

The prognosis of noncutaneous, nonlymphomatous malignancy after heart transplantation: data from the spanish post-heart transplant tumour registry

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Abstract

Introduction. Malignancy is a major complication in the management of solid organ transplant patients. Skin cancers show a better prognosis than other neoplasms, but not all others are equal: Ideally, patient management must take into account the natural history of each type of cancer in relation to the transplanted organs. We sought to determine the prognosis of various groups of noncutaneous nonlymphomatous (NCNL) cancers after heart transplantation (HT).

Methods. We retrospectively analyzed the records of the Spanish Post-Heart-Transplant Tumour Registry, which collects data on posttransplant tumors in all patients who have undergone HT in Spain since 1984. Data were included in the study up to December 2008. We considered only the first NCNL post-HT tumors.

Results. Of 4359 patients, 375 developed an NCNL cancer. The most frequent were cancers of the lung ($n = 97$; 25.9%); gastrointestinal tract ($n = 52$; 13.9%); prostate gland ($n = 47$; 12.5%; 14.0% of men), bladder ($n = 32$; 8.5%), liver ($n = 14$; 3.7%), and pharynx ($n = 14$; 3.7%), as well as Kaposi's sarcoma ($n = 11$; 2.9%). The corresponding Kaplan-Meier survival curves differed significantly ($P < .0001$; log-rank test), with respective survival rates of 47%, 72%, 91%, 73%, 36%, 64%, and 73% at 1 year versus 26%, 62%, 89%, 56%, 21%, 64%, and 73% at 2 years; and 15%, 51%, 77%, 42%, 21%, 64%, and 52% at 5 years post-diagnosis, respectively.

Conclusion. Mortality among HT patients with post-HT NCNL solid organ cancers was highest for cancers of the liver or lung (79%–85% at 5 years), and lowest for prostate cancer (23%).

Malignancy is one of the main causes of death after heart transplantation (HT).¹ The prognosis is better for skin cancer than for lymphomas or noncutaneous solid tumors,² but little is known of differences in life expectancy among patients with noncutaneous nonlymphomatous (NCNL) tumors. Ideally, patient management should take into account the natural history of each type of cancer, which may differ from its natural history among nontransplant patients. Most studies of post-HT malignancy have concerned single centers and/or short follow-up periods.^{3 and 4} In this study, we have determined survival rates among patients with various types of NCNL cancer using the records of the Spanish Post-Heart-Transplant Tumour Registry (SPHTTR), which collects data on posttransplant tumors in all patients who have undergone HT in Spain since 1984.²

Methods

Patients

Candidates for inclusion in the study were the 5301 patients who, according to the SPHTTR, underwent HT between 1984 and December 2008 when aged ≥ 15 years. Of these 5301, we excluded 942 who died within 3 months of HT. Of the remaining 4359, 729 (16.7%) developed 997 tumors before January 2009: 517 skin cancers (51.8%), 81 lymphomas (8.1%), and 399 NCNL tumors (40.1%). This study concerned the 375 first post-HT tumors that were NCNL. The study protocol was approved by the clinical research ethics committee of each collaborating center.

Statistical Analysis

The variables were the location and histopathologic type of tumor, the date of diagnosis, the date of death, and the survival status at the end of the study period (December 31, 2008). Kaplan-Meier curves for survival after diagnosis were constructed using data for 368/375 patients with first NCNL post-HT tumors, 7 of which were discovered post mortem. The significance of differences among the Kaplan-Meier curves of the various types of NCNL tumors was estimated using a log-rank test. The criterion for statistical significance was $P < .05$.

Results

The 375 patients with first post-HT tumors that were NCNL constituted 51.4% of the 729 patients developing tumors; 8.6% of the 4359 patients at risk. Some 90.1% of the 375 were men. The mean value \pm standard deviation (SD) of age at HT was 54.6 ± 9.3 years, with 54 (14.4%) subjects <45 years; 110 (29.3%), aged 45–54 years; 166 (44.3%), aged 55–64 years; and 45 (12.0%), aged ≥ 65 years. The mean \pm SD follow-up time after tumor diagnosis was 2.6 ± 3.1 years.

The 7 most common types of first NCNL tumors were, in descending order, cancers of the lung ($n = 97$; 25.9%), gastrointestinal tract ($n = 52$; 13.9%), prostate gland ($n = 47$; 12.5%; with 14.0% of men), bladder ($n = 32$; 8.5%), liver ($n = 14$; 3.7%), and pharynx ($n = 14$; 3.7%), as well as Kaposi's sarcoma ($n = 11$; 2.9%). Figure 1 shows the corresponding Kaplan-Meier postdiagnosis survival curves, which differed significantly ($P < .0001$). The actuarial 1-year survival rates were 47% for lung cancer, 72% for gastrointestinal cancer, 91% for prostate cancer, 73% for bladder cancer, 36% for liver cancer, 64% for pharynx cancer, and 73% for Kaposi's sarcoma. The corresponding 2-year rates were 26%, 62%, 89%, 56%, 21%, 64%, and 73%; and the 5-year rates were 15%, 51%, 77%, 42%, 21%, 64%, and 52%, respectively.

