Transplant International ISSN 0934-0874

ORIGINAL ARTICLE

Excess risk of cancer in renal transplant patients

Michèle Kessler,[1,2] Nicolas Jay,[2] Rachel Molle[1,2] and Francis Guillemin[2,3]

1 Department of Nephrology, University Hospital of Nancy, Vandoeuvre les Nancy, France
2 EA 4003, University Hospital of Nancy, Vandoeuvre les Nancy, France
3 Department of Clinical Epidemiology and Evaluation, University Hospital of Nancy, Vandoeuvre les Nancy, France

Keywords:
de novo cancer, epidemiology, excess risk, kidney transplantation.

Correspondence
Professor Michèle Kessler, Service de Néphrologie, Hopitaux de Brabois, CHU de Nancy, 54500 Vandoeuvre les Nancy, France.
Tel.: +33-383153169; fax: +33-383153531;
e-mail: m.kessler@chu-nancy.fr

Received: 14 January 2006
Revision requested: 10 February 2006
Accepted: 26 July 2006

doi:10.1111/j.1432-2277.2006.00383.x

Summary

Cancer data were reviewed in 488 patients who underwent renal transplantation and received cyclosporine at our centre from January 1985 to December 1995. Incidence of nonmelanoma skin cancer (NMSC) was standardized on the age and sex distribution of the French population. For cancer other than NMSC, we calculated the ratio of observed to expected numbers of cancer cases in the RT population, based on age- and sex-specific incidence for cancer in France. Standardized incidence ratios (SIR) were calculated for all cancers and for specific cancer types encountered. Over 4638 patient-years of exposure, 51 (10.4%) transplant recipients developed a first NMSC which was significantly associated with older age at transplantation ($P < 0.0001$) and the 1991–1995 transplantation period ($P = 0.0008$). Fifty-six recipients developed cancer other than NMSC over the period. The SIR for all cancer was 2.2 (1.5–3.0) in males and 3.0 (1.9–4.6) in females. The SIR for specific cancer types revealed significant excess for native kidneys [13.0 (5.2–26.8)] prostate cancer [3.6 (1.5–3.0)] and post-transplant lymphoproliferative disorder (PTLD) [9.5 (3.1–22.1)] in males, and cervical cancer [25.3 (9.3–55.0)], native kidneys [26.4 (5.4–77.2)] and PTLD [28.9 (9.4–67.6)] in females. Incidence of NMSC and some types of other cancer is high in cyclosporine-treated patients. Optimizing monitoring practice might be useful to identify subjects with significant excess risk for specific types of solid tumours.

Introduction

An increased incidence of cancer in immunosuppressed and immunodeficient patients is now well established. Since the first report of *de novo* cancer occurring in patients who have had kidney transplantation [1], many studies have indicated a high frequency of cancer in this population. Published studies of post-transplant cancer risk have used differing methodologies that make comparison of results difficult. According to several registries, the most frequent types of tumours are nonmelanoma skin cancer (NMSC) and virus-related tumours [2,3] Nevertheless a recent US study examining recipients in 1995–2001 suggested that most tumours occurred more frequently after kidney transplantation than in the general population [2–4]. Recently it has been suggested that newer agents such as mycophenolate mofetil and sirolimus were not linked with post-transplant malignancies and might have antitumour properties [5], but long-term data are still lacking.

In this cohort study, we reviewed for cancer occurrence the records of all patients transplanted in our unit over an 11-year period in the cyclosporine era. The transplantations were performed according to standardized protocols using a homogeneous immunosuppressive regimen. Cancer incidence was well documented by careful patient follow-up. The main objective of the study was to compare the observed incidence of *de novo* cancer in renal transplant patients standardized for age and sex with the overall incidence of cancer in France. A secondary objective was evaluation of the influence of demographic factors on cancer occurrence.

