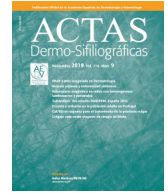




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Actas Dermo-Sifiliográficas

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Research Letter

Oncologic Safety in Solid Organ Transplant Recipients With a Past Medical History of Early-stage Melanoma: A Retrospective Cohort Study

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18 To the Editor,

Q2 The survival of solid organ transplant recipients (SOTRs) has improved in recent decades due to advances in surgical techniques and optimization of immunosuppressive regimens.¹ Despite this, chronic immunosuppression increases the risk of neoplasms, with tumors showing more aggressive behavior.² The incidence rate of melanoma is on the rise, making it increasingly common to assess the suitability of patients with this history for transplantation. This decision should be individualized, considering the initial stage, disease-free interval, urgency of transplantation, the possibility of using a living donor, and comorbidities.^{3,4} Available evidence derives from retrospective series and expert recommendations, with no studies conducted in our setting.^{5,6} Our objective was to analyze the outcomes of SOTRs with a history of melanoma and compare them with a non-transplanted control cohort.

We conducted a retrospective, multicenter cohort study. The cohort included patients undergoing solid organ transplantation (SOT) with a past medical history of melanoma. The control cohort was obtained from the melanoma registry of the *Xarxa Catalana de Melanoma*, matched using propensity score (1:10) by age, sex, year of diagnosis, and stage. Overall survival, disease-specific survival, and progression-free survival were analyzed using Kaplan–Meier curves and the log-rank test ($P < .05$). The analysis was performed using R (4.2.2, R Core Team, Vienna, Austria). The study was approved by the ethics committee of our center.

The SOTR cohort included 11 patients, 91% male, all European, with a median age at melanoma diagnosis of 52 years (Q1;Q3 50;60). Two melanomas were in situ and 9 were invasive (IA–IIB). Sentinel lymph node biopsy was performed in 7 cases, all negative. The median time bet-

ween diagnosis and transplantation was 10.4 years (Q1–Q3, 3.4–15.5); 2 patients underwent transplantation within 2 years. Four patients developed keratinocyte carcinomas before or after transplantation.

In 2 renal transplant recipients, an mTOR inhibitor was used due to a past medical history of melanoma or multiple keratinocyte carcinomas. The remaining patients received classical immunosuppression (corticosteroid, antimetabolite, and calcineurin inhibitor). After a median follow-up of 16.4 years (Q1;Q3 7.7–18.9), only 1 patient with a past medical history of lentigo maligna presented late local recurrence, successfully treated surgically. No metastases were recorded. Two patients died from causes unrelated to melanoma (Table 1).

After matching, no significant differences were observed in clinical and histological characteristics between the transplanted and control cohorts (Table 2). Survival analysis using Kaplan–Meier curves showed that transplanted patients with a past medical history of melanoma had progression-free, disease-specific, and overall survival comparable to the control group (Fig. 1).

Our results indicate that SOTRs with a history of early-stage melanoma do not have a worse prognosis vs non-transplanted patients. Previously published series have shown variable results. An early series described post-transplant recurrence rates close to 19%, although without Breslow data, limiting interpretation.⁷ Subsequent studies with larger sample sizes did not confirm this poor prognosis, showing low recurrence rates and limited progression.⁸ The study by Mary Zwald et al., based on U.S. registries, showed that 22/901 SOTRs with a history of melanoma died from melanoma. However, the initial stage of these patients is unknown.⁹

The choice of immunosuppressive regimen remains key. mTOR inhibitors seem to reduce the incidence rate of cutaneous neoplasms vs conventional drugs, although evidence on their specific impact on melanoma is limited.¹⁰

The >10-year interval between melanoma diagnosis and transplantation observed in our series does not align with current recommendations. Two patients with early-stage melanoma underwent transplantation within 2 years, consistent with timelines proposed by a

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◇ Members of the GEDOC Working Group (Spanish Group of Dermato-Oncology and Surgery) are listed in Appendix 1.

