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Effect of the COVID-19 Pandemic on Delayed Skin Cancer Services

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KEYWORDS

• Surgical delay • Evidence-based guidelines • Time to surgery • Skin cancer • COVID-19 • COVID-19 delays • Survival

KEY POINTS

- Guidelines during the pandemic suggest that surgical treatment of melanoma in situ may be deferred for up to 2 to 3 months, with priority given to T1-T4 lesions.
- Operating rooms should be used sparingly during lockdown periods to limit potential virus transmission and to maximize ventilator capacity.
- Sentinel lymph node biopsy may be delayed for certain skin cancers according to the NCCN guidelines.
- Dermatologists should evaluate skin cancer lesions on a case-by-case basis when following these guidelines.
- Longer term studies are needed to determine if the COVID-19 lockdown had any impact on skin cancer outcomes.

INTRODUCTION

The COVID-19 pandemic has dramatically impacted implementation of health care services in the United States. Since the first reported US cases in January 2020, the virus has surpassed 25 million infections causing more than 525,000 deaths nationally. A state of emergency was declared by the World Health Organization on March 11, 2020, followed shortly in the United States with state-sanctioned lockdown orders starting from March 19, 2020.[1] During lockdown, hospitals reported a substantial decrease in surgical volume when compared with previous years to accommodate pandemic-related medical resources and personnel.[2] As a result, health care systems have been pressured to manage essential supplies and human capital while mitigating risk of viral transmission.[3]

For all patients with cancer, many faced delays in obtaining a diagnosis, whereas others experienced delays in starting or maintaining treatment.[2–4] Patient compliance toward scheduled but deferable visits also reportedly contributed to these totals.[5] For skin cancer, the total number of lesions diagnosed and treated during lockdown periods decreased, with clinical priority given to tumors with high-risk histopathologic features.[6–9] To date, we could not find any studies reporting outcomes for patients with skin cancer affected by COVID-19.

Evidence-based recommendations from several dermatologic research centers have been proposed to facilitate delivery of care to patients with skin cancer.[10–14] In this review, we summarize available 2020 pandemic guidelines from the National Comprehensive Cancer Network (NCCN), the American College of Mohs Surgery (ACMS), the European Society of Medical Oncology, Society of Surgical Oncology (SSO), the British Association of Dermatologists (BAD), and the British Society for Dermatologic Surgery

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(BSDS) and describe the general impact of COVID-19 on skin cancer diagnosis and treatment recognizing that information regarding the impact on long-term outcomes is still limited. Although these guidelines were written for COVID-19 surges and may not be active at the time of this publication, future surges with potentially new COVID-19 variants or new viruses may lead to a reactivation of these recommendations.

MELANOMA TREATMENT GUIDELINES DURING THE PANDEMIC

In 2020, melanoma comprised approximately 5.6% of all US cancer cases, and caused most deaths from skin cancer.[15,16] The risk of metastasis is approximated by histopathologic features, such as primary tumor thickness, ulceration, anatomic location, and regional lymph node involvements.[17] Mortality has been shown to vary significantly based on pathologic stage. From 2010 to 2016, Surveillance, Epidemiology, and End Results data showed a 5-year survival rate of 99% and 66% in localized and regional disease, respectively, and 27% for melanomas with distant metastases.[18]

Skin cancers diagnosed during lockdown also differed from prelockdown tumors in several notable ways. Ricci and colleagues[19] compared histopathologic features for melanomas diagnosed before and after Italy's 54-day lockdown period and observed increased thickness (mean thickness of 0.88 mm and 1.96 mm, respectively), ulceration (odds ratio [OR], 4.9; 95% confidence interval [CI], 1.4–17.3), and nodular subtype (OR, 5.5; 95% CI, 1.3–25.1) in postlockdown melanomas compared with prelockdown melanomas. Although these factors have been previously described as independent adverse prognostic factors, further investigation is required to thoroughly characterize and examine the effect of pandemic delays on long-term survival.[12,20]

