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Insight into the management of patients with melanoma in times of the COVID-19 pandemic – a single-center experience

Uvid u lečenje obolelih od melanoma za vreme pandemije COVID-19 – iskustvo jednog centra

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Abstract

Background/Aim. Despite all innovations in medicine, melanoma still has a rising incidence and high mortality and thus represents a significant challenge for the healthcare system. The pandemic of the coronavirus disease 2019 (COVID-19), spanning three years, redirected healthcare resources, suspended preventive programs, and strained the healthcare system, significantly impacting melanoma management. The aim of this study was to assess the influence of the COVID-19 pandemic on the treatment of melanoma patients. **Methods.** This retrospective study analyzed melanoma patients treated at a single tertiary care center over two distinct three-year periods: pre-COVID period (2017–2020) and the COVID-19 pandemic period (2020–2022). The following data were collected and compared: patient demographics, melanoma characteristics, time intervals from biopsy to surgery, and the share of thin and thick melanoma. **Results.** During the COVID-19 pandemic period, there was a 30% reduction in melanoma patients compared to the pre-COVID-19 period. The decline was most pronounced in 2020 when the state of emergency was introduced in the country. Thin melanoma percentage as a measurement of successful screening programs decreased significantly during the COVID-19 pandemic (11.57% vs. 24.01%), while median Breslow thickness remained stable. The distribution of different histological types was consistent across both periods. The average time from biopsy to surgery remained similar between the two periods, around 40 days. **Conclusion.** Despite challenges posed by the COVID-19 pandemic, melanoma remains a critical healthcare issue. This study emphasized the significance of prioritizing melanoma care in emergencies, ensuring patient identification and timely treatment in order to optimize survival and minimize treatment costs.

Key words:
biopsy; dermatologic surgical procedures; diagnosis; melanoma; covid-19; plastic surgery procedures.

Apstrakt

Uvod/Cilj. Uprkos svim inovacijama u medicini, za melanom se i dalje beleže porast incidence i visoka smrtnost, zbog čega predstavlja značajan izazov za zdravstveni sistem. Pandemija koronavirusne bolesti 2019 (COVID-19), koja je trajala tri godine, preusmerila je resurse zdravstvene zaštite, obustavila preventivne programe i opteretila zdravstveni sistem, što je uticalo na lečenje obolelih od melanoma. Cilj rada bio je da se proceni uticaj pandemije COVID-19 na lečenje obolelih od melanoma. **Metode.** Retrospektivnom studijom su obuhvaćeni oboleli od melanoma koji su lečeni u jednom tercijarnom zdravstvenom centru tokom dva trogodišnja perioda: pre-COVID-19 perioda (2017–2019) i perioda pandemije COVID-19 (2020–2022). Prikupljeni su i uporedeni sledeći podaci: demografske karakteristike bolesnika, karakteristike melanoma, vremenski interval od biopsije do radikalne hirurške intervencije i udeo tankih i debelih melanoma. **Rezultati.** Tokom perioda pandemije COVID-19, u odnosu na period pre pandemije, zastupljenost obolelih od melanoma je smanjena 30%. Najveći pad registrovan je tokom 2020. godine, u vreme uvedenog vanrednog stanja u zemlji. Procenat tankog melanoma, kao mera uspešnih programa skrininga, značajno se smanjio tokom pandemije COVID-19 (11,57% naspram 24,01%), dok se srednja debljina melanoma, prema skali Breslow, nije značajno promenila. Distribucija različitih histoloških tipova melanoma bila je nepromenjena u oba perioda. Prosečno vreme od biopsije do hirurškog zahvata ostalo je slično između dva perioda, oko 40 dana. **Zaključak.** Uprkos

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izazovima koje je donela pandemija COVID-19, melanom ostaje kritično pitanje zdravstvene zaštite. Ovo istraživanje je istaklo značaj davanja prioriteta lečenju obolelih od melanoma u urgentnim okolnostima, kako bi se obezbedila rana identifikacija bolesnika i njihovo pravovremeno lečenje, u cilju njihovog boljeg preživljavanja i manjih troškova lečenja.

