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ORIGINAL ARTICLE

Low incidence of malignancy after transplantation in Chinese heart allograft recipients

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Summary

This study sought to assess the incidence of neoplastic disease after transplantation in Chinese heart allograft recipients. A total of 156 patients (130 male and 26 female; mean age, 45.8 ± 15.7 years), surviving more than 30 days after transplantation, were enrolled in this study. The mean follow up duration was 51.2 ± 33.0 months. Six patients (3.8%) developed neoplastic diseases after transplantation: post-transplant lymphoproliferative diseases in four and solid tumors in two patients. There was no skin cancer or Kaposi's sarcoma. Solid tumors affected the prostate, liver and urinary bladder in two patients. The cumulative incidence of neoplastic disease was 2.1% at 1 year, 3.6% at 5 years, and 10.1% at 10 years after transplantation. The incidence of post-transplant neoplastic disease was low in Chinese heart allograft recipients. It resulted from a relative paucity of Kaposi's sarcoma and skin cancers in Chinese population.

Introduction

The continuous improvement in clinical outcome after heart transplantation has established heart transplantation as a standard and efficient therapy for end-stage heart failure [1]. The overall 1-, 5- and 10-year survival rates for heart transplantation were 80, 70 and 50% with a constant mortality rate of 4% per year [1]. Long-term survival is limited by transplant coronary artery disease and the complications produced by the toxicities of maintenance immunosuppression (malignancy, infection, and renal failure) [1–3]. Transplant coronary artery and malignancy, as expected, increase over time.

The development of malignancy is a well-recognized complication in transplant recipients with prolonged use of immunosuppression [4,5]. The incidence of post-transplant neoplastic diseases depends on the type of organ transplantation and length of time after transplantation [5]. Most reports documented a higher incidence in heart than in kidney transplant recipients. This considerable discrepancy in cancer frequency is likely to be due to the more intense immunosuppression used to prevent and treat allograft rejection in the heart than the kidney. Multicenter registry of the International Society for the Heart and Lung Transplantation in 2003 reported that the cumulative incidence of neoplastic diseases was 3.4 and 18.2% at 1 and 5 years after heart transplantation (data obtained from http://www.ishlt.org).

In Asia, the first clinical heart transplantation was performed by Wada in 1968. Because of poor result, no active heart transplantation program was done for almost two decades. In July 1987, the first heart transplantation was started in Taiwan. Although Taiwan is a small island with a population of 22 million, most of the heart transplantations performed in Chinese are done in Taiwan [6]. However, the incidence of post-transplant neoplastic disease in Chinese heart allograft recipients has not been reported. This study sought to assess the incidence of neoplastic disease after transplantation in Chinese heart allograft recipients.

Patients and methods

Patient population

From July 1987 to December 2002, 171 heart transplants were performed in 169 patients. Patients who underwent

retransplantation or died within 1 month after transplantation were excluded from this study. Thus, a total of 156 patients (130 males and 26 females; mean age at transplantation, 45.8 ± 15.7 years; range: 6 months to 71 years) were enrolled in this study. Heart transplantation was indicated by the following heart diseases: dilated cardiomyopathy in 84 patients (54%), ischemic cardiomyopathy in 50 patients (32%), and other cardiac diseases in 22 patients (14%).

Immunosuppression

All patients received triple-drug immunosuppressive therapy according to our heart transplantation protocol [7]. Since 1995, we started to use rabbit antithymocyte globulins for induction therapy. Azathioprine (4 mg/kg) was given 1 h before the operation. Solumedrol (1000 mg) was infused while release of the aortic cross-clamp. Rabbit antithymocyte globulin 1.5–2.5 mg/kg/day was given after transplantation for 5 days. Cyclosporine was started orally within 5 days after transplantation or after the recovery of renal function. Cyclosporine dose was adjusted according to renal function and serum cyclosporine level, which was maintained at the trough level of 300–500 ng/ml during the first 3 months after transplantation and 200–300 ng/ml 1 year after transplantation. Azathioprine was given at 1–2 mg/kg/day after transplantation, with the dose adjusted to maintain a white blood cell count 4000–6000/mm^3. Prednisone (0.5 mg/kg/day) was started on the second postoperative day and tapered to 0.2 mg/kg/day by the first month after transplantation. Tacrolimus (FK-506) and mycophenolate mofetil (Cellcept) were used for recurrent rejection or severe adverse reactions to cyclosporine and azathioprine [8].

