

# The impact of COVID-19 pandemics on malignant melanoma: the experience of a single center

## O impacto da pandemia COVID-19 no melanoma maligno: a experiência de um centro

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### Abstract

**Introduction:** The pandemic outbreak of coronavirus disease 2019 (COVID-19) greatly restricted routine healthcare services across Europe, including cancer diagnosis and treatment. Amongst skin cancers, malignant melanoma (MM) is responsible for most deaths. **Objective:** This study aimed to compare the number and characteristics of diagnosed MM cases before and during the pandemic in a Portuguese secondary hospital. **Methods:** This was an observational, retrospective study comparing a pre-pandemic (diagnosis from March 2019 to February 2020) and a pandemic group of patients with MM diagnosis (diagnosis between March 2020 and February 2021). **Results:** A total of 59 patients were included, 44 in the pre-pandemic group and 15 in the pandemic period. In the first year of the pandemic, there was a significantly lower number of MM diagnoses compared to the precedent year (15 vs 44,  $p < 0.01$ ), without significant differences in tumor characteristics. The time from referral to first consultation was slightly shorter in the pandemic group (median of 36 vs 76 days,  $p = 0.056$ ). **Conclusions:** This study provides evidence of a reduction in MM diagnosis during the first year of the COVID pandemic, despite no significant differences in prognostic factors. As the pandemic persists, one must emphasize the importance of early MM diagnosis and treatment.

**Keywords:** Skin cancer. Severe acute respiratory syndrome coronavirus 2. Malignant melanoma. Coronavirus disease of 2019.

### Resumo

**Introdução:** A pandemia Coronavírus 2019 restringiu consideravelmente os serviços de saúde de rotina em toda a Europa, incluindo o diagnóstico e tratamento de cancro. De entre os cancros da pele, o melanoma maligno (MM) é o responsável pela maioria das mortes. **Objetivo:** Este estudo teve como objetivo comparar o número e características dos MM diagnosticados antes e durante a pandemia num hospital secundário português. **Métodos:** Estudo observacional, retrospectivo, que comparou o grupo de doentes pré-pandémico (diagnóstico de MM de março de 2019 a fevereiro de 2020) e pandémico (diagnóstico de MM entre março de 2020 e fevereiro de 2021). **Resultados:** Foram incluídos 59 doentes, 44 do grupo pré-pandémico e 15 no período pandémico. No primeiro ano da pandemia, houve uma redução significativa dos diagnósticos

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de melanoma maligno relativamente ao ano anterior (15 vs. 44,  $p < 0,01$ ), sem diferenças significativas nas características dos tumores. **Conclusões:** Este estudo mostra uma redução dos diagnósticos de MM durante o primeiro ano da pandemia, embora sem diferenças significativas nos fatores de prognóstico. Com a persistência da pandemia, deve-se enfatizar a importância do diagnóstico e tratamento precoce do MM.

**Palavras-chave:** Cancro da pele. SARS-CoV-2. Melanoma maligno. COVID-19.

## Introduction

The pandemic outbreak of COVID-19 greatly restricted routine healthcare services across Europe, including cancer diagnosis and treatment<sup>1-3</sup>. The first COVID-19 case in Portugal was confirmed on 2<sup>nd</sup> March 2020. The country entered a lockdown (state of emergency) two weeks later, which began to be lifted on 2<sup>nd</sup> May 2020<sup>3</sup>.

Most healthcare settings implemented minimal services, which, along with the fear of the population getting infected with COVID-19, led to the cancellation or suspension of programmed activity<sup>4,5</sup>. Globally, the World Health Organization estimated that 40% of countries reported partial or complete disruptions in cancer treatment<sup>6</sup>.

Therefore, it is essential to assess whether healthcare limitations led to a reduction in the diagnosis and delays in the treatment of skin cancer, particularly MM since it is responsible for most skin cancer deaths<sup>2,5</sup>.

The outcome of MM depends primarily on tumor thickness, which, in turn, is related to the time to diagnosis<sup>2</sup>. Thin MMs are preferentially diagnosed through screening by experienced dermatologists, whereas patient-identified MMs are tendentially thicker and diagnosed at advanced stages<sup>7</sup>.

A model based on melanoma rate of growth built by Tejera-Vaquerizo estimated that a 3-month diagnosis delay in melanoma would represent an upstaging of 45% of cases and a 2% loss in 5-year survival<sup>8</sup>.

