Oncologic Issues and Kidney Transplantation: A Review of Frequency, Mortality, and Screening

William S. Asch and Margaret J. Bia

Kidney transplant recipients are at increased risk for development of malignancy compared with the general population, and malignancies occur at an earlier age. This increased risk, as expressed by the standard incidence ratio (SIR), varies widely, but it is highest in malignancies triggered by oncogenic viruses. For other cancers, this increased risk is the direct consequence of immunosuppressants promoting tumor growth and lowering immune system tumor surveillance. In this review, we briefly discuss the common malignancies with increased risk after kidney transplantation, explore the pros and cons associated with screening, and summarize current prevention and treatment recommendations.

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Key Words: Kidney transplant, Malignancy, Immunosuppression, Cancer screening

Introduction

Oncologic issues are important in patients with ESRD before and after kidney transplant. In the following review, we will review the incidence of cancer in kidney transplant recipients (KTRs), mechanisms for their increased incidence, and the effect on mortality. We will also briefly describe the malignancies that are most uniquely common to KTRs and review guidelines for prevention and screening. We will end with a discussion of when changes in immunosuppression should be considered based on the frequency of the cancer and the putative role of immunosuppression in its occurrence.

Pretransplant Issues

First, a word about cancer in patients with ESRD and its effect on their being listed for kidney transplant. In previous years, such patients would be denied listing until an appropriate cancer-free interval had elapsed. However, in more recent years, United Network for Organ Sharing (UNOS) regulations allow patients to be listed but made temporarily unavailable, which enables them to accrue time as they wait. Guidelines for suggested disease-free waiting periods for various cancers were published several years ago,1 and to our knowledge they have not been updated. Details such as tumor size and pathologic description clearly affect this decision.

Post-transplant Incidence and Causes

The overall risk of cancer post-transplant is considerably higher than in the general population,2 and it is higher than in dialysis patients.3,4 In more recent publications on this topic, the higher frequency of cancer in KTRs has been expressed as a standard incidence ratio (SIR), which is the incidence in KTRs compared with age-matched controls.3,5 In Table 1, we have compiled a list of the SIRs for common cancers in the post-transplant population on the basis of data from several references.2,3,6-13 Not only is the overall risk of cancer higher in KTRs, but it also occurs at an earlier age. For example, female KTRs 25 to 30 years old have a similar risk for cancer as do women 55 to 60 years old.14 Similar occurrence of cancer at a younger age exists for male KTRs.14 Although cancer risk is still elevated in older KTRs, it is not as dramatic as in younger patients (Fig 1). Accordingly, our efforts should target this higher risk (and by extension, more likely to derive benefit), younger group of patients.

Not all cancers occur at an increased frequency post-transplant. As depicted in Table 1, nonmelanoma skin cancer (NMSC) predominates as the most frequent cancer post-transplant, followed by post-transplant lymphoproliferative disorder (PTLD) and genitourinary and gynecologic cancers (cervix and vulva). Colon cancer occurs approximately 2 times more commonly. It is worth emphasizing that several common cancers, most notably breast and prostate, do not occur at an increased frequency and thus do not call for special consideration with regards to screening or changes in immunosuppression.

Reasons for the increased incidence of malignancy post-transplant relate to the direct effects of immunosuppressants as well as their effects to suppress immune surveillance and to stimulate the activation of oncogenic viruses.7,15 Calcineurin inhibitors, such as cyclosporine and tacrolimus, have been demonstrated to stimulate transforming growth factor-β, interleukin-6, and vascular endothelial growth factor to promote...
tumor growth in animal models. Azathioprine sensitizes DNA to ultraviolet A radiation and cyclosporine inhibits DNA repair in ultraviolet-B-damaged keratinocytes, thus explaining the higher frequency of skin cancer with these agents. Immunosuppression can also activate oncogenic viruses, which can immortalize infected cells by disrupting cell-cycle control, which then can lead, in a setting of induced lowered immune surveillance, to tumorigenesis. Such is thought to be the mechanism of the increased frequency of PTLD associated with activation of Epstein-Barr virus (EBV), Kaposi’s sarcoma (associated with human herpes virus 8), cervical and vulvar cancer associated with human papilloma virus (HPV), and hepatocellular carcinoma associated with hepatitis C virus and hepatitis B virus (Table 2).

