



## Patient experiences with isolated limb perfusion for malignant melanoma – A qualitative study

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### ABSTRACT

**Purpose:** In recent years, the incidence of malignant melanoma has rapidly increased worldwide. Among patients with recurrences, approximately 5% develop in-transit metastases, which can potentially be treated with isolated limb perfusion (ILP). However, little is known about patient experiences with this treatment. A more thorough understanding might guide future research and clinical care. In this study, we aimed to describe patients' experiences of ILP treatment.

**Methods:** This study included eight patients who participated in a semi-structured interview, conducted at one occasion between 3 and 11 months after their ILP treatment. The mean interview duration was 26 min. Data were analyzed using qualitative inductive content analysis according to the methods of Elo-Kyngäs and Graneheim and Lundman.

**Results:** Our analysis yielded three categories, each built on two subcategories: **positive experiences after ILP treatment** emerged from the sub-categories *reduced tumor burden* and *living a less restricted life*; **negative experiences after ILP** was built on the subcategories *fear of relapse* and *complications and side effects*; and **experiences of healthcare** was founded on the subcategories *need for correct information* and *being viewed as sicker than experienced*.

**Conclusion:** Participants showed greater focus on the healthy parts of their lives, even when negative symptoms occurred after ILP treatment. They also described how healthcare workers focused on their illness. Based on these findings, we suggest the following means of providing good nursing care to ILP patients: give correct information, strive to reduce patients' negative symptoms, support their daily living needs, and provide emotional support to reduce fear of recurrence.

### 1. Introduction

In recent years, the incidence of malignant melanoma has increased rapidly worldwide, and it is predicted that this trend will continue. Malignant melanoma is currently the sixth most common cancer in Sweden (Lyth et al., 2015, 2016; Whiteman et al., 2016). Most patients are diagnosed at an early disease stage, and have a promising prognosis. However, approximately 5–8% of patients with melanoma recurrences will develop in-transit metastases, i.e., multiple recurring tumor deposits in superficial lymph vessels, most often confined to the limbs (Pawlik et al., 2005). Among these patients, quality of life (QoL) is mainly reduced by the tumor burden (Bagge et al., 2016), but also by fear of disease recurrence (Noorda et al., 2007).

Patients with high tumor burden or rapidly recurrent in-transit metastases may undergo treatment with isolated limb perfusion (ILP) rather than local surgical resection (Olofsson et al., 2013). ILP is a regional and palliative treatment that can achieve complete response in two-thirds of patients; however, it has not been shown to prolong survival (Moreno-Ramirez et al., 2010). Up to 50% of patients who show an initial complete response experience local recurrences (Olofsson et al., 2013) but, fortunately, ILP can safely be repeated with similar response (Belgrano et al., 2019). During ILP, the affected limb is isolated from the rest of the body via surgical isolation of the blood supply. Catheters are inserted into the limb's main blood vessels, and a heart-lung machine is connected. The limb is heated to 40 °C and the chemotherapeutic agent melphalan is perfused through the extremity for

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**Table 1**

Levels of acute limb toxicity due to isolated limb perfusion, according to the Wieberdink grading system (Wieberdink et al., 1982).

Grade I	No reaction
Grade II	Slight erythema and/or edema
Grade III	Considerable erythema and/or edema with some blistering; slightly disturbed motility
Grade IV	Extensive epidermolysis and/or obvious damage to deep tissues, causing definite functional disturbances; threat of or manifest compartmental syndrome
Grade V	Reaction that may necessitate amputation

60 min. Upon completion of perfusion, the extremity is rinsed with crystalloids, and circulation is restored. This technique enables delivery of melphalan at 10- to 20-fold higher concentrations than the doses achieved with systemic administration, with little or no systemic side effects (Nieweg and Kroon, 2014).