Ključne reči:
biopsija; hirurgija, dermatološka, procedure; dijagnoza; melanom; covid-19; hirurgija, rekonstruktivna, procedure.

Introduction

Melanoma is still one of the most important health care issues, with constantly rising incidence and highest mortality of all skin cancers. It represents not only important health problems but also critical economic concerns that must be considered while creating health strategies and estimating the direct cost of treatment.

In the last three years, the pandemic of coronavirus disease 2019 (COVID-19) has redirected our focus on a new threatening disease that has almost paralyzed healthcare systems worldwide. Our country was not spared of all the problems that other wealthier countries also faced on a daily basis. All human and technical resources were allocated for treating COVID-19 patients, as our priority was keeping the COVID-19 pandemic under control. In the meantime, all preventive and educational programs for the people at risk of getting melanoma, including the screening programs, were suspended. Keeping up with the strict protocols for melanoma treatment [obtaining a biopsy of suspected skin tumors, sentinel lymph node biopsy, and surgery scheduling] was sometimes impossible, clearly exceeding healthcare system availability.

All studies confirmed a strong impact of time to definitive treatment of melanoma on overall survival. Studies confirmed that delay of surgery beyond 29 days for stage I melanoma negatively affects the overall survival of the patient [1]. The current recommendation for definitive treatment of primary melanoma is 3 to 4 weeks after diagnosis in the United States and 4 to 6 weeks in Europe [2, 3]. Postponing adequate treatment will definitely have a negative impact on the course of the disease, the disease-free period, the cost of treatments, and most importantly, the survival of the patient.

Methods

This research was designed as a retrospective study that included patients who underwent melanoma surgery in a single tertiary care center (Clinic for Plastic and Reconstructive Surgery, University Clinical Center of Vojvodina, Serbia) in two distinct periods: three-year non-COVID-19 period 2017–2019 and three-year COVID-19 pandemic time 2020–2022. The study was approved by the Ethics Committee of the University Clinical Center of Vojvodina (No. 00-217).

We compared these two periods to search for the influence of the COVID-19 pandemic on the healthcare system and melanoma patients. Patient general information (age, gender), clinical and pathohistological characteristics of melanoma (localization, type of melanoma, maximal depth of tumor in mm, time lap between biopsy of melanoma and definitive radical surgery, share of thin melanoma with maximum depth lower than 1 mm, share of thick melanoma with maximum depth greater than 4 mm) were taken from medical documentation and compared between the two groups.

Statistical analysis was performed with the SPSS 20 software. Descriptive statistics were shown using mean and standard deviation. Wilcoxon test was used to determine the existence of statistically significant differences between the two dependent samples for variables that do not follow a normal distribution. Mann-Whitney independent samples *t*-test was used to determine the existence of statistically significant differences between the two independent groups for variables that do not follow a normal distribution. All tests were performed on a 0.05 significance level unless pointed differently.

Results

Results presented in Figure 1, in the three-year pre-COVID-19 period (2017–2019), show that 356 patients underwent melanoma surgery, 30% more than in the three-year COVID-19 time (2020–2022) when 273 patients underwent the same surgery. The results also show that there were no significant differences in gender distribution between the two cohorts, pre-COVID-19 and COVID-19 time (Chi-square test was 0.0249, $p = 0.87$).

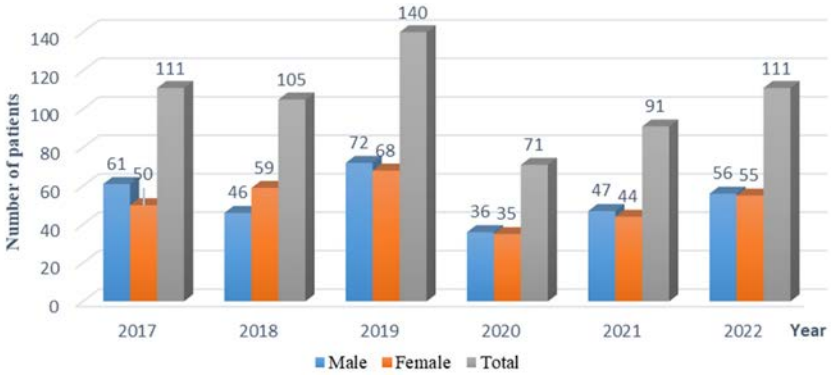

Fig. 1 – Gender distribution of patients in the pre-COVID-19 period (2017–2019) and the COVID-19 period (2020–2022).