Although death from cancer is a major contributor to mortality in KTRs, recent data challenge the notion that this is true across all age ranges. Examining death rates from cancer as reported in U.S. Renal Data Service data from 1990 to 2004, an increased mortality from cancer in younger patients (standardized cancer mortality ratio [SCMR] > 1) was found; however, the death rate was lower from cancer in older patients (SCMR < 1), especially those with diabetes. The authors attribute these results to competing risks of death from other causes in older KTRs, a finding that has implications for screening, depending on age group. When comparing death from cancer across all age groups, the overall SCMR was 0.96 (95% confidence interval 0.92-1.00).

**Description of Common Cancers Post-transplant**

Certain post-transplant malignancies deserve special mention because of their increased frequency and high SIR. Guidelines for detection and screening have been described in Chapters 18-20 on malignancy in the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines for the care of the kidney transplant patient and commentary on these guidelines.

**Skin Cancer**

NMSC is the most common post-transplant malignancy. Risks include fair skin phenotype, geographic location close to the equator, and time post-transplant. The reported SIR of NMSC after kidney transplantation varies, but it is accepted to be high, ranging from 33 to 100. Although the incidence of basal cell carcinoma exceeds that of squamous cell carcinoma 4:1 in the general population, the SIR for squamous cell carcinoma greatly exceeds that of basal cell carcinoma, making it more common after transplantation (ie, the ratio reverses). Coupled with the high incidence of NMSC in the general population, it is not surprising that studies estimate approximately one third of all KTRs will have an episode of NMSC within 10 years after transplantation. Immunosuppressive medications also play a role, with azathioprine and cyclosporine being most implicated.

**Colorectal Cancer**

Colorectal cancer is the second leading cause of death from cancer in the United States. Although it remained a significant cause of death, the mortality associated with colorectal cancer declined over the last decade. Colonoscopic screening allows for the detection and excision of adenomatous polyps in their slowly progressive precancerous phase. Until recently, an increased risk of colorectal cancer after transplant was not clearly established, and screening guidelines, as a consequence, were controversial.

The SIR for colorectal cancer was just under 2. However, we now know that the SIR is higher than previously expected and that transplant recipients may see benefit from screening. Also, in studying the frequency of EBV positivity in advanced colorectal adenomas and invasive cancer, Park and colleagues noted that these lesions are identified in younger transplant recipients at a rate comparable to nontransplanted controls of more advanced age. In particular, this cohort of transplant recipients from Korea had a 12-fold increased risk of advanced neoplasia. Furthermore, the frequency of neoplasia seen in patients in their forties was comparable to patients 10 to 20 years older in the control group. Using this finding as evidence, the authors concluded that colorectal cancer screening was beneficial and recommended that screening should start at a younger age than recommended for the general population.

**Ano-Genital Cancer**

Genital HPV infections are the most common sexually transmitted disease in the United States and are the
causative factor behind most cases of cervical cancer. In particular, HPV-16 and HPV-18 are implicated in approximately 70% of cases. The association between HPV infection and malignancy is not limited to the cervix. In fact, 85% of anal carcinomas and over half of vaginal, vulvar, and penile cancers are linked to HPV infection.27,28 Like colon cancer, a precancerous phase precedes development of cervical cancer and allows for disease prevention through screening.

Immunosuppression clearly increases the risk of anogenital cancer in KTRs. The SIRs are greatest for vulvar and vaginal cancer (SIRs 45 and 36, respectively) and are moderately increased for cervical and anal cancer (SIRs 6.6 and 10, respectively).12,13 Furthermore, these neoplasms are frequently larger, more undifferentiated, and more multifocal compared with the general population. In addition, despite appropriate treatment, lesions are also more likely to persist and recur in the immunosuppressed host. Consequently, the morbidity and overall disease burden associated with ano-genital lesions are greatly increased in the immunosuppressed patient.29

In women older than 30 years of age, HPV positivity increasingly represents chronic infection and warrants screening. Indeed, women with chronic infection have the highest risk for future development of cervical and vulvar cancer.30

