

Miriam TEUSCHER^{1,2}
 Katharina DIEHL³
 Marthe-Lisa SCHAARSCHMIDT⁴
 Juliane WEILANDT^{1,5}
 Bianca SASAMA¹
 Jan OHLETZ⁶
 Andreas KÖNNECKE⁷
 Wolfgang HARTH⁶
 Uwe HILLEN⁷
 Wiebke Katharina PEITSCH¹

¹ Department of Dermatology and Phlebology, Vivantes Klinikum im Friedrichshain, Landsberger Allee 49, 10249 Berlin, Germany

² Faculty of Medicine, Charité University Medicine Berlin, Charitéplatz 1, 10117 Berlin, Germany

³ Mannheim Institute of Public Health, Social and Preventive Medicine, Medical Faculty Mannheim, Heidelberg University, Ludolf-Krehl-Str. 7-11, 68167 Mannheim, Germany

⁴ Department of Dermatology, Venereology and Allergology, University Medical Center Mannheim, Heidelberg University, Theodor-Kutzer-Ufer 1-3, 68167 Mannheim, Germany

⁵ Dermatologie Spandau, Moritzstr. 1, 13597 Berlin, Germany

⁶ Department of Dermatology and Allergology, Vivantes Klinikum Spandau, Neue Bergstr. 6, 13585 Berlin, Germany

⁷ Department of Dermatology and Venereology, Vivantes Klinikum Neukölln, Rudower Str. 48, 12351 Berlin, Germany

Reprints: Wiebke Katharina Peitsch <wiebke.ludwig-peitsch@vivantes.de>

Article accepted on 02/11/2020

Effects of the COVID-19 pandemic on care of melanoma patients in Berlin, Germany: the Mela-COVID survey

Background: The COVID-19 pandemic imposes major challenges for care of cancer patients. **Objectives:** Our aim was to assess the effects of the pandemic on treatment and appointments of patients with malignant melanoma based on a large skin cancer centre in Berlin, Germany, and identify reasons for, and impact factors associated with these changes. **Materials & Methods:** Patients with melanoma treated from January 1st 2019 received a postal survey with questions on impairment due to the pandemic, fear of COVID-19, fear of melanoma, changes in therapy and/or appointments, including reasons for the changes. Impact factors on postponed/missed appointments were examined using descriptive analyses and multivariate logistic regression. **Results:** The response rate was 41.3% ($n = 324$; 57.4% males; mean age: 67.9 years). Among 104 participants currently receiving therapy, four (3.8%) reported treatment changes due to the pandemic. Postponements or cancellations of appointments occurred in 48 participants (14.8%), most frequently, at their own request (81.3%) due to fear of SARS-CoV-2 infection (68.8%). Current treatment was associated with a reduced chance of postponing/missing appointments (OR = 0.208, $p = 0.003$), whereas a high or very high level of concern for COVID-19 (OR = 6.806, $p = 0.034$; OR = 10.097, $p = 0.038$), SARS-CoV-2 infection among close acquaintances (OR = 4.251, $p = 0.026$), anxiety disorder (OR = 5.465, $p = 0.016$) and AJCC stage IV (OR = 3.108, $p = 0.048$) were associated with a higher likelihood of postponing/missing appointments. **Conclusion:** Among our participants, treatment changes were rare and the proportion of missed/delayed appointments was rather small. The main reasons for delays/cancellations of appointments were anxiety and concern for COVID-19.

Key words: anxiety, cancer, COVID-19, melanoma, pandemic, SARS-CoV-2

Following the Coronavirus disease 19 (COVID-19) outbreak in Wuhan, China, and worldwide spread, the World Health Organization declared a global pandemic on March 11th 2020. Due to rapidly increasing new infections, lockdown was proclaimed in Berlin, the capital of Germany, on March 23rd (*supplementary figure 1*). At the time of data cut-off for our study (June 30th 2020), >10 million people had been infected with severe acute respiratory syndrome virus 2 (SARS-CoV-2) worldwide, among them 194,259 in Germany and 8,220 in Berlin [1, 2].

Anticipating unprecedented pressure on hospitals and intensive care units (ICUs), as experienced in Italy and Spain, resources were rapidly rededicated to, and concentrated on patients with COVID-19 [3]. Extensive safety procedures were implemented to prevent nosocomial infections of patients and staff [4]. In dermatology departments, elective admissions and surgery of benign lesions

were cancelled and staff were reallocated to support care for patients with COVID-19.

Patients with cancer are particularly threatened by the pandemic [5-8]. Firstly, they may be more prone to severe SARS-CoV-2 infections due to immunosuppression. In a Chinese study, cancer patients had a more severe course and poorer outcome of COVID-19 than others, particularly if they recently underwent surgery or chemotherapy [9, 10]. Similar findings were obtained in an international study comparing cancer patients and age-matched controls with COVID-19 [11]. According to the UK Coronavirus Cancer Monitoring Project, 52% of the patients had a mild course of COVID-19, but 28% died [12]. The risk of death was significantly associated with advanced age, male sex and comorbidities including hypertension and cardiovascular disease. Chemotherapy in the past four weeks, immunotherapy, targeted therapy and radiotherapy had no effect on mortality after adjusting for these factors [12].