All patients were followed monthly at special cardiac transplantation clinic. Standard chest roentgenogram, blood tests, electrocardiogram and physical examinations were routinely performed at regular intervals.

We evaluated the post-transplant course of the 156 heart transplant patients to determine the incidence and specific type of post-transplant malignancies. The mean follow up duration was 51.2 ± 33.0 months (range: 1–139 months; median, 51.3 months). None of them was lost of follow up.

Statistical analysis

The results are expressed as mean ± SD or as frequencies for the categorical variables. The survival curve and cumulative incidence of post-transplant neoplastic diseases was plotted by the Kaplan–Meier method. Statistical differences between groups were calculated using Fisher exact test. Differences were considered significant at $P < 0.05$.

Results

Post-transplant neoplastic diseases

Among the 156 heart transplant patients, six patients (3.8%) suffered from seven malignant neoplasms. There were post-transplant lymphoproliferative diseases in four and solid tumors in two patients. There was no skin cancer or Kaposi's sarcoma.

Solid tumors affected the prostate, liver, and urinary bladder in two patients. One patient aged 68 years had synchronous double cancers with hepatocellular carcinoma of the liver and small cell carcinoma of the urinary bladder 5 years after transplantation. He underwent combined radical cystectomy with ileal conduit diversion and atypical hepatectomy. Pathology showed distal liver metastasis of bladder cancer in addition to primary hepatocellular carcinoma. He died of sepsis 5 months after operation. The other patient aged 65 years had prostate cancer and bone metastasis 7 years after transplantation. He underwent total orchiectomy and received antiandrogen therapy with bicalutamide 50 mg/day. He is still alive at the time of follow up.

The Kaplan–Meier survival curve of the 156 patients was shown in Fig. 1. The 1-, 5- and 10-year survival rates were 87.1, 70.6 and 61.7%. Causes of death were surgical bleeding in seven patients, acute allograft failure in two patients, infection in 21 patients, acute rejection in 11 patients, transplant coronary artery disease in seven patients, arrhythmia in two patients, multiple organ failure in three patients, and miscellaneous in seven patients.

For 132 patients who survived >1 year after heart transplantation, the cumulative incidence of renal dysfunction with serum creatinine of $\geqslant$2.0 mg/dl after transplantation was 23.0 ± 3.8%, 36.1 ± 4.3, 53.9 ± 4.9, and 57.3 ± 5.8% at 6-month, 1-year, 5-year and 10-year after transplantation.

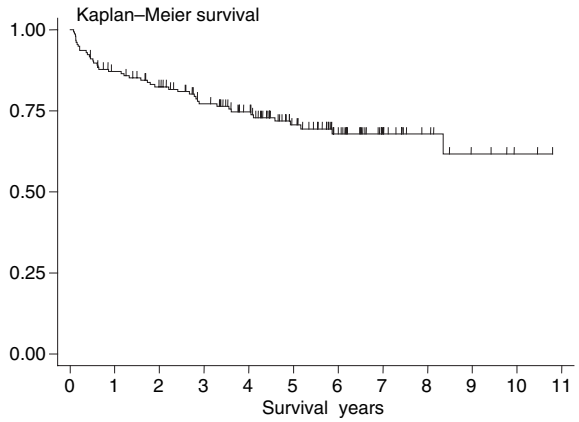

Figure 1 Actuarial survival curve by Kaplan–Meier method.

