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Sexuality in patients with hematological malignancies: From a patient, partner and health-care professional perspective



Corien Eeltink

Sexuality in patients with hematological malignancies: From a patient, partner and health-care professional perspective

Corien Eeltink

2022

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VRIJE UNIVERSITEIT

**SEXUALITY IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES: FROM A PATIENT, PARTNER AND
HEALTH-CARE PROFESSIONAL PERSPECTIVE**

ACADEMISCH PROEFSCHRIFT

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de Vrije Universiteit Amsterdam,
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Table of contents

<i>Chapter 1.</i>	General introduction and outline	2
Part I	Sexual function in patients with hematological malignancies	15
<i>Chapter 2.</i>	Sexual problems in patients with hematological diseases: a systematic review	16
<i>Chapter 3.</i>	Fertility and sexual function in female Hodgkin lymphoma survivors of reproductive age	45
<i>Chapter 4.</i>	Self-reported sexual function in sexually active male Hodgkin lymphoma survivors	62
Part II	Addressing sexuality in clinical practice	77
<i>Chapter 5.</i>	Perceived need for information of patients with hematological malignancies: a literature review	78
<i>Chapter 6.</i>	Discussing sexuality in cancer care: towards personalized information for cancer patients and survivors	106
<i>Chapter 7.</i>	Health-care professionals' perspective on discussing sexual issues in adult patients after hematopoietic cell transplantation	112
<i>Chapter 8.</i>	Recommended patient information sheet on the impact of hematopoietic cell transplantation on sexual functioning and sexuality	141
<i>Chapter 9.</i>	General discussion	155
<i>Chapter 10.</i>	Summary	169
	Samenvatting	173
	List of publications	176
	Dankwoord	181
	Curriculum Vitae	184

Chapter 1

Introduction and outline

“Every person has a right to seek, receive and discuss information related to sexuality”

General introduction

In recent years the prognosis of patients with a hematological malignancy (HM) has greatly improved due to an increasing treatment armamentarium [1]. Consequently, the long-term impact of anti-cancer treatment is becoming increasingly important. Sexuality is one of the domains that is negatively affected not only during treatment but also following treatment [2-4]. Sexuality is a basic need of people and has several purposes, for example reproduction, lust, or to express love. Sexuality provides the positive effects on well-being that people need, such as distraction, relaxation, comfort and intimacy. People can be sexually active into old age, with their partner or only through masturbation [5-7].

Many cancer patients desire and deserve a “normal life”, and sexuality is seen as an integral part of this future life. However, it seems that health-care providers (HCPs) are often unaware of the sexual dysfunction that patients experience, as not only patients feel reluctant to discuss these issues, but also HCPs do not address sexuality for the same reason [8-24]. In addition, detailed insight into sexual function as such and into the way HCPs and patients address sexuality in routine care is scarce.

Sexual function and dysfunction

Knowledge of the human sexual response cycle is fundamental to understand sexual (dys)function [25]. There are two key models that represent human sexual function. The oldest is according to Masters & Johnson (1969) and Kaplan (1979), a sexual based linear model that distinguishes four different phases of sexual function: desire, arousal, orgasm, and resolution, following each other in a sequential manner in both men and women (Fig.1) [25, 26]. In contrast, Basson (2001) who has focused particularly on women, makes a distinction between male and female sexual functioning [27]. She constructed a non-linear model of female sexual response based on intimacy and integrated responsive and spontaneous sexual desire in a circular model of overlapping phases of sexual response (Fig.2)[27].

Sexual dysfunction is broadly defined as the inability to fully enjoy sexuality [DSM-5][28]. Sexual dysfunction occurs when the physical reaction in either the sexual response or sexual activity is missing or diminished. It can happen in one or more phases of the sexual response cycle: desire, arousal, and orgasm, and it can also be a result of pain (upon penetration and overall difficulty having intercourse). In the general population sexual dysfunction is common, 40–45% of adult women and 20–30% of adult men report at least one sexual dysfunction [29, 30]. The most frequent sexual dysfunctions for men are premature ejaculation and erectile dysfunction [5, 6, 30, 31]. For women, desire and arousal dysfunctions and problems achieving

orgasm are the most common sexual dysfunctions [5]. In addition, there is a large proportion of women who experience multiple sexual dysfunctions [6]. The pathophysiology of sexual dysfunction is heterogeneous, ranging from biological (e.g. vascular, hormonal, neurological, urological, iatrogenic, obesity, or poor health) and psychological (e.g. emotional problems, depression, anxiety) to social causes (e.g. sexual abuse, use of alcohol/ tobacco/ opioids/ or recreational drug abuse, marital problems, difficulty talking about the sexual relationship with the partner, no sexual partner, sexual dysfunction in the partner, lower level of educational attainment and unemployment) [6, 30-34]. In patients with HMs any of these components may play a role in sexual dysfunction.



Figure 1. Human Sexual Response Cycle by Masters & Johnson and Kaplan [25, 26]

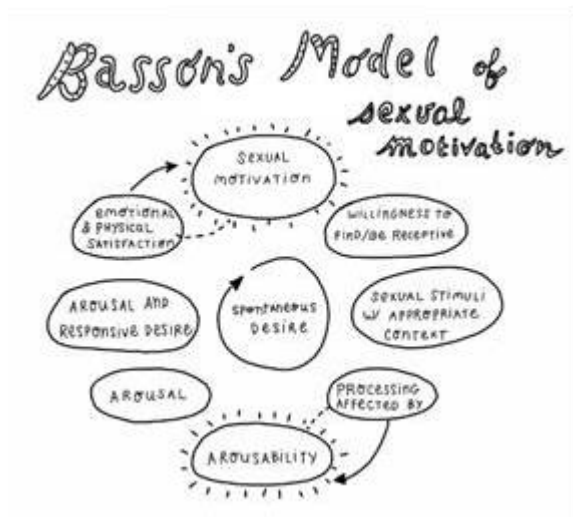


Figure 2. Female Sexual response Cycle by Basson [27],

<https://www.lifeworkspsychotherapy.com/bassons-sexual-response-cycle-teaches-us-sexuality/>