There are already studies across Europe documenting the impact of the pandemic on MM diagnosis and prognosis in several countries<sup>4</sup>. Most of them report a reduction in the number of MM diagnoses in the pandemic era, along with a higher Breslow depth index and TNM staging<sup>4</sup>. One single similar Portuguese study was conducted in IPO Porto, one of the largest cancer-dedicated hospitals in Portugal<sup>3</sup>. The authors compared the impact of the COVID-19 outbreak on the short-term survival of several types of cancer, comparing a period of 4 months after the beginning of the outbreak in Portugal (2<sup>nd</sup> March 2020) with the same period in the previous year<sup>3</sup>. A reduction of 30% of patients diagnosed with melanoma was noted after the pandemic onset, however,

without impact on short-term survival<sup>3</sup>. However, this study doesn't particularize the characteristics of melanoma diagnoses before and during the pandemic, which would be important to assess prognosis and impact beyond short-term survival<sup>3</sup>.

This study aims to compare the number of diagnosed MM before and during the pandemic in a Portuguese secondary hospital and determine if there were differences in tumor characteristics, namely Breslow depth index, mitotic rate, ulceration, and tumor stage.

## Methods

This was an observational, single-center, retrospective study, including patients diagnosed with cutaneous MM between March 2019 and February 2021 at the Dermatology Department of Hospital de Braga, Portugal.

The demographical clinical and anatomopathological data were collected from clinical files. Patients without histopathological confirmation of MM were excluded from the analysis.

A comparative analysis of two groups: pre-pandemic (MM diagnosis from March 2019 to February 2020) and pandemic (diagnosis of MM from March 2020 to February 2021), was performed.

The patient's identity was not disclosed in this research. All procedures were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

The collected data were analyzed using the statistical software for Windows, Statistical Package for the Social Sciences v27 (IBM Corp., Armonk, New York, United States of America). Categorical variables were described by frequency and proportion; summary statistics (median, range) were used to report continuous data. Differences between the two groups were tested by Mann-Whitney *U* test (for continuous variables) and by the Chi-squared test (for categorical variables), as appropriate. A two-sided *p*-value of  $< 0.05$  was considered statistically significant.

**Table 1.** Characterization of patients and tumors

		Pre-pandemic n (%)	Pandemic n (%)	p-value
Number of diagnoses		44 (74.6%)	15 (25.4%)	< 0.01*
Age (years; median)		72	67	0.565
Sex	Male	16 (36.4%)	6 (40%)	0.801
	Female	28 (64.6%)	9 (60%)	
MM localization	Head	23 (52.3%)	4 (26.7%)	0.286
	Trunk	7 (15.9%)	4 (26.7%)	
	Upper limb	7 (15.9%)	2 (13.3%)	
	Lower limb	7 (15.9%)	5 (33.3%)	
MM	In situ	18 (40.9%)	5 (33.3%)	0.603
	Invasive	26 (59.1%)	10 (66.7%)	
MM subtype	LM	15 (34.1%)	4 (26.7%)	0.469
	MM acral in situ	1 (2.3%)	0 (0%)	
	MM in situ	2 (4.6%)	1 (6.7%)	
	LMM	2 (4.6%)	1 (6.7%)	
	MM acral	0 (0%)	1 (6.7%)	
	SSMM	17 (38.6%)	8 (53.3%)	
	Nodular MM	6 (13.6%)	0 (0%)	
	MM NOS	1 (2.3%)	0 (0%)	
Breslow thickness (mm; median)		1.08	1.2	0.806
Ulceration <sup>a</sup>	Yes	8 (18.2%)	0 (0%)	0.089
	No	18 (10.9%)	10 (66.7%)	
Number of mitosis (median)		2.5	1	0.213
Stage	0	18 (40.9%)	5 (33.3%)	0.469
	IA	9 (20.5%)	3 (20%)	
	IB	5 (11.4%)	4 (26.7%)	
	IIA	1 (2.3%)	2 (13.3%)	
	IIB	4 (9.1%)	1 (6.7%)	
	IIC	5 (11.4%)	0 (0%)	
	NOS	2 (4.6%)	0 (0%)	
Referral source	Family doctor	33 (75%)	12 (80%)	0.322
	Dermatology dept	3 (6.8%)	3 (20%)	
	Emergency dept	4 (9.1%)	0 (0%)	
	Other speciality	1 (2.3%)	0 (0%)	
	External	3 (6.8%)	0 (0%)	
Time to first dermatology appointment (days; median)		73	36	0.059
Time to surgery (days; median)		23	13	0.393

MM: malignant melanoma; LM: lentigo maligna; LMM: lentigo maligna melanoma; SSMM: superficial spreading malignant melanoma; NOS: not otherwise specified; dept: department; p bold\*: statistically significant (< 0.05) calculated by Chi-squared test; °: in the invasive melanomas.

