

Donor cancer

Date written: July 2004

Final submission: June 2005

GUIDELINES

No recommendations possible based on Level I or II evidence

SUGGESTIONS FOR CLINICAL CARE

(Suggestions are based on Level III and IV evidence)

- **Cancer is transmissible through organ donation and the risk of transmission, although in the order of 0.015%, cannot be fully eliminated.**
- **Deceased and living donors under the age of 50 years should have prior and current cancer excluded by clinical history and clinical examination. Female donors of reproductive age with death due to intra-cerebral haemorrhage should be screened for metastatic choriocarcinoma by testing serum b-HCG concentration. Skin, breast and large colon cancer are the commonest cancers in the general population under 50 years of age and should be specifically considered.**
- **Deceased and living donors over the age of 50 years should have prior and current cancer excluded by clinical history and clinical examination. Investigations should include Prostate Specific Antigen testing in males. Cancer of the prostate in males, breast in females, large bowel, lung, melanoma, stomach, pancreas, kidney and bladder, lymphoma and leukaemias are the commonest cancers in the general population aged over 50 years, and should be specifically considered.**
- **A donor will be excluded if they are confirmed or suspected to have, or have had a diagnosis of cancer which may be transmitted to the recipient. Donors and organs should be examined thoroughly at the time of retrieval and frozen sections taken of any suspect lesions. A formal post-mortem is desirable in all cases.**
- **Exceptions to the above may be made in the case of:**
 - **non-metastatic, non-melanoma skin cancer**
 - **carcinoma in situ of the cervix**
 - **other cancers known to have been fully eradicated from the donor.**

- **Donors with primary intracerebral tumours may be acceptable in the absence of neurosurgical intervention. Specific consent should be sought from the recipient of organs from such donors.**

Background

Cancer is transmissible through deceased and living donor organ, cell and tissue transplantation. Once transmitted, the immunosuppressed state of the recipient permits rapid expansion and spread of cancer. Death of the renal allograft recipient from transmitted cancer is reported to occur in approximately 50% of patients (Kauffman et al 2002a). The allograft response can be used to contribute to treatment through rejection of the cancer, especially those responsive to immunotherapy such as melanoma.

Reports of transmission of cancer through clinical renal transplantation are all observational. It has been widely accepted that donors with known cancers should be excluded from donation, with the exception of localised squamous cell and basal cell carcinomas of the skin (EBPG 2000, guideline II.1), and some neurological malignancies which are thought not to metastasise to extra-neural organs (Buell 2004; Kauffman et al 2002c). There is thus restricted data on which to apply an evidence-based protocol.

The objectives of this guideline are:

- to provide a practical and applicable protocol, based on the evidence that is available, for the selection of deceased kidney donors, and
- to provide a practical and applicable protocol, based on the evidence available for the assessment of living donors, prior to kidney donation.

Search strategy

Databases searched: MeSH terms and text words for kidney transplantation and cadaveric organs were combined with MeSH terms and text words for diabetes, hypertension, viruses, bacterial infections, non-heart beating, marginal donor, paediatric donor, aged donor, and donor with prior cancer. These were then combined with the Cochrane highly sensitive search strategy for randomised controlled trials and search filters for identifying prognosis and aetiology studies. The search was carried out in Medline (1966 – November Week 2 2003). The Cochrane Renal Group Trials Register was also searched for trials not indexed in Medline. A further search was carried out in Medline (January 2004) using the text words donor malignancy, renal transplantation and liver transplantation.

Date of searches: 12 December 2003; January 2004.

What is the evidence?

The sources of data (Level III or IV) that contribute to the evaluation of the risk of donor cancer are:

- the incidence of cancer in either the general or potential donor populations by age, sex and type of cancer
- the reported cases of cancer transmitted through kidney transplantation, and
- the reported risks of transmitting cancer from donors known to have cancer or a prior history of cancer.

Summary of the evidence

Incidence of cancer in the general population by age, sex and type of cancer

The incidence of cancer in the general Australian population is recorded through the State Cancer Registries. Figures 1 and 2 (Appendix) demonstrate the rates of different cancers in males and females in New South Wales by age cohort. If a background risk of 20 cases per year in 100,000 (or 1 in 5,000) individuals is selected, then the cancers that reach that level under the age of 50 years are: breast, melanoma and large bowel (Figure 1).

