


## Dermatologic Surgery

**Impact of delay in follow-up due to COVID-19 pandemic on skin cancer progression: a real-life experience from an Italian hub hospital**

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**Abstract**

**Background** The COVID-19 pandemic required the setting of a national lockdown in Italy from March 9, 2020, until May 18, 2020; therefore, most of the non-COVID-19 activities were postponed. As a consequence, many follow-up visits in patients with previously excised skin cancers were delayed. The aim of this retrospective real-life case-control study is demonstrating that delay in follow-up led to an increased incidence of advanced melanoma and keratinocyte cancers on the total of surgically excised skin cancers.

**Methods** The incidence of excised advanced melanoma and keratinocyte cancers in our dermato-surgery division in the period May 18 to November 18, 2020, was compared to the same time span of 2019. All data were collected from the electronic database of our department. Odds ratio with 95% confidence interval was used to assess the risk of excised advanced skin cancers in 2020 compared to 2019.

**Results** From May to November 2019, we performed 265 surgical excisions, while during the pandemic in 2020, we completed 280 surgeries. The number of advanced skin cancers excised between May 18 and November 18, 2020, was significantly higher compared with the same period in 2019 (54 vs. 22, OR: 2.64; 95% CI: 1.56–4.47;  $P = 0.0003$ ). Significant differences were also observed regarding the number of surgically removed advanced BCCs (OR 2.15; 95% CI 1.14–4.07;  $P = 0.0187$ ) and advanced SCCs (OR 4.60; 95% CI 1.31–16.18;  $P = 0.0175$ ).

**Conclusion** These results confirm that delay in follow-up and, consequently, postponed surgical excisions are related to an increased incidence of advanced skin tumors, resulting in poorer prognosis lifelong. Follow-up visits should be carried on even during COVID-19 pandemic, avoiding significant delays as much as possible.

**Introduction**

Spreading of the COVID-19 pandemic required the setting of a national lockdown in Italy from March 9 until May 18, 2020; therefore, most of the non-COVID-19 activities were postponed. This new setting of a national health system has rapidly changed the approach to skin cancer screening and follow-up. In particular, many follow-up visits in patients with previously excised melanoma and keratinocyte cancers were delayed. Furthermore, the annual dermatologic checkup visits were frequently postponed. As a consequence, a substantial increase in the number of avoidable cancer deaths all over the world is expected as a result of diagnostic delays due to the COVID-19 pandemic.<sup>1</sup>

During the pandemic, our Dermatology Department has continued to guarantee urgencies, clinical trials scheduled visits,

follow-up of patients under treatment with biologics, and the most important dermato-oncology follow-up and urgent dermato-surgical procedures.<sup>2,3</sup>

However, many patients skipped their scheduled appointments due to logistic reasons or for fear of possible contagion. We hypothesized that the delay on diagnosis and follow-up has critically impacted tumor burden and progression of melanomas and keratinocyte cancers. To confirm this hypothesis, we have analyzed the database of our dermato-surgery division, assessing the incidence of advanced melanomas and advanced keratinocyte cancers during the period of May 18 to November 18, 2020, and compared these data with that of the same period of the previous year (May 18 to November 18, 2019). The definition of advanced tumors was determined on the basis of histological, surgical, and clinical criteria.

The aim of this retrospective real-life single-center study was to understand the impact of delaying the follow-up visits on tumor burden. Therefore, we estimated the delay in scheduled dermatologic follow-up visits at Humanitas Research Hospital of Rozzano, in the metropolitan area of Milan, for patients diagnosed with skin cancers during the period May 18 to November 18, 2020 (compared with the same time span in 2019); then, we assessed the incidence of advanced melanoma and advanced keratinocyte cancers (BCC and SCC) on the total of surgical excisions in the period May 18 to November 18, 2020, and we compared these findings with data from May 18 to November 18, 2019.

## Materials and methods

This is a single-center retrospective real-life case-control study performed analyzing the electronic database of our dermatologic department. We considered a 6-month period, from May 18 to November 18, to compare the surgical activity of two consecutive years (2019 and 2020). We considered the 6-month period in 2020 (immediately after the first pandemic wave in Italy) as the case group and the same time span in 2019 as the control group. Of these patients, we analyzed demographics, tumor risk factors, and mean time occurring between the last two follow-up visits. All patients were followed up in our oncological dermatology clinic. All surgical excisions were performed by the same surgical team both in 2019 and in 2020. For this reason, operator-dependent factors were ruled out when analyzing data.

We have chosen to define “advanced melanoma” (aM) as all melanomas with a pTNM staging of pT1b or more, based on the histological examination.

We have considered as “advanced squamous cell carcinoma” (aSCC) the following categories:

- 1) G2/G3 squamous cell carcinomas
- 2) Squamous cell carcinomas whose excision required an advanced reconstructive surgery due to the tumor size or the location (e.g., grafts or flaps)

- 3) Squamous cell carcinomas that were not surgically removable but eligible for radiotherapy or immunotherapy or targeted therapy.

