



Humanistic burden of disease for patients with advanced melanoma in Canada

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Abstract

Background Metastatic melanoma is a highly aggressive cancer, often striking in the prime of life. This study provides new information directly from advanced melanoma (stage III and IV) patients on how their disease impacts their health-related quality of life (HRQL).

Methods Twenty-nine in-depth, qualitative interviews were conducted with adult patients with advanced melanoma in Canada. A semi-structured interview guide was used. Interviews were transcribed verbatim and key concepts were identified using a grounded theory analytic approach.

Results Many patients' journeys began with the startling diagnosis of an invasive disease and a vastly shortened life expectancy. By the time they reached an advanced stage of melanoma, these patients' overall functioning and quality of life had been greatly diminished by this quickly progressing cancer. The impact was described in terms of physical pain and disability, emotional distress, diminished interactions with friends and family, and burden on caregivers.

Conclusion Our findings provide evidence of signs, symptoms, and functional impacts of advanced melanoma. Signs and symptoms reported (physical, mental, and social) confirm and expand on those reported in the existing clinical literature. Primary care physicians should be better trained to identify melanomas early. Oncology care teams can improve on their current approaches for helping patients navigate treatment options, with information about ancillary services to mitigate disease impacts on HRQL, such as mental health and social supports, as well as employment or financial support services.

Keywords Melanoma · Qualitative · Health-related quality of life · Cancer · Burden of disease · Patient interviews

Background

Melanoma is an aggressive cancer originating in pigment-producing cells known as melanocytes, with one of the fastest rising incidences of all cancers [1, 2]. Approximately 15% of melanoma patients are diagnosed during their mid-40s or early 50s, 22% between ages 55 and 64, and 22% between ages 65 and 74 [3]. While the 5-year survival rate for all melanoma patients is approximately 90%, patients with metastatic disease have a median survival of 5 to 8 months and an estimated

5-year survival rate of just 19% or less, depending on the location of the metastases [4].

Risk factors for melanoma include fair complexion, blonde or red hair, white ethnicity, tendency to freckle, easily burnt or tanned skin, history of blistering sunburns, family history, immunosuppression, and dysplastic nevi [5]. Genetics are also a factor, with at least four genes identified as having involvement in familial melanoma [6]. Major predictors of survival differ by stage: in stage I and II, tumor thickness, mitotic rate, and ulceration predict survival; in stage III, the number of metastatic nodes, tumor load, tumor thickness, and ulceration has the most prognostic value; and the site of distant metastases and serum lactate dehydrogenase level are the strongest predictors among stage IV patients [7].

Melanoma is known to cause physical and mental health deficits that lead to impairments in patients' ability to function, collectively referred to as the humanistic burden on patients' health-related quality of life (HRQL). Fatigue and physical functioning are the most commonly reported

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HRQL domains across published studies, particularly during treatment and as measured by the EORTC QLQ-C30 [8–14]. Several studies have examined the prognostic value of HRQL scores with respect to survival and/or disease progression. Worse global HRQL; lower physical, social, and role functioning; and increased symptoms such as fatigue, pain, and appetite loss were predictive of disease progression/survival [12, 15, 16].

Including the patient's perspective as an element of health outcomes in oncology is increasingly recognized as a necessary complement to traditional measures like survival and recurrence rates [17]. To date, few publications have reported on the functional and emotional impact of advanced melanoma using qualitative interview methods [18–20]. The objective of this study was to describe the humanistic burden of advanced melanoma from the patients' perspective.

Methods

Study design

This was a qualitative, non-interventional study to explore the experience of patients with advanced melanoma (stage III and IV) in Canada.

Target population and recruitment

Recruitment was facilitated by Canadian patient advocacy associations, who made initial contact with members and determined patient eligibility. Patients were recruited from seven provinces: Alberta, British Columbia, Manitoba, New Brunswick, Ontario, Quebec, and Saskatchewan. Patients met all of the following inclusion criteria: had advanced melanoma (stage III or IV, self-report of doctor diagnosis), 18 years of age or above, spoke English or French, and were willing and able to participate in the study and give written informed consent.

