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Advanced stage melanoma at presentation following the peak of the pandemic: a COVID-19 cancer canary in a coal mine

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Abstract

Background: For melanoma patients, timely identification and tumor thickness are directly correlated with outcomes. COVID-19 impacted both patients' ability and desire to see physicians. We sought to identify whether the pandemic correlated with changes in melanoma thickness at presentation and subsequent treatment timeline.

Methods: Retrospective chart review was performed on patients who underwent surgery for melanoma in an academic center surgical oncology practice from May 2019 – September 2021. Patients were split into two cohorts: “pre-pandemic” from May 2019 to May 2020 and “pandemic,” after May 2020, representing when these patients received their initial diagnostic biopsy. Demographic and melanoma-specific variables were recorded and analyzed.

Results: 112 patients were identified: 51 patients from the “pre-pandemic” and 61 from the “pandemic” time period. The pandemic cohort more frequently presented with lesions greater than 1mm thickness compared to pre-pandemic (68.8% v 49%, $p=0.033$) and were found to have significantly more advanced T stage ($p=0.02$) and overall stage disease ($p=0.022$). Additionally, trends show that for pandemic patients more time passed from patient-reported lesion appearance/change to diagnostic biopsy (5.7 ± 2.0 v 7.1 ± 1.5 months, $p=0.581$), but less time from biopsy to operation (42.9 ± 2.4 v 52.9 ± 5.0 days, $p=0.06$).

Conclusions: “Pandemic” patients presented with thicker melanoma lesions and more advanced stage disease. These results may portend a dangerous trend toward later stage at presentation, for melanoma and other cancers with rapid growth patterns, that will emerge as the prolonged effects of the pandemic continue to impact patients' presentation for medical care.

Introduction

No one could have predicted what was to come with the advent of the SARS-CoV-2, COVID-19 (COVID), pandemic. Beyond the catastrophic toll of the number of cases and deaths, the COVID pandemic has inflicted a tremendous secondary effect on population health in the preventative care fields and health screenings. Various lockdowns and restrictions around the nation and re-prioritization of medical resources effectively ceased many preventative care practices including cancer screening [1]. Another effect of the pandemic has been a decrease, estimated at 40% or more, of face-to-face interactions between primary care physicians (PCPs) and patients [2]. Additionally, in the northeast of the United States (New Jersey, Delaware, and Pennsylvania) there was temporary closure of dermatologists' offices which prevented in person screening and care [3]. Considering PCPs and dermatologists are often the "gatekeepers" for timely diagnosis and treatment for diseases such as melanoma, this undoubtedly affected screening, diagnosis, and treatment during the pandemic worth investigating [4].

Melanoma tumor thickness is directly correlated to its disease-specific 10-year survival rates [5]. Additionally, timely screening leading to earlier identification and diagnosis is proven to result in thinner, or earlier stage, melanomas with superior outcomes [6]. Compounding this issue of screening in the COVID pandemic, was the fact that many patients showed hesitancy to present to their healthcare provider for issues unrelated to COVID, with one study estimating that percentage ranging from 37-45% [7]. Updated recommendations and guidance were given for surgical treatment of melanoma during the pandemic but that guidance could not have accounted for patient preference or access for initial lesion evaluation in regional offices that were forced to close [8]. While some studies have predicted that the pandemic would create access issues for patients with melanoma, few have reported on the actual effects seen in the US [8, 9].

Areas of the country that were particularly impacted by COVID-19 were affected by both the forced closure of physicians' offices and patients' hesitancy to visit their physician for

changes in skin lesions. In this study we sought to identify if there were differences in melanoma thickness at presentation between pre-pandemic and pandemic patient cohorts. Our hypothesis was that due to the aforementioned reasons, melanoma patients would have thicker, more advanced lesions in the pandemic cohort. Moreover, we attempted to elucidate where the delay was resulting from in the screening, diagnosis, and treatment timeline by measuring the time between changes noticed by the patient in their melanoma lesions, shave biopsies, initial office visits with their surgeon, and eventual operation.

Methods and Materials

This study was determined to be exempt by the Institutional Review Board of Thomas Jefferson University in 2021 (45 CFR 46.101; Control #21E.813).

Inclusion and Exclusion Criteria and Data Collection.