<https://doi.org/10.1016/j.ad.2026.104663>

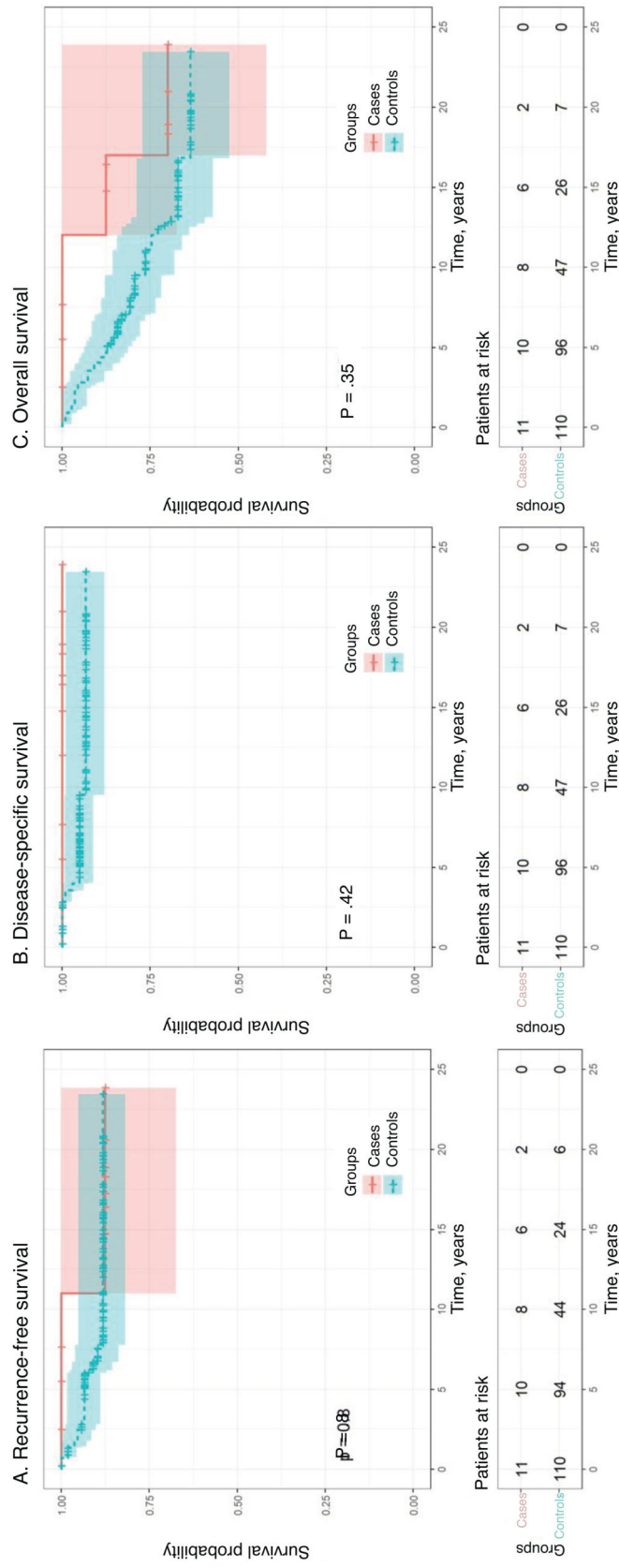


Fig. 1. Kaplan–Meier survival curves for the group of SOTR patients with pre-transplant melanoma (cases, in red) and for the group of melanoma patients from the *Xarxa Catalana de Melanoma* (controls, in green). Recurrence-free survival curve (A), disease-specific survival curve (B), and overall survival curve (C). The log-rank test was used as the hypothesis test.

Table 1

Clinical characteristics of the 11 transplanted patients with a past medical history of melanoma.

Sex/age at melanoma diagnosis	TNM stage 8th Ed	Transplanted organ	Years to transplantation	Immunosuppressants	Recurrence	Months of follow-up after melanoma diagnosis	Death
M/61	IB	Kidney	3.4	PRED + TAC + EVE	No	66	No
M/72	0	Kidney	6.2	PRED + TAC + EVE	Yes (local)	145	Yes (sepsis)
F/52	0	Kidney	1.3	PRED + TAC + MIC	No	30	No
M/61	IIB	Kidney	16.0	PRED + TAC + MIC	No	227	No
M/51	IA	Liver	1.0	CsA + TAC	No	207	Yes (heart disease)
M/49	IIA	Kidney	10.4	PRED + TAC + MIC	No	220	No
M/39	IA	Liver	15.4	TAC + MIC	No	287	No
M/54	IB	Kidney	10.5	PRED + TAC + MIC	No	177	No
M/59	IA	Liver	6.4	TAC	No	92	No
M/51	IB	Kidney	15.7	PRED + TAC + MIC	No	248	No
M/48	IA	Lung	15.5	PRED + TAC + MIC	No	197	No

M: male; F: female; PRED: prednisone; TAC: tacrolimus; EVE: everolimus; MIC: mycophenolate mofetil; CsA: cyclosporine.