Study procedures

Individual interviews were conducted in either English or French by one of five trained interviewers and were completed in a single session lasting 45 to 60 min, during which patients shared their stories and answered questions about their experiences with advanced melanoma. Interviews conducted in French were translated by a professional translation service provider to ensure proper language translation of the French-Canadian language into English. The interviews were audio-recorded and transcribed verbatim using a professional linguist and superior machine assisted rapid translation that ensures accuracy and consistency in the translation process.

Most interviews ($n = 18$; 62%) took place in one of two central locations (Montreal and Vancouver), scheduled to align with an advocacy group forum. These interviews took place in an office suite. Seven others ($n = 7$; 24%) took place at locations convenient to patients within each of the five remaining provinces, and these interviews were scheduled directly with the interviewers. Four interviews (14%) were conducted by telephone with patients who were unable to travel to any interview location. Each patient received a standard stipend.

Prior to completing the interview, patients were provided with an overview of the study and the patient information letter and informed consent form. The interview was guided by open-ended questions that were part of a pre-specified interview guide. Open-ended questions designed to elicit personal experience without leading the patient, for example, "First, will you describe what has it been like for you since you were diagnosed with advanced melanoma?" and, "Please describe any changes in how your body feels or functions since you were diagnosed with advanced melanoma?", were developed to allow patients to describe their experiences spontaneously. Patients were queried about specific symptoms and impacts on functioning or well-being if they did not mention them spontaneously.

Data analysis

Transcripts were coded to identify themes important to patients. Grounded theory data collection and analysis methods were used to identify important concepts from the patient point of view without applying an a priori theoretical model [21, 22]. This allows for the elicitation of patients' experiences rather than using broader themes developed through the eyes of the researcher, as in traditional content analysis [23]. Grounded theory is widely used for analyzing exploratory qualitative data [24, 25].

Interview questions for this study were designed based on a melanoma literature review, collaboration with clinical experts, and patient advocacy groups to include key concepts based on previously known symptoms and impacts. The interview guide is a set of questions exploring patients' general experience of the effects of melanoma on their symptoms and quality of life. An initial code book was developed by the research team, such that the concept elicitation interview guide was the starting point. Codes were created to capture key concepts in the guide by interviewers. For example, for a probe asking about diarrhea as a side effect of treatment, a code for the experience of diarrhea was created.

After the first two transcripts were coded by all researchers independently, the coding scheme was further developed to capture new, emerging symptoms, experiences, and HRQL impacts. Each transcript was then coded and independently reviewed by another researcher. Discrepancies and changes to the coding scheme were harmonized among the research

team, ensuring reliability of coding. All data was analyzed using ATLAS.ti [26].

Results

Sample characteristics

Patients' sociodemographic and clinical characteristics are shown in Table 1. Twenty-nine adult patients with advanced melanoma participated in this study. A majority ($n = 18$; 62%) were female, with a mean age of 52 (range = 28–69). Seven of the ten Canadian provinces were represented, and five patients (17%) identified themselves as French speaking (three of the five requested a French-speaking interviewer). All patients had at least a secondary school education. Ten (34%) were receiving disability, and nine (31%) were retired or semi-retired, the remaining nine were either employed, students, or unemployed. Regarding clinical characteristics, 20 patients (69%) were either in stage III or IV when first diagnosed, and 22 patients (76%) were in stage III or IV at the time of the interview, while three (10%) reported being in remission and four (14%) had achieved no evidence of disease (NED).

Patients' experience with signs and symptoms of advanced melanoma

Patients' reports of pre-diagnosis disease-related symptoms varied. Four patients (14%) reported being asymptomatic prior to their diagnoses, while others recalled feeling tired ($n = 3$; 10%), having pain ($n = 2$; 7%), itchy moles ($n = 2$; 7%), flu-like symptoms ($n = 1$; 3%), or gastrointestinal problems ($n = 1$; 3%) preceding their diagnosis. Visible signs that alarmed patients or their family and friends enough to seek medical treatment included lumps or nodes ($n = 5$; 17%) and suspicious moles ($n = 8$; 28%). One patient elaborated,

“It was a mole on my left thigh. I had been looking at it and thought I was being proactive ... you know what, this doesn't look right. I'm just going to go get it taken off. So I did ... and so when he told me, I was in shock.”

