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# **COVID-19** is Affecting the Presentation and Treatment of Melanoma Patients in the Northeastern United States

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## ABSTRACT

**Background.** Covid-19 significantly affected healthcare delivery over the past year, with a shift in focus away from nonurgent care. Emerging data are showing that screening for breast and colon cancer has dramatically decreased. It is unknown whether the same trend has affected patients with melanoma.

**Methods.** This is a retrospective cohort study of melanoma patients at two large-volume cancer centers. Patients were compared for 8 months before and after the lockdown. Outcomes focused on delay in treatment and possible resultant upstaging of melanoma.

**Results.** A total of 375 patients were treated pre-lockdown and 313 patients were treated post-lockdown (17% decrease). Fewer patients presented with in situ disease post-lockdown (15.3% vs. 17.9%), and a higher proportion presented with stage III-IV melanoma (11.2% vs. 9.9%). Comparing patients presenting 2 months before versus 2 months after the lockdown, there was an even more significant increase in Stage III-IV melanoma from 7.1% to 27.5% (p < 0.0001). Finally, in Stage IIIB-IIID patients, there was a decrease in patients receiving adjuvant therapy in the post lockdown period (20.0% vs. 15.2%).

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A. C. Berger, MD e-mail: adam.berger@rutgers.edu; ab2047@cinj.rutgers.edu **Conclusions.** As a result of the recent pandemic, it appears there has been a shift away from melanoma in situ and toward more advanced disease, which may have significant downstream effects on prognosis and could be due to a delay in screening. Significantly patients have presented after the lockdown, and fewer patients are undergoing the recommended adjuvant therapies. Patient outreach efforts are essential to ensure that patients continue to receive preventative medical care and screening as the pandemic continues.

The COVID-19 pandemic significantly affected healthcare delivery over the past year, with a shift in focus toward emergent and urgent care and away from nonurgent and preventative care. Shortly following the onset of the COVID-19 in the United States, many different medical boards and societies, as well as the U.S. Surgeon General, released recommendations for the care of various types of patients during the pandemic, including cancer patients. In the setting of the COVID-19 healthcare crisis and limited resources, many activities deemed "elective" were delayed, including cancer screening and even surgical management of cancer patients.

Widely available data exist to demonstrate that screening for many cancers has dramatically decreased since the onset of the pandemic. Comparing 20 different U.S. institutions from April 2020 (during COVID-19 pandemic) with April 2019 as a control, breast and colorectal cancer screening declined by 89.2% and 84.5%, respectively.<sup>1</sup> Other studies have likewise demonstrated the negative impact on screening of breast, colorectal, and lung cancers.<sup>2–4</sup> In some reports, this has translated into fewer cancer diagnoses: endometrial cancer diagnoses are 35% lower<sup>5</sup>; newly diagnosed melanomas decreased 67% in April 2020 compared with April 2019 in one study.<sup>1</sup> A third study from Italy found that cancer diagnoses during weeks 11–20 of 2020 were 45% lower than during the same weeks of 2019, with decreased melanoma and nonmelanoma skin cancer diagnoses accounting for more than half of the missing cancers.<sup>6</sup> However, others have found that after a period of pausing screening, cancer diagnoses are much higher than before. Van Haren et al. reported that suspicious lung nodules on screening computed tomography (CT) increased from 8% pre-pandemic to 29% postlockdown.<sup>4</sup> Another study reported observations of significantly higher numbers of skin cancers post-lockdown.<sup>7</sup>

The incidence of melanoma is currently increasing faster than any other preventable cancer in the United States.<sup>12</sup> Melanoma is an aggressive disease that can have a poor prognosis. Surgery is designed to treat melanoma during the radial growth phase before nodal or distant metastasis.<sup>11</sup> There are 6,850 deaths attributable yearly in the United States to melanoma, and death rates increase corresponding with increasing tumor stage.<sup>13–15</sup> Early detection of melanoma is paramount to favorable diseasefree and overall survival.