Table 2Differential baseline characteristics of the 2 cohorts: Cases: SOTR patients with pre-transplant melanoma. Controls: non-SOT patients with melanoma, matched by sex, age, stage, and year of diagnosis from the Xarxa Catalana de Melanoma (*Hospital Clínic de Barcelona and Hospital Germans Trias i Pujol de Badalona*).

	Cases (N = 11)	Controls (N = 110)	P value
<i>Age at melanoma diagnosis</i>			
Median (Q1,Q3)	52.0 (50.0, 60.0)	55.0 (41.9, 70.3)	.836 ^a
<i>Sex</i>			1.000 ^b
Female	1 (9.1%)	10 (9.1%)	
Male	10 (90.9%)	100 (90.9%)	
<i>Breslow index</i>			.798 ^a
Median (Q1, Q3)	1.1 (0.9, 1.3)	1.1 (0.6, 1.8)	
In situ (or NA)	2	20	
<i>Invasion</i>			1.000 ^b
Invasive	9 (81.8%)	90 (81.8%)	
In situ	2 (18.2%)	20 (18.2%)	
<i>Ulceration</i>			.357 ^b
No	9 (81.8%)	86 (89.6%)	
Yes	2 (18.2%)	10 (10.4%)	
NA	0	14	
<i>Mitosis</i>			.839 ^a
Median (Q1, Q3)	0.0 (0.0, 0.4)	0.0 (0.0, 0.9)	
NA	3	37	
<i>Histological subtype</i>			.748 ^b
Lentigo maligna	1 (9.1%)	14 (13.2%)	
Superficial spreading melanoma	10 (90.9%)	68 (64.2%)	
Acral lentiginous melanoma	0 (0.0%)	7 (6.6%)	
Nodular	0 (0.0%)	10 (9.4%)	
Others	0 (0.0%)	7 (6.6%)	
NA	0	4	
<i>Location</i>			.738 ^b
Acral	0 (0.0%)	8 (7.5%)	
Head and neck	3 (27.3%)	20 (18.9%)	
Lower extremities	2 (18.2%)	10 (9.4%)	
Trunk	5 (45.5%)	53 (50.0%)	
Upper extremities	1 (9.1%)	15 (14.2%)	
NA	0	4	
<i>TNM stage 2018 ed.</i>			1.000 ^b
0	2 (18.2%)	20 (18.2%)	
IA	4 (36.4%)	40 (36.4%)	
IB	3 (27.3%)	30 (27.3%)	
IIA	1 (9.1%)	10 (9.1%)	
IIB	1 (9.1%)	10 (9.1%)	

NA: not available.

^a Kruskal–Wallis test.^b Fisher's exact test.

2021 expert consensus. This consensus establishes waiting periods according to stage: no interval (in situ), 1 year for IA–IIA, between 1 and 2 years for IIIA, and 2–4 years for stages IIB–IIIB. For higher stages, at least 5 years is recommended, always on an individualized basis. Sentinel lymph node biopsy is key, as the recommended interval depends on its result.⁴ In the era of effective therapies even for advanced disease, defining an optimal waiting time remains complex.

As in other similar studies, our work is likely subject to selection bias toward melanomas with better prognosis. In addition, the sample size and low number of events limit interpretation of the results. Nevertheless, it reflects routine clinical practice in tertiary referral centers in Spain.

Patients with early-stage melanoma may be suitable candidates for SOT, with recurrence and survival rates comparable to those of the non-transplanted population. Dermatologists play an essential role in the evaluation and follow-up of these patients, in close coordination with multidisciplinary teams.

Conflicts of interest

None declared.

Appendix A. Appendix 1

Members of GEDOC Working Group (*Spanish Group of Dermato-Oncology and Surgery*) (Barcelona, Spain): Sonia Segura Tigell (Barcelona), Cristina Vico Alonso (Madrid), Pablo Luis Ortiz Romero (Madrid), Susana Puig Sarda (Barcelona), and Vicente García-Patos Briones (Barcelona).

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