Wide local excision (WLE) remains the mainstay treatment of early and localized lesions. Current guidelines recommend 1-cm margins for melanomas less than or equal to 2 mm, and 2-cm margins for thicker lesions greater than 2 mm.[21] In the absence of delays, complete surgical excision should be performed 4 to 6 weeks after the initial diagnosis. Mohs surgery is used for melanomas with poorly distinguished visible margins (ie, lentigo maligna melanoma and acral melanoma), including those in cosmetically sensitive areas.[22]

Appropriate intervals for melanoma time to definitive surgery have been widely studied, although there is a lack of consensus.[23] A 2020 literature review of surgical delay and mortality in primary cutaneous melanoma yielded five total studies that addressed surgical delays of 1 month or longer.[24] From this sample, only two studies reported an association between delayed WLE and poor survival outcomes, both of which derived samples from the National Cancer Database. Conic and colleagues[25] stratified National Cancer Database melanomas by pathologic stage and discovered a significant mortality risk among stage 1 melanomas exclusively (30–50 days: hazard ratio, 1.05; 95% CI, 1.01–1.1; 60–89 days: hazard ratio, 1.16; 95% CI, 1.07–1.25). Basnet and colleagues[26] independently found a significant increase in overall survival for time to definitive surgery intervals less than 60 days, compared with after 60 days.

According to the NCCN, surgical treatment of T0 (melanoma in-situ) and T1 melanomas could have been delayed during pandemic surges for up to 3 months, with priority given to T3 and T4 melanomas.[14] If a substantial proportion of residual lesion remained after biopsy for T1 melanomas, then a complete biopsy with narrow surgical margins or elliptical excision with 1-cm surgical margins was recommended. In the setting of limited operating room capacity, sentinel lymph node biopsy (SLNB) for lesions greater than 0.8 mm were recommended for deferral for up to 3 months. For melanomas staged N1 and higher, the NCCN recommended deferral of lymphadenectomy if regional lymph nodes were palpable. Likewise, the BAD and BSDS suggested deferral of WLE for stage T0 and T1a melanomas based on histopathologic features of the biopsy.[11] The ACMS suggested deferral of melanoma in situ for up to 2 to 3 months, and reiterated NCCN guidelines for management of T0 and T1a melanomas.[12] The European Society of Medical Oncology endorsed a tiered system (high, high/medium, low) for guidelines based on value-based prioritization.[27] High priority surgeries included any curative resection for stage III lesions, procedures associated with neoadjuvant trials. High/medium priority surgeries included WLE and SLNB for new invasive melanomas staged T1b or higher, WLE alone for T1a or lower tumors, and resection of oligometastatic disease. There were no surgeries designated in the low priority category. Lastly, the SSO endorsed a case-by-case evaluation of melanomas before surgery.[28] WLE for T0 melanomas could have been deferred for up to 3 months. Surgical treatment of T3 and T4 melanomas held priority over T1 and T2 melanomas, although gross complete resection recommended for any melanoma with a large degree of residual lesion present because of incomplete biopsy. SLNB should have been performed for lesions

with greater than 1 mm thickness and could otherwise be deferred for up to 3 months. The SSO guidelines included precise language to recommend documentation of tumor anatomic location in the event of surgical delay and encouraged that surgeries occur in the outpatient setting. Pandemic guidelines for all skin cancers are summarized in **Table 1**.

KERATINOCYTE CANCER TREATMENT GUIDELINES DURING THE PANDEMIC

Keratinocyte cancers (KC), primarily comprised of basal cell carcinomas (BCC) and squamous cell carcinomas (SCC), represent the most common malignancy in fair-skinned populations.[29] Predisposing factors for KCs include chronic exposure to UV radiation, male gender, and an immunocompromised state. Risk of metastasis correlates to histologic factors, such as subtype (eg, superficial, nodular, or infiltrative) and depth of the primary tumor.[15,16] Generally, BCCs are slow-growing tumors that have a small estimated risk of metastasis (0.003%–0.55%),[30] whereas SCCs are fast-growing tumors with considerable likelihood to metastasize (0.5%–16%).[31]