The impact of HM treatment on sexual function

HMs are malignant diseases arising in hematopoietic and lymphoid tissues [35]. There is a pronounced clinical variety in those diseases, caused by the cellular origin of the disease and the extent of proliferation of malignant cells. In general, there are myeloid malignancies, originating from myeloid precursor cells and lymphoid malignancies originating from lymphoid malignant cells. In both of these types of malignancies there is either an accumulation of highly proliferative young precursor cells with a maturation arrest leading to acute leukemias or an accumulation of mature hematopoietic cells giving rise to chronic leukemias or lymphoproliferative malignancies. In general, acute leukemias can potentially be cured with intensive chemotherapy often consolidated with stem cell transplantation, from either the patient (autologous stem cell transplantation) or a related or unrelated donor (allogeneic stem cell transplantation). In contrast, chronic diseases have a more indolent course. The type of chemotherapy is often, but not always, less intense. Therapy is given on a periodic basis, as generally indolent diseases cannot be cured. In this thesis, the focus is on patients diagnosed with acute leukemias, such as Acute Myeloid Leukemia (AML), Myelodysplastic Syndromes (MDS), Acute Lymphoid Leukemia (ALL), and aggressive malignant lymphomas, as well as more chronic hematological malignancies such as myeloproliferative neoplasms (MPN), indolent lymphomas, and multiple myeloma (MM). The majority of patients diagnosed with HMs are over the age of 65. In Europe, the incidence of HM is between 0.5% and 2.9% of all cancer cases in 2018, of which non Hodgkin lymphoma has the highest incidence [36].

Little is known about the impact of HMs on sexual function. To our knowledge, only one study focused on sexual function in HMs at the time of diagnosis [37]. Behringer et al. reported that sexual function before treatment was negatively influenced by a higher disease stage [37]. Symptoms that might affect sexual function, fatigue and distress, are common symptoms among HM patients [37-41]. Fatigue may result in loss of sexual desire and arousal problems [42]. However, the exact impact of fatigue on sexual function in HM is not well understood. In addition, HM patients may be at risk for distress because of the immediate intensive treatment or because of delayed treatment in the case of indolent diseases [41]. Meanwhile, it is known that the psychological impact of HM can impact sexual function as well [6, 42-45].

In addition to the disease itself, sexual dysfunction can also occur as a result of treatment modalities for HMs [46, 47].

- Alkylating agents and/or irradiation of the pelvic area can lead to damage of the gonads which are responsible for sexual dysfunction [42, 46-53]. Sexual desire is strongly guided by androgen

hormones. Subsequently, problems with sexual interest/desire can occur when abrupt premature menopause in women and hypogonadism in men is induced by HM treatment. Fatigue, pain, nausea, distress and an impaired body image contribute to sexual dysfunction after treatment as well [42].

- Sexual arousal problems involves minimal vaginal lubrication in women and erectile dysfunction in men. Genital arousal is mainly guided by circulation and good neural connections from the centers in the spinal cord to the external genitals. Neurotoxic agents can cause autonomous neuropathy [46, 47, 50] and as a consequence, arousal problems in women and men. Irradiation of the pelvic area might impair the peripheral nerves and pelvic blood flow. Yet again, fatigue, pain, nausea, distress and an impaired body image contribute to sexual arousal problems as well [42].
- Genital pain during sexual activity in women is often a result of minimal vaginal lubrication or genitourinary atrophy. Premature menopause can lead to vaginal and/or vulvar atrophy, causing continuous discomfort and/or pain, as well as vaginal dryness.

As also observed in cancer patients in general, sexual dysfunction in HM patients may be enhanced by psychological and social factors [54]. As a result of all of the mentioned factors, intimate partners can experience sexual dysfunction as well [55, 56].

Sexual health-care

Sexuality and body image are important aspects of QoL, their disruption can negatively affect QoL of HM patients [42, 57-59]. Reduced sexual function may have negative implications on QoL of HM patients, and therefore sexual health-care should be integrated in cancer rehabilitation during and after treatment [59-62].

It is clear from previously described data that before HM treatment starts, patients need to be informed about the impact that HM might have on both sexuality and sexual function during treatment but also after treatment [63-65]. When no introductory information is provided about the impact of HM and its treatment on sexuality, patients are unable to address sexuality issues. Indeed, patients who received sexual education reported a significantly better sexual outcome after HM treatment [64-66]. During follow up, this information should be offered according to the individual's needs [67]. For some, knowing that sex and reproduction are affected is sufficient, and they do not always need support in case of sexual dysfunction [68]; for others however, individually tailored specific suggestions or even intensive treatment will be needed. There is little doubt that as patients live longer, sexual issues will become more important [69, 70]. Nevertheless, for numerous reasons HCPs report that sexual health-care is not routinely provided [71]. As a consequence, it is the HCP who needs to address sexuality issues and determine whether supportive care is

needed in relation to sexual dysfunction. To encourage patient-HCP communication, sexual health-care should at least consist of patient information (oral and/or written) before treatment [72, 73], followed by open communication providing information that normalizes the appearance of sexual dysfunction during treatment and follow up [66, 68]. However, to be able to inform patients and partners and to meet their supportive care needs in a personalized way, HCPs need to understand 1) what the effects are of HM's and their treatments on sexuality, and 2) what patients really want to know about sexuality before and after treatment.

Aim and research questions

The main aim of thesis is to obtain more knowledge on sexual (dys)function that HM patients may face during and after treatment, how health-care providers address sexuality in clinical practice, and on the need on information among HM patients. In order to optimize care for patients with sexual dysfunction, this knowledge is crucial to develop high quality information on sexuality tailored to HM patients in the future.

The main research questions are:

1. What is the prevalence of sexual problems among patients with HM diseases, and are there associations with *fertility status, and sociodemographic and clinical characteristics*?
2. What are the information needs on sexuality among patients and partners within the first 18 months of treatment for HMs?
3. How often do HCPs throughout Europe discuss sexual issues with HM patients, and what are barriers and facilitators to communication?

Outline of this thesis

This thesis consists of two parts, each with a different objective. The objective of the first part of the thesis is to investigate sexual dysfunction in patients affected by HMs. In a systematic review (**Chapter 2**) we describe the findings of previous research: the prevalence of general sexual dysfunctions and sexual problems of patients treated for a HM. In order to better understand sexual dysfunction and the affected domains of sexual function, we carried out a survey among female Hodgkin lymphoma survivors of reproductive age (**Chapter 3**) and among sexually active male Hodgkin lymphoma survivors in complete remission (**Chapter 4**).