Using the same background risk rate of 20 in 100,000 over the age of 50 years, it can be seen in Figure 2 that many cancers occur with this frequency in the general population. Those cancers with the highest risk are: prostate in males, breast in females, large bowel, lung, melanoma, stomach, pancreas, kidney and bladder, lymphoma and leukaemias.

A report from the US found occult renal cell carcinoma in 5 (0.9%) deceased renal donors aged 46–60 years, 4 of which were found by palpation by the transplant surgeon (Carver et al 1999). A deceased organ donor screening protocol in Italy found 5 occult prostate cancers, 1 renal oncocytoma, and 2 occult thyroid carcinomas in 271 potential deceased donors with a median age of 54 years (range: 2–83; Fiorentino et al 2003).

These data imply that in potential donors under the age of 50 years, in addition to a standard clinical history, specific clinical examination should be undertaken of the breasts and skin, and screening of the large bowel undertaken at laparotomy for deceased donors. All living donors should undergo screening consistent with current National Health & Medical Research Council recommendations (EBPG 2000, guideline II.3).

These data imply that in potential donors over the age of 50 years, in addition to a standard clinical history and physical examination, specific clinical examination should be undertaken of the breasts, skin and lymph nodes. In deceased donors, rectal examination of males, as well as examination of the large bowel, stomach, pancreas, abdominal lymph nodes and liver at the time of laparotomy should be undertaken. In male living donors, a rectal examination and in both sexes, occult blood testing of the stool would be recommended. In female living donors, breast mammography or ultrasound would be recommended. Investigations should include a Prostate Specific Antigen test in male donors over 50 years of age.

Reported cases of cancer transmitted through kidney transplantation

The largest report of donor-related malignancies comes from the United Network for Organ Sharing (UNOS) (Kauffman et al 2002a). Nine of 34,933 deceased donors were known to have transmitted cancer (1 in 3,881 donors). The transmitted tumours in renal allograft recipients included melanoma, lung, neuroendocrine small cell, renal oncocytoma, and papillary with unknown primary. Two living donors were known to have transmitted breast and lung cancer, respectively.

Global reporting to the Cincinatti Transplant Tumor Registry, now renamed the Israel Penn International Transplant Tumor Registry (IPITTR) has recorded 69 donors with non-central nervous system (CNS) and 8 with CNS malignancies who transmitted the malignancy to one or more recipients. The non-CNS tumours were: renal cell carcinoma, melanoma, choriocarcinoma, lung, colon, breast, prostate and Kaposi's sarcoma. The transmitted CNS malignancies were from donors with medulloblastoma, malignant meningioma, CNS lymphoma and grade III and IV astrocytomas (Kauffman et al 2002b, Buell 2004).

In Australia, the known transmitted cancers from donors to recipients are of melanoma (1 donor to 2 recipients, no deaths) and renal cell carcinoma (2 recipients from 2 donors, one death). The overall rate of cancer transmission in kidney transplants reported to the UNOS database between 1994 and 2001 was 12 in 59,694 or 0.015% (Feng et al 2002; Feng et al 2003).

The reported risks of transmitting cancer from donors known to have cancer or a prior history of cancer are high. The IPITTR has recorded transplantation of 237 cadaver organs and 33 living donor organs from 163 deceased and 33 living donors. Transmission of the tumour occurred in 117 recipients, suggesting an overall transmission rate of 43%. The reporting bias of the IPITTR would suggest that this is the maximum transmission rate that could be expected from donors with known cancer (Kauffman et al 2002b).

CNS malignancies

UNOS has reported the absence of transmission of CNS tumors from 397 donors to 1220 organ transplant recipients (574 kidneys) between 1992 and 1999. (Kauffman et al 2002c). Chui et al 1999 reported the Australian experience of 154 recipients from 46 organ donors with intracerebral malignancy without known transmission. The IPITTR reported a transmission rate from 22 donors with low grade (I and II) astrocytomas of 0%, but 25% from grade III, and 40% from grade IV astrocytomas (Buell 2004); ventriculoperitoneal shunt or craniotomy carried a 46% transmission risk (Buell 2004).

Non-CNS malignancies

The UNOS Transplant Tumor Registry (Kauffman et al 2000) has reported organ donation in 650 recipients over a two-year period, of organs from 257 donors with a prior history of cancer, 60% of them more than 5 years prior to donation. In total, 188 recipients had donors with a prior history of CNS tumors, 207 with skin, 154 with genitourinary, 38 breast and 63 with miscellaneous cancers. There were no transmitted cancers. In updates of the UNOS data (Feng et al 2003; Feng et al 2002), renal cell carcinoma was reported to have a 61% transmission rate,

melanoma 77%, choriocarcinoma 93%, Kaposi's sarcoma 67%, lung 41%, breast 29%, prostate 29% and colon 19%.

