

Re: Impact of Cigarette Smoking on Kidney Transplant Recipients: a Systematic Review

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Sir,

I read with great interest the review article by Nourbala and colleagues¹ published recently in your most valuable journal, titled "Impact of cigarette smoking on kidney transplant recipients: a systematic review." This review focused its message on drawing the attention of whether the history of cigarette smoking prior kidney transplantation have adverse effects on patient and graft survival rates. They concluded that cigarette smoking was an independent risk factor for patient death. In addition, graft survival correlated with a history of cigarette smoking and the 95% confidence interval of the relative risk for graft failure ranged from 1.06 to 2.3.

I agree that donor smoking has adverse effects on kidney allograft outcomes; however, there are controversial reports. In a retrospective study recently published,² lower graft survival was seen in kidney transplant recipients who received kidneys from living donors with a history of cigarette smoking prior transplantation. A similar conclusion was reported in the study that analyzed the United Network for Organ Sharing (UNOS) dataset from 1994 to 1999, by Lin and colleagues.³ In contrast, previous studies by Cho and coworkers based on the UNOS data in 1995 and 1998,^{4,5} and the Regional Organ Procurement Agency of Southern California, Los Angeles,⁶ showed graft survival was not affected if the donor has a history of cigarette

smoking. We also found no correlation between lower glomerular filtration rates and donor smoking in 269 kidney transplant patients who received a kidney from a living donor (unpublished data); however, our study is continued with recruitment of more kidney transplant recipients, which will be presented later.

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Re: Risk Factors Profile and Cardiovascular Events in Solid Organ Transplant Recipients

Sir,

We read with great interest the review article recently published in the *Iranian Journal*

of Kidney Diseases, titled "Risk Factors Profile and Cardiovascular Events in Solid Organ Transplant Recipients" by professor Ghods.¹

This review focused its message on drawing the attention of the high prevalence of risk factors and cardiovascular events after organ transplantation, especially in kidney transplant recipients. According to this review, the prevalence of cardiovascular disease risk factors increases or remains higher after kidney transplantation. The cardiovascular risk factors in these patients divide into traditional and nontraditional risk factors, which immunosuppressive agents categorized as a traditional risk factor.¹ They may cause posttransplant diabetes mellitus, dyslipidemia, hypertension, and hyperhomocysteinemia, and studies involving withdrawal of these agents have generally shown improvement in parameters such as blood pressure and dyslipidemia.²

We agree that cardiovascular disease is the leading cause of mortality among kidney transplant recipients.³ Traditional risk factors do not adequately explain coronary heart disease risk after kidney transplantation.⁴ Immunosuppressive agents could also play role as a nontraditional risk factor for cardiovascular events. They have potentially a direct adverse influence on the immunologic protective mechanisms in atherosclerosis. It was shown that a number of protective immune responses have also been identified. For example, one of the most important of these is carried out by the regulatory T cells, which are powerful inhibitors of atherosclerosis in several mouse models.⁵ Regulatory T cells inhibit the development of autoimmunity by controlling the activity of autoreactive T cells. If the function of regulatory T cells is compromised in hypercholesterolemic mouse models of atherosclerosis, the development of disease becomes much more aggressive.⁶ In addition, immunization of hypercholesterolemic animals with low-density lipoprotein (LDL) preparations reduces atherosclerosis, suggesting that vaccination may represent a useful strategy for disease prevention or modulation.⁷ Antibodies against oxidized LDL have been demonstrated in atherosclerosis, which may be protective.⁸ Serum anti-oxidized LDL antibody titer is an independent predictor of cardiovascular mortality in a cohort of patients with end-stage renal disease.⁸ In another study revealed that because antibodies may

protect or neutralize pathogens and immunogens, humoral immunity to oxidized LDL can reduce the incidence of atherosclerosis. The protective role of T cell-dependent antibody was demonstrated in rabbits and mice immunized with oxidized LDL.⁹

In conclusion, immunosuppression in transplantation may cause deficient atheroprotective cellular and humoral immune reactivity. Non-traditional markers add a lot to explain the increased rate of cardiovascular disease in transplantation, especially effects by immunosuppression and renal transplantation. Accelerated atherosclerosis in transplantation probably due to both destructive immunologic forces, inflammatory activity, and adversely affected protective immunologic mechanisms targeting atheroantigens.

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