A retrospective chart review was performed on patients referred for surgical oncology treatment of biopsy-proven melanoma to a single surgical oncology practice at an academic medical center. The study dates were July 2019 – September 2021. Patients were divided into two cohorts: “pre-pandemic” from May 2019 to May 2020 and “pandemic,” after May 2020. These dates represented when the patients received their biopsy. Inclusion criteria included: patients receiving surgery for melanoma. Exclusion criteria included a previous diagnosis of melanoma and surgery solely for a site of metastatic melanoma.

Demographic data was recorded including age, gender, race, ethnicity, insurance status, as well as personal or family history of any skin cancer.

Melanoma Tumor Characteristics and Diagnosis and Treatment Timeline Outcomes.

Melanoma-specific tumor characteristics were recorded and analyzed. These included melanoma tumor thickness of lesion, histology, presence of ulceration, TNM staging, and overall staging [10]. In cases where the thickness measured on shave biopsy and final wide local

excision differed, the larger thickness was used for staging and analysis. The anatomic location of the melanoma was recorded.

The time in days from initial biopsy to surgeon's office as well as surgeon office visit to operation were collected. When available, time in months between when the patient reported noticing a lesion/change in lesion and biopsy was recorded.

Statistical Analysis.

Chi-square and Welch's *t* test were used to compare categorical and continuous outcome variables, respectively. For all comparisons two-sided statistical significance was set a priori at $p < 0.05$. All statistical analyses were performed using Stata/MP 17.1 (Statacorp, College Station, TX).

Results

Demographics.

One hundred and twelve patients met inclusion criteria for analysis. There were 51 patients in the "pre-pandemic" cohort and 61 patients in the "pandemic" cohort. There were no significant differences between the cohorts in the age, sex, race, ethnicity, or insurance status of the patients (TABLE 1). In addition, there were no statistically significant differences between the cohorts in personal history or family history of any skin cancers or histology type of the melanoma lesion at time of diagnosis (TABLE 1).

Melanoma Tumor Characteristics.

The pandemic cohort more frequently presented with melanoma lesions thicker than 1mm compared to pre-pandemic (68.8% v 49%, $p=0.033$) (TABLE 2). The pandemic cohort also more frequently presented with melanoma lesions with greater T stages compared to pre-pandemic ($p=0.02$) (TABLE 2). Additionally, on final pathology there was a statistically significant difference in distribution of overall stage using the American Joint Committee on

Cancer (AJCC) TNM staging system 8th edition, with 49.0% of patients presenting at overall stage greater than Stage 1A in the “pre-pandemic” cohort compared to 68.9% in the pandemic cohort ($p=0.022$) (TABLE 2) [10]. There were no statistically significant differences in presence of ulceration, N stage, and M stage (TABLE 2). Although there was no significant difference in location of melanoma between the cohorts, it is notable that the pandemic cohort had an increased percentage of anterior trunk and upper extremity melanomas with a decreased percentage of posterior trunk melanomas (TABLE 2).

Diagnosis and Treatment Timeline Outcomes.

In the pandemic cohort, trends showed a strong, but insignificant trend towards less time passed from biopsy to operation (42.9 ± 2.4 v 52.9 ± 5.0 days, $p=0.06$) and from initial office visit with a surgeon to operation (21.0 ± 1.3 v 27.5 ± 3.6 days, $p=0.06$) (TABLE 3). Interestingly a non-significant trend was found for longer patient-reported time between patients’ noticing a change in their lesion to initial diagnostic biopsy (5.7 ± 2.0 v 7.1 ± 1.5 months, $p=0.581$) (TABLE 3).

Discussion

The temporary closures and limited access to outpatient primary care and subspecialty practices brought on by the COVID-19 pandemic presented a new barrier to healthcare for patients outside of the traditional social determinants of health, especially in the northeast of the country [3]. However, in the case of melanoma, where demographic factors are relatively uniform, the effects of the pandemic serve as a noteworthy example of how access barriers can result in later stage of disease at presentation. In particular, it highlights how the effect of barriers to healthcare can impact patients prior to their interaction with the medical system.