Upon beginning of treatment, patients reported difficulty at times distinguishing between symptoms arising from the disease versus its treatment. Of those symptoms that could be attributed specifically to the disease, the most severe symptoms experienced were linked to brain lesions. Such symptoms, including seizures, severe headaches, blurred vision, and nausea, led to a diagnosis of melanoma for two patients (7%). One patient stated,

Table 1 Sociodemographic and clinical characteristics of study sample

	N (%)
Age (mean years)	52
Gender	
Female	18 (62.1%)
Male	11 (37.9%)
Primary language	
English	24 (82.8%)
French	5 (17.2%)
Province	
Alberta	2 (6.9%)
British Columbia	13 (44.8%)
Manitoba	1 (3.5%)
New Brunswick	1 (3.5%)
Ontario	7 (24.1%)
Quebec	4 (13.8%)
Saskatchewan	1 (3.5%)
Education	
Completed secondary school	4 (13.8%)
Some college courses (in QC-CEGEP)	1 (3.5%)
Completed college (in QC-CEGEP)	8 (27.6%)
Some university or technical college	4 (13.8%)
Completed university (bachelor)	6 (20.7%)
Postgraduate	6 (20.7%)
Work	
Employed full-time	6 (20.7%)
Part-time	2 (6.9%)
Student/part-time	1 (3.5%)
On disability or leave of absence	10 (34.5%)
Unemployed	1 (3.5%)
Retired	9 (31.0%)
Marital status	
Married	26 (89.7%)
Single/never married	3 (10.3%)
Disease stage at diagnosis (patient self-report)	
Do not know/no answer	2 (6.9%)
Stage 0	1 (3.5%)
Stage I	2 (6.9%)
Stage II	4 (13.8%)
Stage III (locally advanced cancer)	11 (37.9%)
Stage IV (metastatic)	9 (31.0%)
Disease stage at interview (patient self-report)	
NED	4 (13.8%)
Remission	3 (10.3%)
Stage III (locally advanced cancer)	4 (13.8%)
Stage IV (metastatic)	18 (62.1%)

“Oh, it was severe – the changes. My diagnosis was brought on after I suffered a couple of seizures. So I had a seizure. I didn't know it was a seizure.”

Another patient remembered,

“I was having blurred vision, double vision, severe – like debilitating headaches, nausea, vomiting. Yeah, I couldn’t stand noise at all...I was just really unwell, though, I guess. It’s hard to stand up for yourself when you’re not feeling good.”

Physical impact of advanced melanoma on patients’ lives

The most common disease-related physical impacts reported by patients ($n = 13$; 45%) related to sleep problems, primarily due to anxiety, stress, and/or worry related to their condition; and some patients’ troubles sleeping were due to pain or discomfort. One patient explained,

“At the beginning, after my first surgery, I was always tired, I was always going back to bed during the day... That’s the bad days. I was sleeping almost all day long. I was getting up, I was not able to make it for the entire dinner. I was functioning at reduced speed, I was not able to do anything the day [sic], anything I was usually able to do.”

Expanding on how their sleep was impacted, eight patients (28%) reported needing to take naps or at least lie down due to their symptoms, and five (17%) reported sleeping more than usual due to their illness.

For many patients, the physical impact was debilitating. A third of patients ($n = 10$; 34%) reported that the use of a limb had been impaired due to either tumors or neurological symptoms when their melanoma metastasized in the brain. Five patients (17%) reported having become generally inactive either because their symptoms and/or an extended recovery time left them feeling tired/fatigued, or low in energy. As one patient articulated,

“I was active. I liked to go on – when I go on trips with my wife, we like to go and walk in these – these trails, wilderness trails and that – and we’re – really like to do that. And I noticed that I just didn’t have the energy to go. I still don’t have the energy to go. And you know, that’s – and that was part – you know, you’ve got one doctor telling you, oh no, you can do this.”