Due to a prioritization of resources for COVID-19 and other critically ill patients, the majority of dermatology clinics were not open during the Spring of 2020 at the height of the lockdown in New Jersey and Pennsylvania.<sup>8</sup> Furthermore, the National Comprehensive Cancer Network (NCCN) published specific guidelines detailing melanoma care during the pandemic.<sup>9</sup> These included delaying treatment of T0-2 tumors up to 3 months, prioritizing T3-4 patients for resection, delaying surveillance imaging in asymptomatic stage IIB/IIC patients for at least 3 to 6 months, delaying resection of metastatic melanoma lesions unless patients were symptomatic, utilizing neoadjuvant therapy to delay surgery when possible, and converting postoperative visits to telemedicine when possible.<sup>10,11</sup> Additionally, adjuvant therapy could be delayed up to 12 weeks postoperatively, and symptom checks with medical oncology were encouraged to be converted to telemedicine visits.

Despite this emerging evidence that delays in cancer screening, largely based on breast and colorectal cancer, relates to patients presenting with more advanced cancers, it is not yet well described whether the same trend has affected patients with melanoma. The purpose of the current study is to determine whether patients with melanoma had delays in care secondary to the COVID-19 pandemic and whether these delays contributed to possible upstaging of patients.

#### METHODS

Following internal review board approval, a retrospective cohort study was performed of patients undergoing surgical management for a primary diagnosis of cutaneous melanoma at Rutgers Cancer Institute of New Jersey in New Brunswick, New Jersey and Fox Chase Cancer Center in Philadelphia, Pennsylvania, These two large-volume National Cancer Institute-designated Comprehensive Cancer Centers are located in the Northeastern United States, an area significantly affected by the current COVID-19 pandemic and subject to widespread lockdowns in the Spring of 2020. Data were collected using a combination of direct electronic medical record review and extraction from the data warehouse. Demographic data as well as timing of initial biopsy, initial surgical oncology consultation, and surgical procedures were collected. Tumor and treatmentrelated data, including detailed biopsy and surgical pathology, as well as details regarding adjuvant therapy, also were collected.

Based on the date of the initial surgical oncology presentation, patients were compared for 8 months before the lockdown (August 2019–March 2020) and after the lockdown (May 2020-December 2020). A subanalysis was performed of patients treated 2 months before the lockdown (January-February 2020) to 2 months after the lockdown (May 2020-June 2020) to capture the subset of patients most likely to have experienced cancelled medical appointments and other delays during the initial wave of COVID-19 cases in the Northeastern United States.

Outcomes focused on delay in treatment and possible resultant upstaging of melanoma. Thus, time from dermatologist visit and biopsy to initial surgical consultation and time from initial surgical consultation to definitive operation were determined. Additionally, clinical and pathologic tumor-staging information and information on adjuvant therapy was recorded. Categorical variables were compared using Fisher's exact test, and continuous variables were compared using two-sample *t* test. *p* value <0.05 was considered significant. All statistical analyses were performed using Stata SE, version 14 (College Park, TX).

#### RESULTS

A total of 688 patients underwent surgical management of melanoma at our two centers (CINJ: 489; FCCC: 199) between August 2019-December 2020. The cohort from CINJ had higher incidence of melanoma in situ (CINJ 20.0%, FCCC 8.5%) and fewer patients with more advanced disease (stage IIIA-IV: CINJ 7.4%, FCCC 17.6%) likely due to regional practice and referral patterns. Other than these differences, however, trends in the difference pre- and post-lockdown are similar between the two cohorts. A total of 375 patients were treated before the lockdown, whereas 313 patients were treated after the lockdown. This demonstrates a 17% decrease in treatment of melanoma patients post-lockdown compared with prelockdown. The mean age was 65.4 (range 22–100) years. 57.2% of the cohort was male, and 95.5% of patients were Caucasian. Insurance was private in 48.7% of patients, Medicare in 41.4%, combined private and Medicare in 5.1%, Medicaid in 2.6%, and uninsured/self-pay in 1.9%, The primary site of melanoma included: 25.4% head and neck, 40.1% truncal, and 34.3% extremity. None of these preoperative/demographic factors were different between the pre-lockdown and post-lockdown cohorts.