**Table 1. The Standard Incidence Ratio of Selected Cancers After Kidney Transplantation**

<table>
<thead>
<tr>
<th>SIR* &gt; 5</th>
<th>SIR 2-5</th>
<th>SIR &lt; 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaposi’s sarcoma</td>
<td>Cervical</td>
<td>Breast</td>
</tr>
<tr>
<td>Nonmelanomatous skin</td>
<td>Thyroid</td>
<td>Ovarian</td>
</tr>
<tr>
<td>PTLD/NHL</td>
<td>Melanoma</td>
<td>Uterine</td>
</tr>
<tr>
<td>Kidney</td>
<td>Esophageal</td>
<td>Pancreatic</td>
</tr>
<tr>
<td>Vulvar</td>
<td>Multiple myeloma</td>
<td>Brain</td>
</tr>
<tr>
<td>Penile</td>
<td>Leukemia</td>
<td>Prostate</td>
</tr>
<tr>
<td>Ano-genital</td>
<td>Oropharyngeal</td>
<td>Testicular</td>
</tr>
<tr>
<td>Liver</td>
<td>Bladder</td>
<td>Lung</td>
</tr>
<tr>
<td>Lip</td>
<td>Colon</td>
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</table>

*The SIR reflects the fold-increased risk of a malignancy in the kidney transplant recipient compared with the general population.

**Table 2. Malignancies Known or Suspected to Be Associated With Viral Infection**

<table>
<thead>
<tr>
<th>Malignancy</th>
<th>Virus Associated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical, vulvar, vaginal, and anal cancer</td>
<td>HPV-16 and -18</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>HBV and HCV</td>
</tr>
<tr>
<td>PTLD</td>
<td>EBV</td>
</tr>
<tr>
<td>Leukemia and lymphoma</td>
<td>HTLV-1</td>
</tr>
<tr>
<td>Kaposi’s sarcoma</td>
<td>HHV-8</td>
</tr>
</tbody>
</table>

**Suspected Viral Associations**

- Prostate cancer: Polyomavirus BK
- Brain cancer: JC virus
- Brain, bone, and mesothelioma cancer: SV-40

**Abbreviations:** NHL, non-Hodgkin Lymphoma; PTLD, post-transplant lymphoproliferative disorder; SIR, standard incidence ratio.

PTLD

PTLD is a well-recognized complication unique to solid organ and allogenic bone marrow transplantation. It is a disorder describing not just a single disease, but a spectrum of disease states ranging from benign lymphoproliferation to metastatic neoplastic lymphocyte growths. Most cases show B-cell proliferation and are classically associated with EBV infection after transplantation in the seronegative host (ie, primary infection).

The rate of PTLD after kidney transplantation is approximately 1% to 4%. Although there is no truly comparable disease in immunocompetent individuals, PTLD is 20-fold more likely to occur than non-Hodgkin lymphoma in the general population.32 Because of differing intensities of immunosuppression, the rate of PTLD development after organ transplantation correlates with the intensity of immunosuppression. Hence, the rate for KTRs is intermediate between liver and heart transplants who have lower and higher risks, respectively. The highest risk occurs in EBV naïve recipients receiving EBV-positive organs. Because this occurrence is more likely in younger recipients, PTLD is more common in pediatric KTRs.

Presenting symptoms vary widely and include fevers, night sweats, weight loss, and lymphadenopathy. Although uncommonly seen in non-Hodgkin lymphomas,
central nervous system involvement is common in the transplant recipient with PTLD (occurring in ~30% of cases). Furthermore, PLTDb involves the kidney allograft has been described and should prompt the clinician to consider PTLD as a cause of allograft dysfunction in the early post-transplant period of EBV naive recipients. 

PTLD treatment options cover a broad range of therapies from immunosuppression reduction to aggressive chemotherapy with Rituximab-CHOP in more severe cases. Rituximab treatment alone can be considered in low-risk cases when the patient fails to improve with immunosuppression reduction alone. At first glance, treatment with antivirals targeting EBV makes sense. However, most EBV-transformed cells do not express thymidine kinase, a requirement for antiviral drug activation. 

Overall, PTLD remains a condition associated with significant morbidity and mortality. Indeed, in some cases sacrificing the allograft is necessary to control disease. 