Common complications after ILP include swelling, redness, stiffness, pain, and reduced mobility in the treated limb. These toxicity symptoms are classified according to the Wieberdink scale, which includes grades I–V (Table 1), and the majority of patients develop complications of grades I–III (Wieberdink et al., 1982).

Since the introduction of ILP treatment in the early 1960s, several published studies have investigated response rates, complications, surgical techniques, and safety (Belgrano et al., 2019; Dossett et al., 2016; Katsarelias et al., 2018; Nieweg and Kroon, 2014; Olofsson Bagge et al., 2014; Olofsson et al., 2013; Testori et al., 2011). Only a few studies have examined patient experiences with ILP treatment by investigating patient-reported outcomes, such as post-treatment QoL and symptoms (Bagge et al., 2016; Jiang et al., 2015; McClaine et al., 2012; Noorda et al., 2007). To our knowledge, only one previous study has used a qualitative approach to more deeply explore the emotional impact of locally advanced cutaneous melanoma (Weitman et al., 2018), and no study has specifically investigated patients undergoing ILP in this context. Ashton highlighted this knowledge gap in 2012, concluding that nurse's lack of knowledge when caring for patients undergoing ILP treatment could place these patients at risk (Ashton, 2012). Thus, in the present study, we aimed to describe patients' experiences of ILP treatment.

## 2. Methods

### 2.1. Study design

This study was designed as a qualitative inquiry, with patients participating in individual semi-structured interviews on one occasion within their first year after ILP treatment. The interview guide included open-answer questions (Supplement 1). Data were analyzed using content analysis with an inductive approach.

### 2.2. Participants

All ILP procedures in Sweden are performed at Sahlgrenska University Hospital in Gothenburg. We identified 19 patients with melanoma in-transit metastases who underwent treatment with ILP in 2016. Our initial goal was to conduct face-to-face interviews, to avoid missing non-verbal information. Therefore, we selected the sample based on geographical range for convenience (Polit and Beck, 2008). We identified 11 patients who lived reasonably near Gothenburg, and invited these patients to participate in the study. Six of the 11 patients were willing to participate. To enrich our data collection, we also included two additional patients who lived further away, and who were interviewed by telephone. Data analysis revealed that the telephone interviews were just as rich as the face-to-face interviews. Altogether, this study included eight patients treated with ILP due to malignant melanoma. Table 2 presents their demographic data.

**Table 2**

Demographic data of participants who underwent isolated limb perfusion to treat melanoma in-transit metastases.

Characteristic	Number or median (range)
Participants	8
Gender, male/female	4/4
Age	69 (61–78) years
Time from treatment to interview	3.5 (3–11) months
Interview time	27.5 (16–43) min
Treated limb, leg/arm	7/1

### 2.3. Data collection

The interviews were conducted between December 2016 and January 2017. Participants chose where the interview took place: at home, at the hospital, or by telephone. Five patients participated in face-to-face interviews (three at the hospital and two in participant's homes), and three participated in telephone interviews. One participant who lived nearby Gothenburg chose to be interviewed by phone rather than face-to-face. All interviews were recorded and transcribed verbatim by two authors (Ekenberg and Wesslau). Due to the possibility that the deep conversations or questions might elicit emotions that caused mental discomfort, all participants were informed that they could receive follow-up support from a counselor, nurse, and/or doctor, if needed. None of the participants requested such support after the interviews.

### 2.4. Data analysis

Data were analyzed using a qualitative content analysis method, following the methods of Elo & Kyngäs (Elo and Kyngas, 2008) and Graneheim & Lundman (Graneheim and Lundman, 2004). First, the interview transcripts were carefully read several times to acquire an overall understanding of the content. Meaningful units that captured the essence of the participants' experiences of ILP treatment were highlighted and condensed into brief phrases, and these phrases were labeled with codes. This initial analysis was performed by two of the authors (Ekenberg and Wesslau). Next, a triangulation was performed by the same two authors together with a third author (Engström), and the codes were sorted into subcategories. Finally, similar subcategories were grouped into main categories. Table 3 shows an example of the analysis process.