Primary management for KC includes WLE, electrodessication and curettage, and Mohs micrographic surgery. Mohs surgery has been shown to be the most effective treatment modality for high-risk or recurrent KC in some reports.[17] A meta-analysis of treatments used in KC reported an aggregated 5-year cure rate of 99% and 97% for previously untreated BCC and SCC, respectively.[32] A more recent prospective study from the Netherlands found no statistical difference in recurrence rates between surgical excision and Mohs surgery for treatment of BCC.[33] For SCC in particular, surgical delays longer than 18 months were associated with significantly increased likelihood of thicker and invasive tumors (OR, 4.18; 95% CI, 2.45–7.13), although this association is not yet well-established for delays relevant to pandemic lockdown periods.[20]

The NCCN recommended deferral of KC, including BCC, SCC, dermatofibrosarcoma protuberans, and other rare tumors, unless the physician estimated a high risk of metastasis or debilitating progression within 3 months. Following local excision, adjuvant therapy should be postponed for N0 and N1 tumors without extension invasion of large caliber nerves. The ACMS recommended deferral of BCC management for up to 3 months for small and well-differentiated lesions unless the patient was symptomatic.[12] Deferral of slowly enlarging and well-differentiated SCC/SCC in situ was also recommended, although no discrete time period is suggested. SCC that was symptomatic or contained significant risk factors, such as rapid growth, poor differentiation, ulceration, and perineural invasion, should have been prioritized. The BAD and BSDS recommended deferring surgical excisions of BCC for 3 to 6 months unless the patient was highly symptomatic or endorsed high potential for significant growth.[11] Surgical treatment of SCC/SCC in situ that were small and well-differentiated may have also been reasonably deferred unless the lesion demonstrated rapid growth, poor differentiation, ulceration, and/or perineural invasion. High-priority lesions should have been carefully evaluated on a case-by-case basis to assess the risks and benefits of treatment with the concurrent risk of COVID-19 exposure.

MERKEL CELL CARCINOMA TREATMENT GUIDELINES DURING THE PANDEMIC

Merkel cell carcinoma (MCC) is a highly aggressive neuroendocrine-derived skin cancer that resides within the basal layer of the epidermis (eg, deep skin and hair follicles).[34] This lesion commonly affects individuals who are elderly (median age of diagnosis, 75–80 years) and immunocompromised.[35,36] These underlying conditions have been associated with increased risk of requiring intensive care because of COVID-19,[37] thus extra precautions should be taken during treatment to limit potential exposure to the virus in this patient population.

Treatment of MCC requires careful consideration of tumor stage and patient-specific factors. WLE with clear margins is performed to prevent local recurrence and regional metastasis of early stage tumors, although has not been shown effective in stand-alone treatment.[38,39] Mohs micrographic surgery has been recommended to effectively remove smaller lesions in cosmetically sensitive areas, or to monitor local recurrence during adjuvant therapy.[40] To note, Brisset and colleagues[41] reported lower survival of patients treated with Mohs excision when compared with those treated with radical excision supplemented by cervical block dissection, although the chart review was limited to 22 patients. Surgical treatment is usually accompanied by adjuvant radiation therapy, particularly in patients suspectable to local-nodal recurrence. Because of the high-risk nature of the lesion, there are limited studies available to date that describe outcomes related to surgical delay in MCC.

According to the NCCN, treatment should not have been deferred because of the COVID-19

Table 1
Summary of surgical treatment guidelines for skin cancer

		NCCN[10,14]	BAD/BSDS[11]	ACMS[12]	ESMO[27]	SSO[28]
MCC		Do not defer treatment with the exception of lesions <1 cm in elderly populations. Given low OR capacity, delay SLNB from excision if wound is allowed to granulate.	Prioritize rapidly enlarging tumors, poorly differentiated tumors, perineural tumors, ulcerated and symptomatic lesions.			
KC	BCC	Defer up to 3 mo unless the physician estimates a high risk of metastasis or debilitating progression.	Defer up to 3–6 mo unless the patient is highly symptomatic or endorses high potential for significant growth.	Defer up to 3 mo for small and well-differentiated lesions unless the patient is symptomatic.		
	SCC	Defer up to 3 mo unless the physician estimates a high risk of metastasis or debilitating progression.	Defer SCC/SCC in situ unless the lesion demonstrates rapid growth, poor differentiation, ulceration, and/or perineural invasion.	Prioritize SCC that are symptomatic or contain significant risk factors, such as rapid growth, poor differentiation, ulceration, and perineural invasion.		

