SURGICAL MANAGEMENT OF CUTANEOUS MELANOMA IN THE ERA OF COVID-19 PANDEMIC: A SINGLE CENTER EXPERIENCE

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Timely started surgical treatment represents the gold standard in melanoma therapy and keeps mortality at a low level. The pandemic caused by SARS-CoV-2 has affected the availability of health care both nationally and globally. The aim of this study was to examine the impact of the COVID-19 pandemic on newly operated cutaneous melanoma in patients and to contribute to identifying the impact of the pandemic on the healthcare system in Serbia. We conducted a single institution retrospective study including patients who consecutively underwent surgery for cutaneous melanoma at the Clinic for Plastic and reconstructive Surgery, University Clinical center of Niš, between January 1, 2018 and March 15, 2023. We compared the pre-pandemic (01/Jan/18 -14/Mar/20) and pandemic (15/Mar/20 - 15/Mar/23) periods by evaluating patient age, sex, body distribution, Breslow thickness, pT staging, mitotic index rate and ulceration status. No differences were observed between age (p = 0.666), sex (p = 0.720), body distribution (p = 0.109), Breslow thickness (p = 0.172), pT staging (p = 0.274), mitotic index rate (p = 0.257), and ulceration status (p = 0.787) in the two examined groups. Statistically significant differences were observed in the melanoma subtype ($\chi^2 = 9.241$; p = 0.026). Distribution of lentigo maligna in patients diagnosed with melanoma during the pandemic was statistically lower. To date, the diagnostic delay caused by COVID-19 has generally not led to unfavorable characteristics of the primary cutaneous melanoma. Follow-up studies are needed in the coming years to identify the potential impact on stage distribution and long-term survival. Acta Medica Medianae 2023; 62(3): 95-102.

Key words: COVID-19, melanoma, surgical treatment, Breslow thickness, diagnostic delay

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Introduction

Melanoma is one of the most malignant tumors in human population and the most malignant skin tumor. The incidence of melanoma varies around the world and it has been steadily rising in recent decades. Timely started surgical treatment represents the gold standard in melanoma therapy and keeps mortality at a low level (1, 2, 3). Patients with a higher Breslow index and the presence of ulceration at the time of diagnosis have a worse prognosis and a more aggressive form of the disease (4). Melanomas detected in a screening program are usually thinner than melanomas detected by selfexamination (5).

The pandemic caused by SARS-CoV-2 has affected the availability of health care both nationally and globally (6). Elective surgical procedures were not performed during the lockdown while surgical treatment of cancer was postponed (7). Delaying the surgical treatment of melanoma is devastating for the patient and leads to increased health care costs (8).

As a consequence of the delay in screening programs and surgical treatment of melanoma, many studies have indicated a significant decrease in the number of newly diagnosed patients with melanoma (9-11), while on the other side the Breslow thickness was higher (11 - 19). An increase in the number of patients in stage II of the disease and higher was also noted (20). On the other hand, many studies indicate that the COVID-19 pandemic had no effect on melanoma thickness (19, 21-24).

According to our knowledge, there is only one study on the impact of the COVID-19 pandemic on patients with cutaneous melanoma in the Republic of Serbia, which includes only patients operated on at the Clinic for Burns, Plastic and Reconstructive Surgery of the University Clinical Center of Serbia (25).

Aim

The aim of this study was to examine the impact of the COVID-19 pandemic on newly operated cutaneous melanoma in patients and to contribute to identifying the impact of the pandemic on the healthcare system in Serbia.

Material and methods

We conducted а single institution retrospective study including patients who consecutively underwent surgery for cutaneous melanoma at the Clinic for Plastic and Reconstructive Surgery, University Clinical Center of Niš, between January 1, 2018 and March 15, 2023. The clinic is also a tertiary national referral center for skin cancer patients for the region of southeastern Serbia. Medical history and a clinical records database of the Clinic for Plastic and Reconstructive Surgery were used as the sources of data for this study. Demographic characteristics (gender, age), localization of melanoma and TNM classification according to the American Joint Committee on Cancer (TNM classifications for cutaneous melanoma, eighth edition) were analyzed.

The study procedures were carried out in accordance with the Declaration of Helsinki.

The following statistical parameters are presented by descriptive statistical analysis: arithmetic mean, standard deviation, absolute frequency (N), and structure index (%). The comparison of the frequency of occurrence of individual modalities of attribute features between groups was performed by Pearson χ^2 test. The mean values of the numerical features between the two independent groups of respondents were compared by Student's T-test or Mann-Whitney Utest. Statistical analysis was performed using an Excel program from the Microsoft Office software package and an SPSS program (version 18.0). The threshold for statistical significance was the level of statistical error less than 5% (p < 0.05). The results of the statistical analysis are presented in tables and graphs.