The objective of the second part of this thesis is to give insight into how sexual issues should preferably be addressed and which barriers would prevent such approaches. By reviewing the informational

needs of patients with a HM (**Chapter 5**), and by investigating what patients and partners actually want, we identified the sexuality information needs among patients and partners within the first 18 months of treatment for HMs (**Chapter 6**). Furthermore, we assessed the frequency of discussing sexual issues by the HCP and the exact barriers and facilitators to discussing sexuality (**Chapter 7**).

Lastly, we collected information from the systematic literature review on what is known about the impact of treatment for HM diseases on sexual function and the patients' preferences in an attempt to address an unmet need. The (unfulfilled) informational needs of the patient and the fact that only a minority of HCPs routinely addresses sexuality have heightened the need for easily available information for patients and their partners. For this scope, a patient information sheet is highly recommended and has therefore been developed (**Chapter 8**).

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Part I

Sexual function in patients with hematological malignancies

Chapter 2

**Sexual problems in patients with hematological diseases:
a systematic review**



**Corien Eeltink, Alaa Embaby, Luca Incrocci, Hans Ket, Sarah Liptrott, Irma Verdonck-de Leeuw,
Sonja Zweegman**

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Abstract

Purpose Sexual problems are frequently reported by recipients of hematopoietic stem cell transplantation (HCT). However, little is known about the impact of hematological malignancies and their treatments, without HCT being a part of the treatment regimen. The goal of this systematic review was to examine the prevalence of various sexual problems of patients treated for hematological malignancies without HCT.

Methods The work focused on online databases available from their inception until 11 November 2020. The data related to sexuality in adult patients diagnosed with hematological malignancies. Selected studies were appraised for methodological quality.

Results Twenty-four studies were included. Twenty-two studies were observational cross-sectional cohort studies, and two studies had a prospective longitudinal design; fourteen studies used non-validated instruments; only two studies used the multidimensional concept of sexuality; six studies compared sexual problems in the target population with reference data. Based on the few high-quality studies, sexual problems occurred in 18-50% of acute leukemia, Hodgkin lymphoma, and non-Hodgkin lymphoma patients.

Conclusion Understanding sexual problems in patients treated for hematological malignancies without HCT is not only hampered by the variability in methodology, but also by the lack of research on patients using novel therapies. The exact impact of the diagnosis and treatment of a hematological malignancy on sexual function remains to be answered. Longitudinal studies focusing on the effects of the diagnosis and treatment of hematological malignancies on sexuality using validated questionnaires and comparison with normative data are hugely needed.

Introduction

Hematological malignancies (HM) are diverse and arise from either the lymphoid or myeloid hematopoietic cells. HM range from acute diseases, such as acute lymphoid or myeloid leukemias and aggressive lymphomas arising from precursor cells, to more chronic diseases such as chronic lymphoid or myeloid leukemias and indolent lymphomas arising from more mature hematopoietic cells. The survival rates of both acute and chronic HM patients are increasing as a result of improved diagnostic procedures, innovative non-chemotherapeutic treatment regimens, such as tyrosine kinase inhibitors (TKIs), immune therapy and optimal use of supportive care [1]. Moreover, the fact that autologous and allogeneic hematopoietic stem cell transplantations (HCT) can be applied at older age due to reduced conditioning regimens and better supportive care contributes to improved survival.

This survival often comes, however, with a price of acute side effects and chronic sequelae of more intense and continuous treatment, among which are sexual problems [2-4]. Sexual concerns are especially common after HCT, a treatment which offers the highest change for long-term survival in fit patients with high-risk HM, such as acute leukemia (AL) and myelodysplastic syndromes (MDS). Exposure to total body irradiation, high-dose alkylating agents, and graft versus host disease is known to affect sexuality leading to problems in sexual desire, arousal, and the orgasm phase of the sexual response cycle [2-8]. However, it is assumed that most HM patients without HCT as a part of the treatment regimen, including patients affected by Hodgkin lymphoma (HL), non-Hodgkin lymphoma (NHL), and chronic leukemias, older patients with multiple myeloma (MM) and MDS, and patients with myeloproliferative neoplasms (MPN), are confronted with changes in sexual function as well. HM can seriously impact sexuality during treatment but also in the survivorship period, as a result of biological factors such as fatigue, gonadal dysfunction, neurological changes, and changes to pelvic blood flow [3, 9-11]. Moreover, psychological factors such as depression, anxiety, and use of antidepressants [12] can also have significant consequences on sexual functioning, along with social factors, and impair the sexual relationship with the partner [13].

Patients as well as health-care professionals (HCPs) find it difficult to initiate and discuss sexual issues. A lack of knowledge about management strategies is one of the barriers often cited by HCPs for not addressing sexuality [14,15]. Furthermore, it is essential that patients and their partners are well informed about cancer treatment as they prepare for changes that may affect their sexual life. They also need to understand the risk of sexual difficulties and what treatment or support is available [16]. Patients and their partners want open communication about intimacy and sexuality and many are disappointed by the

information and support they receive [17-19]. People cope better when sexual issues have been aired [22,21]. However, to be able to inform patients and partners, and to meet their supportive care needs, HCPs need to understand the effects of HMs and their treatments on sexuality.

HCPs of patients with HM have repeatedly reported that a lack of knowledge influences discussing sexual issues with their patients [16]. According to the literature this lack of knowledge can only partly be justified. In contrast to the increasing body of literature about the impact on sexuality among survivors after HCT [2, 3, 8], it seems that far less is known about the sexual problems after HM without a HCT. This systematic review aims to investigate the prevalence of various sexual problems among HM patients without HCT.

Methods

Search strategy

This review was conducted following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guidelines [22]. Systematic searches were performed in the databases PubMed, Ebsco/APA PsycINFO, and Ebsco/CINAHL (by CE, AE, and JK) from inception up to 11 November 2020. See Appendix 1 for the full search strategies. The search included indexed terms and free-text words for ‘hematologic cancer’ and ‘sexuality’ or ‘oncologic quality of life questionnaires’. We did not exclude publications by date.