### 2.5. Ethical considerations

This study was approved by the Regional Ethical Review Board in Gothenburg (Dnr 484-15). All participants received both verbal and written information before study participation, and all participants signed a written consent form.

## 3. Results

Our analysis of the interviews yielded three categories—*positive experience after ILP*, *negative experience after ILP*, and *experiences of healthcare*—each built from two subcategories. *Positive experience after ILP* emerged from the sub-categories *reduced tumor burden and living a*

**Table 3**  
Example of the inductive content analysis process.

Meaning units	Condensed meaning units	Code	Subcategory	Category
"If I'm sitting at a table and it is curved, it's swelling. It still does; it's swelling immediately. I am so swollen in the foot; I have a lot of pain"	"I am so swollen in the foot. I have a lot of pain"	Swelling and pain	Complications and side effects	Negative experience of ILP treatment
"You're not tired, you just don't have any energy. I've never been through that before ... I've been so tired that I almost fainted before, but not being without energy"	"You're not tired, you just don't have any energy"	Loss of energy, fatigue	Complications and side effects	
"It's still swollen and now the skin is ulcerated. I don't know exactly what is in the skin that burns like fire; it just feels like something is working. ... so I woke up some night, yes this was many weeks ago ... I thought the skin cracked, it felt like pulling a razor blade at the skin."	"It's still swollen and now the skin is ulcerated"	Swelling, pain, and ulceration	Complications and side effects	

less restricted life. Negative experience after ILP was built on the subcategories *fear of relapse* and *complications and side effects*. Experiences of healthcare was founded in the subcategories *need for correct information* and *being viewed as sicker than experienced* (Fig. 1).

### 3.1. Positive experiences after ILP treatment

#### 3.1.1. Reduced tumor burden

Participants described how living with malignant melanoma and in-transit metastases often involved a high tumor burden and rapidly recurring metastases. Many participants had previously undergone repeated surgical treatments with tumor removal, and had negative experiences with incomplete surgery or rapid recurrences. After ILP, the participants experienced a more sustainably reduced tumor burden, because their tumors decreased in size or even disappeared completely.

"To run and cut all the time and wait for it to heal, and when it's healed, a new one turns up—it's not that nice ... so [ILP] was actually nice." (Participant 1)

"No, it hasn't come back. It is so.... Well, just on this thigh then as it is done, it is so easy to see if there is anything or not. No, it's just as good as any." (Participant 6)

#### 3.1.2. Living a less restricted life

Participants expressed that the reduced tumor burden enabled them to live a less restricted life, which included returning to work, continuing with hobbies (e.g., walking in the forest), driving their car, and being able to find clothes and shoes to wear. They also experienced a greater ability to spend time with friends and family. Support from relatives, friends, and employers was important for facilitating the participants' resumption of a more normal life after treatment. Such support was described as "helping out" with simple things (e.g., driving the car), meeting over a cup of coffee, or providing psychosocial support when they needed someone to talk to. When the participants were able to continue to live life "as usual", with support and help from family, friends, and colleagues, they described it as reclaiming life.

"We have parking lots that are quite far from our office, but he (the supervisor) said that I was welcome to park outside the building. But I thought—no ... now, maybe we should try to be a bit normal here (laughing). But it's very nice they want me to come back." (Participant 7)

"It was so lucky that I was not alone ... I have my husband here at home. Yep, and he is so helpful." (Participant 5)

### 3.2. Negative experiences after ILP treatment

#### 3.2.1. Fear of relapse

Uncertainty regarding the sustainability of the treatment outcome, and about their future health, led to feelings of stress among the participants.

"... no, so it's ... in some ways, a little uncertain, because we have no answer. So to speak... you simply have to live with it..." (Participant 3)

Life after ILP treatment was also described as involving continuous emotional shifts between believing in the future and, at the same time, experiencing agony. The side effects of treatment were stated to be easier to tolerate than the fear of disease relapse. The time pending treatment was also experienced as a difficult time, and patients suffered anxious thoughts about the malignant melanoma.

