

# Immunosuppression in Patients with Transplanted Kidneys

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## Introduction

An increased incidence of cancer is linked to immunodeficiency. It is unclear, though, whether immunodeficiency and the emergence of several primary cancers are related. As kidney transplant recipients have a higher risk of cancer due to their long-term use of immunosuppressant, we examined this connection in the current study. The majority of multiple tumours occurred at the same time, and there was rarely any correlation between cancer and episodes of rejection. It would be reasonable to conclude that, from a purely theoretical and statistical perspective, long-term transplanted patients potentially have a higher risk of developing MPMs. In the general cancer population, one-ninth of patients are at higher risk of developing a second tumour over the course of a lifetime [1].

Although there have been numerous reports of an increased incidence of various tumour types in immunodeficient patients, and immunosuppression is undoubtedly a risk factor for the multicancer syndrome, the evidence to date has not been strong enough to support a link between immunodeficiency and multiple primary malignancies in transplant recipients.

## Description

The most effective treatment for people with end-stage renal disorders is kidney transplantation. The use of increasingly potent immunosuppressive medications has significantly reduced the rate of rejection and improved outcomes, which has contributed to the growing success of this strategy. However, long-term usage of immunosuppressive medications raises the risk of cancer. Immunosuppression in transplant recipients is known to be associated with cancer development. An increasing amount of evidence has evolved over the past few decades illustrating the immune system's dual function in cancer, being engaged in both tumour formation (through chronic inflammation through the innate immune system) and tumour management and removal (through the adaptive immune system). For instance, renal cell carcinoma has historically been thought to be immunogenic since immunosuppressed patients have a higher prevalence of the disease. Additionally, this tumour kind is customarily thought to respond well to immunotherapy. Therefore, it is now widely acknowledged that immunosuppressive medications used in transplant recipients may cause immunological abnormalities, impairing the immune response and encouraging the emergence of a secondary immunodeficiency (ID), which might ultimately hasten the onset of malignancy. Additionally, the prevalence of multiple primary malignancies (MPMs) is rising overall and is predicted to continue to rise in the upcoming years. Each tumour must meet the following criteria in order to be considered an MPM: it must be a solid tumour, have a histological diagnosis of malignancy, be topographically distinct from other tumours, and not include tumours that are metastases of the primary [2].

They can appear simultaneously (both cancers appear at the same

time), synchronously (the second tumour appears within six months of the first tumour), or metachronously (both tumours appear at different times) (i.e., the second tumour appears more than six months after the first tumor). The chances of acquiring MPMs is, however, potentially higher in transplant patients who develop tumours, recover from them, and continue to receive immunosuppressive therapy than in the general population. The issue of MPMs in transplant patients should be thought of from this angle. The relationship between secondary immunodeficiency and the emergence of MPMs in transplant recipients is the main topic of this research.

We chose kidney-transplanted individuals expressly to explore the association between immunosuppression and MPMs for a number of reasons. First, among patients who have received solid organ transplants, kidney recipients are the most numerous group and have the longest follow-up (kidney transplantation was the first solid organ transplant carried out; from a single cadaver donor it is generally possible to obtain two kidneys for two different kidney recipients; living kidney donation is a perfectly codified procedure which is carried out worldwide). This population is hence representative. Second, because kidney transplants recipients have a long median overall survival (more than 10 years), they are more likely to be exposed to immunosuppressive medications. As a result, it is possible to assess in these patients whether there is a correlation between immunosuppression and the development of cancer(s) over an appropriate timeframe [3].

Immunosuppressants are typically taken at full dosage after kidney transplantation, allowing for the evaluation of their actual effects on tumorigenesis. Last but not least, in this population, the failure of a transplanted organ does not always result in death because dialysis can be resumed. As a result, in these patients, the natural course of the disease may also be assessed if immunosuppressive medication is reduced, modified, or discontinued [4].

Today, highly excellent outcomes can be attained in terms of the short- and medium-term survival of both organs and patients thanks to the high standards in surgical, anaesthesiological, and intensive-care operations as well as in the clinical management of patients undergoing transplantation. However, the long-term problems described in these patients, particularly the emergence of malignancy, have partially overturned these findings. When compared to the overall population of people their age, this group of individuals' tumour incidence, aggressiveness, and prognosis appear to be markedly elevated [5].

## Conclusion

According to calculations, tumour prevalence peaks at around 45 percent at 20 years following kidney transplant and ranges from 20 to 30 percent at 10 years. Immunosuppressive therapy is unquestionably the key factor hastening the development of malignancy in organ transplant recipients. Indeed, individuals receiving immunosuppressants for conditions other than transplantation also have a higher chance of developing neoplasms. Recent research has revealed that some immunosuppressants, such as calcineurin inhibitors, azathioprine, and thymoglobulin, exert a direct oncogenic effect in addition to the indirect oncogenic effect that all immunosuppressive medications have because they change the immune response. By preventing DNA repair and apoptosis and by promoting the synthesis of transforming growth factor-beta (TGF-beta) and vascular endothelial growth factor, calcineurin inhibitors encourage oncogenesis, neoplastic development, and metastasization (VEGF). Azathioprine and its derivatives have the ability to accelerate UV-induced DNA damage while preventing DNA repair. Thymoglobulin appears to encourage the genomic changes brought on by oncoviruses.

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