Inclusion criteria

A study was eligible for inclusion if it reported quantitative, patient-reported data relating to sexuality in patients ≥ 18 years of age diagnosed with HM: HL, NHL, acute and chronic leukemias, MM, MDS and MPN. Only publications in English language were included.

Exclusion criteria

Studies were excluded if:

- 1) Reporting questionnaire validation and not patients results.
- 2) Sexual function was evaluated during induction therapy only.
- 3) Outcomes were not quantified.

4) Results described combined HM and cancer populations without distinction in the analysis.

5) Reporting on survivors of HCT.

Screening, data extraction, and quality evaluation

Title and abstracts of all retrieved records were screened by two independent reviewers (by CE and AE). Further, full text review was performed for all potentially eligible records. To ensure accuracy, data was extracted by two independent reviewers (by CE and AE) to assess study type, number of participants and response rate, participant characteristics (age, gender, type of HM, type of HM treatment, time since treatment), and quantitative outcome measures (prevalence of sexual problems). Disagreement about the selection and data extraction was resolved by team discussion (by CE, AE, and SZ) with full agreement on the present selection. Based on the sexual response cycle [5-7], data were categorized into 6 sexual problems categories:

1) decrease in sexual activity.

2) decrease in sexual desire.

3) sexual arousal difficulties (erectile dysfunction in men and vaginal dryness and dyspareunia in women).

4) problems reaching orgasm.

5) problems with sexual satisfaction.

6) sexual problems not further specified.

An appraisal of the methodological quality of each study was assessed using the checklist published by the US National Heart, Lung and Blood Institute for observational cohort and cross-sectional studies (<https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools>). In order to evaluate the risk of bias, 14 questions needed to be examined to assess the quality of the methodology (research question (q1), study population and studied population (q2, 3 and 4), sample size justification (q5), exposure assessed and sufficient timeframe to observe effect (q6, 7, 8, 9 and 10), outcome measures (q11), adequate blinding (q12), follow up rate (q13), and statistical analysis (q14). All answers were rated as follows: 0=no, cannot determine, not applicable or not reported, 1=yes. Figure 2 (Appendix 2) provides an overview of the quality appraisal by 14 items of included studies. In a second step, an overall quality score was calculated for each

manuscript. This calculated overall quality appraisal score could range from 0-14. A higher score indicates a lower risk of bias and higher quality.

Results

Study selection

We identified 3795 records, and, after title and abstract screening, 90 manuscripts were considered potentially relevant. Following a full-text review, 65 manuscripts were rejected, while 25 manuscripts met the selected criteria, representing 24 studies (two manuscripts reported on the same study performed among two different populations) (Fig.1).

The included studies were published between 1979 and 2020. The majority of studies came from Europe ($n=12$) (United Kingdom ($n=4$)[23-26], Germany ($n=3$)[27-29], the Netherlands ($n=3$)[30-32], Denmark ($n=1$)[33], and Norway ($n=1$)[34]) and from the USA ($n=8$) [35-43]. The methods and sample characteristics of the 24 studies are shown in Table 1. The median age of the patients at the time of the published studies was between 30 and 44 years old (range 18-90). The studies reported data on sexual problems in patients with AL, chronic myeloid leukemia (CML), MPN, HL, and NHL. No studies were found that reported prevalence data of sexual problems of patients with chronic lymphatic leukemia, MM and MDS. The type of first-line treatments for lymphoma ($n=7377$) and AL ($n=878$) varied over the years but were either chemotherapy with/without involved field radiotherapy or radiotherapy alone. CML patients ($n=163$) were receiving a maintenance treatment IFN versus no IFN after low-dose continuous or high-dose intermittent busulphan and 6-thioguanine, or hydroxurea [25]. MPN patients ($n=2088$) were either not receiving medication or were treated with interferon, cyto reduction therapy, anagrelide, warfarin, immunomodulators, or steroids [44]. The follow up ranges from 1 year since diagnosis [36] up to more than 30 years post-treatment [23].

Characteristics of the studies

Most of the studies ($n= 22$) were observational cross-sectional cohort studies. Two studies had a prospective longitudinal design measuring from prior to treatment until 27 months [28] and at 3 years after treatment (median)[26]. Six studies compared data on sexual problems among HM patients (HL and NHL) with a general population [28,30-32,38,43].

Quality assessment

Figure 2 (Supplement) provides an overview of the quality appraisal of included studies. The mean overall quality score was 6.2 (range 2-9). The studies with scores ≥ 7 were all studies that had measured and adjusted for confounding variables [24,25,28,31,35-38,42,44,45]. The longitudinal studies and studies that described sexual problems of patients less than 5 years following treatment were regarded as having used a sufficient timeframe to see the effect of treatment on sexual problems [24-26,28,40,42]. All studies clearly stated the aim of the study, 15 studies focused on sexual function or sexual satisfaction [23,26,28-30,32-36,38,40,42,43,45,46], five studies focused on quality of life (QoL) [25,27,31,39,41], and four studies focused on the impact of symptoms and side effects on sexual function [24,37,44,47].

Most studies (21/24) defined the study population. In total, ten of the 24 studies used validated questionnaires either to measure sexual problems [30-32,42,43,45,46] or to measure QoL [23], or distress related to sexual problems [37,44]. Of the seven validated questionnaires measuring sexual problems, the International Index Erectile Function was used twice, all others; Female Sexual Function Index, Maudsley Marital Questionnaire, National Health and Social Life Survey and Brief Sexual Function Inventory, were used once. Finally, the Sexual Activity Questionnaire and the Maudsley Marital Questionnaire were used partly while both were adapted [31,42]. Two of the 24 studies combined a validated questionnaire with a study-specific questionnaire to assess sexual problems [30,32], while ten studies used only a study-specific questionnaire [24,25,27-29,34-36,38,41,47], and six studies obtained quantitative data by means of a structured interview [26,33,35,36,39-41].

Just two studies used the multidimensional concept of sexuality [36, 37, 43].