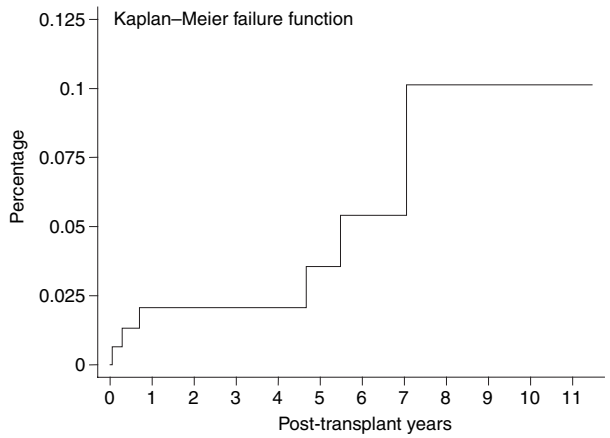

Figure 2 Cumulative incidence of neoplastic diseases after heart transplantation by Kaplan–Meier method.

As shown in Fig. 2, the cumulative incidence of neoplastic disease was 2.1% at 1 year, 3.6% at 5 years, and 10.1% at 10 years after transplantation.

Comparison with western series

The comparison of patient characteristics and incidence of post-transplant malignancy was listed on Table 1. Only those series published in recent 10 years was listed for comparison [9–15]. The incidence of all-cause post-transplant neoplastic diseases in western series ranged from 6.7 to 15.6%. The incidences of all-cause malignancy and solid malignancy were compared between our series and Pham *et al.*'s series [14] because both groups had similar age at transplantation and mean follow up duration. In our patients, there was a lower incidence of all-cause malignancy (3.8% vs. 15.2%, $P < 0.001$ by Fisher exact test), but there was no difference in the incidence of solid malignancy (1.2% vs. 3.3%, $P = 0.281$ by Fisher exact test).

The cumulative incidences of all-cause neoplastic diseases at 1 and 5 years after heart transplantation in our patients were compared with those of the International Society for the Heart and Lung Transplantation registry (http://www.ishlt.org). In our patients, there was a lower 5-year cumulative incidence of all-cause malignancy (3.6% vs. 18.2%, $P < 0.001$ by Fisher exact test), but there was no difference in 1-year cumulative incidence of all-cause malignancy (2.3% vs. 3.4%, $P = 0.804$ by Fisher exact test). In our patients, the incidence was especially low for Kaposi's sarcoma, skin cancers, and solid cancers (1.2% vs. 2.6–6.3%). Skin cancers and Kaposi's sarcomas that were common in western series were not present in our patients.

Types of solid malignancies after heart transplantation were listed in Table 2. Lung cancer was the main cause of solid cancers after transplantation in western series. However, none of our patients had lung cancer after transplantation.

Discussion

Compared with transplant coronary artery disease, i.e. the most common long-term complication of heart transplantation, post-transplant neoplastic disease is a relatively uncommon complication [1]. However, patients with

Table 1. Comparison of post-transplant neoplasms between Chinese and western patients.

Author	Hsu	Rinaldi	Curtil	Goldstein	Pham	Mihalov	Dresdale	Tenderich
Year	2005	2001	1997	1995	1995	1996	1993	2001
Country	Taiwan	Italy	France	USA	USA	USA	USA	Germany
Number	156	474	267	633	608	307	112	1080
Age (years)	45.8 ± 15.7	48.6 ± 12.1	47 ± 15	42.6 ± 18.3	43.1 ± 16.4	45.1	47.6	NA
Male (%)	83	85	83	78.3	81	81	83	NA
DCM (%)	54	47	49	52.9	36	NA	36	NA
Follow up	51.2 ± 33.0	71.1 ± 43	NA	NA	51.6 ± 27.6	33.4	41.5	NA
Incidence								
All-cause (%)	3.8	11.6	6.7	NA	15.2	15.6	8	10.38
PTLD (%)	2.6	2.3	1.1	NA	9.0	6.8	0	1.2
Skin/lip (%)	0	1.1	0	NA	2.6	6.5	3.8	3.0
Kaposi's sarcoma (%)	0	1.3	0	NA	NA	NA	0.9	NA
Solid cancer (%)	1.2	6.3	5.6	2.6	3.3	NA	3.6	NA
Annual incidence (year)								
1 (%)	2.1	NA	NA	NA	NA	4.5	NA	NA
5 (%)	3.6	NA	NA	NA	NA	22	NA	NA
10 (%)	10.1	24	NA	NA	NA	NA	NA	NA

DCM, dilated cardiomyopathy; PTLD, post-transplant lymphoproliferative disease; NA, not available.