Patients and methods

All patients who underwent first kidney transplantation at the Nephrology and Transplantation department of the Nancy University Hospital between 1 January 1985 and 31 December 1995 were included in the study. They received homogeneous immunosuppressive treatment by induction with antilymphocyte globulins followed with dual (cyclosporine–prednisone) or triple (cyclosporine–prednisone–azathioprine) therapy. Each patient was considered exposed to risk of cancer from the day of transplantation to 31 December 2003, date of death, return to dialysis or last visit for the patients lost to follow-up. Recipients were censored for analysis at graft failure because no follow-up data were available after that point. We retrieved the following information from the medical records: date of birth, gender, dates of transplantation, last visit, death or return to dialysis and diagnosis of cancer (date and type). Patients with past history of cancer before renal transplantation were excluded. Diagnosis of cancer was made on presentation of clinical symptoms or through systematic monitoring for skin, cervix, prostate and native kidneys cancers. During the study period, usual follow-up of the recipients was a visit once a month during the first year, every 2 months during the second year and every 3 months from year 3. These visits were alternated between our centre and the local nephrology units which referred the patients for renal transplantation in a regional collaborative network. Before transplantation, females on the waiting list had cervical smears once a year and mammography every 2 years and males above 50 had measurement of prostate-specific antigen (PSA) once a year. After transplantation, the same screening was continued and recipients had a systematic dermatology consultation and ultrasound examination of native kidneys in the postoperative period and then once a year. The type of cancer was confirmed by histological examination (at biopsy or surgery) in all patients. For patients who had multiple skin malignancies, the first skin cancer only was taken into account. For other cancer all primary tumours were documented.

The observed incidence rates for cancer were calculated by dividing the number of cancer cases by the number of patient-years of exposure since renal transplantation. Cancer incidence estimates for cancer other than NMSC are available in France, the FRANCIM network which collects the data from 17 population-based registries throughout the country [6] and cancers were coded and grouped according to the FRANCIM classification.

For NMSC, observed incidence in each 5-year age band and sex was expressed as number of cases by patient-years at risk. Using direct standardization, we calculated incidence standardized on age and sex distribution in the French population 1999 census [7]. In France, during the study period, a census was done once every 9 years and we considered that 1999 results were the most appropriate to reflect population structure and to allow generalization of our results. For other cancers, indirect standardization was used and we calculated the ratio of observed to expected numbers of cases of cancer in the kidney transplantation population. Expected numbers were based on age- and sex-specific incidence for cancer in France in 1995 [6]. In the absence of other data for general population during the study period, standardization could not be done by calendar year. Standardized incidence ratios (SIR) with 95% confidence interval were calculated for all cancers and for specific types of cancer encountered based on the assumption of a Poisson distribution for cancer occurrence. Cancers were coded and grouped according to the FRANCIM classification [7].

Time to cancer occurrence was modelled using Kaplan–Meier estimates and differences between groups, by sex, age and calendar period (1985–1990 and 1991–1995) at first renal transplantation were analysed using the Cox regression model. Data were analysed using SAS statistical software (V9.0, SAS France, Gregy-Sur-Yerres, France).

Results

Four hundred and eighty-eight patients who received a first kidney graft during the study period were included and followed during an average of 9.5 ± 5.2 years, representing 4638 patient-years of exposure. Among them, 12 patients had pre-emptive transplantation. There were 326 (66.8%) males and 162 (33.2%) females. Age at transplantation was 42.6 ± 12.6 years (42 ± 12.3 in males and 43.6 ± 13.0 in females: $P = 0.19$). Two hundred and thirty-one transplantations were performed during the 1985–1990 period and 257 during the 1991–1995 period. A total of 73 patients died, 143 returned to dialysis and three received a second graft. One hundred and seven (21.9%) patients (72 men and 35 women) developed a first cancer. Fifty-one had skin cancer and 56 other cancers.

Skin cancer

Crude incidence of NMSC was 11.7 per 1000 patient-years (12.8 in males and 9.4 in females). The incidence of NMSC, standardized on the French population was 9.1 per 1000 patient-years (CI 95% 6.4–31.2). It was not significantly higher in males than in females. The basal/squamous cell carcinoma ratio was around one in both genders (25:26). One melanoma was observed. Age and time since renal transplantation (RT) at diagnosis of first NMSC were similar in females and males (55.1 ± 11.7 vs. 60.5 ± 7.5, $P = 0.127$ and 5.4 ± 3.7 vs. 6.4 ± 3.4, $P = 0.351$ respectively). Considering era of transplantation,

patients were significantly older during the 1991–1995 period: 44.3 ± 13.2 vs. 40.7 ± 11.6 years in 1985–1990 ($P = 0.001$). Kaplan–Meier estimates showed that NMSC occurred more frequently in older patients (log rank test $P < 0.0001$) (Fig. 1a) and in patients transplanted during the 1991–1995 period (log rank test $P = 0.0008$) (Fig. 1b).

