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Malignancy after Heart Transplantation: Difference in incidence and prognosis between genders. Data from the Spanish post-Heart Transplant Tumor Registry

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On behalf of The staff of all the Spanish heart transplant centers.

Background: Malignancy is one of the leading causes of mortality in the long term follow up after heart transplantation (HT). Male sex has been described as an independent risk factor for developing cancer in this group of patients. However, the real incidence of all type of neoplasm and its impact prognosis in mortality in both group of sex remains unknown.

Purpose: The aim of this study was to assess the incidence of malignancy and the disparity in its relative weight as a cause of death between genders.

Methods: Observational longitudinal study of heart transplant patients from the Spanish post-HT Tumor registry (SPHTTR) who underwent HT in this country from 1984 to 2017. Re-transplant, combined transplant patients and those with survival less than 3 months since HT were excluded. Incidence and mortality rates per 1000 person-year for all tumors, skin cancer (including melanoma), lymphoma and non-skin solid malignancy (NSSM) were calculated for both groups of sex. The main end-point of the study was death for any causes related to cancer following HT. Survival curves since first diagnosis of neoplasia were constructed using Kaplan

Meier estimates and comparisons among genders were performed using long-rank test.

Results: A total of 5865 patients (81.6% male, 18.4% female) were included in the analysis. Incidence and mortality rates in both genders are summarized in Table 1. Total cumulative incidence rate of all tumors, non-skin solid malignancy and lung cancer were higher in men patients (All tumors: 44.8 vs 25.7 per 1000 person-year; female to male RR 0.68, 95% CI 0.60–0.78, $p < 0.001$). Mortality rates were also higher in male patients for all types of tumors (RR 0.76, CI 95% 0.62–0.94, $p = 0.01$) and for NSSM (RR 0.60, 95% CI 0.44–0.80, $p = 0.001$) albeit not for cutaneous neoplasia or lymphoma. Survival curves are shown in figure 1 and display significant differences among both genders ($p = 0.0037$).

Conclusions: Incidence of malignancy post-HT is higher in men than in women specially for skin cancer and de novo solid tumors. The relative weight of cancer as a cause of death was also higher in men than in women, furthermore, this could have impact prognosis in HT survivors.

Table 1

Type of tumor	Female		Male		Female to Male Incidence RR		Female to male mortality RR	
	Incidence rate*	Mortality rate*	Incidence rate*	Mortality rate*	RR	p-value	RR	p-value
All tumors	25.7 (22.8–29.0)	94.0 (77.3–114.3)	44.8 (42.9–46.8)	129.6 (120.9–138.9)	0.68 (0.60–0.78)	<0.001	0.76 (0.62–0.94)	0.01
Skin cancer	12.6 (10.6–15.0)	63.2 (45.4–88.0)	24.4 (23.0–25.9)	70.4 (62.6–79.1)	0.62 (0.52–0.74)	<0.001	0.88 (0.62–1.25)	0.481
Lymphoma	2.0 (1.3–3.0)	137.8 (80.0–237.3)	2.5 (2.1–3.0)	237.5 (187.9–300.2)	0.84 (0.52–1.36)	0.483	0.58 (0.32–1.06)	0.076
NSSM	11.1 (9.3–13.4)	125.0 (95.2–164.0)	17.5 (16.4–18.8)	234.7 (214.0–257.5)	0.75 (0.62–0.92)	<0.001	0.60 (0.44–0.80)	0.001

NSSM: Non-skin solid malignancy. *Per 1000 person-year.

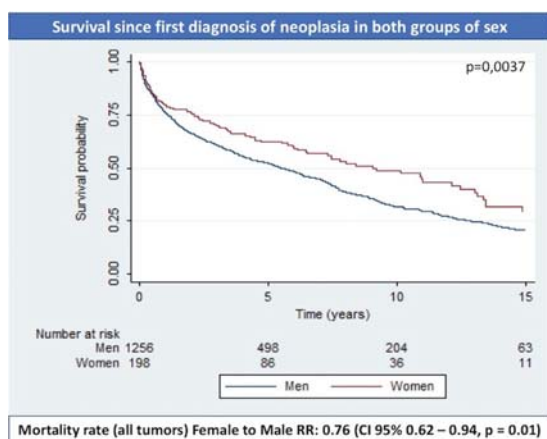


Figure 1