Our definition of “advanced basal cell carcinoma” (aBCC) includes the following categories:

- 1) Basal cell carcinomas that were not totally excised due to their size or location
- 2) Basal cell carcinomas whose excision required an advanced reconstructive surgery due to the tumor size or the location (e.g., grafts or flaps)
- 3) Basal cell carcinomas that were not surgically removable but eligible for radiotherapy or chemotherapy or targeted therapy.

Data are presented in the text and in the tables as means and percentages, when appropriate. Means were compared with Student's *t* test. Odds ratio (OR) with 95% confidence interval (95% CI) was used to assess the risk of excising advanced skin cancers in 2020 (case group) compared with 2019 (control group). For all statistical analyses, a *P*-value inferior to 0.05 was considered significant.

## Results

Our patients' characteristics are shown in Table 1. Demographics and risk factors for skin cancers (including personal and family history, previous immunosuppressive therapies, and radiotherapy) were comparable among patients undergoing surgery from May 18 to November 18, 2020, versus May 18 to November 18, 2019. Mean age of patients who underwent dermatologic surgery between May and November 2019 was 64.3 years, while it was 65.4 years in 2020. In 2019, 72 of our patients (32.1%) had a personal history of skin cancer, compared with 70 patients (29.5%) in 2020. Follow-up periods, however, were significantly different between the two groups, as the vast majority of the patients skipped or postponed their follow-up visit, going from a mean of 6.2 months between the last two

**Table 1** Patient demographics and risk factors for skin cancers

	May 18 to November 18, 2019	May 18 to November 18, 2020	<i>P</i> -value
Number of patients	224	237	n/a
Mean age	64.3	65.4	0.62
Sex	116 males, 108 females	135 males, 102 females	0.26
Previous skin cancers	72 (32.1%)	70 (29.5%)	0.55
Family history	30 (13.4%)	26 (11%)	0.45
Previous immunosuppressive therapies	24 (10.7%)	24 (10.1%)	0.84
Previous radiotherapy	12 (5.4%)	15 (6.3%)	0.66
Previous phototherapy	9 (4%)	10 (4.2%)	0.91
Mean time between last two follow-up visits	6.2 months	8.5 months	0.0003

dermatologic visits in patients diagnosed with skin cancer in May–November 2019 to 8.5 months in those undergoing surgery in May–November 2020 ( $P = 0.0003$ ).

From May to November 2019, we performed 265 surgical excisions for 224 patients with a mean age of 64.3 years. During the pandemic in 2020, we completed 280 surgeries on 237 patients.

In May–November 2019, we excised 22 advanced skin cancers (8.3% of all surgeries): four advanced melanomas, 15 advanced basal cell carcinomas, and three advanced squamous cell carcinomas. During the same time span in 2020, 54 advanced skin tumors were surgically removed (19.3%): we performed eight excisions of advanced melanoma, 32 of advanced basal cell carcinoma, and 14 of squamous cell carcinoma. Complete data are available in Table 2.

The difference between the number of advanced skin cancers excised between May 18 to November 18, 2020, was significantly higher compared with the same period in 2019, with an OR of 2.64 (95% CI: 1.56–4.47;  $P = 0.0003$ ). Significant differences were also observed regarding the number of surgically removed advanced BCCs (OR 2.15; 95% CI 1.14–4.07;  $P = 0.0187$ ) and advanced SCCs (OR 4.60; 95% CI 1.31–16.18;  $P = 0.0175$ ).

**Comment**

The COVID-19 pandemic has deeply changed our routine clinical and surgical activities, forcing us to consider new ways to guarantee a cancer care and follow-up in order to avoid the negative impact on patients’ life expectancy created by delay. The benefits of this care should be balanced against the risk of COVID-19 new contagion for outpatients and staff during visits and surgeries, in any clinical field and department.<sup>1</sup>

During the first pandemic wave, we had to reorganize the dermatologic department and its clinical and surgical activities in order to reduce the possibilities of contagion among outpatients and site staff.<sup>2</sup> The oncological follow-up was guaranteed for all invasive melanoma and squamous cell carcinoma, and

also for all patients affected by basal cell carcinoma at high risk for location and clinical/histological subtypes. All patients diagnosed with noninvasive keratinocyte cancers or melanoma at the previous oncological visit were postponed, skipping the scheduled follow-up. We recovered all the delayed or canceled appointments, and we performed these visits right after the first apex of the COVID-19 pandemic in Italy.