In the multivariate analysis, a higher age at first renal transplantation and the 1991–1995 period were significant and independent risk factors for developing skin cancer [RR = 1.09 per year (1.06–1.12) and 1.99 (1.04–3.80) respectively].

Cancer other than NMSC

The most frequent types of cancer were cancer of the cervix, native kidneys and post-transplant lymphoproliferative disorder (PTLD) in females and cancer of native kidney, prostate, lips and mouth, lung and PTLD in males (Table 1). Overall, a first cancer was diagnosed in males at 56.4 ± 10.5 years and 6.2 ± 4.3 years after RT. In females, age at diagnosis was 50.7 ± 14.9 and time since RT 5.8 ± 4.6 years.

The SIR for all cancer types significantly exceeded one, indicating an excess risk in the RT population over that in the general population in males [2.2 (1.5–3.0)] and females [3.0 (1.9–4.6)] (Table 1). The SIR for individual types of cancer in males and females was significantly higher than one for cancer of the prostate in males and cervix in females and cancer of native kidneys and PTLD in both genders. The incidence for lung, colon, rectum, bladder and breast cancer did not differ significantly from the general population.

With Kaplan–Meier analysis the probability of cancer occurrence according to transplantation era increased

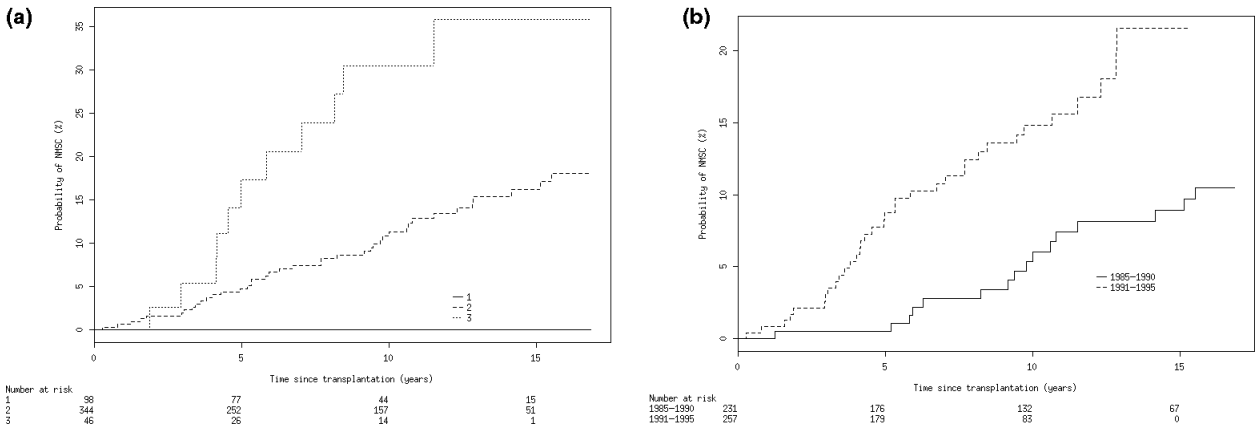

Figure 1 (a) Probability of first nonmelanoma skin cancer by age group. Group 1: <30 years; group 2: 30–59 years; group 3: >59 years. (b) Probability of first nonmelanoma skin cancer by transplantation era.

Table 1. Standardized incidence ratio (SIR) for nonskin cancers compared with the general population in France.