Renal Cell Carcinoma
Renal cell carcinoma (RCC) occurs with an increased frequency compared with the general population but not necessarily greater than the risk in dialysis patients. Major risk factors for this include previous RCC and the acquired cystic disease present in many ESRD patients. Patients with tuberous sclerosis and analgesic-abuse nephropathy may also be at increased risk. It is unclear whether screening would benefit KTRs, and recent KDIGO guidelines advised against screening because of a lack of evidence because screening could detect many small lesions that may not progress rapidly enough to affect morbidity or mortality.

Breast Cancer
On the basis of current incidence rates, 1 in 8 women will develop breast cancer, making it the most common malignancy affecting women and the second-leading cause of malignancy-related death in women. Despite being so common overall, the SIR for breast cancer in KTRs is estimated at 1.25, indicating that the baseline risk increases very modestly after transplantation. There are also some data indicating that for solid organ transplants in general, the SIR for breast cancer is 0.85 (ie, suggesting that breast cancer may be less likely to occur after transplantation and immunosuppression than it is in the general population). The same is true for prostate cancer (ie, no significant increase in SIR).

Screening and Prevention Post-transplantation
Cancer screening guidelines established for the general population cannot simply be extended to the immuno-suppressed transplant recipient. However, in the absence of studies either confirming or refuting the benefits of malignancy screening, transplant clinicians have turned to the population recommendations for guidance.

Acknowledging that transplant recipients are far more likely to die of cardiovascular disease (CVD) than malignancy, the decision not to screen a patient is also often appropriate. In 2003, Kiberd and colleagues recommended that cancer screening in patients with a life expectancy less than 5 to 7 years be deferred given that most strategies produce little or no demonstrable benefit within the first 5 years. Also included in this do-not-screen group are those patients who are likely to lose their allograft within 5 years and not be candidates for retransplantation.

The importance of lifestyle modifications in preventing malignancies after kidney transplant cannot be overlooked. Most importantly, all KTRs who smoke should be encouraged to quit. The primary benefit of smoking cessation is a reduction in CVD and morbidity; however, patients also benefit from a reduced risk of malignancy.

There are excellent data describing the value of the physical exam in skin cancer screening. This is not the case for other malignancies associated with visible or easily palpable changes amenable to physical-exam-based detection. PTLD (via lymphadenopathy screening), thymus cancer, oral cancer, penile cancer, and male anal cancer are examples of such malignancies. However, although no good information describing the value of physical exam screening for these cancers exists, logic would suggest that this would be a cost-effective strategy that should be considered further. Studies to determine the relative value of exam-based screening in KTRs need to be done. The pros and cons of screening are listed in Table 3.

Skin Cancer
All KTRs should be advised of the increased risks associated with sun exposure. They should also be educated regarding the importance of minimizing sun exposure during peak daylight hours, wearing full-coverage clothing including wide brimmed hats, and applying sunscreen with a sun protection factor of 30 or higher on any exposed skin. All KTRs should receive total-body skin examinations (TBSEs) by a dermatologist. The timing of the initial examination can be determined after a simple assessment of the patient’s risk. Timing of subsequent TBSEs can be determined by the dermatologist on the basis of the findings. Consideration should be given to discontinuing azathioprine in any KTR developing skin cancer. Furthermore, although the disease threshold above which a switch from a calcineurin to mammalian target of rapamycin inhibitors should be considered is debated (ie, the number of lesions per year and how aggressive), the switch does appear to reduce the burden of subsequent skin cancers in high-risk patients.
## Table 3. The Pros, Cons, and Screening Recommendations for Kidney Transplant Recipients