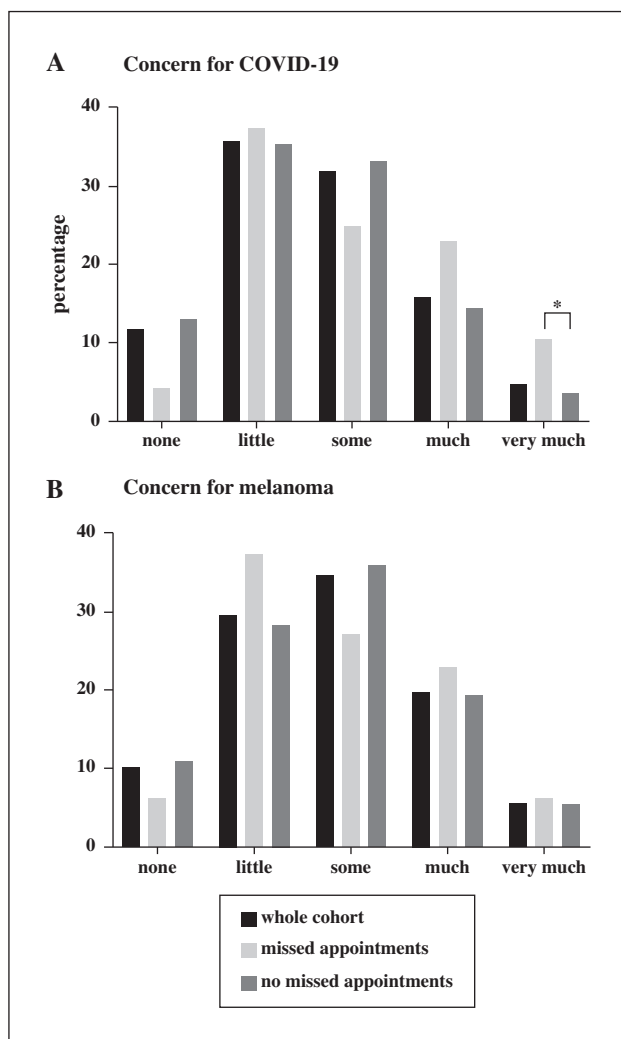


Figure 1. Concern for COVID-19 (A) and melanoma (B) in the total cohort and in subgroups of individuals with or without postponed or missed appointments. Differences between subgroups with and without postponed/missed appointments were compared using post hoc test; * $p < 0.05$.

Secondly, a delay in diagnosis and treatment imposes major risks on patients with cancer, including melanoma [5, 7, 8, 13, 14]. According to a US American study, encounters due to melanoma decreased by 51.8% in April 2020 compared to April 2019 [15]. Based on a growth model, the effect of the lockdown on melanoma thickness and prognosis predicted a 45% risk of upstaging to a higher T-stage and decrease of 10-year survival from 90% to 87.6% after a three-month diagnostic delay [16]. Indeed, an Italian study showed increased thickness of primary melanomas in the post-lockdown era [17]. To counteract these effects, many dermatologists pursued treatment conforming to guidelines for SARS-CoV-2-negative melanoma patients when the benefits outweighed the risks and resources were sufficient [3, 18-21].

Regarding follow-up of melanoma patients during the pandemic, there are no standard recommendations. Decisions on postponing or maintaining appointments should be

made after weighing up the risk of SARS-CoV-2 infection versus the risk of missing disease progression and/or treatment-related complications, considering tumour stage and burden, current treatment, age, comorbidities and risk of COVID-19 exposure. Decision-making is complicated by the fact that the duration and development of the pandemic are unknown.

The Vivantes Skin Cancer Centre (HTZ) comprises three departments of dermatology located in different districts of Berlin (Friedrichshain, Neukölln, and Spandau). The aim of our study was to analyse the effects of the COVID-19 pandemic on treatments and appointments of melanoma patients from the HTZ and to identify reasons for, and determinants associated with these changes.

Patients and methods

Study population

Inclusion criteria were diagnosis of invasive melanoma American Joint Committee on Cancer (AJCC) 2017 stage I-IV, treatment and/or examination and/or consultation due to melanoma in the HTZ between January 1st 2019 and June 30th 2020, age ≥ 18 years and capacity to consent. Potential participants were identified via primary case and follow-up lists prepared for certification as cancer by the German Society of Oncology (Deutsche Krebsgesellschaft). All patients fulfilling inclusion criteria were contacted by mail. The study was performed according to the principles of the Declaration of Helsinki and approved by the Ethics Committee of the Faculty of Medicine of Charito University Medicine Berlin (EA4/082/20).

Data collection

Data were collected between May 15th 2020 and June 30th 2020. Patient information, two copies of the informed consent form and the questionnaire were sent by post. All patients willing to participate were asked to return one copy of the signed informed consent and the completed questionnaire in a prepaid envelope within four weeks. Contact to the study team was offered by phone, fax, e-mail or post in case of queries.

The questionnaire comprised information on sociodemographic characteristics (age, sex, marital status, household members, education, employment) and melanoma-related aspects (time since diagnosis, previous treatments, treatment since February 1st 2020). General health state was assessed using the EuroQoL 5-Dimension 5-Level (EQ-5D-5L) health-related quality of life score [22]. Comorbidities including hypertension, cardiovascular, pulmonary and liver disease, diabetes, arthropathy, thyroid disease, immunological diseases, allergies, depression, anxiety disorder, other mental illnesses, lipometabolic disorders, non-melanoma skin-cancer and other cancers could be chosen from a list. Respondents could indicate unstated comorbidities as free text. In addition, they were asked for current or past SARS-CoV-2 infections affecting themselves, household members and/or close acquaintances and for the place of treatment (outpatient, isolation ward of a hospital, or ICU). The level of concern for COVID-19 and melanoma were assessed on 5-point scales (from “zero”

to “very high”) and by indicating numbers between 0 (no concerns) and 100 (greatest concern).

Furthermore, the survey contained questions about alterations in treatment (pause, postponement, stoppage or change) and melanoma-related appointments (postponement or cancellation) due to the pandemic. Participants reporting alterations were asked to indicate whether the change was requested by themselves or by medical providers, and to specify reasons (fear of SARS-CoV-2 infection, sickness, risk-benefit consideration, lack of resources, closure of the doctor’s office, or other reasons).

A medical documentation form comprising information on the history of melanoma (AJCC 2017 stage, time since diagnosis, current tumour manifestation), previous treatments, current treatment (since February 1st 2020), treatment response, goal (adjuvant or palliative), and comorbidities was completed for all participants by one of the authors (MT). Effects of the pandemic on treatment and appointments were recorded from the medical provider perspective. Reasons for changes were classified as patient-related and medical provider-related.