Gender distribution in different age groups in the general sample (2017–2022) is presented in Figure 2. It shows that there is a significant difference in gender distribution with the dominance of women in younger age groups (< 50) compared with male dominance in older age groups (Chi-square test $p < 0.01$).

The number of patients who underwent melanoma surgery in 2020, according to the mount, is presented in Figure 3. There were no patients who underwent melanoma surgery in April in our hospital.

The median depth of melanoma was 2.5 mm, and, according to the Mood's median test, there was no statistically significant difference in the median values for melanoma depth *per* year, $p = 0.34$ (Table 1).

According to the Chi-square test, there was a significant difference in the presence of thin melanoma (maximal depth < 1 mm) in the pre-COVID-19 and COVID-19 time, but for a level of significance of $p < 0.1$ ($p = 0.065$) as presented in Tables 2 and 3.

The difference in the distribution of thick melanoma (> 4 mm) in pre-COVID-19 and COVID-19 periods is statistically significant ($p < 0.05$) (Table 3).

The distribution of different histological types of melanomas is presented in Table 4. According to the Chi-

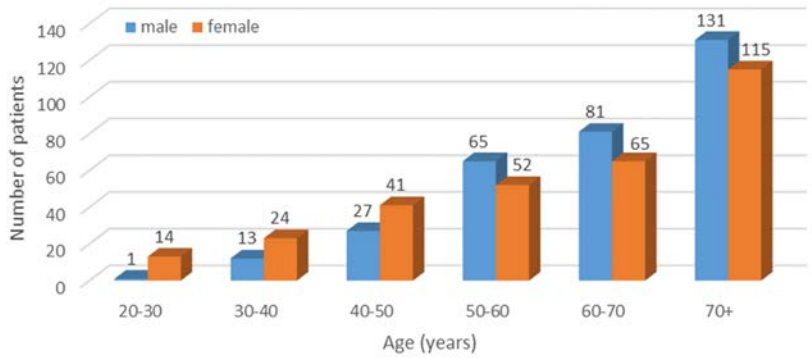

Fig. 2 – Gender distribution of patients in different age groups: dominance of women in younger age groups (< 50) vs. male dominance in older age groups ($p < 0.01$).

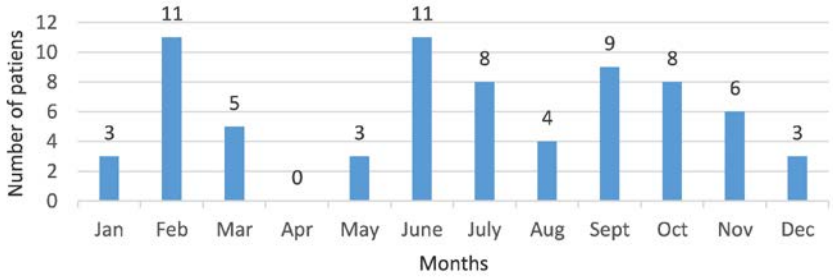

Fig. 3 – Number of patients who underwent melanoma surgery in 2020.

Table 1

Average depth of melanoma *per* year from 2017 to 2022

Parameter	Year					
	2017	2018	2019	2020	2021	2022
Melanoma depth (mm)	2.20	2.00	3.00	1.70	3.00	2.40

Values are presented as median values.

Table 2

Distribution of thin melanoma *per* year

Melanoma depth (mm)	Year					
	2017	2018	2019	2020	2021	2022
≥ 1	82	79	108	61	81	95
< 1	29	26	32	10	10	16
Total	111	105	140	71	91	111

Values are presented as numbers.