"Yes, it has been like a rollercoaster, and so ... some days... hmmm ... What's worst is not knowing whether you will manage this or not [the ILP]. Will it succeed? ... Before you knew what to do ... Do I get one more Christmas? ... What are the odds? I will have another grandchild

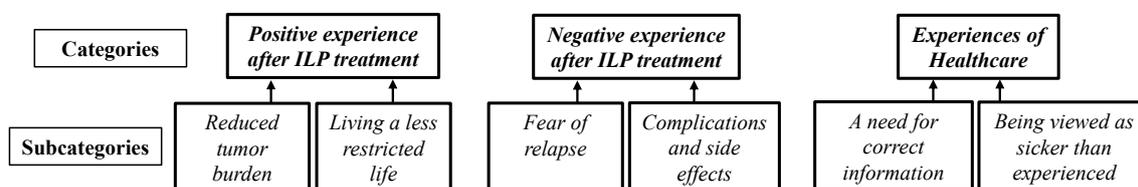


Fig. 1. The overall results based on the eight interviews.

next year; will I see them? I'm not afraid of dying, but perhaps I am scared of the journey leading there." (Participant 2)

### 3.2.2. Complications and side effects

All participants experienced swelling and stiffness after ILP treatment. Swelling commonly occurred soon after the treatment, and increased for several weeks before finally declining. However, for a few participants, the swelling persisted for significantly longer than two weeks. Symptoms of stiffness typically began later than the swelling, but stiffness was experienced as a more permanent side effect. Both swelling and stiffness caused several limitations in daily life (e.g., difficulties driving a car or going for a walk), which led to the participants feeling involuntarily isolated. Participants also experienced decreased sensation and blistering, which caused limitations when selecting clothes or shoes.

*"I have not been able to wear any shoes. It was so swollen and eh...I had a hard time walking." (Participant 8)*

The experience of pain varied among participants, from very little pain to strong pain. Additionally, the duration varied from pain lasting only a short time after treatment to more persistent pain over time. One participant experienced strong persistent pain, and described that it caused social and emotional isolation.

*"It hurt; it did. And I was so worried that somebody was going to touch my leg, so it was worse when I was out somewhere...Yes, [whenever someone was] just ... near the leg, it felt like an open wound." (Participant 7)*

Participants also commonly described symptoms of fatigue and loss of energy, to the extent that a simple task, such as laundering, could seem overwhelming.

*"This loss of energy, that you have no energy at all, that you are not really tired, but you have no energy. I've never felt like this before ...I've been tired to the point of fainting ... but I have not experienced a total loss of energy. It's just like the treatment has taken all my energy..." (Participant 2)*

### 3.3. Experiences of health care

#### 3.3.1. A need for correct information

All participants reported that they were well informed by the caregiver who had administered the ILP, with regards to symptoms and complications that might occur. Possessing knowledge of what to expect (e.g., knowing which reactions were normal) made participants feel less worried and more satisfied with the treatment.

*"I don't think there was anything missing. As I was leaving, I met with the doctor, and I received a telephone number that connected directly to him...in case anything came up...I felt satisfied, and I received answers to all the questions that I had...so it was good." (Participant 5)*

Several participants expressed dissatisfaction and disappointment with their primary healthcare. Two participants stated that they felt as if they had received a "death sentence". They also described being "forced" to take sick leave for several months pending the treatment, despite their wish to work—a situation that led to unnecessary distress

and suffering. Then, when they were first referred to the special unit, they received a less critical prognosis.

*"It started before Christmas you know... About one year ago... I went to the health center where they thought... it will be better, but nothing happened. But now I have changed to another primary health center..." (Participant 4)*

Some of the participants from regions other than Gothenburg experienced dissatisfaction with their referral hospital, due to the lack of knowledge and information provided before and after the ILP treatment. They described feelings of being forsaken and having no one to talk to after their treatment, which led to strong feelings of frustration.