There was no delay in care after biopsy seen comparing the two groups, with an average 34 days between dermatologist biopsy and definitive surgery pre-lockdown and 35 days post-lockdown (p = 0.385). On subgroup analysis, no difference in care delays was seen by age. However, compared with other insurance groups, those with Medicaid did experience greater delays between dermatologist biopsy and definitive surgery (61 days pre-lockdown and 53 days post-lockdown); however, there was no increase in this delay secondary to the pandemic, and the number of patients with Medicaid in this cohort was so small (18 patients) that this was not further explored in this analysis. Additionally, we did note that several patients had significant delays in presentation to dermatology after identifying lesions at home or were delayed in their routine skin screening appointments due to the pandemic. However, this was unable to be quantified as we did not have this information available for all patients included in the study.

Despite no overall delay in care between biopsy and surgery identified due to the pandemic, fewer patients presented with in situ disease post-lockdown (15.3% vs. 17.9%, p = 0.412), and a higher proportion presented with advanced disease (stage III and IV melanoma, 11.2% vs. 9.9%, p = 0.618; Table 1). Interestingly, the presentation of advanced disease does not seem to be related to increased T-stage "upstaging" from clinical pathology (from biopsy) to surgical pathology. T-stage upstaging occurred in 8.5% of patients pre-lockdown and in 9.9% of patients post-lockdown (p = 0.596). Furthermore, subanalysis identified no trends in upstaging seen by primary disease site or by age.

In an attempt to cone down on what affects we might see for the period immediately after the most drastic lockdown conditions eased, we focused on the time period immediately surrounding the lockdown. Patients presenting to the surgeon from January-February 2020 were compared with those presenting from May-June 2020. In this immediate post-lockdown group, in situ disease was decreased to 9.8% of patients compared with 15.2% of patients immediately pre-lockdown (p = 0.452), and patients with more advanced, stage III and IV melanoma were significantly increased: 27.5% of patients compared with 7.1% (p = 0.001).

To isolate further the effects attributable to the lockdown and minimize seasonal effects on melanoma referrals and practice patterns, we additionally compared patients presenting in January and February 2019 with those presenting in January and February 2020, expecting no change in presentation patterns, as well as patients presenting in May and June 2019 with those presenting in May and June 2020, expecting to see a change. In the January/February 2019 group, there were 68 patients, 10 of whom had in situ disease (14.7%) and 11 of whom had stage III/IV disease (16.2%). In the January/February 2020 group, there were 101 patients (48.5% increase in patient presentations compared with previous year), 20 of whom had in situ disease (19.8%) and 9 of whom had stage III/IV disease (8.9%). In the May/June 2019 group, there were 72 patients, 16 of whom had in situ disease (22.2%) and 8 of whom had stage III/IV disease (11.1%). Finally, in the post-lockdown group (May/June 2020), there were only 20 patients (70.6% decrease in patient presentations compared with previous year, p < 0.001), 1 of whom had in situ disease (5.0%) and 6 of whom had stage III/IV disease (30.0%; Table 2). These findings supported the differences in presentation seen pre- and post-lockdown were not only due to seasonal variation.

Finally, in Stage IIIA-IIIC patients, a greater number of patients who were offered adjuvant therapy by medical oncology refused treatment in the post-lockdown period (20.0% pre vs. 15.2% post, p = 0.767). One additional patient was noncompliant with their adjuvant regimen during the height of the pandemic and unfortunately developed a brain metastasis 8 months postoperatively.

### DISCUSSION

The current study highlights the shift in focus away from nonurgent and preventative medical care due to the pandemic. As a result, fewer melanoma patients are presenting to surgical clinics. Furthermore, many patients have had delayed evaluation by a dermatologist and possibly a surgeon. Thus, more patients were diagnosed with later-stage melanomas, which may lead to worse prognosis. This shift is especially pronounced in the group of patients presenting in the first 2 months after the lockdown period. These patients will need to be surveilled carefully moving forward.