	Male		Female	
Type	*n*	SIR (95% CI)	*n*	SIR (95% CI)
All cancers	38	2.19 (1.55–3.00)	21	3.01 (1.86–4.60)
Native kidneys	7	13.01 (5.23–26.81	4	35.20 (9.58–90.1)
Prostate	8	3.59 (1.55–7.06)		–
Cervix		–	6	25.28 (9.27–55.02)
Non Hodgkin Lymphoma	5	9.48 (3.08–22.13)	5	28.95 (9.40–67.56)
Lips and mouth	3	1.59 (0.33–4.6 4)	0	0.00 (0.00–31.22)
Colon and rectum	2	0.89 (0.11–3.22)	0	0.00 (0.00–4.73)
Pancreas	1	3.61 (0.09–20.12)	0	0.00 (0.00–49.95)
Lung	5	1.70 (0.55–3.96)	1	4.57 (0.11–25.46)
Bladder	1	1.02 (0.03–5.67)	1	11.72 (0.29–65.31)
Breast	1		1	0.35 (0.01–1.97)
Oesophagus	1	1.43 (0.04–7.99)	0	0.00 (0.00–103.17)
Thyroid	1	7.40 (0.19–41.24)	0	0.00 (0.00–26.40)
Larynx	1	1.48 (0.04–8.27)	0	0.00 (0.00–189.80)
Myeloma	0	0.00 (0.00–27.71)	1	17.26 (0.43–96.17)
Others	2		2	

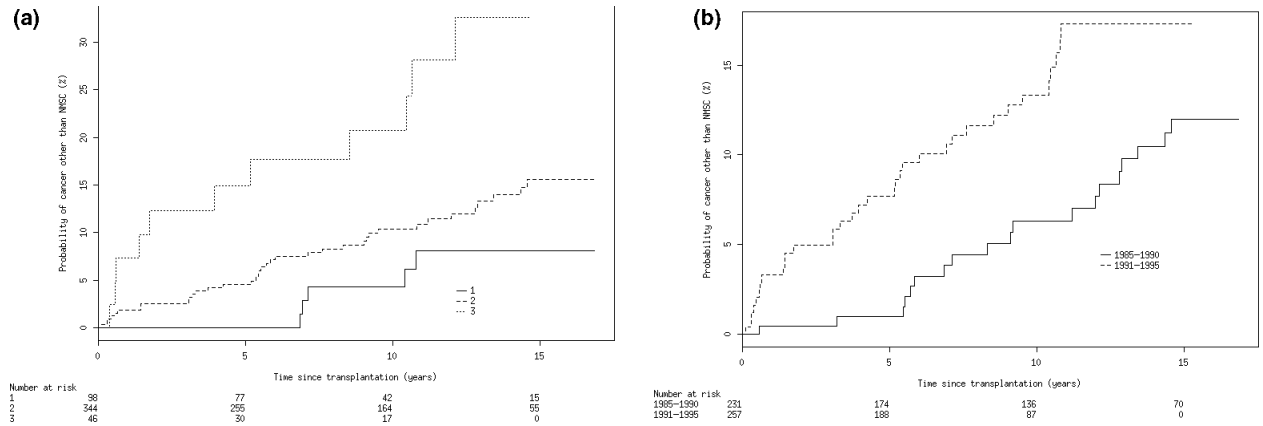

Figure 2 (a) Probability of cancer other than NMSC by age group. Group 1: <30 years; group 2: 30–59 years; group 3: >59 years. (b) Probability of cancer other than NMSC by transplantation era.

with age (log rank test $P = 0.0006$) (Fig. 2a) and appeared significantly more frequent during the 1991–1995 period when compared with the 1985–1990 period (Fig. 2b) (log rank test $P = 0.014$). This variable was included in the multivariate analysis, as a stratifying variable, because it did not meet risk proportionality requirement for the Cox model. Age at first RT was found to be a significant predictor of nonskin cancers [RR = 1.04 per year (1.02–1.07)]. Gender had no significant influence [RR = 1.08 (0.63–1.86)].

Discussion

The present investigation compared for the first time the risk of cancer in renal transplant patients in France with that of the general population. Follow-up duration was longer than many previous studies. The data on both skin and nonskin cancers were highly reliable and complete.

Compared with published data, our study showed that patients exclusively receiving cyclosporine and prophylactic antilymphocyte antibodies displayed a crude incidence of NMSC of 11.7 per 1000 patient-years during the first 10 years following transplantation. This result observed in a period during which the immunosuppressive regimen was kept unchanged is quite similar to that obtained in Italy [8] and in the Netherlands [9], a country not very far from our region. Because of the lack of a French registry for NMSC, we could not calculate the excess risk. SIR was found to be 24 in the Dutch study. Australian renal transplant patients have a very high incidence of NMSC [10] but in fact, considering the high incidence of skin cancer in the general population, the excess risk is quite similar to that observed in countries with much lower sunlight exposure. In our study, like in the general population, age was the main risk factor of NMSC. As age of potential recipients is increasing, the crude incidence of skin cancer will probably increase. The increased incidence of NMSC during the 1991–1995 period is independent of the increasing age of our transplant population and may illustrate the increasing risk of skin cancer in the general population. In the general population, the basal cell/squamous cell carcinoma ratio is 5:1 to 8:1 [11]. We found among renal transplant recipients, a ratio of 0.9:1 for the first skin cancer; this ratio is even lower when multiple skin tumours are considered [8, 12].