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Pros to Screening</th>
<th>Cons to Screening</th>
<th>How to Screen</th>
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<tbody>
<tr>
<td>Skin</td>
<td>• Noninvasive and evidenced based&lt;br&gt;• High yield&lt;br&gt;• Inexpensive&lt;br&gt;• Detection can prevent progression&lt;br&gt;• Supported by KDIGO guidelines&lt;sup&gt;8&lt;/sup&gt;</td>
<td>None except cost of dermatology visit&lt;br&gt;None except cost of dermatology visit</td>
<td>• Referral to dermatology for total body skin exam&lt;sup&gt;8&lt;/sup&gt;&lt;br&gt;Timing of initial exam can be based on sun exposure risk&lt;sup&gt;40,41&lt;/sup&gt;</td>
</tr>
<tr>
<td>Colorectal</td>
<td>• Provides opportunity to catch lesions early in the precancerous phase&lt;br&gt;• Disease occurs in transplant recipients at a younger age&lt;br&gt;• Supported by KDIGO guidelines&lt;sup&gt;8&lt;/sup&gt;</td>
<td>No proof that this reduces mortality in KTRs.&lt;br&gt;No proof that this reduces mortality in KTRs.</td>
<td>Screening colonoscopy and FOBT as recommended for the general population&lt;sup&gt;8&lt;/sup&gt;&lt;br&gt;Consider screening KTRs at age 40 or 5 y after transplantation ( whichever comes first)&lt;sup&gt;11&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ano-genital (cervical)</td>
<td>• Detection of precancerous lesion prevents progression&lt;br&gt;• Early detection helps prevent repetitive and more aggressive gynecologic procedures&lt;br&gt;• May also detect ano-genital lesions at time of exam&lt;br&gt;• Supported by KDIGO guidelines&lt;sup&gt;8&lt;/sup&gt;</td>
<td>No proof that this reduces mortality in transplant recipients&lt;br&gt;No proof that this reduces mortality in transplant recipients</td>
<td>Visual examination by Ob/Gyn for anal, vulvar, and vaginal lesions&lt;sup&gt;8&lt;/sup&gt;&lt;br&gt;Pap smear testing.</td>
</tr>
<tr>
<td>PTLD</td>
<td>• Evidence supports screening in EBV naïve KTRs&lt;br&gt;• Detection can prevent progression if immunosuppression is reduced&lt;br&gt;• High mortality when detected late&lt;br&gt;• Supported by KDIGO guidelines&lt;sup&gt;8&lt;/sup&gt;</td>
<td>• Cost of PCR testing&lt;br&gt;• Testing not standardized between centers&lt;br&gt;• No accepted threshold level above which intervention is indicated</td>
<td>Quantitative serum EBV PCR testing once in the first week after transplant, then at least monthly for the first 3-6 mo after transplant, and then every 3 mo until the end of the first post-transplant year&lt;sup&gt;8&lt;/sup&gt;</td>
</tr>
<tr>
<td>Renal cell carcinoma</td>
<td>• Frequency of acquired cystic disease associated with renal cell carcinoma in ESRD patients&lt;br&gt;• Supported by KDIGO guidelines&lt;sup&gt;8&lt;/sup&gt;</td>
<td>• Cost/inconvenience of ultrasound imaging&lt;br&gt;• Disagreement as to how to manage smaller lesions with less alarming characteristics&lt;br&gt;• The American Society of Transplantation found no evidence to advise screening&lt;sup&gt;47&lt;/sup&gt;</td>
<td>Ultrasound imaging</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>• Data modeling suggests that breast cancer screening in nondiabetic Caucasian KTRs is cost-effective.&lt;sup&gt;36&lt;/sup&gt;&lt;br&gt;• Supported by KDIGO and European transplant guidelines.&lt;sup&gt;8,51&lt;/sup&gt;</td>
<td>• Data modeling suggests that older and diabetic KTRs are unlikely to see a survival benefit because of competing causes of death&lt;sup&gt;36&lt;/sup&gt;</td>
<td>Mammography for female KTRs between 50 and 69 y with an option to screen after the age of 40 y&lt;sup&gt;47,51&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

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Abbreviations: EBV, Epstein-Barr Virus; FOBT, fetal occult blood test; KDIGO, Kidney Disease: Improving Global Outcomes; PCR, polymerase chain reaction; KTRs, kidney transplant recipients; Ob/Gyn, obstetrician/gynecologist; PTLD, post-transplant lymphoproliferative disorder.
Colorectal Cancer
Although there is presently no proof that screening for colorectal cancer will reduce mortality in KTRs, following the screening guidelines established for the general population seems wise and was recommended by the KDIGO workgroup. As such, all KTRs older than 50 years of age should be referred for a screening colonoscopy. If the KTR has a positive family history for colorectal cancer, screening should start at an age 10 years younger than that at which the family member was diagnosed. Furthermore, given that KTRs appear to have a risk for colorectal cancer comparable to those in the general population 10 to 20 years older, consideration can be given to routine screening starting at age 40 or 5 years after transplantation.