Melanoma	Defer T0/T1 melanomas up to 3 mo, with priority given to T3/T4 melanomas. Prioritize complete biopsy with narrow surgical margins or elliptical excision with 1 cm surgical margins if large amount of residual lesion remains. Given low OR capacity, defer SLNB >0.8 mm for up to 3 mo. Defer lymphadenectomy for N1+ tumors if regional lymph nodes are palpable.	Defer T0/T1a melanomas based on histopathologic features.	Defer T0 up to 2–3 mo. Defer T0/T1a melanomas based on histopathologic features.	High priority: any curative stage III melanoma resection, procedures associated with neoadjuvant trials, procedures addressing postsurgical complications. High/medium priority: WLE and SLNB for new invasive melanomas staged T1b or higher, WLE alone for T1a or lower tumors, and resection of oligometastatic disease.	Defer T0 up to 3 mo, with priority given to T1/T2 melanomas Prioritize gross complete resection for residual lesion in the setting of incomplete biopsy. SLNB performed only for >1 mm melanomas, otherwise defer for up to 3 mo.

Guidelines uniformly endorse urgent surgical excision, particularly for when high-risk features, such as increased thickness, poor differentiation, ulceration, and/or perineural invasion, are present. When evaluating a biopsy for high-risk features, specimen size and depth should be appropriate to provide the recommended clinical information.

Abbreviations: ACMS, American College of Mohs Surgery; BAD/BSDS, British Association of Dermatologists/British Society for Dermatological Surgery; BCC, basal cell carcinoma; ESMO, European Society of Medical Oncology; KC, Keratinocyte cancer; MCC, Merkel cell carcinoma; NCCN, National Comprehensive Cancer Network; OR, operating room; SCC, squamous cell carcinoma; SLNB, sentinel lymph node biopsy; SSO, Society of Surgical Oncology; WLE, wide local excision.

Table 2
Synopsis of studies for the impact of COVID-19 on skin cancer outcomes

Paper	Study Characteristics	Key Findings
Barruscotti et al, 2020[6]	Retrospective review of all surgical excisions performed in the dermatologic surgery room at Fondazione IRCCS Policlinico San Matteo from February 22–May 3, 2020 (n = 163).	Melanoma diagnoses in the 2020 lockdown period was reduced 60% from previous years (prevalence, 3.7%; 95% CI, 1–8). 30% relative decrease in all dermatologic surgical activity.
Earnshaw et al, 2020[7]	Retrospective review of a cancer tracking database in the UK from February to April 2020.	34.3% reduction in urgent skin cancer referrals during the study period. Largest decrease observed in April 2020 (56.4% lower cases than April 2019). Lower total skin cancers diagnosed in March 2020 compared with previous years.
Nolan et al, 2020[8]	Prospective cohort of patients undergoing skin cancer surgery from 32 plastic surgery units in the United Kingdom from March 16–June 14, 2020 (n = 1549). Retrospective patient data on melanoma surgery (March 23–June 14, 2020) from 20 plastic surgery units (n = 501).	Treatment of KC decreased by 27%–47% throughout April and May 20. SCCs prioritized over BCCs, and at the pandemic's peak SCCs comprised 71% of excisions. 77% of Mohs micrographic surgeons stopped procedures.
Filoni et al, 2021[9]	Retrospective review of all dermatologic and surgical activity performed in an Italy-based melanoma skin unit from February 23–May 21, 2020.	When compared with the previous calendar year, surgical excisions during lockdown increased 31.7% and SLNBs decreased 29%. Dermatologic follow-up decreased 30.2%, whereas surgical follow-up decreased 37%.
Ferrara et al, 2021[4]	Standards-based audit retrospective review comparing the number first diagnoses of tumors finalized during weeks 11–20 of 2020 at an Italian pathology unit (n = 2751).	All cancer diagnoses fell in 2020 by 44.9% compared with 2018 and 2019. Melanoma and KC represented 56.7% of all missing diagnoses.
Nicholson et al, 2020[48]	Survey study for all BSDS members practicing Mohs over the course of 3 wk starting April 27, 2020 (n = 47).	49% of respondents stopped Mohs surgery. When Mohs was performed, 35% reported decrease use of grafts/flaps, 81% reported increased use of dissolvable sutures, and 29% reported increase prescribing of prophylactic antibiotics.

