression on the prognosis of renal transplant recipients and explore new treatment schemes.

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LETTER TO THE EDITOR

Assessment of advanced age candidates for liver transplantation warrants more caution

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Abstract

For patients with fulminant liver failure and end-stage liver disease, liver transplantation remains the only effective treatment. Over the years, as a result of the ageing population, the average age of liver transplant donors and recipients has increased and currently about one quarter of patients receiving transplantation in the United States are above the age of 65. Recently, a study reported that patients aged 65 years or older had lower one-year survival compared to a younger cohort. Herein, we express our opinion about this interesting publication.

Key Words: Liver transplantation; Elderly patients; Age in liver transplantation; Frailty; Transplant assessment; Liver transplant outcomes

Core Tip: As a result of the ageing population, the average age of liver transplant candidates has increased over the years and about one quarter of recipients receiving transplantation in the United States are over 65 years of age. The study reported that patients aged 65 years or older had lower survival at one year compared to a younger cohort. In addition, they have identified congestive heart failure to be strongly associated with poor outcomes in elderly. In this letter to the editor, we express our opinion about these interesting findings.

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TO THE EDITOR

We read with great interest the study from Kleb *et al*[1]. The authors analysed the outcome of 260 elderly patients (65 years old) undergoing liver transplantation (LT) with the aim of identifying features associated with futility, defined as death within 90 d post transplantation. In this retrospective study, Kleb *et al*[1] demonstrated that congestive heart failure (CHF) is strongly associated with futility of LT in elderly patients. Furthermore, patients aged 65 years or older had even when adjusting for severity of liver disease and comorbidities.

LT is a life-saving procedure and it is the only efficient treatment for chronic liver diseases and acute liver failure. However, organ shortage is one of the main challenges that the transplant community continues to face. Indeed, donor availability is becoming an increasing problem globally, limiting the wider spread of LT. As a result of the ageing population, average age of donors and recipients has increased throughout the decades and about one quarter of LT recipients in the United States are over the age of 65[2]. In addition to the standard transplant assessment, when considering patients in this age group, close attention should be paid to cardiovascular diseases, frailty and performance status. Commonly, elderly recipients have more medical conditions, higher waitlist and post-transplant mortality as opposed to a younger cohort.

In a large study it has been demonstrated that, in recipients without hepatocellular carcinoma, advanced age at registration has been shown to be a considerable risk factor behind patients being too unwell to undergo transplantation and it has been linked with higher waitlist mortality[3]. With a competing risk analysis, Su *et al*[3] have shown interesting results with regards to age and transplantation. In fact, patients aged 64 to 69 years displayed higher waiting list mortality with an adjusted hazard ratio of 1.73 as opposed to 2.04 for those aged ≥ 70. In addition, age was linked to less likelihood of LT, with an adjusted hazard ratio of 0.89 and 0.86 in patients aged 64 to 69 years and ≥ 70 years, respectively.

This is one of several studies which highlight the relation between advanced age and LT outcomes. Interestingly, the authors identified CHF to be strongly associated with poor outcomes. Although the results by Kleb *et al*[1] are compelling, they need to be interpreted with caution. The data presented have been retrospectively reviewed, but some important indexes to estimate frailty and comorbidities, such as the Charlston Comorbidity Index[4] and Liver Frailty Index[5] have not been calculated. This would add a more precise evaluation of the pre-transplant status and comorbidities of the recipients that can influence outcomes. Secondly, the causes of death within 90 d from LT have not been reported. Therefore, it is difficult to estimate the clear relation between advanced age alone and futility, as death could be related to post-operative complications such as graft dysfunction, infection, or immunosuppression rather than recipient age itself. Thirdly, the cohort for this study is from a single-centre, hence as yet we cannot translate this to a broader population.

By way of conclusion, the authors have to be congratulated for their work. They have demonstrated with a well-conducted analysis that recipients aged 65 years and older had increased mortality at one year compared to patients below the age of 65. This finding is of great interest and warrants a thorough assessment of potential recipients with advanced age. In particular, as underlined also by other authors[6], a meticulous pre-transplant cardiological evaluation appears to be of high importance in elderly. Identifying additional pre-operative factors that can guide the decision-making to select low-risk patients in a wider population would be of great interest.

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