Postoperative Survival Outcomes in Early-Stage Melanoma: A Systematic Review of Real-World Studies in Four Latin American Countries

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Introduction

- Melanoma is a significant public health concern worldwide, with cases increasing significantly over the last 30 years due to factors like ultraviolet radiation exposure and aging population[1]
- Early cancer detection and treatment greatly influence survival rates, with the 5-year relative survival rate for stage I melanoma being over 99% in US.[3] In contrast, more advanced melanoma stages were associated with poor survival outcomes
- In Latin America, the burden of melanoma is growing, with Latin America reporting 15,520 new cases and 4,132 deaths in 2022.[2] However, there is limited data on survival outcomes in this region, particularly for early-stage (non-metastatic) cases
- To fill this gap, this review synthesizes real-world data on survival outcomes in early-stage melanoma across Argentina, Brazil, Colombia, and Mexico, which represent three-quarters of the total new cases and deaths in this region
- This review may offer valuable insights for managing high-risk melanoma patients in the evolving treatment landscape, which now includes adjuvant immunotherapy, as compared to the adjuvant therapy options available prior to 2022. The ultimate goal is to enhance patient outcomes and healthcare strategies across Latin America

Objective

To describe survival outcomes in early-stage melanoma in four Latin American countries: Argentina, Brazil, Colombia, and Mexico.

Methods

- **Study design:** A protocol was developed for this systematic review, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[6] The study was designed using the PICOT framework, which stands for Population, Intervention, Comparison, Outcome, and Time. The eligibility criteria for study selection are shown in **Figure 1**

Figure 1. PICOT question

Population(s)	Individuals with early-stage, non-metastatic melanoma in Argentina, Brazil, Colombia, and Mexico who underwent surgery
Intervention	Not restricted
Comparisons	Not restricted
Outcomes	Overall survival (OS), disease-specific survival (DSS), disease-free survival (DFS) and recurrence-free survival (RFS)
Time	Published from January 2015 to Dec 2023
Study design	Observational studies (prospective and retrospective cohort studies, case-control studies, cross-sectional studies, registry/database studies)
Other	No language restrictions were applied

Search strategy:

- A search strategy was conducted in four databases (Embase®, LILACS, SCOPUS, and SCIELO) to identify articles published from January 2015 to December 2023. The search strategy included keywords and medical subject headings (MeSH) related to melanoma and survival outcomes. Endnote was used as a reference management software to collate references and remove duplicate records

Study selection process:

- Two reviewers (JF, CIP) independently screened the abstracts or titles. Two reviewers (FV, CIP) independently assessed full-text articles and classified them as included studies or excluded studies
- Any disagreements were solved through discussion or by involving a third review author (MR)

Data extraction:

- Data were extracted using a standardized form, including study characteristics, patient demographics, and survival outcomes

Results

- A total of 1,474 references were identified, 122 articles underwent full-text review, and 18 were included
- Seven (38.9%) studies were from Mexico, seven (38.9%) from Brazil, three (16.7%) from Colombia and one from Argentina (5.5%) and the study periods varied from 1982 to 2021
- The most frequent histology were acral lentiginous and nodular melanoma
- The majority of studies utilized the TNM (AJCC) staging system, and three studies (Nunes et al, 2018A; Featherston et al, 2021; Almeida et al, 2023) used only T classification/tumor thickness (Breslow depth)
- Among 18 studies, 12 reported OS, 5 DSS, 2 DFS, and 2 RFS (**Table 1**)
- The 5-year OS by stage ranged: Stage I: 89% to 100% (n=5 studies); Stage II: 60% to 83.4% (n=6); and Stage III: 33% to 68.5% (n=6)
- The 5-year DSS by stage ranged: Stage I: 49% to 92.4% (n=4); Stage II: 39% to 70.1% (n=4); Stage III: 36% to 53.5% (n=4)
- Only one study reported DFS by stage: Stage I: 69%; Stage II: 81%
- Only one study reported aggregated RFS for stages I-III: 5-year RFS: 81.5%; 10-year RFS: 67.8%

Table 1. Main characteristics of the studies of real-world reporting postoperative survival outcomes in early-stage melanoma