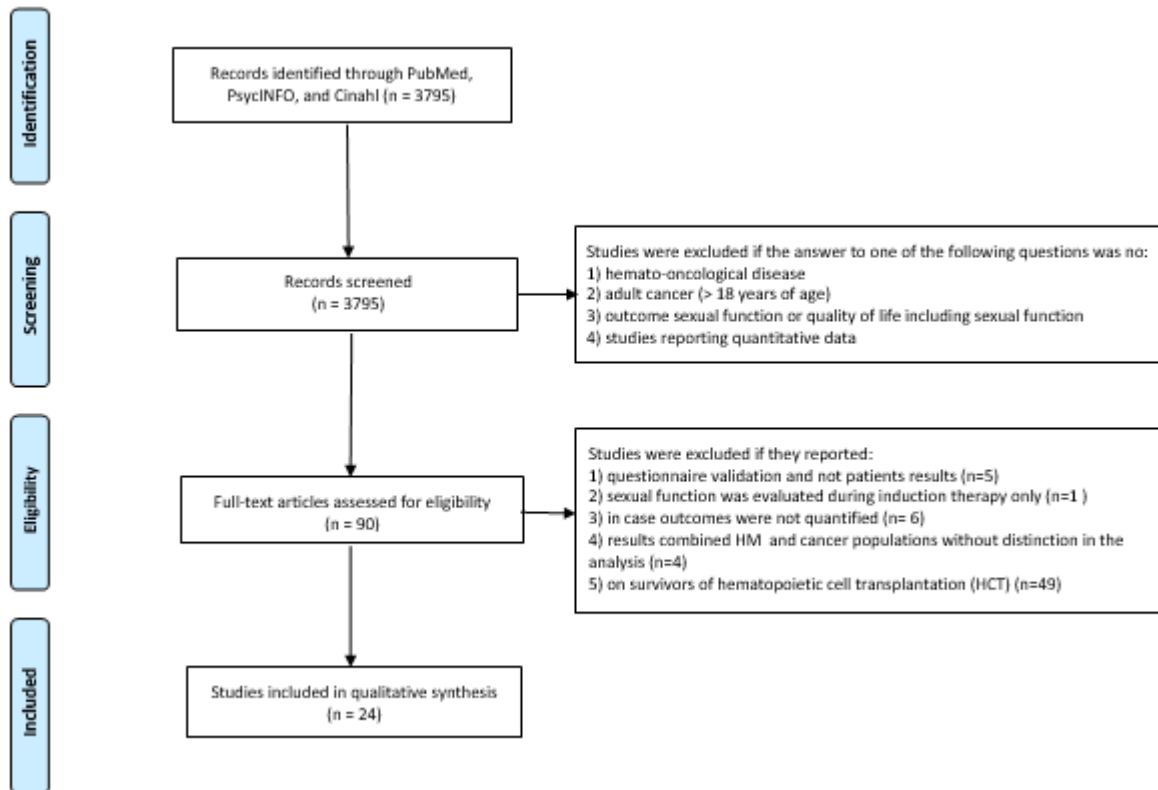


Fig 1. Flow of studies through selection process

Outcomes

In total, 24 studies reported data on sexual problems derived from a total of 10,506 HM patients, with samples ranging from 16 patients to 3208 patients [28,33]. Most studies included both females and males. In 17 studies that reported the response rate, this was at least 50% (range 52-97%) [23-25,28,31,33-38,41-45,47]. In seven studies, the response rate was not reported [26,27,29,30,32,40,46].

Ten studies reported on decrease in sexual activity [24,25,31,33,35,36,38,40-42], 14 studies reported on decrease in sexual desire [23-26,29,31,33-36,38,41-43], 12 studies reported on sexual arousal difficulties (erectile dysfunction in men and vaginal dryness and dyspareunia in women) [29,32,35,36,38-40,42,43,45,46], four studies reported on problems reaching orgasm [29,39,42,45], nine studies reported on problems with sexual satisfaction [23-25,31,35,40], and 14 studies reported sexual problems (not further specified) [23-25,27,28,30,32,34-37,40,42,44,45] (Table 2).

Table 1 Methodological and sample characteristics of the 24 studies

Author (year)	Study population type of treatment (%)	Gender	Response rate (%)	Age at time of diagnosis	Age at time of study	Time since diagnosis	Design	Validated instrument	Non-validated instrument
Greaves et al. (2014) [23]	AL, n = 112, CT, NR	♀n = 46, ♂n = 66	56	Mean 36.5, SD 14.5	Mean 54.8, SD 12.3	Mean 18.4, SD 10.3	Cross	Functional Assessment of Cancer Therapy -BMT	
Messeret et al. (2008) [27]	AML, n = 249, CT, NR	♀n = 149, ♂n = 100	NR	Median 47	NR	Median 9, range 5-22	Cross	No	Leukemia-specific late effects
Watson et al. (1998) [24]	AML, n = 311, CT, NR	♀n = 145, ♂n = 166	89	NR	Median 43	Mean 14 mo after therapy	Cross	No	Leukemia-BMT-specific module
Kornblith et al. (1998) [35]	AL, n = 206, CT, 68%, AD 38% ara-C	♀n = 105, ♂n = 101	75	Mean 36.4, range 12-74	Mean 43.6, range 21-90	Mean 5.6, range 1-17	Cross	No	Structured interview (QNR)
Homewood et al. (2003) [25]	CML, n = 163, BU and 67H, HU, IFN maint vs no maint	♀n = 80, ♂n = 83	85	NR	Mean 56.8, range 24-79	NA	Cross	No	Leukemia-BMT-specific module
McFarland et al. (2018) [37]	MPN, n = 117, NR	♀n = 69, ♂n = 45	78	NR	Mean 57.7, SD 14.8	Range < 1, y > 10 y	Cross	The Distress Thermometer and Problem List	
Geyer et al. (2016) [44]	MPN, n = 1971, NR	♀n = 1060, ♂n = 911	52	NR	Mean 59.2	NA	Cross	Myeloproliferative Symptom Assessment Form	
Eelink et al. (2020) [32]	HL, n = 30, CT (40% ABVD, 60% BEACOPP) and 30% RT (IF)	♂n = 30	NR	NR	Median 38, range 22-63	Median 47 mo, range 9-83	Cross	International Index Erectile Function	Additional self-report QNR sexual function
Greaves et al. (2014) [23]	HL, n = 280, CT and/or RT	♀n = 114, ♂n = 166	56	Mean 28, SD 11.5	Mean 53.1, SD 11.9	Mean 25.1, SD 10.0	Cross	Functional Assessment of Cancer Therapy -BMT	
Eelink et al. (2013) [30]	HL, n = 36, CT (11% MOPP, ABV, 31% ABVD, 58% BEACOPP) and 61% RT (IF)	♀n = 36	NR	NR	Mean 32, SD 4	Median 70 mo	Cross	Female Sexual Function Index	Additional self-report QNR sexual function
Behringer et al. (2013) [28]	HL, n = 3208, CT (ABVD or BEACOPP) followed by RT (IF) vs no RT	♀n = 1382, ♂n = 1826	77	NR	Mean 36, SD 13.3	Range 0-27 mo	Long	No	Sexual functioning scale
Recklitis et al. (2010) [38]	HL, n = 465, 93% RT and 37% CT, NS	♀n = 234, ♂n = 231	61	Mean 26.6, SD 9.95	Median 44	Mean 18.3, SD 7.3	Cross	No	Survey including 6 items inquiring about occurrence of sexual problems