*"Who would you talk to? What would you ask for? Nobody knew anything." (Participant 3)*

#### 3.3.2. Being viewed as sicker than experienced

Participants often stated that although they viewed themselves as quite healthy, others viewed them as sick. Participants stated that their diagnosis of malignant melanoma and the ILP treatment did not cause any major differences in their daily lives, and they perceived themselves as quite healthy. However, they experienced opposite attitudes from both the healthcare community and society (i.e., family), which indicated that others regarded them as much sicker than they actually experienced themselves to be. This situation was described as very frustrating.

*"I never viewed myself as sick. I still do not see myself as sick, but everyone says I'm sick. I don't have any ... except that my leg hurt, I'm not ... Once I broke my ankle and then I thought I was disabled." (Participant 2)*

*"I have an old mother who is 88 years old who considers me sick. And I say "I am not sick." For sick, I think it is when you lie at home with a 40-degree fever and feel really ill. But, I mean, I feel like not sick. I feel as usual." (Participant 7).*

## 4. Discussion

In our present study, we found that our participants experienced a less restricted life after undergoing ILP treatment, because ILP alleviated their tumor burden, whereas previous surgical procedures had not. Being able to live a more active life after treatment enabled for example that some patients could return to work. Some patients described improvements of physical functions, such as being able to talk a walk, and of their psychosocial functions. They also stated that it was easier to find functional clothes and shoes to wear after ILP treatment. These findings differ from those reported by [Weitman et al. \(2018\)](#), who investigated patients' experiences of living with locally cutaneous melanoma, without receiving any treatment. They found that patients reported problems finding functional clothing, and described how decreased physical functioning caused limitations in patients' daily lives ([Weitman et al., 2018](#)).

All of the participants in our present study felt healthier when their tumor burden was reduced, and could thus experience a higher QoL. [Albrecht and Devlieger \(1999\)](#) have described a paradox in which humans with serious illnesses can experience an excellent QoL. They

hypothesized that patients were able to achieve a balance between their body, soul, and spirit, enabling them to maintain harmonious relationships within their social networks and in their environments. Information and a strong social network were identified as factors that increased well-being and health, while pain and isolation led to illness (Albrecht and Devlieger, 1999). This phenomenon has also been recognized in patients with malignant melanoma, who have reported a high QoL despite severe illness in several studies (Bagge et al., 2016; Jiang et al., 2015; McClaine et al., 2012). Indeed, one study reported that patients with severe illnesses perceived a QoL higher than that perceived by the healthy population (Noorda et al., 2007). In our study, participants felt increased well-being when their tumor burden had decreased, and when they simultaneously experienced support from their relatives, employers, and caregivers.

Participants in our study also experienced negative side effects after ILP treatment, including swelling, stiffness, and pain in the treated limb, and anxiety when their treatment outcome remained uncertain. These experiences are all known to affect QoL (Ashton, 2012). In the study by Weitman et al. (2018), swelling was the most commonly reported bothersome symptom and, as in our present investigation, fewer patients reported problems with pain (Weitman et al., 2018). These findings highlight several important nursing care needs for ILP patients. Firstly, nurses must check that symptoms, such as swelling and pain, are not abnormal and that they pose no risk for the patients (Ashton, 2012). Secondly, nurses should ensure that patients receive accurate support and symptom relief, such that they avoid isolation and negative hospital experiences (Felder, 2004; Ferrell and Coyle, 2010). Finally, nurses have to make sure that patients experience continuing support when dealing with fears of recurrence (Lamprell and Braithwaite, 2018). Our patients experienced insecurity and anxiety arising from uncertainty regarding disease progression and from fear of relapse. Physically, participants described a feeling of not daring to look at their own limbs, for fear of potentially finding new metastases. Fear of relapse has been previously described by patients with malignant melanoma (Bell et al., 2017), and by patients with other cancer types, including colorectal cancer (Custers et al., 2016). Nurses can address this particular type of fear by using, e.g., “The Cancer Worry Scale” for early identification of those patients requiring additional interventions (Custers et al., 2014). According to Ashton (2012), patients who experience a recurrence of melanoma will likely benefit from additional emotional support and further information about their treatment plans.