Table 2. Case distribution of solid malignancy after transplantation between Chinese and western patients.

Author	Hsu	Rinaldi	Curtil	Goldstein	Pham	Dresdale	Tenderich
Number	3	31	16	17	20	4	93
Lung	0	12	11	7	10	0	22
Bowel	0	5	0	0	0	2	21
Stomach	0	2	1	0	0	0	
Liver	1	2	0	0	0	1	
Pancreas	0	2	0	0	0	0	
Head/neck	0	2	1	2	3	0	3
Biliary tract	0	1	0	0	1	0	
Urologic	2	2	2	5	2	1	35
Breast	0	1	0	0	1	0	
Gynecologic	0	1	0	1	2	0	6
Miscellaneous	0	1	0	0	1	0	6

post-transplant cancers usually were diagnosed in advanced diseases and recurrence was common because of the continued use of immunosuppression [14,16].

Penn and Starzl first reported the association of neoplastic diseases with post-transplant immunosuppression in 1972 [17]. In 1978, before the introduction of cyclosporine, Krikorian *et al.* [18] reported a cumulative incidence of neoplastic diseases 2.7 ± 1.9 and 25.6 ± 11.0% at 1 and 5 years after heart transplantation. This figure seemed not changed recently. Data from the multicenter registry of the International Society of Heart and Lung Transplantation in 2003 reported a cumulative incidence of 3.4 and 18.2% at 1 and 5 years after heart transplantation. In our patients, there was a lower cumulative incidence of neoplastic disease 2.1% at 1 year, 3.6% at 5 years, and 10.1% at 10 years after transplantation.

The incidence of all-cause post-transplant neoplastic diseases was 3.8% in our patients. This frequency is much lower compared with the western series of Dresdale *et al.* [15] and Pham *et al.* [14], who reported cancer incidences of 8.2 and 15.2%, respectively. Mihalov *et al.* [12] even observed 48 malignant neoplasms in 307 patients (15.6%) with a mean follow up duration of 33.4 months. Multicenter database from the Cincinnati Transplant Tumor Registry [5] estimated a frequency of all-cause post-transplant neoplastic diseases in heart recipients of around 6%. Compared with these western series, the incidence of all-cause post-transplant neoplastic disease was low in Chinese heart allograft recipients.

The incidence of neoplastic diseases was related to the use of immunosuppression, recipient age at transplantation and length of follow up after transplantation [5]. Couetil *et al.* [4], Oechslin *et al.* [19], and Fortina *et al.* [20] reported there was no relationship between type of immunosuppression and tumor development. It was considered that cancer was a complication of intense immunosuppression itself. The exact role of each specific agent has not been resolved. In our study, 144 of 156 patients had induction therapy with antithymocyte globulins and all the patients had triple maintenance immunosuppression. There was also no difference in age, gender, etiology of heart disease and follow up duration between our patients and most of the western series (Table 1). It was unlikely that the low incidence of post-transplant malignancy in our patients resulted from the differences of the risk factors that we already knew.

Penn [5] reported that the predominant tumors in heart allograft recipients are skin cancers, lymphomas, and Kaposi's sarcomas. Skin cancers account for nearly 28% of malignancies, whereas lymphoma is one of the most common malignancies after heart transplantation, accounting for 42% of all cases. Solid organ tumors have been reported less frequently, and lung cancer is the predominant one. Hosenpud *et al.* [1] reported that skin cancers and lymphomas accounted for 37.3 and 29.0% of all malignancies at 1 year, and 52.1 and 12.5% of all malignancies at 5 years after heart transplantation. It was quite possible that type of malignancies contributed to the low incidence of malignancies after transplantation in our patients.