Table 1 (continued)

Author (year)	Study population type of treatment (%)	Gender	Response rate (%)	Age at time of diagnosis	Age at time of study	Time since diagnosis	Design	Validated instrument	Non-validated instrument
Aksay et al. (2008) [46]	HL, n = 38, 100% CT (3-14 cycles NS), 79% RT	♂n = 38	NR	NR	Mean 40.2 SD 11, range 18-55	Mean 7.7, range 0-20y	Cross	International Index Erectile Function	
Abrahamson et al. (1998) [34]	HL, n = 459, CT (MVPP or LVPP) and/or RT	♀n = 204, ♂n = 255	82	Mean 32, range 15-60	Mean 44, range 19-74	Range 3-23	Cross	No	Self-constructed QNR
Brierley et al. (1998) [47]	HL, n = 353, CT and/or RT (32% MOJP-type and RT), RT (42% MRT and 17% IF)	NR	97	NR	NR	NR	Cross	No	Structured QNR
Van Tulder et al. (1994) [31]	HL, n = 81, CT and/or RT (4% VBL, 11% MOJP, 100% MRT)	♀n = 39, ♂n = 42	92	NR	♀ Mean 42.8, SD 11; ♂mean 44.3, SD 11.1	Mean 14, SD 2	Cross	Maudsley Marital QNR	
Boorm et al. (1993) [39]	HL, n = 85, CT (25% MOJP, 25% PAVE, 14% ABVD, 3% VBM0, and RT 48%, RT alone 37%)	♂n = 85	88	NR	Mean 32.3, range 21-60	Mean 37 mo, range 1-7.5y	Cross	No	Structured interview
Hannah et al. (1992) [40]	100% splenectomy, CT and/or RT NS	♂n = 24	NR	NR	Mean 35.2, SD 6.8	Mean 34.9 mo	Cross	No	Structured interview
Kreuger et al. (1987) [29]	HL, n = 33, CT (COPP)	♀n = 14, ♂n = 19	NR	NR	♀ Median 31, range 19-39; ♂median 32, range 19-53	Median 5, range 1-17	Cross	No	QNR
Fobair et al. (1986) [41]	HL, n = 403, CT (5%), CT and RT (58%) RT (38%)	♀n = 181, ♂n = 222	95	Mean 27	Mean 36	Median 9	Cross	No	Structured interview (QNR)
Kornblith et al. (1990) [36]	HL, n = 273, 78% received alkylating agents (MP), 16% RT + CT, 4% RT	♀n = 109, ♂n = 164	74	Mean 29.6, range 6-56	Mean 37, range 20-66	Mean 5.9, range 1-20	Cross	No	Structured interview (QNR)
Specht et al. (1984) [33]	HL, n = 16, CT (44% MOJP) or MRT (56%)	♂n = 16	70	Mean 29, range 16-36	NR	Mean 72 mo, range 48-125 mo	Cross	No	Structured interview (QNR)
Chapman et al. (1979) [26]	HL, n = 40, CT (MMVP)	♀n = 40	NR	NR	Median 30, range 20-51	Median 36 mo, range 10-78	Long	No	Structured interview (QNR)

Table 1 (continued)

Author (year)	Study population type of treatment (%)	Gender	Response rate (%)	Age at time of diagnosis	Age at time of study	Time since diagnosis	Design	Validated instrument	Non-validated instrument
Kim et al. (2017) [45]	NHL, $n = 738$, 89% CT (R-CHOP, CHOP, R-CVP, CVP) and 15% RT (pelvic area)	♀ $n = 313$, ♂ $n = 425$	56	NR	♀ Mean 55.0, SD 11.4, ♂ mean 55.6, SD 12.5	Mean 6.2	Cross	National Health and Social Life Survey	
Graess et al. (2014) [23]	NHL, $n = 326$, CT and/or RT, NS	♀ $n = 150$, ♂ $n = 176$	56	Mean 45, SD 13	Mean 61.8, SD 11.8	Mean 16.8, SD 8.5	Cross	Functional Assessment of Cancer Therapy -BMT	
Beckjord et al. (2011) [42]	NHL, $n = 222$, 51% CT and 49% CT plus other treatment	♀ $n = 99$, ♂ $n = 123$	73	Mean 57.73, SD 14.81	NR	Mean 3.54, SD 0.84	Cross	Sexual Activity QNR / Sexual Functioning QNR	
Aksoy et al. (2008) [46]	NHL, $n = 21$, 100% CT (3–14 cycles NS), 55% RT	♂ $n = 21$	NR	NR	Mean 40.2, SD 11.0, range 18–55	Mean 8, range 10 mo to 20 y	Cross	International Index Erectile Function	
Kiserud et al. (2009) [43]	HL + NHL, $n = 246$, CT and/or RT, NS	♂ $n = 236$	85	Mean 32, SD 9.4	Mean 47, SD 10.2	Mean 15	Cross	Brief Sexual Function Inventory	

Hematological malignancy: AL, acute leukemia; AML, acute myeloid leukemia; CML, chronic myeloid leukemia; MPN, myeloproliferative neoplasm; HL, Hodgkin lymphoma; NHL, non-Hodgkin lymphoma