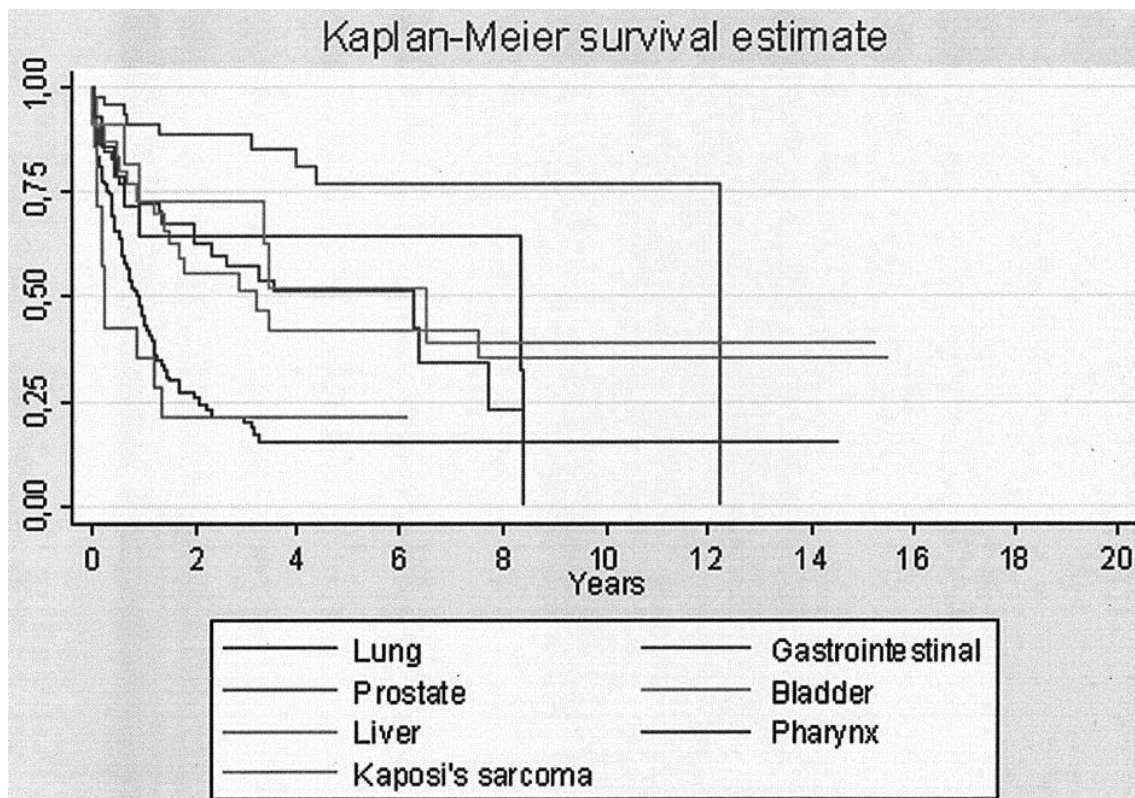


Fig 1. Kaplan-Meier survival curves for the 7 most common types of noncutaneous nonlymphomatous tumor among Spanish heart transplant patients.

Among the 37 women with first tumors of a NCNL type, there were 7 cervical cancers (19%), 5 breast cancers (14%), 2 endometrial cancers (5%), 2 ovarian cancers (5%), and 1 cancer of the vulva (3%), but survival statistics for these types were not calculated because of the small numbers of cases.

Discussion

Overall, the 5-year survival rate among Spanish HT patients developing NCNL tumors was about 32%,² confirming differences among neoplasms, as are known among the general population. Five-year survival rates, for example, in decreasing order were prostate (77%) > pharyngeal (64%) > Kaposi's (52%) \approx gastrointestinal (51%) > bladder (42%) > liver (21%) > lung (15%) cancer. As far as we know, evidence for differences of this kind have only previously come from small, single-center studies, such as that of El-Hamamsy et al.⁴ These differences are important, because they may influence the therapeutic approach to various types of cancer. For a condition with a relatively optimistic prognosis such as prostate gland cancer, it may be hypothesized that the oncological benefits of a severe reduction in immunosuppression might be outweighed by the accompanying increase in the risk of rejection. It remains to be seen whether such dilemmas will be irrelevant by the advent of mammalian target of rapamycin inhibitors, the use of which, together with partial or total withdrawal of calcineurin inhibitors, has been reported to slow the progression of cancer in patients with kidney grafts.^{5, 6 and 7}

Although classification differences and other issues prevent direct comparisons of percentages, the survival rates (prostate > pharyngeal > Kaposi's \approx gastrointestinal > bladder > liver > lung cancer) may be compared, for example, with those observed 5-year rates for 55–64 and 65–74 year-olds in the EURO CARE-4 study of cancer in the European population in general (7): prostate > bladder > gastrointestinal tract \approx pharyngeal > lung > liver cancer. The worse relative prognoses of lung cancer and cancer of the bladder invite further research.

The main weakness of this study was that, because of the limitations of the SPHTTR, it failed to distinguish between deaths from cancer and those from other causes. It also naturally shares the drawbacks common to all registry-based studies, which derive from the heterogeneity of the treatments, which were decided by each patient's medical team at their own discretion. Its strength is its size: 4359 patients at risk including, 375 who developed NCNL cancers.

In conclusion, the mortality among HT patients with post-HT NCNL solid organ cancers varied widely among types of cancer. It was greatest for cancers of the liver or lung (79%–85% at 5 years), and lowest for prostate cancer (23%).

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Appendix

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