In the interviews, participants who were recruited from outside the Gothenburg area described a sense of being forsaken, with no one to talk to. Some patients had received incorrect information about their primary disease, which was perceived as frustrating and prompted unnecessary worries. On the other hand, the information received from the hospital that administered ILP was considered very good, leading to feelings of satisfaction and greater calmness. These findings imply a need for better education and greater information training for physicians who deliver a malignant melanoma diagnosis (Lamprell and Braithwaite, 2018). Furthermore, using skilled interaction, good communication, and listening, nurses can acquire accurate information about each individual patient's physical, psychological, spiritual, and social needs before and after the ILP treatment (RCC, 2016). The findings of our present study suggest that all patients should receive a telephone follow-up with a clinical nurse who is specialized in surgery or oncology, and who has profound knowledge of ILP treatment. In addition to this planned telephone follow-up, patients should be able to get in touch when needed. Such increased support could foster greater feelings of security in patients, and a satisfied and secure patient is likely to experience better health, despite severe illness.

Importantly, nurses who care for ILP patients must pay attention to and support patients' daily living needs, rather than only focusing on patients' illnesses. The participants in our study all tried to live as normally as possible, and did not view themselves as being as sick as the healthcare providers did. In a systematic review, Maguire et al. (2013)

explored the supportive care needs of people living with lung cancer, and reported similar findings—i.e., patient's made efforts to live as normally as possible, even though their lives were dominated by treatments and test results. The authors' conclusions, as well as our present findings, warrant further studies to address this topic, both in the clinic and in future research.

#### 4.1. Study limitations

This study had several strengths and limitations. Both authors who conducted the interviews were employees of the department where ILP treatment was performed, which can be considered as both a strength and a limitation. This setting carries the risk that the authors' might unconsciously base their interpretations on past experiences, which might be irrelevant in the study context (Polit and Beck, 2008). Additionally, the participants might feel a dependency on the interviewers, leading them to construct answers that they think would satisfy the researcher. On the other hand, participants could experience the interview situation as helpful, and appreciate the opportunity to share their experiences with someone they trust (Ryan et al., 2009).

The main limitation of our study was that the sample size was quite small. Thus, caution must be used about transferability of the present results to other patients. Although the collected data were quite rich, our results are insufficient to fully cover the vast complexity and variety of patients' experiences when undergoing palliative ILP treatment. Nevertheless, the interviewed participants could be viewed as being representative of the small population of patients who undergo this unique treatment.

## 5. Conclusion

Patients with in-transit metastases of melanoma who undergo ILP treatment experienced a reduced tumour burden, which facilitated a less restricted life and improved health. Simultaneously, patients experienced various grades of negative symptoms, such as swelling, fatigue, and pain, as well as a fear of relapse. The participants exhibited a greater focus on the healthy parts of their lives, but experienced that healthcare workers and relatives focused more on their illness. Patients' feelings of well-being were reduced by receiving incorrect information about their disease and treatment, and by others viewing them as sicker than they felt.

It is important that healthcare services provide adequate care for these patients. Based on our present findings, we suggest the following means of providing good nursing care to ILP patients: giving correct information, striving to reduce patients' negative symptoms, supporting their daily living needs, and providing emotional support to reduce fears of recurrence. One way to address these needs may be to offer all patients follow-up with a nurse who is specialized in surgery or oncology, and who has profound knowledge of ILP treatment and its impact on patients' health.

#### Declaration of competing interest

None declared.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejon.2019.101672>.

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