Statistical analyses

Statistical analyses were performed using IBM SPSS Statistics 25. For subgroup analyses, participants were stratified according to age, sex, marital status (single or widowed vs. married or in a partnership), school degree (low or intermediate vs. higher education entrance qualification [A-levels, “Abitur” or “Fachabitur”]), AJCC 2017 stage (I, II, III or IV), current tumour burden (yes/no), current melanoma treatment (yes/no), kind of current treatment (surgery, radiotherapy, adjuvant or palliative systemic treatment), EQ-5D-5L (<1 or 1), presence or absence of each comorbidity in the list, any comorbidity (yes/no), <5 or ≥5 comorbidities, level of concern for COVID-19 and melanoma (zero, low, moderate, high and very high; 0-100), and current or past SARS-CoV-2 infections affecting the participants (yes/no), household members (yes/no) or close acquaintances (yes/no). Differences were tested for statistical significance using Chi-square tests for categorical variables and Mann-Whitney-U-tests for linear variables due to lack of normal distribution.

Associations between characteristics and changes in appointments were further investigated using multiple logistic regression analyses. The basic model contained postponed/missed appointments as a dependent variable and sex, age, AJCC stage, current treatment, anxiety disorder, concern for COVID-19 and melanoma and number of comorbidities (<5 vs. ≥5) as independent variables. To assess the impact of specific comorbidities, we additionally calculated regression models for each comorbidity instead of including the number of comorbidities. A *p* value ≤0.05 was considered significant.

Results

A total of 784 patients were contacted by post. Of these, 324 provided informed consent and returned completed questionnaires (response rate: 41.3%). All questionnaires were included in the final analyses.

Sociodemographic and disease-related characteristics

Among all participants, 57.4% were male, and the mean age was 67.9 years (*table 1*). Seventy-one percent lived in a partnership, and 27.9% were working. Approximately one third (34.3%) rated their health state as optimal (EQ-5D-5L = 1). Most participants suffered from melanoma stage I (48.5%), followed by stage II (20.1%), stage III (17.6%) and stage IV (13.9%) (*supplementary table 1*). The average time since diagnosis was 32.1 months. One hundred and four participants (32.1%) received treatment between February 1st 2020 and the time of data collection. Among these, 63.5% obtained systemic treatment, 47.1% surgery and 2.9% radiotherapy (*supplementary table 1*). The treatment goal was curative in 74.0%. One third of all participants (32.1%) received systemic treatment.

Impairment by the COVID-19 pandemic

One patient probably acquired COVID-19 during a hospital stay for wide excision of his melanoma and sentinel lymph node biopsy (SLNB) in March 2020. He was treated as an inpatient in an isolation ward for nine days and fully recovered. One participant reported SARS-CoV-2 infection of his wife. SARS-CoV-2 infections among close acquaintances were recorded by 15 participants (*table 2*).

The mean score for concern for COVID-19 was 35.1 on a scale of 0-100, and the mean score for concern for melanoma was 38.1. Altogether, 15.8% of participants reported a high level and 4.7% a very high level of concern for COVID-19 (*table 2, figure 1A*), while 19.8% reported a high and 5.6% a very high level of concern for their melanoma (*table 2, figure 1B*). More than three quarters (76.3%) reported a high or very high level of decreased social contact during the pandemic. Among working participants, 57.4% indicated a high or very high level of decreased professional contact (*table 2*).

Changed or postponed treatments

Four of 104 participants currently receiving melanoma treatment (3.8%) changed or postponed their therapy due to the pandemic (*supplementary table 2*). The first participant received hypofractionated radiotherapy after neurosurgery for brain metastasis. The second deferred wide excision of primary melanoma due to COVID-19 outbreak in another hospital. The third postponed wide excision and SLNB at her own request. For the fourth participant, adjuvant pembrolizumab was changed from 200 mg, three times a week, to 400 mg, six times a week. Moreover, one patient each reported cancellation of rehabilitation and physiotherapy.

Postponed or missed appointments

Between February 1st 2020 and the start of study participation, 48 patients (14.8%) postponed or cancelled a melanoma-related appointment because of the pandemic, most frequently at their own request (81.3%) and due to fear of SARS-CoV-2 infection (68.8%) (*figure 2*). Participants were most afraid of SARS-CoV-2 infection from other patients (54.2% of 72 answers), followed by

Table 1. Sociodemographic characteristics of the whole cohort and subgroups of individuals with or without postponed/missed appointments.

Characteristic	Whole cohort	Postponed/missed appointments		<i>p</i> ^b	
	<i>n</i> = 324 ^a <i>n</i> (%)	Yes, <i>n</i> = 48 ^a <i>n</i> (%)	No, <i>n</i> = 276 ^a <i>n</i> (%)		
Sex					
Female	138 (42.6)	18 (37.5)	120 (43.5)	0.439	
Male	186 (57.4)	30 (62.5)	156 (56.5)		
Age, years					
Mean (SD)	67.9 (13.4)	69.4 (12.3)	67.6 (13.6)	0.450	
Median (IQR, range)	69 (20, 28-95)	70.5 (16.5, 37-90)	69 (20, 28-95)		
<60	85 (26.2)	10 (20.8)	75 (27.2)	0.357	
≥60	239 (73.8)	38 (79.2)	201 (72.8)		
Partnership					
Single ^c	94 (29.0)	17 (35.4)	77 (27.9)	0.289	
Partner ^d	230 (71.0)	31 (64.6)	199 (72.1)		
Living alone^e					
Yes	76 (23.5)	12 (25.5)	64 (23.2)	0.726	
No	247 (76.5)	35 (74.5)	212 (76.8)		
School degree^e					
Low/intermediate	163 (50.8)	23 (50.0)	140 (50.9)	0.909	
High ^f	158 (49.2)	23 (50.0)	135 (49.1)		
Education^e					
None	18 (5.6)	5 (10.6)	13 (4.7)	0.301	
Apprenticeship	135 (41.9)	20 (42.6)	115 (41.8)		
Master qualification	36 (11.2)	3 (6.4)	33 (12.0)		
University degree	133 (41.3)	19 (40.4)	114 (41.5)		
Employment status^e					
Not working	233 (72.1)	37 (78.7)	196 (71.0)	0.276	
Working	90 (27.9)	10 (21.3)	80 (29.0)		
EQ-5D-5L^e					
Mean (SD)	0.877 (0.184)	0.846 (0.213)	0.882 (0.178)	0.433	
<1	209 (65.7)	33 (70.2)	176 (64.9)		0.482
1	109 (34.3)	14 (29.8)	95 (35.1)		

EQ-5D-5L: EuroQoL 5-Dimension 5-Level health-related quality of life score; IQR: Interquartile range; *n*: number; SD: standard deviation.