(*continued on next page*)

Table 2
(continued)

Paper	Study Characteristics	Key Findings
Schauer et al, 2020[47]	Retrospective study of a UK hospital laboratory database January 27–March 22, 2020; and March 23–May 18, 2020 (inclusive) (n = 17).	Most cases represented early or thin melanomas (7% and 44% for prelockdown and during lockdown). Malignant melanoma detection rates were higher during lockdown (5.73%).
Ricci et al, 2020[19]	Cross-sectional study of all consecutive primary malignant melanomas from the Pathology Registry of IDI-IRCCS (Rome, Italy) during the COVID-19 pandemic (n = 237).	Mean number of melanomas diagnosed per day: 0.6 during lockdown vs 2.3 prelockdown vs 1.3 postlockdown. Mean Breslow thickness was 0.88 (95% CI, 0.50–1.26) prelockdown and 1.96 (95% CI, 1.16–2.76) postlockdown. Proportion of ulceration was 5.9% (95% CI, 2.4%–11.7%) prelockdown and 23.5% (95% CI, 10.8%–41.2%) postlockdown.
Valenti 2021[46]	Retrospective study of excised advanced melanoma and keratinocyte cancers in an Italian dermatosurgery division from May 18–November 18, 2020 (n = 265).	The number of advanced skin cancers was significantly higher during lockdown (54 vs 22; OR, 2.64; 95% CI, 1.56–4.47; P = .0003). The number of advanced SCCs (OR, 4.60; 95% CI, 1.31–16.18; P = .0175) and BCCs (OR, 2.15; 95% CI, 1.14–4.07; P = .0187) was significantly higher during lockdown.
Marson 2021[43]	Retrospective study of 143 US dermatology practices (350 providers) covering 4.7 million patients across 13 geographically distributed states.	Average monthly number of skin cancers decreased during lockdown compared with before (cutaneous melanoma mean difference, −126.5; cSCC, −2086.6; BCC, −3305.8) and immediately after (cutaneous melanoma, −144.7; cSCC, −2057.7; BCC, −3370.0). Largest decreases were observed during April 2020 (cutaneous melanomas, −69.6%; SCCs, −77.7%; BCCs, −85.9%).
Andrew 2021[44]	Retrospective review of data from the Northern Cancer Network from March 23–June 23, 2020 compared with the same period in 2019.	Skin cancer diagnoses decreased 68.61% (P<.01). Waiting times were decreased during COVID-19 compared with before (median 8 d and 12 d, respectively; P<.0001).

We found 11 studies that reported short-term skin cancer outcomes because of the pandemic, only one of which was based in the United States. At the time of this review, no studies were found reporting long-term patient outcomes because of surgical treatment delay.

Abbreviation: BCC, basal cell carcinoma; BSDS, British Society for Dermatological Surgery; KC, Keratinocyte cancer; SCC, squamous cell carcinoma.

pandemic because of high risk of disease progression,[10] with the exception of lesions less than 1 cm in elderly populations (favorable T1 tumors with no immunosuppression or angioinvasion).[42] Delayed surgery of MCC may increase the likelihood that the patient requires adjuvant radiotherapy. In the setting of limited operating room capacity, SLNB could be deferred from WLE or Mohs excision if the wound was allowed to granulate. NCCN guidelines also emphasized cutoffs in pathologic stage to guide treatment. For example, MCC diagnosed at stage III (or higher) should require careful evaluation of patient comorbidities by the physician to determine treatment (eg, definitive resection with complete lymphadenectomy or off-label immunotherapy). The BAD and BSDS recommended prioritizing treatment of all "rapidly-enlarging tumors, poorly-differentiated tumors, perineural tumors, ulcerated and symptomatic lesions" in addition to careful multidisciplinary evaluation of complex cases.[11]