Our study of a population of patients treated at an academic medical center, in a region of the United States that was particularly impacted early in the pandemic, identified a significant trend towards thicker melanoma lesions and later stage overall disease associated with the pandemic. Another subtle, but noteworthy finding, was that in our study we observed relatively

more lesions in areas easily visualized by patients (i.e., upper extremity, anterior trunk) and less lesions in those classically picked up by physicians (i.e., posterior trunk/flank) during the pandemic. We also began to clarify what level of the care process most impacted the diagnosis and treatment of these melanoma patients. Initially, the decreased time between diagnosis and treatment in our study may be counterintuitive, but upon further contemplation is likely explained by the tier prioritization system enacted by many institutions globally and in the US, which placed emergency surgeries *as well as* cancer-related operations in the highest tiers [11]. Our university hospital prioritized the surgical care of trauma, acute care, and cancer patients throughout the height of the pandemic. Our surgical practice markedly increased the utilization of telehealth for office visits to provide care while minimizing exposures. Interestingly, our results demonstrate that these prioritization efforts during the height of the pandemic were associated with a decrease in time between diagnostic biopsy and date of surgery as well as time between the initial surgeon's office visit and date of surgery for patients with malignant melanoma. All of these findings highlight the complexity of barriers to access within the medical system as well as the positive potential for prioritization efforts and technology to improve efficiency of care delivery.

In the context of timely cancer screening and treatment, melanoma represents a uniquely aggressive, routinely monitored cancer diagnosis. Specifically, doubling time for melanoma is estimated to be around 94 days [12] as compared to 241 days for invasive breast cancer [13], 440 days for 600 days for lung adenocarcinoma [14], and 936 days for colorectal adenocarcinoma [15]. Our study sought to characterize the early pandemic effects given the knowledge that this cancer would present itself earliest based on rapid growth pattern. In addition, it was selected to serve as a warning for slower growing cancer diagnoses that will inevitably be affected by the continued backlog of cancer screening and patient hesitation to return for routine health screenings caused by the pandemic and its aftereffects.

Increased tumor thickness is a well reported prognostic factor for melanoma outcomes [16]. Our findings of a significant increase in presentation of melanomas with greater than 1 mm in thickness and greater overall stage are consistent with those reported by Ricci *et al* who observed an increase in melanoma thickness amongst Italian patients during their pre-pandemic phase from 0.88mm to 1.96mm during the pandemic [17]. Interestingly, they also found an increase in ulceration rates from 5.3% to 23.5%, which was not present in our cohort [17]. Of note, Ricci *et al* also measured the number of new diagnoses of melanoma per day, which decreased from 2.3 pre-pandemic, to 0.6 during the height of the pandemic, and rose only to 1.3 as the pandemic restrictions decreased [17]. This lends evidence to our concern that the true deficit in these patients receiving timely treatment during the pandemic is time to diagnosis as opposed to time between diagnosis and treatment.

Several helpful guidelines have been published on the surgical management of malignant melanoma once diagnosed in the context of the resource-limited pandemic [18-21]. However, there exists a paucity of data and guidelines on how to bolster screening efforts during these times [8, 22]. We suggest that disease-specific screening guidelines should be created for melanoma among dermatologic, surgical, and cancer-related societies, to prepare for a potential *next* practice-altering event. These may include promoting telehealth visits to assess lesions that may be high risk and warrant a timely in-person office visit for biopsy.

Limitations of the study include that it is of a single academic institution in a region that was impacted early and throughout the pandemic. While the generalizability of these findings remains to be seen, we believe that these trends will likely persist in larger scale studies which will inevitably be published in the years to come. Second, some of our findings, namely the time between patient-reported lesion change and diagnosis/treatment variables, failed to reach significance due to a lack of power with limited numbers of patients able to recall noticing their lesion change as well as the potential for recall bias. Finally, our study was retrospective in nature and, thus, can be subject to the biases associated with these types of studies.

Conclusions

In this study we identified that patients presenting with melanoma during the height of the pandemic had thicker lesions and presented at more advanced stages of melanoma. Based on the results of this study, this concerning trend is more likely related to patients' hesitancy or barriers to present to the healthcare setting during the pandemic since the times from diagnostic biopsy and initial surgeon's office visit to operation were both shorter during the pandemic. It will be important in the coming months and years to closely surveil for patients who may have been lost to follow up in terms of their cancer screening. These findings of advanced stage, thick melanomas may serve as the proverbial canary in a coal mine associated with lack of screening and decreased access to care, as well as serve as an example of the need for screening guidelines in pandemic or resource-limited circumstances.