	First author (year)	No. patients	Study period	Clinical staging n (%)				Histology (%)	RFS/DFS/DSS/OS (%)
				Stage I	Stage II	Stage III	Stage IV		
ARG	Featherston (2021)	<70 years: 150	2005-2020	38 (25)	58 (39)	40 (26.5)	14 (9.5)	NR	5y OS: 87
		≥70 years: 44		10 (22.7)	12 (27.3)	13 (29.5)	9 (20.5)	NR	5y OS: 63
COL	Duarte (2017)	90	2003-2009	28 (31.1)	29 (32.2)	25 (27.8)	5 (5.6)	ALM: 100	5y OS: 54 5y OS by stage I–II: 71
	Rodríguez-Betancourt (2022)	132	2006-2015	26 (19.7)	25 (18.9)	10 (7.6)	26 (19.7)	ALM: 18.2; LMM: 7.6: SSM: 17.4; NM: 25.8; NR: 31.1	5y OS by stage I: 100; II: 76 ; III: 68.5
	Ospina Serrano (2023)	759	2011-2021	184 (24.2)	228 (30)	241 (31.7)	–	ALM: 27.8; SMM: 18.2; NM: 16.6; LMM: 10.8; Other: 26.6	5y OS: 83.2 10y OS: 71.1 5y OS by stage: 0/I: 97; II: 80; III: 65 5y-RFS: 81.5 10y-RFS: 67.8
BRA	Vazquez (2015)	1073	1997-2011	296 (27.6)	271 (25.3)	214 (19.9)	168 (15.7)	SMM: 32.9; NM: 26.8; ALM: 7.1; LMM: 3.7; Other: 29.5	5y DSS: 67.6 5y DSS: I: 91.4; II: 70.1; III: 46.5
	Nunes (2018A)	157	1997-2014	15 (9.6)	13 (8.3)	20 (12.7)	78 (49.7)	ALM: 25.5; NM: 22.9; SMM: 7.0; Other: 44.6	5y RFS: 48.2 5y OS: 61
	Nunes (2018B)	529	1997-2014	51 (12.3)	184 (44.3)	147 (35.4)	16 (3.8)	NM: 41.2; ALM: 44.3; SMM: 3.7	5y OS by stage: I: 89; II: 60; III: 33
	Vicente (2019)	459	2001-2012	73 (16.3)	147 (32.9)	133 (29.8)	80 (17.9)	NM: 38.9; SMM: 34.4; ALM: 21.2; Other: 5.6	5y DSS: 51.1
	da Costa (2019)	1848	1996 -2015	510 (27.6)	422 (22.8)	317 (17.2)	270 (14.6)	SMM: 35.1; ALM: 21.3; Other: 3.6; NR: 33	5y DSS: 68.8 5y DSS by stage: I: 92.4; II:69.5; III: 53.5
	Borges de Barros Primo (2023)	154	2002-2014	38 (24.7)	116 (75.3)	-	-	ALM: 86.4; Non-ALM: 13.6	5y DFS by stage (ALM) I-II: 72.7; I: 69; II: 81
	Almeida (2023)	105	2001-2021	13 (16.4)	42 (53.2)	18 (22.8)	6 (7.6)	Cutaneus melanoma	5y OS: 92.4
MEX	Luna-Ortiz (2018)	226	1982-2012	66 (34.7)	63 (33.2)	38 (20)	23 (12.1)	Cutaneous melanoma	5y DFS: 94 5y OS: 88
	Lino-Silva LS (2016)	1219	2005-2014	161 (19.3)	233 (27.8)	261 (31.2)	182 (21.7)	ALM:44.1; SMM: 17.4; NM: 37.3; LMM: 1.2	5y DSS: 52.3 5y DSS by Stage: I: 49; II: 39; III: 36
	Lino-Silva (2019)	715 ALMs	2000-2015	164 (27.6)	367 (51.3)	136 (19)	48 (2.1)	ALM: 62.5	5y DSS: 46.3 5y DSS by Stage: I: 53.3; II: 52.7; III: 40.8
		429 non-ALM		169 (39.4)	199 (46.4)	46 (10.7)	15 (6.5)	Non-ALM: 37.5	5y DSS: 55.7 5y DSS by Stage: I: 66; II: 60.8; III: 48.4
	Lino-Silva (2022)	742	2005–2015	142 (19.1)	307 (41.4)	269 (36.3)	24 (3.2)	Cutaneous melanoma	5y OS: 75.9 5y OS by Stage: I: 96.2; II: 83.4; III: 54.4
	Lino-Silva (2023)	306	2005-2018	-	137 (44.8)	154 (50.3)	15 (4.9)	ALM	5y OS: II: 75.2; III: 55.8
	Pérez-Aldrete (2019)	323	2000-2010	69 (22)	84 (27)	17 (5)	29 (9)	NM: 28; SMM: 21; LMM: 19; ALM: 15; Other: 17	Mean OS: 77 (mean follow-up: 7 years)
	Zepeda-Najar (2021)	707	2005-2015	196 (27.7)	233 (33)	255 (36.1)	23 (3.3)	ALM: 55.4; NM: 21.9; SMM: 14.1; LMM: 8.5	5y OS by Stage: I: 96.6; II: 80.5; III: 58.3

NR, Not reported; ALM, Acral lentiginous melanoma; LMM, lentigo malignant melanoma; NM, nodular melanoma;.SMM, superficial spreading melanoma.

Discussion and conclusions

- This review provides valuable insights into the survival outcomes of early-stage melanoma in Latin America, which can inform healthcare strategies and improve patient management in this region
- The most common histological types were acral lentiginous and nodular melanoma
- There is a need for standardized reporting of survival outcomes, including RFS, to better understand long-term patient outcomes. Limited RFS data highlights a need for better long-term follow-up.
- OS varied significantly by stage. Stage I had better prognosis (5-year OS: 89% to 100%) than stages II and III, that had 5-year OS of 60% to 83.4% and 33% to 68.5%, respectively.
- Most studies reported adjuvant therapy, mainly radiotherapy and systemic therapy (chemotherapy and interferon alpha). This highlights the need for more innovative therapies such as adjuvant immunotherapy to improve survival outcomes.
- These real-world results represent findings prior to the introduction of new therapies, such as immunotherapy with pembrolizumab for early-stage melanoma indication.

References

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