Compared with expected occurrence in the French population, we observed a significant excess risk of cancer other than NMSC in both genders when all cancers were considered. Our results are similar to the SIR calculated in Denmark [12]. Comparison for specific type of cancer is difficult because the definition of cancer sites differed from one study to another: for example, we used the FRANCIM classification [7] which is different from the ICD-9.CM. On the other hand, grouping of cancers was different depending on the number of cases observed. The increased incidence of PTLD after renal transplantation has been known for more than three decades [13–15]. The use of potent antilymphocyte antibodies for prophylaxis of acute rejection was found to be associated with a higher risk for PTLD [14]. In the present study where nearly all patients received prophylactic antilymphocyte antibodies, crude incidence of PTLD (2.2 per 1000 patient-years) seems lower than in the collaborative transplant study [14].

We found a significant excess risk for cancer of native kidneys. In Japan, the relative risk of renal cell carcinoma (RCC) in renal transplant patients was 80-fold higher than that in the general population [16]. This increased risk was confirmed by some studies in the USA [4] but not by the EDTA-ERA study [13] or the Danish registry [12]. As in dialysis patients, the main risk factor for the development of RCC is probably the development of

acquired cystic kidney disease in the setting of prolonged uraemia [17] and conflicting results could be explained by differences in policies of bilateral nephrectomy prior to transplantation which was rarely done in our transplanted patients. It could also be related with differences in screening strategy. During the study period, we performed an ultrasound examination once a year for RCC with special regard to the native kidneys; in case of doubtful finding a computed tomography scan was initiated. It has been suggested that RCC in kidney transplant patients is quite aggressive [18] warranting careful screening both before and after transplantation. International recommendations for screening renal transplant recipients for RCC are conflicting: not recommended by the guidelines of the American Society of Transplantation [19] it was recommended by the European Best Practice Guidelines for Renal Transplantation [20]. The differences among international guidelines relate to the uncertainty surrounding whether early detection results in better survival for transplant patients with RCC.

Excess of cancer of the cervix of the uterus appears to be significant in our female transplant population in whom an annual smear was performed to screen for cervical neoplasia. A general trend to increased risk was confirmed by data coming from Japanese [16] and European registries [13]. Cervical cancer appears to be aetiologically related to infection with oncogenic strains of human papilloma virus (HPV). In transplanted women, the increased risk of cervical cancer could be because of either reactivation of latent HPV or inability to contain a primary infection. There is considerable evidence that regular screening reduces the incidence of invasive cancer in the general population; the interest of such a policy was also shown in renal transplant women [21].

There is controversy about the incidence of prostate cancer both in the general population and in renal transplant recipients. In the USA, prostate cancer rate was reported to be two-fold higher after RT [4]. In most registry-based studies, the SIR for this type of cancer after RT has not been significant [4, 12, 13, 16]. This may be because of uncertainty of benefit from systematic screening. In our male population in whom PSA was assayed once a year when patients were on the waiting list and after transplantation, and for whom biopsies were systematically performed in the event of increased levels, the crude incidence was two per 1000 patient-years and the SIR were similar to those observed in the Nordic countries [2]. A high incidence of prostate cancer was recently found in a study based on questionnaires mailed to 22 French renal transplant centres [22]. Systematic screening in RT recipients will undoubtedly increase the incidence of localized prostate cancer but this could be because of a lead time bias. Whether this excess is simply an advance of latent cancer with acceleration of carcinogenesis, or true excess that would continue to be observable over a longer follow-up period, needs to be established. In the absence of prospective studies comparing the evolution of prostate cancer in RT recipients with that in the general population, it is therefore difficult to establish whether annual measurement of PSA will modify the evolution of prostate cancer in male RT recipients.