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Tables

Table 1. Demographic data for "pre-pandemic" and "pandemic" patient cohorts

	Pre-pandemic (n = 51)	Pandemic (n = 61)	P value
Age (years), Mean \pm SD	61.3 \pm 2.09	63.0 \pm 1.98	0.541
Female Sex, N (%)	19 (37.3)	29 (47.5)	0.273
White Race, N (%)	49 (96.1)	60 (98.3)	0.456
Non-Hispanic Ethnicity, N (%)	50 (98.0)	59 (96.7)	0.667
Insurance Status, N (%)			0.419
Medicare	22 (44.9)	20 (32.8)	
Medicaid	1 (2.0)	2 (3.3)	
Private	26 (53.1)	39 (63.9)	
Personal History of Skin Cancer, N (%)	16 (31.4)	18 (29.5)	0.669
Family History of Skin Cancer, N (%)	13 (26.0)	18 (29.5)	0.682
Histology, N (%)			0.181
Superficial Spreading	19 (37.3)	17 (27.9)	
Nodular	12 (23.5)	14 (22.9)	
Lentigo Maligna	6 (11.8)	2 (3.3)	
Acral Lentiginous	1 (1.9)	3 (4.9)	
Other	13 (25.5)	25 (41.0)	

Abbreviations: SD = standard deviation

Table 2. Melanoma tumor characteristics for “pre-pandemic” and “pandemic” patient cohorts

	Pre-pandemic (n = 51)	Pandemic (n = 61)	P value
Thickness > 1mm, N (%)	25 (49.0)	42 (68.8)	0.033*
Ulceration Present, N (%)	15 (29.4)	17 (27.9)	0.857
T Stage, N (%)			0.02*
Tis	5 (9.8)	3 (4.9)	
T1	22 (43.1)	16 (26.2)	
T2	15 (29.4)	21 (34.4)	
T3	5 (9.8)	12 (19.7)	
T4	4 (7.8)	9 (14.8)	
N Stage, N (%)			0.322
N0	48 (94.1)	54 (88.5)	
cN0	23 (47.9)	19 (35.2)	
pN0	25 (52.1)	35 (64.8)	
N1	3 (5.9)	3 (4.9)	
N2	0 (0)	3 (4.9)	
N3	0 (0)	1 (1.7)	
M Stage, N (%)			0.119
M0	49 (96.0)	61 (100)	
M1	2 (4.0)	0 (0)	
Overall Stage, N (%)			0.022*
0	5 (9.8)	2 (3.2)	
1A	21 (41.2)	17 (27.9)	
1B	10 (19.6)	16 (26.2)	
2A	8 (15.7)	5 (8.2)	
2B	1 (2.0)	9 (14.8)	
2C	3 (5.9)	5 (8.2)	
3	1 (2.0)	7 (11.5)	
4	2 (3.8)	0 (0)	
Location of Melanoma Lesion, N (%)			0.41
Head/Neck	6 (11.8)	7 (11.5)	
Upper Extremity	15 (29.4)	24 (39.3)	
Lower Extremity	13 (25.5)	15 (24.6)	
Posterior Trunk/Back/Flank	15 (29.4)	10 (16.4)	
Anterior Trunk	2 (3.9)	5 (8.2)	

* denotes statistical significance; Abbreviations: SD = standard deviation

Table 3. Diagnosis and Treatment Timeline for "pre-pandemic" and "pandemic" patient cohorts

	Pre-pandemic (n = 11)	Pandemic (n = 20)	P value
Change in Lesion to Biopsy (months), Mean \pm SD	5.7 \pm 2.0	7.1 \pm 1.5	0.581
	Pre-pandemic (n = 51)	Pandemic (n = 61)	P value
Biopsy to Initial Office Visit with Surgeon (days), Mean \pm SD	25.5 \pm 4.0	22.2 \pm 2.0	0.451
Biopsy to Operation (days), Mean \pm SD	52.9 \pm 5.0	42.9 \pm 2.4	0.060
Initial Office Visit with Surgeon to Operation (days), Mean \pm SD	27.5 \pm 3.6	21.0 \pm 1.3	0.060

Abbreviations: SD = standard deviation