^a For calculation of proportions, the total number of participants in each group (*n* = 324 in the total cohort, *n* = 48 in the subgroup of individuals who postponed/missed an appointment and *n* = 276 in the subgroup of individuals who did not postpone or miss consultations) was set to 100%.

^b Differences between participants who postponed/missed their appointment and participants who kept all appointments were tested for significance using the Chi-square test for binary and categorical variables and Mann-Whitney-U tests for linear variables.

^c No partner, divorced or widowed.

^d In a partnership or married.

^e Missing data: living alone *n* = 1; school degree *n* = 3; education *n* = 2; employment status *n* = 1; EQ-5D-5L *n* = 6.

^f A-levels or higher education entrance qualification.

infection during travel (25%) and infection transmitted by medical staff (20.9%). Medical provider-related reasons, including risk-benefit assessment, closure of a practice, scarcity of resources, and SARS-CoV-2 infection from the practicing dermatologist, were responsible for 27.1% of all postponements/cancellations (figure 2). Appointments in doctors' practices and in the HTZ were postponed/missed equally frequently (*n* = 25 each). Seventy percent of the consultations were postponed, 26% were cancelled, and 4% were initially postponed and then cancelled.

Subgroup analyses according to sociodemographic and disease-related factors and concern for COVID-19 and melanoma (tables 1, 2, supplementary table 1, figure 1) revealed that patients currently receiving treatment were less likely to have postponed/missed appointments than those without current treatment (*p* = 0.005) (supplementary table 1). Conversely, a high or very high level of

concern for COVID-19 (*p* = 0.050) (table 2, figure 1A) and SARS-CoV-2 infection among close acquaintances (*p* = 0.041) (table 2) were associated with a higher proportion of postponed/missed consultations. Significant association between current treatment (OR = 0.208, table 3 table 3), concern for COVID-19 (high: OR = 6.806; very high: OR = 10.097) (table 3) or SARS-CoV-2 infection among close acquaintances (OR = 4.251, *p* = 0.026) and postponement/cancellation of consultations was confirmed by logistic regression analysis. The models additionally suggested a higher probability of postponing/missing appointments for individuals with AJCC stage IV compared to stage I (OR = 3.108) (table 3). Other disease-related or sociodemographic characteristics and concern for melanoma did not show significant association with the appointment variable (tables 1-3, supplementary table 1, figure 1B).

Table 2. Effect of the COVID-19 pandemic and its association with postponed/missed appointments.

Characteristic	Whole cohort n=324 ^a n (%)	Postponed/missed appointment		p ^b
		Yes, n=48 ^a n (%)	No, n=276 ^a n (%)	
SARS-CoV-2 infections				
No	308 (95.1)	43 (89.6)	265 (96.0)	0.058
Yes	16 (4.9)	5 (10.4)	11 (4.0)	
Patient ^c	1 (0.3)	0 (0.0)	1 (0.4)	0.676
Household	1 (0.3)	0 (0.0)	1 (0.4)	0.676
Close acquaintances ^c	15 (4.6)	5 (10.4)	10 (3.6)	0.041
Concern about COVID-19^c				
Scale 0-100				
Mean (SD)	35.1 (27.2)	41.5 (29.5)	34.0 (26.6)	0.110
Median (IQR, range)	30 (40, 0-100)	30 (47.5, 0-100)	30 (40, 0-100)	
5-point scale				
None	38 (11.8)	2 (4.2)	36 (13.1)	0.050
Little	115 (35.7)	18 (37.5)	97 (35.4)	
Some	103 (32.0)	12 (25.0)	91 (33.2)	
Much	51 (15.8)	11 (23.0)	40 (14.6)	
Very much	15 (4.7)	5 (10.4)	10 (3.7)	
Concern about melanoma^c				
Scale 0-100				
Mean (SD)	38.1 (27.7)	39.8 (29.6)	37.8 (27.4)	0.707
Median (IQR, range)	35 (50, 0-100)	32.5 (52.5, 0-100)	35 (50, 0-100)	
5-point scale				
None	33 (10.2)	3 (6.3)	30 (11.0)	0.513
Little	96 (29.7)	18 (37.5)	78 (28.4)	
Some	112 (34.7)	13 (27.1)	99 (36.0)	
Much	64 (19.8)	11 (23.0)	53 (19.3)	
Very much	18 (5.6)	3 (6.3)	15 (5.5)	
Social contact reduction^c				
None	12 (3.8)	3 (6.3)	9 (3.3)	0.180
Little	25 (7.8)	0 (0.0)	25 (9.2)	
Some	39 (12.2)	6 (12.5)	33 (12.1)	
Much	115 (35.9)	16 (33.3)	99 (36.4)	
Very much	129 (40.3)	23 (47.9)	106 (39.0)	
Professional contact reduction				
Total ^d	94 (100.0)	11 (100.0)	83 (100.0)	
None	20 (21.3)	0 (0.0)	20 (24.1)	0.144
Little	6 (6.4)	1 (9.1)	5 (6.0)	
Some	14 (14.9)	2 (18.2)	12 (14.5)	
Much	14 (14.9)	4 (36.4)	10 (12.0)	
Very much	40 (42.6)	4 (36.4)	36 (43.4)	

Significant findings are highlighted in bold. IQR: Interquartile range; n: number; SD: standard deviation.

^a For calculation of proportions, the number of participants in each group was set to 100%.

^b Differences between participants who postponed/missed their appointment and participants who kept all appointments were tested for significance using the Chi-square test for binary and categorical variables and Mann-Whitney-U tests for linear variables.

^c Missing data: SARS-CoV-2 infection of participants n=1; SARS-CoV-2 infection among close acquaintances n=3; concern for COVID-19 scale 0-100: n=10, 5-point scale: n=2; concern for melanoma scale 0-100: n=4, 5-point scale: n=1; social contact reduction n=4.