Treatment: CT, chemotherapy; RT, radiotherapy; IF, involved field; MRT, mantle field radiotherapy; AD, cytarabine, daunorubicin, ara-C, cytosine arabinoside; BU, busulfan; 6-TG, 6-thioguanine; HU, hydroxyurea; IFN, interferon; MOPP-ABV, nitrogen mustard, vincristine, prednisone, procarbazine, doxorubicin, bleomycin, vinblastine, and procarbazine; BEACOPP, cyclophosphamide, doxorubicin, etoposide, procarbazine, prednisone, vincristine, bleomycin; MVPP, mustine, vinblastine, procarbazine, and prednisone; LYPP, chlorambucil, vinblastine, procarbazine, and prednisone; VBM, vincristine, bleomycin, methotrexate; COPP, cyclophosphamide, vincristine, procarbazine, prednisone; VBL, vinblastine; MP, mechlorethamine, procarbazine; MOPP, nitrogen mustard, vincristine, prednisone, procarbazine; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone; CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone; R-CVP, rituximab, cyclophosphamide, vincristine, prednisone; CVP, cyclophosphamide, vincristine, prednisone

Other: SD, standard deviation; *mean*, mean; *mo*, months; *y*, years; *na*, not applicable; *NR*, not reported; *NA*, not applicable; *Cross*, cross-sectional cohort study; *Long*, longitudinal cohort study; *QNR*, questionnaire; *QoL*, quality of life

Table 2 Prevalence of sexual problems

Author (year)	Calculated overall quality appraisal score*	Decrease in sexual activity	Decrease in sexual desire	Sexual arousal difficulties	Sexual pain	Problems reaching orgasm	Problems with sexual satisfaction	Sexual problems not further specified	Comparison to general population
Behringer et al. (2013) [28]	9							49.9% reported severe impairment of sexual function	Worse sexual function in patients with advanced-stage HL
Beckjord et al. (2011) [42]	9	31% not sexual active; 23% not satisfied with frequency	29%	26%		24%	25%	26% considered sexual functioning as a moderate or big problem	
McFarland et al. (2018) [37]	8							10.3% reported sexual problems	
Kim et al. (2017) [45]	8		♀64%, ♂38%	♀48%, ♂49%	32%	♀58%, ♂38%	♀58%, ♂23%	♀32%, ♂42% reported anxiety about performance	
Geyer et al. (2016) [44]	8							64% of patients some degree of sexual dysfunction and 43% experiencing severe symptoms	
Homeswood et al. (2003) [25]	8	62% IFN vs 44% no IFN	55% IFN vs 36% no IFN				51% IFN vs 34% no IFN	45% IFN vs 41% no IFN decrease in ability to have sex;	
Van Tulder et al. (1994) [31]	8	29%	25%				12%		Poorer sexual function (sexual activity, sexual desire, satisfaction) in HL survivors No difference compared to controls
Recklitis et al. (2010) [38]	7	54%	41%		32%				
Watson et al. (1998) [24]	7	35%	24%				18%	18% decreased ability to have sex	
Kornblith et al. (1998) [35]	7	29%	21%	18%	9%		23%	17% feeling unattractive	
Kornblith et al. (1990) [36]	7	21%	18%	13%			31%	37% reported one or more sexual problems	

Table 2 (continued)

Author (year)	Calculated overall quality appraisal score*	Decrease in sexual activity	Decrease in sexual desire	Sexual arousal difficulties	Sexual pain	Problems reaching orgasm	Problems with sexual satisfaction	Sexual problems not further specified	Comparison to general population
Greaves et al. (2014) [23]	6		20%				32%		
Eelink et al. (2020) [32]	6		20%				22%		
Eelink et al. (2013) [30]	6		28%	23%			34%	20% reported a sexual problem	No differences
Kiserud et al. (2009) [43]	6	21%	27%			21%		39% reported one or more sexual problems, 31% reported a sexual dysfunction	No differences
Brierley et al. (1998) [47]	6		7% ongoing and 25% transient						Poorer sexual arousal and satisfaction in HL/ NHL survivors
Aksøy et al. (2008) [46]	5			63%					
Abrahamson et al. (1998) [34]	5			57%					
Bloom et al. (1993) [39]	5					23%		12% ongoing sexual problems, and 16% transient problems	
Fohair et al. (1986) [41]	5	36%	26%						
Specht et al. (1984) [33]	5	0%	0%						
Kreuser et al. (1987) [29]	4		♀21%, ♂11%	♂5%	25%	♀21%, ♂5%			
Chapman et al. (1979) [26]	4		73%						
Messner et al. (2008) [27]	3								17% sexual limitations

*The higher the score, the higher the quality of the studies

Prevalence of sexual problems

Decrease in sexual activity was reported by 29-35% of AL patients ($n=517$)[24,35], 44-62% of CML patients ($n=163$)[25], 0-63% HL and NHL patients ($n=1484$)[31,33,36,38,40-42]. Decrease in sexual desire was reported by 20-24% AL patients ($n=629$) [24, 25, 35], 38-55% patients with CML ($n=163$)[25], 0-73% HL and NHL patients ($n=3476$)[23,26,29,31,33,36,38,41-43,45,47]. Sexual arousal difficulties (e.g. erectile dysfunction in men, vaginal dryness or dyspareunia in women) were reported by 9-18% of AL patients ($n=206$) [35], 5-63% of HL and NHL patients ($n=2145$) [29,36,38-40,42,43,45,46]. Problems in the phase of orgasm were reported by 5-58% of HL and NHL patients ($n=1078$) [29,39,42,45]. Problems in this domain were not reported by patients with other HM. Dissatisfaction with sexual life was reported by 18-32% of AL patients ($n=629$)[23,24,35], 34-51% of CML patients ($n=163$)[25], and 12-58% of HL and NHL patients ($n=2190$) [23,31,36,40,42,43,45]. Various other sexual problems were reported by 17-28% of AL patients ($n=878$) [23,24,27,35], 41-45% of CML patients ($n=163$)[56], 10-64% of MPN patients ($n=2088$)[37,44], 12-50% of HL and NHL patients ($n=5596$)[23,28,30,32,34,36,40,42,45] (Table 2).