Results

A total of 199 patients with cutaneous melanoma were included in the study. During

2018, 65 patients were registered, in 2019 there were 31, 16 in 2020, 30 in 2021, 47 in 2022, and 10 in the first 3 months of 2023 (Figure 1). In the period before the start of the pandemic, 104 cases (52.3%) were registered, while during the pandemic, there were 95 (47.7%). The average number of registered cases per year before the pandemic was 48 ± 24 , while during the pandemic, it was 31±15. Our sample contained almost equal numbers of males (99) and females (100). The most registered cases were in the age group of 61 to 80 years. The mean age of patients in the prepandemic group was 57.5 (SD 15.5), while in the pandemic group, it was 59.5 (SD 14.2). There were no significant differences in sex (p=0.720) and age (p=0.666) of the patients between the pre- and post-COVID groups (Table 1).

In both cohorts, the most common subtype of melanoma was superficial spreading melanoma (SSM), represented by 55.3%, followed by the nodular subtype 31.2%. Other subtypes of melanoma were represented by 13.5%. Statistically significant differences were observed in the melanoma subtype (χ^2 =9.241; p=0.026). Distribution of lentigo maligna in patients diagnosed with melanoma during the pandemic was statistically lower.

Melanoma was most common on the trunk 49.2%, followed by the head and neck 20.1%, as well as the lower 16.1% and upper extremities 14.6%. There were no significant differences between the cohorts before and during the pandemic regarding the individual body distribution of melanoma and if there was an increase in the number of trunk melanomas and a decrease in the number of head and neck melanomas during the pandemic period (p=0.109).

Melanomas operated on in the two periods did not show a significant difference in Breslow thickness (2.1 vs. 2.7; p=0.172). Also there was no statistically significant difference in Breslow thickness during the examined years (p=0.549) (Table 2). There was no statistically significant change in the mitotic rate in the pandemic cohort (p=0.257), although the mitotic index doubled from 1 to 2. An increase in the number of melanomas with ulceration was also not observed. In both experimental groups, most patients were in the T1 stage of the disease. Also, there was no significant difference in the distribution of patients between stages in the groups (p=0.274) (Figure 2).



Figure 1. Number of diagnosed cases per year

Table 1	General	characteristics	of melanoma	patients	before	and a	after	the	onset	of tł	пe
			COVID-19 pa	andemic							

	before COVID-19	COVID-19	
	n=104	n=95	p-value
	(52.3%)	(47.7%)	
Age (mean ± SD)	57.53±15.52	59.52±14.21	0.349 ¹
Age groups			
≤40 years	13(12.5)	9(9.5)	0.666 ²
41–60 years	41(39.4)	37(38.9)	
61–80 years	44(42.3)	46(48.4)	
>80 years	6(5.8)	3(3.2)	
Sex			
Male	53(51.0)	46(48.4)	0.720 ²
Female	51(49.0)	49(51.6)	
Body distribution			
Head and Neck	27(26.0)	13(13.7)	0.109 ²
Trunk	44(42.3)	54(56.9)	
Upper extremities	15(14.4)	14(14.7)	
Lower extremities	18(17.3)	14(14.7)	
Melanoma subtype			
Superficial spreading	61(58.7)	49(51.6)	0.026 ²
Lentigo maligna	13(12.5)	4(4.2)	
Nodular	28(26.9)	35(36.8)	
Others	2(1.9)	7(7.4)	
Breslow thickness (median, 25th–75th percentile)	0.75 (0.40-2.69)	1.0 (0.40-3.70)	0.172 ³
Breslow thickness			
<1 mm	72(69.2)	53(55.8)	0.132 ²
1.01–2 mm	6(5.8)	13(13.7)	

2.01–4 mm	12(11.5)	11(11.6)	
>4 mm	14(13.5)	18(18.9)	
pT staging			
In situ	23(22.1)	20(21.1)	0.274 ²
T1	46(44.2)	30(31.6)	
T2	6(5.8)	11(11.6)	
T3	13(12.5)	14(14.7)	
Τ4	16(15.4)	20(21.1)	
Clark level			
I	23(22.1)	20(21.1)	0.682 ²
	45(43.3)	33(34.7)	
	18(17.3)	19(20.0)	
IV	15(14.4)	19(20.0)	
V	3(2.9)	4(4.2)	
Mitotic index rate (median, 25th–75th percentile)	1.0 (1.0-3.0)	2.0 (0.0-4.0)	0.257 ³
Ulcerations			
Yes	31(29.8)	30(31.6)	0.787 ²
No	73(70.2)	65(68.4)	



Figure 2. Combined pT staging of melanoma patients before and during the pandemic

Year	mean	SD	p-value
2018.	2.32	3.97	
2019	2.23	4.04	
2020.	3.44	4.80	
2021	3.43	4.38	
2022.	1.89	2.70	
2023.	1.80	1.55	0.549