^d 94 patients provided information on professional contacts.

Impact of comorbidities on postponed/missed appointments

More than a half of the participants (55.9%) suffered from hypertension, 33.3% from other cardiovascular diseases, 12.7% from pulmonary diseases, and 4.6% were immunosuppressed. In addition, 8.3% had depression and 4.6% anxiety disorder (*supplementary table 3*). Patients with anxiety disorder postponed/missed their

appointment significantly more frequently than participants without this condition ($p=0.005$) (*supplementary table 3*), a finding confirmed by logistic regression analysis (OR = 5.465, $p=0.016$) (*table 3*). Other comorbidities were not significantly associated with delayed/missed appointments, neither based on bivariate analysis (*supplementary table 3*) nor individual logistic regression models for each comorbidity including age, sex, AJCC stage, current treatment, concern for COVID-19, concern for melanoma, and

Table 3. Logistic regression model including potential determinants for postponed/missed appointments.

Characteristics	OR ^a	CI	p
Male	1.170	0.562-2.434	0.675
Age	1.010	0.979-1.041	0.542
AJCC stage			
II	0.552	0.214-1.422	0.218
III	0.659	0.208-2.085	0.478
IV	3.108	1.010-9.570	0.048
Current treatment	0.208	0.073-0.594	0.003
Anxiety disorder	5.465	1.364-21.900	0.016
≥5 comorbidities	0.934	0.430-2.028	0.862
Concern about COVID-19			
Little	3.845	0.774-19.096	0.100
Some	2.484	0.460-13.399	0.290
Much	6.806	1.156-40.064	0.034
Very much	10.097	1.138-89.591	0.038
Concern about melanoma			
Little	1.761	0.443-6.994	0.421
Some	0.998	0.228-4.363	0.998
Much	1.573	0.327-7.562	0.571
Very much	0.813	0.093-7.130	0.851

Reference categories were as follows: Male: female; AJCC stages II, III and IV: AJCC stage I; current treatment: no current treatment; anxiety disorder: no anxiety disorder; ≥5 comorbidities: <5 comorbidities; concern for COVID-19: none; concern for melanoma: none. Age was incorporated as a linear variable. Significant findings are highlighted in bold.

AJCC: American Joint Committee on Cancer; CI: 95% confidence interval; OR: odds ratio.

^a The dependent variable was postponed/missed appointments (yes=1, no=0), all other independent variables were integrated simultaneously into the model.

anxiety disorder (data not shown). Participants with ≥five comorbidities did not differ from those with <five comorbidities regarding postponed/missed appointments (table 3, supplementary table 3).

Discussion

Many oncology centres experienced substantial reductions in melanoma referrals and/or diagnoses during the first COVID-19 wave [13, 15, 23] while in others, melanoma defied the lockdown [24]. Fortunately, the German health-care system did not tend to collapse during the first wave of pandemic. This has enabled us to continue care for melanoma patients using extensive precautions, following German Onkopedia guidelines [25], recommendations by the Robert-Koch-Institute [26, 27] and guidelines for protection of medical staff and patients [4]. Safety measures included accurate hygiene and disinfection, SARS-CoV-2 swabs prior to plannable procedures and hospital admissions, compulsory face masks for patients and staff, FFP2 masks during surgery in the head/neck region and/or during general anaesthesia, isolation of SARS-CoV-2 infected patients in separate wards, accommodation of patients with unclear COVID-19 status in separate rooms, safety distancing, limitation of concurrent appointments in melanoma clinics and restraint of visitors and escorts. One participant probably acquired SARS-CoV-2 infection from another inpatient in the same room at the beginning of the pandemic, when routine preadmission SARS-CoV-2 swabs had not yet been

implemented. To our knowledge, this was the only nosocomial SARS-CoV-2 infection in a patient from the HTZ.

Treatment changes or postponements

Treatment postponement/change was rare in our cohort. Surgery was postponed in only two patients. In countries more severely affected by the pandemic, such as the USA, the UK and Italy, melanoma surgery had to be triaged more strictly [28-31]. For example, based on multidisciplinary recommendations from the USA, it was proposed to postpone surgery of T1 melanomas for three months if there was no macroscopic residual disease and to delay definite treatment of ≥T2 melanomas if biopsy margins were negative [28].

One patient received hypofractionated radiotherapy for brain metastasis, as recommended by radiotherapy associations [32]. In another, intervals between pembrolizumab infusions were prolonged in accordance with guidelines for management of melanoma during the COVID-19 pandemic [25, 29]. Many other patients already received nivolumab or pembrolizumab at long intervals (*i. e.*, every four or six weeks).

The effects of immune checkpoint inhibitors (ICIs) on SARS-CoV-2 infection are a matter of debate [33-36]. On the one hand, ICIs are suspected to exacerbate cytokine-release syndrome, which may contribute to a fatal outcome of COVID-19. ICI-related pneumonitis might be mistaken for COVID-19-related interstitial pneumonia and vice versa. Co-occurrence of both is likely to be life-threatening. Steroids used for the management of immune-related adverse events contribute to

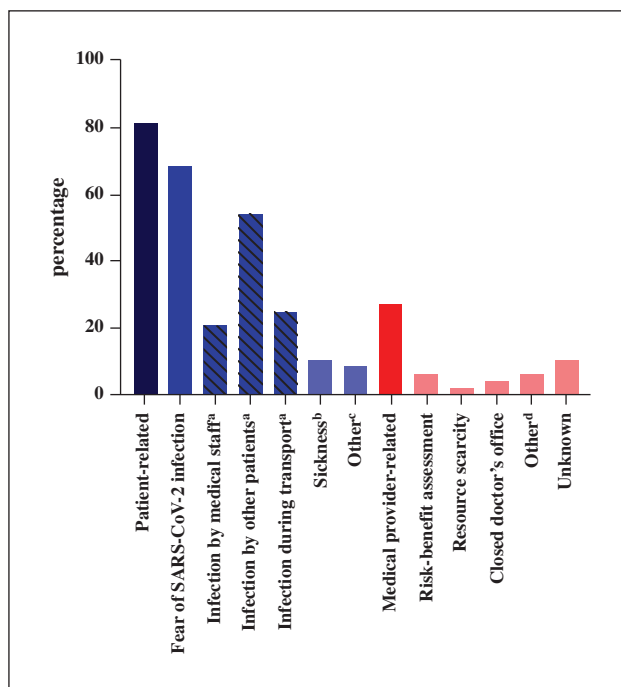


Figure 2. Reasons for postponing or missing appointments. The number of patients who delayed or missed their appointments (n=48) was set at 100%.