TABLE 1 Ch	aracteristics of	f melanoma	patients	before	and	after	lockdown
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	Pre-Covid group $(n = 375)$	Post-Covid group ( $n = 313$ )	p value
Age, yr (mean, range)	65.7 (22–100)	67.0 (29–94)	0.343
Sex, male (%)	234 (62.9%)	182 (58.1%)	0.265
Site of melanoma (%)			0.653
Head/neck	26.7	23.6	
Trunk	39.4	41.0	
Extremity	33.9	35.4	
Insurance (%)			0.152
Private	154 (41.1%)	181 (57.8%)	
Medicaid	8 (2.1%)	10 (3.2%)	
Medicare	148 (39.5%)	137 (43.8%)	
Private+Medicare	23 (6.1%)	12 (3.8%)	
None/self pay	8 (2.1%)	5 (1.6%)	
Time from biopsy to surgical consultation, days (median, range)	17 (3–439)	15 (3–198)	0.361
Time from surgical consultation to surgery, days (median, range)	23 (0-270)	22 (0-218)	0.711
Pathologic staging, %			
0	67 (17.9%)	48 (15.3%)	0.412
1a	163 (43.5%)	134 (4.3%)	0.877
1b	46 (12.3%)	45 (14.4%)	0.431
2a	27 (7.2%)	26 (8.3%)	0.667
2b	21 (5.6%)	10 (3.2%)	0.143
2c	14 (3.7%)	15 (4.8%)	0.569
3a	9 (2.4%)	8 (2.6%)	1.000
3b	7 (1.9%)	6 (1.9%)	1.000
3c	10 (5.1%)	16 (5.1%)	0.110
3d	1 (2.7%)	0 (0%)	1.000
4	1 (2.7%)	5 (1.6%)	0.097

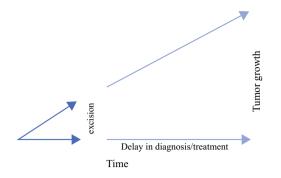
TABLE 2 Characteristics of patient presentation over time

Factor	Jan/Feb 2019	Jan/Feb 2020	% r	p value	May/Jun 2019	May/Jun 2020	% r	p value
Patients (n)	68	101	+48.5%	< 0.001	72	20	-70.6%	< 0.001
In situ, <i>n</i> (%)	10 (14.7%)	20 (19.8%)	+5.1%	0.395	16 (22.2%)	1 (5.0%)	-17.2%	0.079
Stage III/IV, n (%)	11 (16.2%)	9 (8.9%)	-7.3%	0.152	8 (11.1%)	6 (30.0%)	+18.9%	0.032

Given the strain on healthcare resources secondary to COVID-19, many melanoma surgeries were planned to be delayed 3–6 months following diagnosis. In response to these recommendations, a rate of growth model was published by Tejera et al. to demonstrate predicted melanoma growth secondary to melanoma delays<sup>14</sup> (Fig. 1). This model demonstrates a shift away from early disease and toward higher T stages as well as poorer 5- and 10-year overall survivals corresponding with delays up to 3 months. The existing literature pre-pandemic on survival outcomes following delayed surgery is sparse, and the data are mixed. A 2002 study of nearly 1,000 melanoma patients

did not demonstrate impact of time between biopsy and wide local excision on overall survival.<sup>16</sup> However, two separate National Cancer Database (NCDB) studies did demonstrate such an association: one examined stage I-III patients having surgery within or longer than 2 months following biopsy,<sup>17</sup> and another examined early-stage patients who received surgery within or longer than 30 days after biopsy.<sup>18</sup>

Delayed presentation or treatment represents a process outcome that may correspond with more advanced-stage melanomas and ultimately worse oncologic outcomes. As was the concern with delays in screening, a trend toward



**FIG. 1** Melanoma growth with diagnostic or treatment delay (adapted from Tejera et al.  $^{14}$ )

higher stage at presentation in the cohort of patients presenting post-lockdown was observed in the current study. This was similarly seen in a smaller study by Villani et al., who reported a 50% decrease in new melanoma diagnoses post-lockdown, and although there was no difference in median Breslow thickness, there was a slight trend toward invasive disease compared with in situ (56% post-lockdown compared with 44% in 2019 and 55% in 2018).<sup>19</sup> A similar trend to more advanced disease also has been reported in nonsmall-cell lung cancer in Korea with higher presentation of stage III-IV disease in 2020 (74.7%) compared with previous (2017: 57.9%, 2018: 66.7%, 2019: 62.7%).<sup>20</sup> Furthermore, the pandemic has contributed to change in treatment plan: Gasparri et al. performed a survey of European breast centers demonstrating a delay in initiation of treatment for breast cancer following diagnosis in 20% of cases and a 56% rate of treatment modification, such as upfront surgery rather than neoadjuvant therapy or postponing postoperative radiation.<sup>21</sup> Specific to melanoma, a survey of medical oncologists was performed in Italy demonstrating that surgical intervention was delayed, and while there was no delay or reduction in use of immune checkpoint inhibitors (ICIs) for melanoma patients, oncologists reported adopting the longest possible schedule of the ICIs in an effort to reduce hospital admissions.<sup>22</sup>