The incidence of skin cancers increases with time after transplantation. Transplant recipients have a greater tendency for development of squamous cell carcinoma when compared with basal cell carcinoma [16]. Their frequency varied with the amount of sun exposure [20,21] and increased in certain geographical regions [22]. A surprisingly high incidence of skin cancers was reported in Australia [16], Italy [20–22], and Spain [23]. Skin cancers are not common in Chinese population with yellow skin color, in contrast to their common occurrence in Caucasian patients [24]. For general population, pigmentary traits such as red hair, fair skin, lack of tanning ability and propensity to freckle have been identified as genetic risk factors for skin cancers when combined with the environmental risk factor of high ultraviolet light exposure [25]. It has also been reported that poor tanning ability rather than the amount of sun exposure is associated with the development of skin cancers in kidney transplant recipients and warts appearing after the transplantation indicate increased risk [26].

The link between immunosuppression and Kaposi's sarcoma was substantiated by the reports of Penn [5]. Kaposi's sarcoma occurred most often in transplant recipients who were Arabic, Jewish, black, or of Mediterranean ancestry [5]. Lanza *et al.* [27] reported that Kaposi's sarcoma accounted for 30% of all malignancies in South Africa. However, no Kaposi's sarcoma was diagnosed in a French series after heart transplantation [11]. Similarly, no Kaposi's sarcoma was diagnosed in our heart trans-

plant recipients. It was reported that cases of classic Kaposi's sarcoma have been distributed most in Europe, Mediterranean countries, and the Americas. Geographic location, age, gender, and ethnicity might influence the occurrence of Kaposi's sarcoma [28]. Chinese people have the lowest incidence rate of classic Kaposi's sarcoma among all countries [28]. The age-standardized rates of melanoma skin cancers were 2.4 in the world (data obtained from http://www.dep.iarc.fr) and 0.14–0.32 in Taiwan [29]. The age-standardized rate of nonmelanoma skin cancers was 0.39–0.93 in Taiwan [29]. The low incidence of post-transplant neoplastic disease could result from a relative paucity of Kaposi's sarcoma and skin cancers in Chinese population. In addition, the appearance of Kaposi's sarcoma correlates with the human herpesvirus 8 replication [30,31]. It was assumed that the ethnic factor, skin type and possible virus factor contributed to the low incidence of skin cancers and Kaposi's sarcoma after transplantation in our heart allograft recipients.

Among the solid tumors after heart transplantation, lung cancer was particularly common, accounting for up to 50% of the solid malignancies [5]. Those neoplasms that are frequently observed in the general population (cancers of the lung, breast, prostate, liver, and colon) showed no increase or even a decrease after transplantation [5]. The distribution of solid tumors after heart transplantation was quite different between Chinese and western people (Table 2). In general population, southeast Asians had higher risks of cancers of the nasopharynx, stomach, liver, gallbladder, and cervix. Southeast Asians had lower risks of cancer of the oral cavity, colon, rectum, larynx, lung, bladder, nervous system, breast, and prostate [32]. The five most common cancers in the general population around the world were lung cancers, stomach cancers, prostate cancers, colorectal cancers, and liver cancers (data obtained from http://www.dep.iarc.fr). And the five most common cancers in Taiwan were liver cancers, lung cancers, stomach cancers, colorectal cancers, and nasopharyngeal cancers. The age-standardized rates of liver cancers were 14.97 in the world (data obtained from http://www.dep.iarc.fr) and 31.6–34.4 in Taiwan [29].

Because most of transplants have been performed in recipients of renal allografts and many of them have been followed for a long period, it was advisable to have a look of Chinese renal allograft recipients. Hepatitis virus infection was related to the development of hepatocellular carcinoma after transplantation [33]. Taiwan is an endemic area of hepatitis B virus infection. Huo *et al.* [34] and Lee *et al.* [35] demonstrated a high incidence of hepatocellular carcinoma in Chinese renal recipients with hepatitis B virus infection. Urologic malignancies were also prevalent in Taiwan [36]. In our current study, one patient had prostate cancer and one patient had double cancers with hepatocellular carcinoma and bladder cancer. Hepatocellular carcinoma and urologic malignancies were the dominant cause of malignancy in Chinese heart allograft recipients.