^a Regarding fear of SARS-CoV-2 infection, several participants marked more than one answer. Percentages were calculated based on the total number of answers (n=72, 100%).

^b Sickness other than SARS-CoV-2 infection.

^c Other patient-related reasons reported as free text included fear of infecting an immunosuppressed wife with SARS-CoV-2, lack of childcare, wish to postpone follow-up as long as the patient felt healthy and legal requirements for contact.

^d Other medical provider-related reasons comprised SARS-CoV-2 infection of the practicing dermatologist and lack of possibility to realize the planned examinations.

immunosuppression and thereby to a higher risk of severe COVID-19. On the other hand, adjuvant and palliative immunotherapy significantly improve survival of melanoma patients [37]. According to the UK Coronavirus Cancer Monitoring Project [12] and experience from an oncology centre in Milan, Italy [38], immunotherapy did not correlate with particularly severe outcome of COVID-19. Melanoma patients treated with ICIs in Milan or Turin had a lower incidence of symptomatic SARS-CoV-2 infection compared to the general Italian population, indicating that immunotherapy can be safely pursued in the majority of cases [39]. Consensus guidelines recommend to continue offering adjuvant and palliative ICIs when indicated, preferably with PD-1 monotherapy with four- or ideally six-week intervals [25, 29]. The same applies to targeted therapies with BRAF and MEK inhibitors [25, 29].

Changes in appointments

Following consensus guidelines [29], staging and follow-up examinations were condensed and consultation by phone was offered when appropriate. Of our participants, 14.8% postponed/missed appointments, almost always in

agreement with medical providers. Most cancellations were made by the patients themselves due to fear of COVID-19. According to a WhatsApp messenger-based survey of cancer patients from Italy, 37% requested postponement of their appointment [40]. The emotion reported most frequently was fear. In line with this, major impact factors on postponed/cancelled appointments identified in our study were concern for COVID-19 and anxiety disorder. It is likely that participants with close acquaintances with COVID-19 also cancelled consultations more frequently because of increased concern.

Patients with melanoma Stage IV were more likely to postpone/cancel appointments than patients with Stage I, possibly because intervals for close follow-up could be prolonged or because stage IV patients had a worse performance status. According to the WhatsApp survey, patients with an Eastern Cooperative Oncology Group (ECOG) performance status of 2 requested a delay for visits and/or treatment more frequently than those with a better performance status [40].

Current treatment was associated with a reduced risk of postponing/missing appointments, probably because patients currently requiring therapy set greater value on cure from melanoma or relief from symptoms than on avoidance of nosocomial SARS-CoV-2 infection.

Notably, neither advanced age nor comorbidities, except anxiety disorder, conferred a higher likelihood of postponing/missing appointments, even though older age and comorbidities, such as cardiovascular disease, diabetes, chronic obstructive lung disease and immunosuppression, are known to contribute to an increased risk of severe COVID-19 [41].

Delaying melanoma follow-up is a double-edged sword. On the one hand, it contributes to minimizing nosocomial SARS-CoV-2 infection and generates resources for patients with COVID-19. On the other hand, missing melanoma recurrence or progression may be worse than the small residual risk of SARS-CoV-2 infection that remains despite careful prevention [6, 16, 42]. Clearly, telemedicine provides great potential for optimizing care for melanoma patients during the ongoing pandemic [19, 32, 43], even though this method cannot replace laboratory tests, staging examinations and treatments.

Limitations

The conclusions based on the results of this study may not be applicable to countries more severely affected by the pandemic. The rate of treatment change and/or postponed/cancelled appointments may have been different among patients who did not participate in the study. More than two thirds of our respondents had no current treatment. It was probably easier to postpone appointments for these patients who were potentially cured than for patients with ongoing therapy. Furthermore, determinants for postponed/missed appointments may have been overlooked due to the limited cohort size.

Anxiety disorder was self-reported and not further validated. Information about postponed/missed appointments with practicing dermatologists was obtained exclusively from the patient questionnaire. Last, but not least, concern for COVID-19 depends on the development of the pandemic. Our data were collected at the end of the first wave in

Germany, and fear of COVID may decrease thereafter and rise again during further waves.

Conclusion

Among our participants, treatment changes were rare and the percentage of missed/delayed appointments was rather small. Clearly, decisions on delaying or continuing melanoma treatment and follow-up depend on the development of the pandemic, availability of resources, legal requirements, and individual risk-benefit assessment. Instructing patients in-depth about prevention of COVID-19 and discussing individual trade-offs is essential to provide optimal care in this turbulent time [30, 32, 40, 44]. ■

Disclosures. *Financial support: none. Conflict of interests: M.-L. Schaarschmidt has been an advisor and/or received speakers' honoraria and/or received grants and/or participated in clinical trials of the following companies: AbbVie, Ammirall, Biogen Inc., Böhringer-Ingelheim, Celgene, Janssen-Cilag, Eli Lilly, Merck Serono, MSD, Novartis Pharma and UCB.*

J. Weilandt obtained speaker's honoraria from Novartis.

B. Sasama participated in clinical trials from Array Biopharma, Janssen-Cilag, MSD and Sandoz and obtained financial support for participation in conferences from Janssen-Cilag.

J. Ohletz served as investigator for Novartis and received financial support for participation in conferences from Janssen-Cilag and Novartis.

W. Harth was a member of advisory boards of Novartis, obtained honoraria from Novartis and LEO Pharma, and received support for conferences from AbbVie, Ammirall Hermal, Beiersdorf, Dermo Medical, Biofrontera, Celgene, Dermapharm, Dr. Pfleger, Galderma, Hexal, Janssen-Cilag, Jenapharm, Kosmetik vom Wasserfall, LEO Pharma, Medac, Novartis and Pfizer.