Unfortunately, it is likely that these effects of delayed screening will affect not only those who presented in the months following the lockdown. These delays in screening may create a "bottleneck effect," whereby there are a large number of patients eligible for screening surpasses the system capacity, creating continued downstream delays.<sup>23</sup> Once patients do get screened, it is likely that a large number of patients will need to schedule appointments for treatment and management of their (potentially upstaged) cancers, further overwhelming the system.<sup>24,25</sup> Preparing for this bottleneck and surge of cases in the upcoming months and potentially years is paramount to preventing undue morbidity and mortality caused by delays in care.<sup>26,27</sup> As such, it is critical that oncology specialists

work together with primary care providers to encourage patients to resume their normal healthcare schedules and screening.<sup>23,28</sup>

How do we address populations especially at risk for "falling through the cracks" and encourage resumption of normal healthcare visits and cancer screening? First, behavioral interventions to encourage screening and presentation to healthcare providers for concerning symptomatology is paramount.<sup>26,29</sup> These may include public awareness campaigns to assure the legitimacy of medical concerns during the pandemic and risks of cancer and safety of screening procedures on public and social media platforms as well as proactive outreach to patients due for screening.<sup>24,29,30</sup> In-person screening should be safe (following masking and social distancing when possible), and telemedicine should be utilized when possible.<sup>30–32</sup> Specific to melanoma, Villani et al. suggest screening campaigns consistent with patient education on sun protection and self-examination on relevant media platforms and advertising of large, free-screening events.<sup>8</sup>

This study has several limitations. First, it is a retrospective cohort study, and although there were no statistically significant differences between the two groups, there may be unmeasured differences inherent to the study design. Second, these results are from two high-volume NCI-designated Comprehensive Cancer Centers in the Northeastern United States and thus may not be generalizable to other parts of the country or other institutions. Additionally, given the short time period of the study, the number of patients may have left the study underpowered to determine differences in outcomes. Although many differences in outcomes were not statistically significant, we do believe these trends are worth reporting given the novelty of the current situation and possible downstream effects for patients with melanoma during the current healthcare crisis. As such, the current study is limited by the inability to study survival outcomes. We hope in the future to continue to follow these patients and the pandemic's effect on overall survival and disease recurrence. We were not able to quantify what delays may have occurred in patients getting into the dermatology offices, because we did not have access to that data for all patients. Finally, although multiple, temporal comparisons were made to try to isolate the lockdown as a potential cause for change in patient presentations, other factors may have been unmeasured by the current study affecting these results.

Ultimately, it is up to the judgment of the surgeon and other care providers to weigh the risks and benefits of surgery and other treatments during a precarious time, such as the COVID-19 pandemic.<sup>33</sup> Cancer surgery, while often not urgent/emergent, also is not "elective." Intervention

planning should consider risk of delay to the patient and risk to patient of hospital exposure, as well as risk of exposure of hospital personnel and their contacts.

#### CONCLUSIONS

The recent pandemic has shifted focus away from nonurgent medical care. As a result, it appears that more and more patients with melanoma are presenting with advanced disease at diagnosis, which may have significant downstream effects on prognosis. Significantly fewer melanoma patients have presented after the lockdown, and fewer patients are undergoing the recommended adjuvant therapies. Although there does not appear to be a delay from time of biopsy to surgery, there may be delay in routine dermatology visits and obtaining biopsies of skin lesions. We also may see more disparity as the pandemic progresses. Patient outreach efforts are essential to ensure that patients continue to receive preventative medical care as the pandemic continues. Future studies will attempt to examine whether there is a "bottleneck effect" that leads to additional delays in presentation and diagnosis.

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