## Results

A total of 59 patients were included, 44 in the prepandemic group and 15 in the pandemic period.

The characteristics of patients and tumors are described in Table 1.

In the 1st year of the pandemic, there was a significantly lower number of MM diagnoses compared to the

precedent year (15 vs 44,  $p < 0.01$ ), which corresponds to a decrease of 65.9% in the number of diagnoses. Notably, there were no diagnoses in March, April, and May 2020 (the first lockdown period).

There were no statistically significant differences in ages between groups, with a median age of 72 and 67 years of the pre-pandemic and pandemic groups, respectively. Most of the patients were women in both groups (64.6 and 60% in the pre-pandemic and pandemic groups, respectively), without differences in sex distribution.

The most common tumor location was the head in the pre-pandemic group (52.3% of tumors), while in the pandemic group, it was the lower limb (33.3%), although this difference did not reach statistical significance.

Regarding the proportion of *in situ* vs invasive MM, there were no differences between groups, though, in the pandemic group, we found an increase in invasive MM (66.7 vs 59.1%). There were also no differences concerning the MM subtype or staging, with a greater proportion of superficial spreading MM in both groups, consistent with a predominance of lower stages (0 and I).

Breslow depth index was slightly higher in the pandemic group (median 1.2 vs 1.08 mm). However, this difference did not reach statistical significance. We also found no differences in what concerns ulceration or mitotic index.

Regarding the referral source, the family doctor was preponderant in both groups, without significant differences between them. The time from referral to first consultation was marginally significantly shorter in the pandemic group (median of 36 vs 76 days,  $p = 0.056$ ), and there was no significant difference among groups in the time from first dermatology appointment to surgery.

## Discussion

The main finding of this study is a significant reduction in the number of MM diagnoses in the first year of pandemics (a decrease of 65.9% of diagnoses,  $p < 0.01$ ). Similarly, other studies also reported a reduction of MM diagnosis, although with a lower expression<sup>4,7,9-11</sup>. Some of these studies report a more pronounced reduction in *in situ* and thin MM, translating into a higher proportion of invasive MM<sup>4,7,11</sup>. In our study, we observed a slight increase in invasive MM in the pandemic group, although without statistical significance. Since we found a major reduction in the number of MM diagnoses, the reduced sample in the pandemic group may explain the lack of statistical significance; however, we believe that these results are worth mentioning.

Regarding prognostic factors, such as the Breslow depth index, ulceration, or mitotic index, there were no differences between groups, which translates into a similar staging distribution. In contrast, other authors found higher Breslow depths and mitotic rates and, consequently, a shift toward more advanced stages in pandemic groups<sup>4,7,10,11</sup>.

Surprisingly, we found a marginally significant reduction in the time from referral to the first dermatology appointment in the pandemic group. This could be explained by the reduction of referrals of less urgent situations from primary care in this period and the maintenance of the outpatient activity of the Dermatology Department. Similarly, Andrew and associates also found a decrease in skin cancer diagnoses accompanied by a reduction in waiting time for the first appointment during the first 3 months of COVID-19<sup>12</sup>.

In what concerns to the referral source, primary care remained preponderant in both periods, reinforcing the role of the family doctor in the detection of suspected lesions.

The main limitation of this study is the inclusion of one single center with a small sample. This might have impacted the obtention of statistically significant results. Including more centers and cancer referral centers would overcome this limitation and would allow us to see the "bigger picture" and better understand the real impact of the pandemics on MM in Portugal. However, the authors still consider this a relevant study since it is the first of this kind to include Portuguese data. Furthermore, cause-effect relationships are difficult to assess from retrospective observational data, and the impact of confounding factors is unknown. Moreover, we believe the reduction of melanoma diagnoses in the COVID era may reflect a higher threshold in seeking medical care due to fear of infection by the general public rather than a true reduction in melanoma incidence.

## Conclusion

In conclusion, this study provides evidence of a reduction in MM diagnosis during the first year of the pandemic in a Portuguese center. Reasons for this would require further analysis. It can be speculated that this could happen due to limitations on access to Primary care, which is the main referral source of MM patients, and the fear of COVID-19 from the population, avoiding medical consultations. As the pandemic persists, it is essential to reinforce among the population and health professionals the importance of screening and prompt treatment of melanoma.

## Funding

None.

## Conflicts of interest

None.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

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