The other malignancies had similar incidence in the transplanted and general population. This is in agreement with previous studies, particularly for lung and breast cancers [13, 23]. Incidence of breast cancer was found particularly low during the first transplant year [23] but in many transplant centres including ours, screening for breast cancer is systematically performed before enrolment on the wait listing, which would decrease the chance of developing breast cancer early after transplantation. Data coming from the EDTA-ERA registry suggest an increased risk for colonic cancer [13]. This is true only for the 10–20 years after renal transplantation. Our results, similar to those of Birkeland *et al.* [2] showed, after a mean follow-up of 9.5 years, no significant excess risk. Data coming from the USRDS showed that in the 47% of total RT patients who used Medicare, rates for most common malignancies were higher than in the general population [4]. In this study, duration of follow-up was very short (3 years). Many of these tumours may have developed before RT and remained latent for several years before diagnosis. These results highlight the importance of careful evaluation of potential recipients before transplantation to detect latent cancers.

Our study, restricted to an 11-year period has the advantages of homogeneous immunosuppressive treatment prescribed, standardized methods used for ascertainment of cancers, and high degree of completeness and quality of locally recorded data. This gives additional insight for comparing the risk of cancer in a renal transplant population with general population. Nevertheless, our study has some limitations. First, indications for transplantation as well as the type of immunosuppressive treatment favouring cancer occurrence may have affected the representativity of our renal transplantation population. Second, recipients were censored when they went back to dialysis or were lost to follow-up. This could have introduced an underestimation of cancer occurrence. Third, indirect standardization was not done by calendar year because national rates of cancer were only available for 1995. This could have introduced a bias if the risk of cancer in the French population had notably changed during the study period. Fourth, the size of our RT population is relatively small and could be unable to yield a sufficiently reliable determination of cancer incidence.

Journal compilation © 2006 European Society for Organ Transplantation **19** (2006) 908–914

This is probably true for less common cancers. Fifth, surveillance bias is inherent in all studies concerning cohorts of patients with chronic diseases followed regularly for prolonged periods of time. Our cases were not identified through a cancer registry as there is none in our region. Even if cases of cancer in a transplant population were identified through a cancer registry they would never be identified in the same way as cancers usually are in the general population. Identification of cancer in transplant patients was also different: more intensive and less spontaneous; therefore identification of cancer in a transplant population could never be purely population based. The absence of a cancer registry led us to calculate expected cases from 17 other French regional registries. To minimize a potential ecological bias the average of the 17 registries was used.

Our relatively aggressive screening strategy could not be generalized to the transplant population without a careful consideration and further studies are needed to evaluate the impact of screening for skin, cervical and prostate cancer and RCC in the renal transplant population examining both cost and effectiveness issues [24]. Some authors proposed an individualized approach based on patient's age, life expectancy, inherent cancer risk factors [25].

In conclusion, our findings confirm the existence of a high incidence of NMSC in renal transplant recipients on cyclosporine-based immunosuppressive treatment. A significant excess risk for specific types of cancer other than NMSC, particularly native kidneys, cervix and prostate, raises the question of optimizing and standardizing monitoring practice in this population. On the other hand, any excess risk of cancer should be interpreted in light of the absolute risk in the general population to appreciate the real burden of cancer, given the benefit of renal transplantation.

Acknowledgement

This study has been conducted with the support of the Centre d'Epidémiologie Clinique de Nancy INSERM (Institut National de la Santé et de la Recherche Médicale) – CIE 6-Ministère de la Santé – Centre Hospitalier Universitaire de Nancy.