U. Hillen served as investigator for Magnosco and Novartis, was a member of advisory boards of Novartis and Takeda, obtained honoraria from AbbVie, Novartis and OmniaMed, and received support for conferences from Ammirall Hermal, Amgen, Biofrontera, BMS, L'Oreal, MSD, Novartis, Roche, Pierre Fabre and Takeda.

W. K. Peitsch served as investigator for AbbVie, Array Biopharma, Boehringer Ingelheim, Eli Lilly, Janssen-Cilag, MSD, Novartis, Pfizer and UCB Pharma, was a member of advisory boards of BMS, Eli Lilly, LEO Pharma, MSD, Novartis, Pfizer, Roche and UCB Pharma, obtained honoraria from ALK-Abello, AbbVie, Biotest, BMS, Janssen-Cilag, MSD, Novartis, Pfizer, Dr. Pfleger and Roche, and received support for conferences from AbbVie, Actelion, ALK-Abello, Alma Lasers, Ammirall Hermal, ARC Lasers, Asclepion, Beiersdorf, BMS, Celgene, Dermapharm, Dermasence, Eli Lilly, Galderma, GSK, Immunocore, Janssen-Cilag, L'Oreal, La Roche Posay, LEO Pharma, Medac, MSD, Mylan, Novartis, Pierre Fabre, P&M Cosmetics, Pfizer, Roche, Sanofi and Sun Pharma.

M. Teuscher, K. Diehl and A. Könnecke declare no conflicts of interest.

The study was performed without support from the pharmaceutical industry, and the conflicts of interest have no impact on the content of the manuscript.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1684/ejd.2021.4098.

Table S1. Disease and treatment characteristics and their association with postponed/missed appointments.

Table S2. Treatment changes or postponement due to the pandemic.

Table S3. Comorbidities and their association with postponed/missed appointments.

Fig. S1. Number of new SARS-CoV-2 infections per day in Germany and Berlin between February 1st 2020 and July 1st 2020.

References

1. World Health Organization. WHO coronavirus disease (COVID-19) dashboard. Geneva: World Health Organization; 2020. Available at: <https://covid19.who.int/>. (accessed: 05 Aug 2020).
2. Robert Koch-Institut (RKI). Täglicher Lagebericht des RKI zur Coronavirus-Krankheit-2019 (COVID-19) 30.06.2020—aktualisierter Stand für Deutschland. 2020. Available at: www.rki.de/DE/Content (accessed 05 Aug 2020).
3. Wollina U. Challenges of COVID-19 pandemic for dermatology. *Dermatol Ther* 2020; 33(5): e13430.
4. Arbeitsgemeinschaft Wissenschaftlichen Medizinischen Fachgesellschaften e.V. (AWMF). AWMF-S1-Leitlinie: Interdisziplinär abgestimmte Empfehlungen zum Personal- und Patientenschutz bei Durchführung planbarer Eingriffe zur Zeit der SARS-CoV-2-Pandemie. (AWMF Registry No. 017-080, June 2020) AWMF. 2020. Available at: www.awmf.org/uploads/tx_szleitlinien/. (accessed 05 Aug 2020).
5. Raymond E, Thieblemont C, Alran S, Faivre S. Impact of the COVID-19 outbreak on the management of patients with cancer. *Target Oncol* 2020; 15: 249-59.
6. Gomolin T, Cline A, Handler MZ. The danger of neglecting melanoma during the COVID-19 pandemic. *J Dermatolog Treat* 2020; 31: 444-5.
7. Sud A, Jones ME, Broggio J, et al. Collateral damage: the impact on outcomes from cancer surgery of the COVID-19 pandemic. *Ann Oncol* 2020; 31: 1065-74.
8. Alhalabi O, Subbiah V. Managing cancer care during the COVID-19 pandemic and beyond. *Trends Cancer* 2020; 6: 533-5.
9. Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol* 2020; 21: 335-7.
10. Wang H, Zhang L. Risk of COVID-19 for patients with cancer. *Lancet Oncol* 2020; 21: e181.
11. Dai M, Liu D, Liu M, et al. Patients with cancer appear more vulnerable to SARS-CoV-2: a multicenter study during the COVID-19 outbreak. *Cancer Discov* 2020; 10: 783-91.
12. Lee LYW, Cazier JB, Starkey T, Turnbull CD, Kerr R, Middleton G. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. *Lancet* 2020; 395: 1919-26.
13. Earnshaw CH, Hunter HJA, McMullen E, Griffiths CEM, Warren RB. Reduction in skin cancer diagnosis, and overall cancer referrals, during the COVID-19 pandemic. *Br J Dermatol* 2020; 183(4): 792-4.
14. Mugele K, Tschoepe C, Kohlstädt S. Corona-Taskforce warnt weiterhin vor zu spät diagnostizierten Krebserkrankungen. *DKG Forum aktuell* 2020; 35: 178.
15. London JW, Fazio-Eynullayeva E, Palchuk MB, Sankey P, McNair C. Effects of the COVID-19 pandemic on cancer-related patient encounters. *JCO Clin Cancer Inform* 2020; 4: 657-65.