The major limitation of this study was relatively small case number and short follow up. The incidence might be decreased in a small cohort [15] and a higher incidence in larger studies [12,14]. It is important to continue this study and see if these preliminary observations still hold up.

In conclusion, the incidence of post-transplant neoplastic diseases was low in Chinese heart allograft recipients. It could result from a low case number in our study population or from a relative paucity of Kaposi's sarcoma and skin cancers, in Chinese population.

References

1. Hosenpud JD, Bennett LE, Keck BM, Boucek MM, Novick RJ. The Registry of the International Society for Heart and Lung Transplantation: 18th Official Report-2001. *J Heart Lung Transplant* 2001; **20**: 805.
2. Fraund S, Pethig K, Franke U, *et al.* Ten year survival after heart transplantation: palliative procedure or successful long term treatment? *Heart* 1999; **82**: 47.
3. McGiffin DC, Kirklin JK, Naftel DC, Bourge RC. Competing outcomes after heart transplantation: a comparison of eras and outcomes. *J Heart Lung Transplant* 1997; **16**: 190.
4. Couetil JP, McGoldrick JP, Wallwork J, English TA. Malignant tumors after heart transplantation. *J Heart Transplant* 1990; **9**: 622.
5. Penn I. Incidence and treatment of neoplasia after transplantation. *J Heart Lung Transplant* 1993; **12** (6 Pt 2): S328.
6. Chu SH, Hsu RB, Wang SS. Heart transplantation in Asia. *Ann Thorac Cardiovasc Surg* 1999; **5**: 361.
7. Hsu RB, Chu SH, Wang SS, *et al.* Low incidence of transplant coronary artery disease in Chinese heart recipients. *J Am Coll Cardiol* 1999; **33**: 1573.
8. Ko WJ, Chou NK, Chen YS, *et al.* Clinical trial of FK506 in heart transplant patients in Taiwan: report of 7 cases with immunosuppression switch from cyclosporine to FK506. *Transplant Proc* 1998; **30**: 3339.
9. Tenderich G, Deyerling W, Schulz U, *et al.* Malignant neoplastic disorders following long-term immunosuppression after orthotopic heart transplantation. *Transplant Proc* 2001; **33**: 3653.
10. Rinaldi M, Pellegrini C, D'Armini AM, *et al.* Neoplastic disease after heart transplantation: single center experience. *Eur J Cardiothorac Surg* 2001; **19**: 696.
11. Curtil A, Robin J, Tronc F, Ninet J, Boissonnat P, Champsaur G. Malignant neoplasms following cardiac transplantation. *Eur J Cardiothorac Surg* 1997; **12**: 101.