In our hospital, we excised 265 neoplasms from May 18 to November 18, 2019, and 22 of them were invasive or advanced tumors (8.3% – four melanomas, 15 basal cell carcinomas, and three squamous cell carcinomas); in the same time span, in 2020 during the COVID-19 pandemic, we performed 280 excisions, resulting in 54 (19.3%) advanced neoplasms (OR 2.64; 95% CI: 1.56–4.47;  $P = 0.0003$ ). Patients’ characteristics were comparable across the two groups, with the only exception being the time between the last two dermatologic examinations. As a matter of fact, all the patients diagnosed with an advanced skin cancer from May 18 to November 18, 2020, had a delayed follow-up, with a mean time of 8.5 months between the last two dermatologic visits (compared with 6.2 months in 2019,  $P = 0.0003$ ). Thus, our findings underline how during the first apex of the COVID-19 pandemic the delayed follow-up strongly impacted skin cancer diagnosis and treatment, with a higher percentage of advanced melanomas and keratinocyte cancers, compared with 2019.<sup>4,5</sup> As a matter of fact, in 2019, not one of our patients had postponed the oncological follow-up.

Several of our patients decided to delay the follow-up visit because of the fear of new contagion, as happened in other hospitals;<sup>4,5</sup> others were postponed by the hospital during the first pandemic apex (March–April 2020) with only urgencies and COVID-19 care guaranteed, as happened in other hospitals.<sup>3,6</sup> All the consultations skipped during those months were postponed and performed from May to November 2020, resulting in new clinical diagnoses and indications to radical excision.

We think that skipped follow-up visits meant a delay on the diagnosis and, consequently, a delay on surgical excision which resulted in not-radical excision and a histological diagnosis of advanced tumors, with an odds ratio of 2.64 and a  $P = 0.0003$ .

A regular oncological follow-up, even during the COVID-19 pandemic, especially for patients with higher risk of developing skin cancers, could help avoid complicated and invasive surgery procedures (e.g., flaps or grafts) with a consequent better aesthetic result.<sup>7,8</sup> Therefore, a radical excision of a noninvasive skin cancer has a better lifelong prognosis, following a more aesthetically acceptable postsurgery result.

Our study has several limitations, the majority of them being that it is representative of only a single-center experience. Another limitation is due to our dermatologic activity being mainly targeted on high-risk patients sent from primary care services. Thus, many of the selected cases and controls were already at risk for developing advanced melanomas or keratinocyte cancers due to personal or familial dermatologic history, previous radiotherapy, previous or concomitant

**Table 2** Comparison of advanced skin cancers in the same time period, 2019 vs. 2020

	May 18 to November 18, 2019	May 18 to November 18, 2020	P-value
No. patients	224	237	n/a
No. surgical excisions	265	280	n/a
No. advanced skin cancers	22 (8.3%)	54 (19.3%)	0.0003
No. advanced melanoma	4 (1.5%)	8 (2.9%)	0.29
No. advanced BCCs	15 (5.7%)	32 (11.4%)	0.0187
No. advanced SCCs	3 (1.1%)	14 (5%)	0.0175

No., number; BCC, basal cell carcinoma; SCC, squamous cell carcinoma.

immunosuppressive therapy, or previous phototherapy. However, these risk factors were well balanced between our two groups (Table 1).

This retrospective case-control real-life single-center study from a dermatology department of northern Italy has demonstrated a bigger incidence of advanced skin cancers (19.3% of advanced tumors during May to October 2020) compared to the same period of the previous year (8.3% from May to October 2019, OR 2.64; 95% CI: 1.56–4.47;  $P = 0.0003$ ). This statistical analysis shows that not only primarily diagnosed advanced skin cancers became more invasive without a prompt surgical excision but also carcinoma in situ evolved in a more aggressive way.

These results confirm the hypothesis that follow-up delay and, consequently, retarded surgical excision is related to an increased incidence of advanced skin tumors, resulting in poorer consequences for prognosis, aesthetic result, and therapeutic management.<sup>9</sup> Cancer patients' schedules should be carried on even during the COVID-19 pandemic, trying to minimize the delay between follow-up visits.

We all need better models of cancer care and treatment during this pandemic in order to avoid both tumor burden and new contagions in the hospitals among our fragile patients. This report highlights the importance of maintaining a regular follow-up and avoiding, as much as possible, significant delays that could lead to skin tumor progression. As in the current environment, presenting for a clinical skin examination may be viewed as "not strictly necessary" and thus postponed; however, early detection of melanoma and keratinocyte cancers must be encouraged. Telehealth could be used for patients at highest risk of SARS-CoV-2 infection, including elderly patients with multiple risks factors for either skin cancers or respiratory infections, and others who are fearful of visiting doctors. Telemedicine also eliminates the risk of contagion for dermatologists and other healthcare workers.<sup>10</sup> In this context, technological diagnostic strategies such as telemedicine, that has already confirmed its value before and during this pandemic scenario, could represent a new possible support for dermato-oncologists.<sup>11,12</sup>

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