- 16.** Tejera-Vaquero A, Nagore E. Estimated effect of COVID-19 lockdown on melanoma thickness and prognosis: a rate of growth model. *J Eur Acad Dermatol Venereol* 2020; 34: e351-3.
- 17.** Ricci F, Fania L, Paradisi A, *et al.* Delayed melanoma diagnosis in the COVID-19 era: increased breslow thickness in primary melanomas seen after the COVID-19 lockdown. *J Eur Acad Dermatol Venereol* 2020; 34(12): e778-9.
- 18.** Gentileschi S, Caretto AA, Tagliaferri L, Salgarello M, Peris K. Skin cancer plastic surgery during the COVID-19 pandemic. *Eur J Surg Oncol* 2020; 46: 1194-5.
- 19.** Tagliaferri L, Di Stefani A, Schinzari G, *et al.* Skin cancer triage and management during COVID-19 pandemic. *J Eur Acad Dermatol Venereol* 2020; 34: 1136-9.
- 20.** Caliendo V, Picciotto F, Quaglino P, Ribero S. COVID infection and sentinel lymph node procedure for melanoma: management in a dermatology center in a high-risk pandemic area. *Dermatol Ther* 2020; 33(4): e13536.
- 21.** Ueda M, Martins R, Hendrie PC, *et al.* Managing cancer care during the COVID-19 pandemic: agility and collaboration toward a common goal. *J Natl Compr Canc Netw* 2020: 1-4.
- 22.** Herdman M, Gudex C, Lloyd A, *et al.* Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res* 2011; 20: 1727-36.
- 23.** Barruscotti S, Giorgini C, Brazzelli V, *et al.* A significant reduction in the diagnosis of melanoma during the COVID-19 lockdown in a third level center in the north of Italy. *Dermatol Ther* 2020; 33(6): e14074.
- 24.** Schauer AA, Kulakov EL, Martyn-Simmons CL, Bunker CB, Edmonds E. Melanoma defies "lockdown": ongoing detection during COVID-19 in central London. *Clin Exp Dermatol* 2020; 45(7): 900.
- 25.** von Lilienfeld-Toal M, Greinix H, Hein A, *et al.* Coronavirus-Infektion (COVID-19) bei Patienten mit Blut- und Krebserkrankungen. *Onkopedia* 2020, accessed 05 Aug 2020 <https://www.onkopedia.com/de/onkopedia/guidelines/>.
- 26.** Robert Koch-Institut (RKI). *Empfehlungen des RKI zu Hygienemaßnahmen im Rahmen der Behandlung und Pflege von Patienten mit einer Infektion durch SARS-CoV-2.* 2020. Available at: <https://www.rki.de/DE/Content> (accessed 05 Aug 2020).
- 27.** Robert Koch-Institut (RKI). *Coronavirus SARS-CoV-2 - Erweiterte Hygienemaßnahmen im Gesundheitswesen im Rahmen der COVID-19 Pandemie.* 2020. Available at: <https://www.rki.de/DE/Content/> (accessed 05 Aug 2020).
- 28.** Baumann BC, MacArthur KM, Brewer JD, *et al.* Management of primary skin cancer during a pandemic: Multidisciplinary recommendations. *Cancer* 2020; 126: 3900-6.
- 29.** Nahm SH, Rembielak A, Peach H, Lorigan PC. Consensus guidelines for the management of melanoma during the COVID-19 pandemic: surgery, systemic anti-cancer therapy, radiotherapy and follow-up. *Clin Oncol* 2020; 33(1): e54-7.
- 30.** Rossi E, Trakatelli M, Giacomelli L, *et al.* The COVID-19 outbreak in dermatologic surgery: resetting clinical priorities. *J Eur Acad Dermatol Venereol* 2020; 34(10): e543-5.
- 31.** Elmas ÖF, Demirbaş A, Düzayak S, Atasoy M, Türsen Ü, Lotti T. Melanoma and COVID-19: a narrative review focused on treatment. *Dermatol Ther* 2020; 33(6): e14101.
- 32.** Nguyen NP, Vinh-Hung V, Baumert B, *et al.* Older cancer patients during the COVID-19 epidemic: practice proposal of the International Geriatric Radiotherapy Group. *Cancers* 2020; 12: 1287.
- 33.** Bersanelli M. Controversies about COVID-19 and anticancer treatment with immune checkpoint inhibitors. *Immunotherapy* 2020; 12: 269-73.
- 34.** Kattan J, Kattan C, Assi T. Do checkpoint inhibitors compromise the cancer patients' immunity and increase the vulnerability to COVID-19 infection? *Immunotherapy* 2020; 12: 351-4.
- 35.** Citarella F, Russano M, Pantano F, *et al.* Facing SARS-CoV-2 outbreak in immunotherapy era. *Future Oncol* 2020; 16: 1475-85.
- 36.** Quaglino P, Fava P, Brizio M, *et al.* Metastatic melanoma treatment with checkpoint inhibitors in the COVID-19 era: experience from an Italian Skin Cancer Unit. *J Eur Acad Dermatol Venereol* 2020; 34: 1395-6.
- 37.** Leonardi GC, Candido S, Falzone L, Spandidos DA, Libra M. Cutaneous melanoma and the immunotherapy revolution (review). *Int J Oncol* 2020; 57: 609-18.
- 38.** Trapani D, Marra A, Curigliano G. The experience on coronavirus disease 2019 and cancer from an oncology hub institution in Milan, Lombardy Region. *Eur J Cancer* 2020; 132: 199-206.
- 39.** Pala L, Conforti F, Saponara M. Data of Italian cancer centers from two regions with high incidence of SARS CoV-2 infection provide evidence for the successful management of patients with locally advanced and metastatic melanoma treated with immunotherapy in the era of COVID-19. *Semin Oncol* 2020; 47(5): 302-4.
- 40.** Gebbia V, Piazza D, Valerio MR, Borsellino N, Firenze A. Patients with cancer and COVID-19: a whatsapp messenger-based survey of patients' queries, needs, fears, and actions taken. *JCO Glob Oncol* 2020; 6: 722-9.
- 41.** U.S. Centers for disease control and prevention (CDC). *People of any age with underlying medical conditions.* U.S. Department of Health & Human Services, U.S. centers for disease control and prevention (CDC). 2020. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/> (accessed 05 Aug 2020).
- 42.** Cortiula F, Petike A, Bartoletti M, Puglisi F, Helleday T. Managing COVID-19 in the oncology clinic and avoiding the distraction effect. *Ann Oncol* 2020; 31: 553-5.
- 43.** Janda M, Swetter SM, Horsham C, Soyer HP. Virtual melanoma checks during a pandemic. *Br J Dermatol* 2020; 183(4): 752-3.
- 44.** Shankar A, Saini D, Roy S. Cancer care delivery challenges amidst coronavirus disease - 19 (COVID-19) outbreak: specific precautions for cancer patients and cancer care providers to prevent spread. *Asian Pac J Cancer Prev* 2020; 21: 569-73.