Emotional impact of advanced melanoma

Patients overwhelmingly reported an emotional impact of advanced melanoma. For many, the journey began with the startling change from a previously healthy person to someone

with an invasive disease and a vastly shortened life expectancy. Nearly half ($n = 14$; 48%) reported that their sense of self had changed through their illness experience, struggling with self-identifying or being identified by others as a cancer patient or survivor. One patient, for example, explained,

“I don’t want anybody driving me to my appointments because then I’d feel like a cancer patient. I don’t want my neighbors bringing me casseroles because I feel like a cancer patient. You know?”

Patients also discussed their feelings as oscillating between emotional highs and lows over the course of diagnosis, treatment, and progression. One patient described the process as:

“Well, obviously at first when you’re diagnosed, you are probably at one of the lowest points, I guess, emotionally. And then as things progress with treatments and finding out disease progressed instead of getting better, you end up, you know, with hope and then back down at the bottom again, or lower than bottom, I suppose. And then there’s the elation of finding out that one did work, and then you kind of plateau at the top, I think, emotionally.”

Two-thirds of patients ($n = 19$; 66%) reported feeling worried about their disease. In general, patients worried about their future lifespan and quality of life, as well as the impact of their illness, and potentially their death, on loved ones. Other commonly reported emotional impacts included anxiety ($n = 12$; 41%), depression ($n = 11$; 38%), stress ($n = 10$; 34%), loss of control ($n = 9$; 31%), anger or sadness ($n = 7$; 24%), and increased emotional sensitivity ($n = 6$; 21%). One patient stated,

“I find if I get worried [...] if I feel a pain in my gut or if I feel – a symptom that I’ve felt before where it – and it turned out to be cancer-related, that – I shut down and I get really inside my head and almost depressed and worry. Worry, worry, worry.”

and another patient echoed,

“Initially, it’s the anxiety. So you’re dealing with the – and then that can lead to depression. You know, just you get wound up so much...”

The experience of living with melanoma had a considerable effect on many patients’ outlook. While seven (24%) described themselves as having become more realistic, roughly half of the sample ($n = 13$; 45%) discussed living more in the moment and learning to appreciate all the good things they have. Others ($n = 4$; 14%) said they had become more

accepting of or kinder to themselves. One reported becoming calmer through the illness experience:

“So having said all that, (laughter) how has it changed my life? In the sense that I’m calmer, I’m more realistic about myself. I’m kinder to myself, because I treat myself like this is today, this is the best you’ve got is right now ... there’s many gifts that cancer has given me.”

Other emotional impacts mentioned by some patients were: feeling isolated or alone and feeling guilt about burden placed upon family and friends.

Attitudes and experience with disease progression

The rapidity of progression was a concern and a particular challenge for patients. Finding out that one’s disease had progressed was emotionally very difficult for the patients, and many reported being angry, having trouble sleeping, having “charged” emotions, with fear about having to go through a difficult treatment for the second time. Several patients also worried about whether their treatment would be successful, what the next steps would be if it wasn’t, whether their cancer would return, and the risk of acquiring infections during treatment.

Many patients ($n = 13$; 45%) recalled that they had feared that they would die from their illness, and many continued to be concerned that the disease would ultimately be fatal for them. Those who had achieved NED or remission ($n = 5$; 17%) described a constant awareness that their disease status was likely temporary and that the melanoma would return. One patient poignantly described the sadness surrounding coming to terms with one’s own death and all the loss that advanced cancer can bring:

“Since the metastatic? It’s been quite a journey. It’s been – a lot of it has been really hard in that it’s just – you know, fear of death is a lot of it or, you know, coming to terms with that, and reconciling that was probably the most difficult part. And then just the sense of loss, you know, around that. – Once you come to terms with death, it’s – there’s still a sense of loss around family and children and spouse and things like that. So that was a lot of the sadness or that was part of it.”

The social consequences of advanced melanoma

Nearly all patients ($n = 26$; 90%) discussed how their melanoma impacted their social relationships. Common themes included role changes within families, support from others, and difficulties participating in social activities. Most ($n = 16$; 55%) noted the disruptions it caused to daily life within their

homes, especially for those with children, the stress it caused for others, and the burden it put on spouses and other household members to perform tasks formerly done by the patient. Patients felt grateful for the support they had received but some also felt guilt from the perceived burden their disease caused their family and friends.