DISRUPTIONS IN SKIN CANCER CARE DURING THE COVID-19 PANDEMIC

Several clinical observations suggest that COVID-19 lockdown periods have caused disruptions in skin cancer care. There has been a substantial decrease in the number of skin cancers diagnosed[6–9,43,44] and treated[8,9,45] during lockdown (**Table 2**). In the United Kingdom, a prospective cohort study of 2050 patients found a 27% to 47% weekly decrease in the number of keratinocyte cancers treated during their COVID-19 lockdown period (March 16, 2020 to June 14, 2020).[8] SCC were prioritized over BCC, comprising approximately 71% of all excisions during this study period. Andrew and colleagues[44] found a 68.61% decrease in overall skin cancers diagnosed in the United Kingdom when compared with the previous calendar year ($P<.01$). In Italy, Valenti and colleagues found no decrease in total skin cancers diagnosed from May to November 2020 but reported a significant increase of advanced skin cancers diagnosed (54 vs 22; OR, 2.64; 95% CI, 1.56–4.47; $P = .0003$).[46] In this study, advanced skin cancers were defined as melanomas staged T1b or higher (according to TNM staging) or KC with high-risk clinical and histopathologic features as determined by the clinician. Another study reported improved detection of earlier stage during lockdown in London, suggesting the importance of maintained skin referral pathways during pandemics.[47]

In the United States, a multicenter study reported significantly decreased average monthly number of skin cancers diagnosed during pandemic months (March to May 2020), with only a modest increase during the recovery period (BCC, +1.4%; SCC, +3.1%; melanoma, +9.2%) from June to August 2020. A US retrospective chart study found a 43.1%, 44.1%, and 51.2% decrease in cutaneous melanomas, SCC, and BCC diagnosed respectively from March to May 2020. The authors also proposed that the backlog of undiagnosed cancers during the recovery period (June to August 2020) may lead to average diagnostic delays of 1.8 months, 2.1 months, and 1.9 months for melanomas, SCC, and BCC diagnosed, respectively.[43]

In a UK-based survey, approximately half of Mohs surgeons reported discontinuing care during lockdown because of reallocated resources, lack of personal protective equipment, or concerns regarding viral transmission.[48] Postsurgical management was modified by limiting referrals for external reconstruction procedures and the increasing use of dissolvable sutures. In Italy, Filoni and colleagues[9] surprisingly found a 31.7% increase in surgical excisions accompanied by a 29% increase and 64% decrease in SLNB and lymph node dissections, respectively. The increase in surgical excisions was attributed to the reallocation of personnel from elective surgeries into oncologic referral pathways.

Data on skin cancer outcomes during the pandemic are limited because of short follow-up. It has previously been reported that modest delays in cancer care may significantly affect long-term survival. In a model-based study of cancer outcomes affected by the pandemic, a recent study reported an average loss of 0.97 and 2.19 life-years gained per person with surgery delays of 3 and 6 months, respectively, for all cancers.[45]

SUMMARY

The COVID-19 pandemic has had a profound impact on the routine management of skin cancer services. Surgical delays in cancer have historically decreased long-term survival. Consequently, a significant reduction in skin cancer surgery may manifest as increased morbidity and mortality because of undetected tumors, although no outcomes during COVID-19 have been reported yet. Patients with high-risk underlying conditions, such as old age, immunosuppression, and/or previous malignancy history, should be carefully triaged by a multidisciplinary team to mitigate potential COVID-19 exposure.

CLINICS CARE POINTS

- When interpreting these guidelines, tumor-specific factors should be carefully examined in the context of patient history and pandemic status.
- Three cancer centers have made recommendations for the surgical management of MCC. All guidelines endorse urgent surgical excision, particularly for high-risk features, such as increased thickness, poor differentiation, ulceration, and/or perineural invasion present.
- Surgical excision of BCC may be deferred 3 to 6 months for slow-growing and well-differentiated lesions according to the NCCN, BAD/BSDS, and ACMS guidelines.
- Treatment of SCC may be deferred unless significant risk factors are present according to the NCCN, BAD/BSDS, and ACMS.
- Guidelines for melanoma patients suggest deferral of melanoma in situ for up to 2 to 3 months, with priority given to T1-T4 lesions.
- A normal throughput of surgical and diagnostic processes for skin cancer should be maintained to avoid negative consequences associated with postlockdown backlog.
- When triaging cases during lockdown periods, the survival benefit for skin cancer surgery should outweigh the possible risk of COVID-related mortality.

DISCLOSURE

The authors have nothing to disclose.

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