Table 3

Distribution of thin and thick melanoma in the pre-COVID-19 and COVID-19 period

Melanoma depth (mm)	Period (years)	
	2017–2019	2020–2022
Thin		
≥ 1	269 (75.56)	237 (86.81)
< 1	87 (24.44)	36 (13.19)
Thick		
> 4	134 (37.64)	77 (28.21)
≤ 4	222 (62.36)	196 (71.79)
Total, n	356	273

n – number. Values are presented as numbers (percentages).

Table 4

Distribution of different histological types of melanoma *per* year

Type of melanoma	Year						Total
	2017	2018	2019	2020	2021	2022	
Acral	2	4	5	6	2	7	26
In situ	5	2	3	1	–	2	13
LM	4	1	3	–	4	–	12
NM	37	32	44	23	41	41	218
SSM	63	66	85	41	44	61	360
Total	111	105	140	71	91	111	629

LM – *lentigo maligna*; NM – nodular melanoma; SSM – superficial spreading melanoma. Values are presented as numbers.

Table 5

Time interval between biopsy and radical surgery

Parameter	Year					
	2017	2018	2019	2020	2021	2022
Time interval (days)	40 ± 17	40 ± 19	45 ± 17	40 ± 34	37 ± 23	48 ± 35

Values are given as mean ± standard deviation.

square test, there is no statistically significant difference in the distribution of different types of melanoma during the pre-COVID-19 and COVID-19 periods ($p > 0.05$).

The time interval (in days) between biopsy and radical surgery in all examined cases is present in Table 5. Statistical analysis revealed that the average time from biopsy until radical surgery in the pre-COVID-19 period (2017–2019) was 42 days, and during the COVID-19 period (2020–2022), it was 41 days. There is no statistically significant difference in these data ($p = 0.87$). A statistically significant difference was seen only between the years 2021 and 2022 ($p = 0.04$).

Discussion

There are various perspectives when dealing with melanoma issues. Early diagnosis will obviously lead to better survival without the need to implement adjuvant therapies necessary for advanced stages. The economic burden of melanoma is also increasing, not only because of increased incidence but also because of the increased cost of treatments, primarily in advanced stages of the disease where expensive immunotherapy and targeted therapy are included. The figure that illustrates this change the best is the participation of adjuvant therapy in the overall cost of treatment of patients with melanoma. Chevalier et al. [4] published in their study from 2008, before revolutionary targeted therapy was introduced, that the chemotherapy available at that time accounted for only 17% of the total direct cost of melanoma treatment, whereas in a recent study from 2018, Buja et al. [5] stated that medical therapy accounts for 39.2% of all costs. In a situation where the healthcare system is financially overloaded with unexpected costs of treating a new threatening disease – COVID-19, it is the right moment to emphasize the importance of maintaining screening campaigns focused on detecting melanoma in the early stage in all circumstances.

Considering melanoma treatment, several new problems emerged during the COVID-19 pandemic. As the whole healthcare system was on alert, focused on COVID-19, all other non-COVID-19 medical problems were on hold, trying to avoid a crash of the system. All other segments of the healthcare system faced the necessary postponement of diagnostic and therapeutic procedures. The question for the medical community was how this temporary closure of the primary healthcare system for melanoma patients and difficult access to care would affect further clinical picture and outcome of these patients. In a great population-based modelling study conducted in England, Maringe et al. [6] tried to estimate the impact of the COVID-19 pandemic on cancer