The overwhelming majority ($n = 28$; 97%) reported having received support from others during their illness experience, and almost half ($n = 13$; 45%) reported that their relationships with family or friends had improved as a result. One patient articulated the positive aspects of having cancer, saying,

“But there were definitely many, many blessings along the way. I’ve had huge community support and friends come out and really, really step up and really be there for me, so it’s really been a huge eye opener of all the blessings that are – that I have, as well...and it’s been really good for my relationship with my husband and my kids and my mother, and so a lot of good things have come out of it.”

While most of the discussions of social relationships were positive, nine patients (31%) recalled instances in which they perceived others as not supportive. These included family members who did not want to discuss the illness, and significant others who became emotionally distant or even ended their relationship with the patient:

“And the people that I don’t want in my life, I don’t try and sugarcoat it and break their hearts and, you know – just say you don’t support me, you’re not my true friend. Please go. And a lot of people were – will yell and call me names to whatever degree, but I just don’t care. I have my true friends, and then the people that don’t support me – kick them to the curb. (laughter) Or they’ll kick me to the curb, but I don’t really care.”

Despite the marked challenges of living with melanoma, about two-thirds of the sample ($n = 21$; 72%) spoke of efforts to “live normally” for the sake of family members, and a need to perform household chores, run errands, exercise, and raise their children. A typical pattern of impact included restricted social activity due to being tired or out of concern for becoming exposed to contagions while immune-compromised during treatment, while still trying to attend special events such as weddings or vacations, or maintain involvement in specific activities.

Discussion

This was a qualitative, non-interventional study to explore the functional and emotional impact of advanced melanoma on

patients' lives in Canada. The study sample reflects a range of disease severity, but necessarily excludes the experiences of those who were not well enough to participate in interviews. We sought to minimize this limitation by conducting some interviews by telephone in order to include patients too ill to travel to interviews conducted in person.

Many patients' journeys began with the startling change from being a previously healthy person to one with an invasive disease and a vastly shortened life expectancy. By the time patients reached an advanced stage of melanoma, their overall functioning and HRQL had already been greatly diminished by the quickly progressing cancer. The patient's experience was described in terms of physical pain and disability, emotional distress, diminished interactions with friends and family, and burden on caregivers.

The predominant physical symptom was fatigue, to the point of exhaustion and inability to function in everyday life or participate in usual activities. Emotionally, nearly all patients reported feelings of anxiety, stress, sadness, or fear about their future, their families, their treatment successes or failures, and the uncertainty of what lay ahead. However, we also elicited positive findings about the patients' evolving priorities in their lives, and the new appreciation for friends and family that was gained over the course of the cancer journey.

In conclusion, our findings provide evidence of a diverse set of signs, symptoms, and life impacts associated with the advanced melanoma that correspond with and expand on those that we identified in the clinical literature. Most physical impacts were seen as serious and frequent, such as fatigue, anxiety, and sleep problems. Receiving a diagnosis and knowledge of disease progression was associated with mental and social impacts.

Physicians and payers have increasingly demanded information directly from patients on their disease experience. In addition, developers of melanoma treatments and the regulatory bodies that oversee new drug approval need information directly from patients to inform clinical studies supporting new treatments. A lack of patient engagement makes it difficult for agencies responsible for reviewing drugs for approval, and some, such as pCODR (Pan-Canadian Oncology Drug Review), explicitly state that "...understanding the experiences of patients and their caregivers is a key element in making recommendations for drugs under review" [27]. Our research provides a wealth of information directly from patients on how advanced melanoma impacts their physical, mental, and social quality of life. Implications from this study include the need to better understand the impact of advanced melanoma treatment on HRQL, and to ensure that oncologists routinely conduct thorough assessment to identify humanistic burden. Physicians should be trained to identify melanomas early and diagnose the illness before it has advanced. Oncology care teams can improve on their current approaches for helping patients navigate treatment options, with

information about ancillary services to mitigate disease impacts on HRQL, such as depression, anxiety, and social supports, as well as employment support services or financial services.

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Compliance with ethical standards

Conflict of interest Made possible through the support of Merck Canada Inc. The opinions expressed in this publication are those of the authors and do not necessarily reflect the views of Merck Canada Inc.

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