European Journal of Cancer 85 (2017) 122–132

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Health-related quality of life in melanoma patients: Impact of melanoma-related limb lymphoedema

Caroline A. Gjorup [a,*], Mogens Groenvold [b,c], Helle W. Hendel [d], Karin Dahlstroem [a], Krzysztof T. Drzewiecki [e], Tobias W. Klausen [f], Lisbet R. Hölmich [a]

[a] *Department of Plastic Surgery, Herlev and Gentofte Hospital, University of Copenhagen, Denmark*
[b] *Department of Public Health, University of Copenhagen, Copenhagen, Denmark*
[c] *Department of Palliative Medicine, Bispebjerg University Hospital, Copenhagen, Denmark*
[d] *Department of Clinical Physiology and Nuclear Medicine, PET-Center, Herlev and Gentofte Hospital, University of Copenhagen, Denmark*
[e] *Department of Plastic Surgery, Breast Surgery and Burns Treatment, Rigshospitalet, University of Copenhagen, Denmark*
[f] *Department of Hematology, Herlev and Gentofte Hospital, University of Copenhagen, Denmark*

Received 26 April 2017; received in revised form 29 June 2017; accepted 30 July 2017
Available online 15 September 2017

KEYWORDS
Melanoma;
Quality of life;
Surveys and questionnaires;
Patient reported outcome measures;
Surgical procedures;
Lymphoedema;
Cancer;
Survivors;
Time;
Body image

Abstract ***Aim:*** To explore health-related quality of life (HRQoL) in recurrence-free melanoma patients, with a focus on the association between melanoma-related limb lymphoedema and HRQoL.
Methods: HRQoL was evaluated using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30), the breast cancer module (EORTC QLQ-BR23) subscales body image and future perspective, the Functional Assessment for Cancer Therapy-General subscale social/family well-being and the Hospital Anxiety and Depression Scale. Data were analysed using linear and ordinal logistic regression adjusting for age and gender.
Results: A total of 431 melanoma patients who had undergone wide local excision and axillary or inguinal sentinel lymph node biopsy (SLNB) and/or complete lymph node dissection (CLND) participated. No patients had had recurrence of the disease or had received adjuvant radiotherapy. The HRQoL scores improved with time after surgery. Melanoma-related limb lymphoedema was present in 109 patients (25%). Patients with lymphoedema had significantly worse HRQoL scores in the EORTC QLQ-C30 subscales global health status/quality of life, role and social functioning, fatigue, pain and financial difficulties, as well as in the QLQ-BR23 body image subscale. No associations were found between the limb affected (upper or lower

* *Corresponding author*: Department of Plastic Surgery, Herlev and Gentofte Hospital, University of Copenhagen, Herlev Ringvej 75, 2730 Herlev, Denmark.
E-mail address: caroline@gjorup.com (C.A. Gjorup).

http://dx.doi.org/10.1016/j.ejca.2017.07.052

limb), clinical stage of lymphoedema, duration of lymphoedema or type of surgery (SLNB or CLND) and HRQoL. We found an interaction with age and gender in the associations between lymphoedema and HRQoL: younger patients and women with lymphoedema had worse social functioning and women had significantly more impaired body image.
Conclusions: The negative impact of melanoma-related limb lymphoedema on HRQoL emphasises the importance of developing strategies for increasing awareness and improving prevention and treatment of lymphoedema.

1. Introduction

The incidence of melanoma as well as the survival rates are steadily increasing in Europe and in the United States [1,2]. The reported increase in incidence might be partially explained by an increase in risk behaviour in terms of excessive recreational exposure to sunlight [3]. The improved survival is possibly attributed to earlier detection, improved diagnostic methods and in recent years the evolvement in particular immuno- and targeted therapy [4–6]. Recent age-standardised 5-year survival rates are approximately 84% and 91% in Danish men and women, respectively [3]. The current standard of care in patients with American Joint Committee on Cancer stage IB–III disease includes wide local excision (WLE) of the primary melanoma and sentinel lymph node biopsy (SLNB) to detect occult lymph node metastases [7]. If the SLNB is positive, complete lymph node dissection (CLND) at the nodal basin is performed [7]. However, the treatment of melanoma is debated with arguments both for and against the current standard treatment [8–10]. It is therefore of utmost importance to have comprehensive data on the late effects and HRQoL in melanoma patients; such information is needed for informed treatment decision-making.

An important late effect after nodal surgery and in particular after CLND is melanoma-related limb lymphoedema, affecting 2–83% depending on site and type of surgery [11–13]. The detrimental effects of lymphoedema in breast cancer patients are well-documented [14,15]. However, the population of breast cancer patients, the treatment hereof and the areas involved are not comparable to melanoma and melanoma patients. Despite the high prevalence of lymphoedema, only few studies have addressed the impact of lymphoedema on HRQoL in melanoma patients [16–19]. Of these, considerable limitations in the study designs were present, including the definition of lymphoedema based on objective measurements, which likely underestimated the prevalence of lymphoedema and the lack of stratification by site and the type of procedure [16–18,20]. Furthermore, the study populations varied with regard to both the extent of lymph node dissections and the use of adjuvant radiotherapy, which are known risk factors for the development of lymphoedema [16,18]. Finally, the results on the HRQoL were sparingly reported [16,18].

We therefore aimed to assess the impact of clinical lymphoedema on HRQoL in melanoma survivors. Secondary aims were to assess the association between time since surgery and HRQoL, and for the patients with lymphoedema, the association between limbs affected, stage and duration of lymphoedema and HRQoL.

2. Materials and methods

2.1. Participants

A cross-sectional study of patients treated for cutaneous melanoma on the trunk or extremities from January 1997 to February 2015 at the Department of Plastic Surgery at Herlev Gentofte Hospital, Denmark was conducted after Ethics Board approval (journal no.: H-4-2014-127). Patients who were $\geq$18 and $\leq$75 years treated with WLE and unilateral axillary or inguinal SLNB and/or CLND at least 1 year before the study were assessed for eligibility. No patients had had recurrence of the disease or received adjuvant radiotherapy, and no patients were receiving adjuvant therapy. All patients received the following standard of care post-operatively. After axillary or inguinal SLNB alone and axillary CLND, the patients were not recommended to use prophylactic compression garments. After inguinal CLND, the patients were recommended to wear circular knit compression stocking (grade II) daily for 3 months. In case of lymphoedema after 3 months, prolonged use of compression garments was recommended.

The main exclusion criteria were melanoma recurrence or lymphoedema not related to the treatment of melanoma. Further exclusion criteria are listed in Fig. 1. The participants were either in or had ended a 5-year follow-up program at our unit. The participants received the questionnaires using an electronic survey system (SurveyXact). To estimate the possible effect of lymphoedema on HRQoL, we planned to include 435 participants to include approximately 100 participants with lymphoedema [21].