12. Mihalov ML, Gattuso P, Abraham K, Holmes EW, Reddy V. Incidence of post-transplant malignancy among 674 solid-organ-transplant recipients at a single center. *Clin Transplant* 1996; **10**: 248.
13. Goldstein DJ, Williams DL, Oz MC, Weinberg AD, Rose EA, Michler RE. De novo solid malignancies after cardiac transplantation. *Ann Thorac Surg* 1995; **60**: 1783.
14. Pham SM, Kormos RL, Landreneau RJ, *et al.* Solid tumors after heart transplantation: lethality of lung cancer. *Ann Thorac Surg* 1995; **60**: 1623.
15. Dresdale AR, Lutz S, Drost C, *et al.* Prospective evaluation of malignant neoplasms in cardiac transplant recipients uniformly treated with prophylactic antilymphocyte globulin. *J Thorac Cardiovasc Surg* 1993; **106**: 1202.
16. Veness MJ, Quinn DI, Ong CS, *et al.* Aggressive cutaneous malignancies following cardiothoracic transplantation: the Australian experience. *Cancer* 1999; **85**: 1758.
17. Penn I, Starzl TE. A summary of the status of de novo cancer in transplant recipients. *Transplant Proc* 1972; **4**: 719.
18. Krikorian JG, Anderson JL, Bieber CP, Penn I, Stinson EB. Malignant neoplasms following cardiac transplantation. *JAMA* 1978; **240**: 639.
19. Oechslin E, Kiowski W, Schneider J, Follath F, Turina M, Gallino A. Pretransplant malignancy in candidates and post-transplant malignancy in recipients of cardiac transplantation. *Ann Oncol* 1996; **7**: 1059.
20. Fortina AB, Caforio AL, Piaserico S, *et al.* Skin cancer in heart transplant recipients: frequency and risk factor analysis. *J Heart Lung Transplant* 2000; **19**: 249.
21. Caforio AL, Fortina AB, Piaserico S, *et al.* Skin cancer in heart transplant recipients: risk factor analysis and relevance of immunosuppressive therapy. *Circulation* 2000; **102**(19 Suppl. 3): III222.
22. Naldi L, Fortina AB, Lovati S, *et al.* Risk of nonmelanoma skin cancer in Italian organ transplant recipients. A registry-based study. *Transplantation* 2000; **70**: 1479.
23. Espana A, Redondo P, Fernandez AL, *et al.* Skin cancer in heart transplant recipients. *J Am Acad Dermatol* 1995; **32**: 458.
24. McDonald RR, Georgouras KE. Skin disorders in Indo-Chinese immigrants. *Med J Aust* 1992; **156**: 847.
25. Sturm RA. Skin colour and skin cancer – MC1R, the genetic link. *Melanoma Res* 2002; **12**: 405.
26. Lindelof B, Granath F, Dal H, Brandberg Y, Adami J, Ullen H. Sun habits in kidney transplant recipients with skin cancer: a case-control study of possible causative factors. *Acta Derm Venereol* 2003; **83**: 189.
27. Lanza RP, Cooper DK, Cassidy MJ, Barnard CN. Malignant neoplasms occurring after cardiac transplantation. *JAMA* 1983; **249**: 1746.
28. Iscovich J, Boffetta P, Franceschi S, Azizi E, Sarid R. Classical Kaposi's sarcoma: epidemiology and risk factors. *Cancer* 2000; **88**: 500.
29. Yang CY, Hsieh YL. The relationship between population density and cancer mortality in Taiwan. *Jpn J Cancer Res* 1998; **89**: 355.
30. Mendez JC, Procop GW, Espy MJ, Smith TF, McGregor CG, Paya CV. Relationship of HHV8 replication and Kaposi's sarcoma after solid organ transplantation. *Transplantation* 1999; **67**: 1200.
31. Briz M, Alonso-Pulpon L, Crespo-Leiro MG *et al.* Detection of herpesvirus-like sequences in Kaposi's sarcoma from heart transplant recipients. *J Heart Lung Transplant* 1998; **17**: 288.
32. Bouchardy C, Parkin DM, Khlat M. Cancer mortality among Chinese and South-East Asian migrants in France. *Cancer* 1994; **58**: 638.
33. Fornairon S, Pol S, Legendre C, *et al.* The long-term virologic and pathologic impact of renal transplantation on chronic hepatitis B virus infection. *Transplantation* 1996; **62**: 297.
34. Huo TI, Yang WC, Wu JC, *et al.* Kidney transplantation in patients with chronic hepatitis B virus infection: is the prognosis worse? *Dig Dis Sci* 2001; **46**: 469.
35. Lee WC, Shu KH, Cheng CH, Wu MJ, Chen CH, Lian JC. Long-term impact of hepatitis B, C virus infection on renal transplantation. *Am J Nephrol* 2001; **21**: 300.
36. Yang MH, Chen KK, Yen CC, *et al.* Unusually high incidence of upper urinary tract urothelial carcinoma in Taiwan. *Urology* 2002; **59**: 681.