mortality. They analyzed changes in the provision of cancer care during the pandemic, modifications of diagnostic pathways, and treatment schedules, focusing on the impact that delayed diagnosis would have on mortality and concluded that there is an increase in deaths due to cancer ranging from 4.8% for lung cancer to 16.6% for colorectal cancer. We can assume that a similar influence could be expected in melanoma patients as this highly malignant disease also requires early diagnosis in order to expect a good outcome. As shown in our study, there were 30% fewer melanoma patients in our hospital in the COVID-19 period compared to pre-COVID-19 time. Lallas et al. [7] also presented a similar decline of 36.4% during COVID-19 time in the number of melanoma patients in Greece. The drop in the number of patients was especially conspicuous in 2020, marking a 50% decline, as in that period, a state of emergency with a complete lockdown was declared. The state of emergency and lockdown was proclaimed in Serbia on March 15, and there were no patients who underwent melanoma surgery in April in our hospital. Similar trends could be seen in some other studies presenting the situation in their countries [7–9]. That certainly does not mean that melanoma as a disease "disappeared" during the COVID-19 pandemic. We suppose that people were focused on COVID-19, terrified of the deadly disease, and as melanoma does not hurt and does not look urgent, they postponed all preventive check-ups for later. Diagnosing thin melanoma requires preventive check-ups and skin biopsies, as those melanomas are usually unnoticeable. On the one hand, people postponed all "unnecessary" doctor visits, and on the other, primary medical care was mostly inaccessible for non-COVID-19 problems. Our results confirm this assumption, showing a significant decrease in the number of patients with thin melanoma compared to the pre-COVID-19 time (11.57% vs. 24.01%), even though average Breslow thickness in both cohorts did not significantly change as we expected. The majority of studies [7, 10, 11], unlike ours but like the one presented by Ungureanu et al. [12], representing the impact of the pandemic in Romania on melanoma management, marked a significant increase in the thickness of melanoma and an increased proportion of thick melanoma during the COVID-19 time. Unlike them, results presented by Ricci et al. [10], considering Italy, show a lower median thickness of melanoma during lockdown compared to the pre-COVID-19 period (0.66 vs. 0.88 mm). This could open discussion on the level of health education in different countries as it might tell us that people who are educated about health risks did not underestimate other health problems during the COVID-19 pandemic. Other studies also confirm delays in melanoma diagnosis, whose consequences are yet to be determined [12, 13]. A retrospective cohort study from five European cancer centers shows an overall increase in Breslow thickness and a significant delay in diagnosis of cutaneous melanoma [14]. Our results show that the distribution of different histological types of melanoma did not change over the years with the expected dominance of superficial spreading melanoma as described in the literature.

The question arises whether late diagnosis of melanoma, canceled screening programs, postponed radical surgical interventions after biopsy, and deprived adjuvant therapy due to hospital closures and quarantine measurements could lead to worse outcomes for patients and higher costs of treatment as a silent consequence of the COVID-19 pandemic. We shall see that in the coming years, but further studies will certainly address this problem; hence, we can try to change clinical practice during possible future pandemics. All epidemiological studies in the last decade showed a constant rise in new melanoma cases even without COVID-19, and no one could have predicted this disruption to the healthcare system and the damage that it would cause to other diseases, leading probably to the escalation of numbers in all cancer statistics [15, 16].

Our results show that the average time to definitive surgical treatment in this one-center study, before and during the COVID-19 pandemic, was similar (42 vs. 41 days). We initially expected to have a delay in radical surgery of melanoma during COVID-19 time. However, as all other elective surgeries in our hospital were canceled, oncological patients were the only patients who had at least some access to surgery. Luckily, this allowed us to keep the usual protocol for melanoma treatment.

Another unfortunate circumstance that connects these two diseases (melanoma and COVID-19) is the data suggesting that severe acute respiratory syndrome coronavirus 2 is more likely to affect older adult males with chronic comorbidities already at greater risk of melanoma [1, 17].

Employment of all medical staff in COVID-19 departments, regardless of specialty, along with quarantine measures and limited access to primary healthcare, led to some innovative solutions, like the introduction of telemedicine or some sort of teledermatology in diagnosing cutaneous malignancies. Although crisis drives innovation, we were very conservative about this idea and tried to maintain, if possible, all medical sources available for patients "face to face". Dealing with this problem, Gomolin et al. [18] clearly underline in their study the limit of teledermatology and that the consequences of falsely reassuring a person that they do not have melanoma can be fatal.

Conclusion

Following strict guidelines for melanoma treatment in times of pandemics can be challenging. As we can see with the COVID-19 pandemic, closing the health system for all other medical problems in an attempt to solve one problem creates confusion where people are uncertain about where to go and how to address their health issues. Time-sensitive nature of melanoma treatment requires that we keep our focus on this disease in all emergencies to enable expeditious patient identification and early treatment in order to provide the best survival and decrease avoidable melanoma deaths.

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