 Table 2. Breslow thickness during years

Discussion

The Coronavirus, formally known as SARS-Cov-2, detected in Wuhan (China) at the end of December 2019, affected the availability of health care around the world (26). Many studies across different countries have shown a decrease in the number of patients with skin tumors during the pandemic, as the research has shown in Serbia also (25). In some cases, this drop was up to 60% (12, 20, 27). The biggest drop in the number of newly diagnosed patients with skin tumors was in 2020, which corresponds with our results (28). The biggest reduction in the number of newly diagnosed cases was in patients over 60 years old, which is also the case in our study. Our results are partially in line with the results of other authors who indicate the impact of covid-19 on the overall decline in the number of melanoma diagnoses. While the decline in the number of melanoma diagnoses in other authors is present in all years since the beginning of the pandemic, in our study this decline is present only in 2020. (12, 15, 29). Studies have shown that early detection and adequate surgical treatment of thin lesions decrease the mortality rate in the short term. In the long term however, prevention could play a huge role (30).

The results of our study showed an increase in Breslow thickness with a higher mitotic index during the pandemic, which is in agreement with the results of other studies (11-19). In relation to this, we observed an increase in the number of patients in the pT-2 stage and above, which was also discussed by Shannon et al. who observed an increased proportion in pT3-4 stage in patients operated on during the pandemic (13). A three month diagnostic delay according to Tejera et al. results in a significant drop off in the pT-1 stage (40% vs. 27%) and a doubled number of pT-4 cases (16% vs. 30%) as well as decreased five-and ten-year survival rate (31).

Because during the pandemic there is an evident delay in diagnosis and surgical treatment (32, 33), there are still no results on how this will affect five- and ten-year survival rate and how to improve screening programs, due to the lack of data and appropriate guidelines (34, 35).

The strength of our study is in the fact that it is based on the data of one of the largest institutions for the treatment of skin tumors in Serbia. Unfortunately, our study does not include patients with enlarged lymph nodes or distant metastases during this period, which represents a limitation of this study but leaves us space for further research. The sample of this study may contribute to further understanding of the impact of the Covid-19 pandemic and to promote the guidelines on how to improve the screening program and surgical treatment in these times.

Conclusion

To date, the diagnostic delay caused by COVID-19 has generally not led to unfavorable characteristics of the primary cutaneous melanoma. Follow-up studies are needed in the coming years to identify the potential impact on stage distribution and long-term survival.

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HIRURŠKO LEČENJE MELANOMA KOŽE U ERI PANDEMIJE KOVIDA 19: ISKUSTVO JEDNOG CENTRA

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Pravovremeno započeto hirurško lečenje predstavlja zlatni standard u terapiji melanoma i održava mortalitet na niskom nivou. Pandemija koju je izazvao virus kovid 19 uticala je na dostupnost zdravstvene zaštite, kako na nacionalnom, tako i na globalnom nivou. Cilj ove studije je da ispita uticaj pandemije kovida 19 na novooperisane bolesnike sa melanomom kože i da doprinese identifikovanju uticaja pandemije na zdravstveni sistem u Srbiji. Sproveli smo retrospektivnu studiju koja je ukliučivala bolesnike sa melanomom kože hirurški lečene na Klinici za plastičnu i rekonstruktivnu hirurgiju Univerzitetskog kliničkog centra Niš u periodu od 1. januara 2018. do 15. marta 2023. godine. Upoređivali smo periode pre pandemije (01/01/2018 -14/03/2023) i tokom pandemije (15/03/2020 - 15/03/2023) procenom starosti bolesnika, pola, zastupljenosti melanoma na određenim delovima tela, debljine po Breslovu, pT stadijuma, stope mitotičkog indeksa, podtipa melanoma i prisustva ulceracije. Nisu uočene razlike između starosti (p = 0,666), pola (p = 0,720), zastupljenosti melanoma na određenim delovima tela (p = 0,109), debljini po Breslovu (p = 0,172), pT stadijumu (p = 0,274), stopi mitotičkog indeksa (p = 0,257) i prisustva ulceracije (p = 0,787) u dvema ispitivanim grupama. Statistički značajne razlike uočene su kod podtipova melanoma (χ^2 = 9,241; p = 0,026). Distribucija lentigo maligna kod bolesnika sa dijagnozom melanoma tokom pandemije bila je statistički niža. Do danas, kašnjenje u postavljanju dijagnoze melanoma kože, usled padnemije izazvane kovidom 19, generalno nije dovelo do nepovoljnih karakteristika primarnog kožnog melanoma. Potrebno je sprovesti dodatne studije u budućnosti kako bi se identifikovali potencijalni uticaj na distribuciju po fazama i dugoročna stopa preživljavanja. Acta Medica Medianae 2023;62(3):95-102.

Ključne reči: kovid 19, melanom, hirurško lečenje, debljina po Breslovu, dijagnostičko kašnjenje

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