References

1. Murray JE, Gleason R, Bartholomay A. Third report of the human kidney transplant registry. *Transplantation* 1965; **35**: 294–302.
2. Birkeland SA, Storm HH, Lamm LU, *et al.* Cancer risk after renal transplantation in the Nordic countries, 1964–1986. *Int J Cancer* 1995; **60**: 183–189.
3. Kinlen J, Sheil AGR, Peto J, Doll R. Collaborative United Kingdom–Australasian study of cancer in patients treated with immunosuppressive drugs. *Br Med J* 1979; **2**: 1461–1466.
4. Kasiske BL, Snyder JJ, Gilbertson DT, Wang C. Cancer after kidney transplantation in the United States. *Am J Transplant* 2004; **4**: 905–913.
5. Buell JF, Gross TG, Woodle ES. Malignancy after transplantation. *Transplantation* 2005; **80**: S254–S264.
6. Réseau FRANCIM. *Le cancer en France: Incidence et Mortalité. Situation en 1995. Evolution entre 1975 et 1995.* Paris: Ministère de l'emploi et de la solidarité. Secrétariat d'état de la santé, 1995.
7. Recensement de la population mars 1999. Available at: http://www.recensement.insee.Fr/FR/ST_ANA/F2/POPALLPOP1APOP1A1FZFR.html. Accessed 17 August 2006.
8. Naldi L, Fortina AB, Lovati S, *et al.* Risk of non melanoma skin cancer in Italian organ transplant recipients. A registry-based study. *Transplantation* 2000; **70**: 1479–1484.
9. Hartevelt MM, Bouwes Bavinck JN, Kootte AMM, Vermeer BJ, Vandenbroucke JP. Incidence of skin cancer after renal transplantation in the Netherlands. *Transplantation* 1990; **49**: 506–509.
10. Hardie IR, Strong RW, Hartley LCJ, Woodruff PWH, Clunie GJA. Skin cancer in Caucasian renal allograft recipients living in a subtropical climate. *Surgery* 1980; **87**: 177–183.
11. Euvrard S, Kanitakis J, Claudy A. Skin cancers after organ transplantation. *N Engl J Med* 2003; **348**: 1681–1691.
12. Birkeland SA, Lokkegaard H, Storm HH. Cancer risk in patients on dialysis and after renal transplantation. *Lancet* 2000; **355**: 1886–1887.
13. Brunner FP, Landais P, Selwood NH. Malignancies after renal transplantation: the EDTA-ERA registry experience. *Nephrol Dial Transplant* 1995; **10** (Suppl. 1): 74–80.
14. Opelz G, Döhler B. Lymphomas after solid organ transplantation: a collaborative transplant study. *Am J Tansplant* 2003; **4**: 222–230.
15. Penn I, Hammond W, Brettschneider L, Starzl TE. Malignant lymphomas in transplant patients. *Transplant Proc* 1969; **1**: 106–112.
16. Hoshida Y, Tsukuma H, Yasunaga Y, *et al.* Cancer risk after renal transplantation in Japan. *Int J Cancer* 1997; **16**: 517–520.
17. Maisonneuve P, Agodoa L, Gellert R, *et al.* Cancer in patients on dialysis for end-stage renal disease: an international collaborative study. *Lancet* 1999; **354**: 93–99.
18. Pope JC, Koch MO, Bluth RF. Renal cell carcinoma in patients with end-stage renal disease: a comparison of clinical significance in patients receiving hemodialysis and those with renal transplants. *Urology* 1994; **44**: 497–501.
19. Kasiske BL, Vazquez MA, Harmon WE, *et al.* for the American Society of transplantation. Recommendations for the outpatient surveillance of renal transplant recipients. *J Am Soc Nephrol* 2000; **11**: S1–S86.

20. EBPG Expert group on renal transplantation. European best practice guidelines for renal transplantation (part 2). *Nephrol Dial Transplant* 2002; **17** (Suppl. 4): 3–67.
21. ter Haar-van Eck SA, Rischen-Vos J, Chadha-Ajwani S, Huikeshoven FJM. The incidence of cervical intraepithelial neoplasia among women with renal transplant in relation to cyclosporine. *Br J Obstet Gynaecol* 1995; **102**: 58–61.
22. Cormier L, Lechevallier E, Barrou B, *et al.* Diagnosis and treatment of prostate cancers in renal-transplant recipients. *Transplantation* 2003; **75**: 237–239.
23. Stewart T, Tsai SCJ, Grayson H, Henderson R, Opelz G. Incidence of *de-novo* breast cancer in women chronically immunosuppressed after organ transplantation. *Lancet* 1995; **346**: 796–798.
24. Chertow GM, Paltiel AD, Owen WF Jr, Lazarus JM. Cost-effectiveness of cancer screening in end-stage renal disease population. *Arch Intern Med* 1996; **156**: 1345–1350.
25. LeBrun CJ, Diehl LF, Abbott KC, Welch PG, Yuan CM. Life expectancy benefits of cancer screening in end-stage renal disease population. *Am J Kidney Dis* 2000; **35**: 237–243.