Ano-Genital (Cervical) Cancer
In the United States, a routine gynecologic examination with traditional Pap smear screening is recommended for all women older than 21 years of age and is therefore advisable for KTRs. These exams should also include a thorough visual inspection of the anal and vulvar areas, which are also at risk for malignancy. Acute HPV infection is common in women younger than 30 years of age and does not necessarily, at least not in the general population, carry a high risk of chronic infection. The risk of resulting chronic infection and subsequent disease is higher in KTRs.

Gardasil vaccination protects against development of HPV 6-, 11-, 16-, and 18-related genital tract diseases associated with chronic viral infection. Studies are currently underway to determine the efficacy of Gardasil vaccination in women with advanced stage CKD and ESRD. At a minimum, attention should be given to the use of Gardasil in qualifying women pretransplant.

PTLD
Although not all cases of PTLD can be linked to EBV, quantitative polymerase chain reaction screening of the serum of EBV-seronegative recipients transplanted from seropositive donors (ie, high-risk recipients) for EBV viremia should be considered. Because this disease commonly has its onset in the first year after transplant, screening should occur during this interval. There are potential caveats to this screening approach. First, viral load results vary between laboratories because of the lack of an international reference standard. Second, many healthy KTRs will test positive with chronic but low-grade viremia. Treatment of these KTRs poses a dilemma.

RCC
The KDIGO and American Society of Transplantation (AST) workgroups concluded that there was insufficient evidence to recommend RCC screening post-transplant for all KTRs. Pretransplant, the AST’s Evaluation of Renal Transplant Candidates: Clinical Practice Guidelines workgroup concluded that ultrasound of the native kidneys during the candidate evaluation was “reasonable.” Consistent with this practice recommendation, most, if not all, centers screen for acquired cystic disease and suspicious appearing native kidney lesions by ultrasound as a component of the pretransplant evaluation. When a suspicious cyst is detected, the frequency of subsequent monitoring should be based on the recommendation of the ultrasound radiologist. Higher grade findings are managed accordingly. Prior history of RCC, acquired cystic disease, tuberous sclerosis, and analgesic nephropathy are all associated with future development of RCC. Ultrasound imaging on an annual or biannual basis can be considered in these higher risk KTRs, but a benefit on mortality is not established.

Breast Cancer
Mammography screening is widely accepted as the “gold standard” for early breast cancer detection. However, whether there is a mortality benefit from mammography remains controversial. Acknowledging that the rate of breast cancer in KTRs does not appear significantly higher than for women in the general population, the KDIGO workgroup did not make a recommendation for or against mammographic screening. However, the European Best Practice Guidelines Expert Group recommended following the guidelines established for the general population. Note that simulated data suggest that screening is beneficial for nondiabetic Caucasians, but no benefit exists for older and diabetic KTRs. This is because of the high likelihood that older and diabetic KTRs will die from a competing illness. Not screening for breast cancer in these subgroups of KTRs should be considered. The test performance characteristics of mammography are not expected to differ between KTRs and women in the general population.

When Not to Screen
It is generally noted that the benefit of screening diminishes in older individuals or those with a life expectancy less than 5 to 10 years. With enhanced mortality from CVD, judgment regarding screening is needed in many KTRs.

When to Lower Immunosuppression Drugs
Not all cancers occur with increased frequency post-transplant (Table 1). As suggested in the KDIGO guidelines, it may be wise to confine such decisions to cancers in which the SIR is 3 or greater post-transplant. Although there is no evidence to support this recommendation, it makes sense to lower immunosuppression, not in all KTRs with advanced malignancy, but in those whose malignancy is thought to be caused or exacerbated by immunosuppression.
Summary

In KTRs, several, but not all, malignancies occur at a higher frequency (expressed as a SIR) and at a younger age. Direct effects of immunosuppressant drugs and/or their effect to stimulate the proliferation of oncogenic viruses contribute to the cause. KDIGO guidelines for screening, as well as guidelines from other transplant organizations, should be followed, especially in younger KTRs with relatively few comorbidities. Guidelines for when to consider a decrease in immunosuppression are discussed, although there is no evidence to confirm these suggestions.

References