Donor-derived malignancies

A number of tumours have been identified that are derived from donor cells, but which were not present at the time of transplantation. A proportion of post-transplant lymphoproliferative diseases are derived from Epstein-Barr virus negative donors, but there is no evidence that these tumors were present at the time of transplantation. A single case of donor pancreas adenocarcinoma has been reported to have occurred 3.5 years after transplantation, perhaps developing in the pancreas after transplantation rather than being occult at the time of the transplant (Kauffman et al 2002a). Deceased and living donor protocols cannot take into consideration donor-derived malignancies.

What do the other guidelines say?

Kidney Disease Outcomes Quality Initiative: No recommendation.

British Renal Association: No recommendation.

Canadian Society of Nephrology: No recommendation.

European Best Practice Guidelines: Exhaustive list of cancers transmitted and potentially transmissible by transplantation plus authors' opinions. (Level C evidence) EBPG 2000, Section II: Evaluation and selection of donors; pp. 39–51.

International Guidelines:

United Network for Organ Sharing: Transmission of donor malignancies is rare with 18 cases from 34,933 deceased donors, and 3 cases from living donors being reported to UNOS from 1994–2001. Donors with past histories of certain types of cancers may be considered as donors, including certain types of primary CNS tumours. Tumours that pose a high transmission risk include choriocarcinoma, melanoma, lymphoma and carcinoma of the lung, colon, breast, kidney and thyroid. High-risk donors include those who have had glioblastoma multiforme, high-grade astrocytomas, medulloblastomas, and any brain tumour donor who has undergone ventriculoperitoneal shunting. Available at: www.unos.org/

The British Transplantation Society: Standards for Solid Organ Transplantation in the United Kingdom (2003).

Chapter 11.0, Appendices, page 50. Paragraph 2.2. Care must be taken to minimise the accidental transmission of malignant disease from donor to recipient but there is little reliable data from which to accurately predict the risk of tumour transmission. Tumours with a propensity to late recurrence such as breast cancer, malignant melanoma and sarcomas are an absolute contraindication to organ donation. Available at: www.bts.org.uk/

Implementation and audit

ANZDATA and ANZOD need to produce maintain an Annual Report of the outcome of all organ donations from donors with a prior history of cancer.

Suggestions for future research

Monitor the annual rate of refusal of both living and deceased donors on the basis of cancer.

References

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Appendices

Figure 1. Background rate of cancer in the NSW population by sex and age cohort under the age of 50 years. Each line represents a single type of cancer in one sex. Source: NSW Cancer Council Registry.

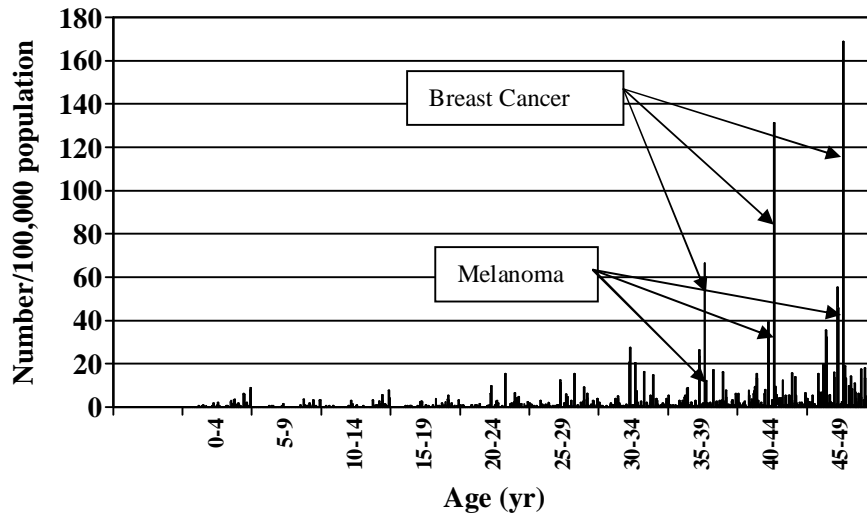


Figure 2. Background rate of cancer in the NSW population by sex and age cohort over the age of 50 years. Each line represents a single type of cancer in either males or females. Source: NSW Cancer Council Registry.