Discussion

To improve understanding of sexual problems among patients treated for HM prior to HCT, we conducted a systematic literature review investigating the prevalence of sexual problems. We found 24 studies reporting quantitative, patient-reported data relating to sexual problems among adult patients diagnosed with HM. Over the last 10 years, in line with an increased interest for quality of life research, six studies focused on sexual function or sexual satisfaction [23,28,30,32,42,45], and two studies focused on the impact of symptoms and side effects on sexual function among patients[37,44]. With regard to the methodology of the identified studies, mainly incomprehensive outcomes were measured among a fairly young population of mostly patients treated for a malignant lymphoma, making it difficult to draw final conclusions.

In order to get at least a multidimensional understanding of sexuality in HM patients, the most common domains according to the sexual response cycle, such as interest, desire, excitement/ arousal, orgasm and satisfaction, need to be assessed [5-7]. Furthermore, the impact on sexual relationship needs to be assessed as well, as we know that an active and satisfying sex life is easily set aside when a serious illness is involved [13]. Our review yielded only one study assessing all the aforementioned domains regarding sexual function [42] with two studies assessing four domains (frequency of sexual activity, desire, arousal and satisfaction) [35,36,45]. All others assessed three domains or even fewer.

To measure sexual problems, a validated questionnaire is required. A mere six validated questionnaires were used to assess sexual function or sexual satisfaction [30-32,42,43,45,46]. Of these six, two, namely the Sexual Activity Questionnaire and the Maudsley Marital Questionnaire, were used partly, and both were adapted [31,42,48,49]. In recent years, two tools that assess multidimensional aspects of sexuality in cancer survivors have been developed. The National Institutes of Health's Patient-Reported Outcomes Measurement Information System® (PROMIS®) Network developed the PROMIS Sexual Function and Satisfaction Measure (SexFS), an item bank which includes many different familiar and less familiar domains. In total, there are 131 items in 18 domains [50-52]. It has a modular approach, and allows user to select only those items that are important for the study sample. The SexFS is suitable for healthy populations and for populations with comorbidity (heart failure, diabetes, cancer, depression, and anxiety) and the SexFS scoring provides a built-in comparison to the general population. Moreover, a brief SexFS is available and consists of 8 items for SExFS version 2 Brief Profile Male, and 13 items for the SexFS Brief Profile Female[52]. The European Organization for the Research and Treatment of Cancer (EORTC) has developed the 22-item Sexual Health Questionnaire (EORTC SHQ-22), a validated patient-reported outcome (PRO) for the assessment of physical, psychological, and social aspects of sexual health in cancer patients and survivors [53]. Both tools measure patients' perceptions of their sexuality by items that have been explicitly reported as relevant by patients themselves, and are meant to be used for all genders and as a stand-alone questionnaire. For reasons of comprehensiveness, we propose to use the brief SexFS male or female questionnaire.

Sexual problems are common in the general population as well as in the cancer population. The causes for sexual problems in both populations are often multiple heterogeneous factors, like biological factors (e.g., vascular, hormonal, neurological, urological, iatrogenic, psychiatric, obesity, or poor health), psychological factors (e.g., emotional problems, depression, anxiety) and social factors (e.g., sexual abuse, alcohol/tobacco/opioids/ recreational drug abuse, marital problems, communication, no sexual partner, sexual dysfunction in the partner, and low education and unemployment) [3,8,12,13,54-60]. As a result of these numerous causes, there is a need for a strong baseline from where we can continue to build. The benefit of one cancer-specific measurement to assess sexual dysfunction in a cancer population is that it can provide this strong baseline.

Research regarding sexual problems in HM patients has mostly focused on patients treated for malignant lymphoma and shows limited reporting on sexual problems across all other HM disease groups, with only one study focusing on CML[25] and two on MPN [37,44] and none on patients with chronic

lymphatic leukemia (CLL), multiple myeloma (MM) or myelodysplastic syndromes (MDS). Unlike the latter, CML and MPN need continuous treatment. For patients with MPN, The Myeloproliferative Neoplasm Symptom Assessment Form (MPN-SAF) is a validated instrument specifically developed for assessing symptom burden, including sexual problems [61]. Geyer et al. reported sexual problems in two-thirds (64%) of MPN patients. In the initial 27-item MPN-SAF, a sexual problem is assessed by one item inquiring for “problems with sexual desire or function”. Sexual problems are common among MPN patients, but unfortunately, it provides limited contribute to our understanding of the extent of the problem. Furthermore, sexual problems associated with current standard therapies like JAK2 inhibitors in MPN and TKIs in CML have not been evaluated. So, understanding sexual problems in HM patients is not only hampered by the variation in methodology but also by the lack of research on patients using novel therapies.

In case of follow-up of more than 5 years, we have to consider that other aspects such as aging and associated health problems can also influence sexual function and then it is difficult to distinguish what the effect of HM or its treatment is [56,62]. Therefore, with the aim to see the effect of treatment on sexual problems, longitudinal studies, and studies that described sexual problems of HM patients less than 5 years following treatment, were regarded as most informative for our understanding of the impact of hematological malignancies (HM) and their treatments on sexuality. Two longitudinal studies [26,28] and four cross sectional studies described sexual problems of survivors less than 5 years following treatment [24,32,40,42]. However, the response rate was not reported in three of these studies [26,32,40]. Subsequently, because of this possible nonresponse bias, these results may not be indicative for sexual problems, leaving three useful studies among three different HM populations, respectively AL, HL and NHL, with prevalence rates of sexual problems varying between 18 and 50% [24,28,42].

Strengths

To our knowledge, this is the first systematic review about the prevalence of sexual problems among HM patients. A systematic approach was used to investigate the prevalence an underreported problem that is important for the HM survivors.

Limitations

Only studies reporting quantitative data were included. It is recognized that qualitative data could supplement further the research findings. Consequently, this systematic review evaluated data presented within the articles which may not be a complete reporting of results. In addition, no prevalence data was

found on the effect of current therapies in HM on sexual function (e.g. immunotherapies, methylating agents, or targeted therapies). This is an important consideration for daily practice, as the novel therapies are increasingly used as standard treatment in HM.

Clinical implications

Most HCPs do not feel comfortable about informing patients and their intimate partners about the changes in sexuality that can occur [15,17,18,63,64], neither are they used to taking a sexual history [65]. As a result, sexuality is not addressed, sexual problems are not assessed, and support will in general not be offered. A PRO like the SexFS or the EORTC SHQ-22 is eminently appropriate to be used by the HCPs to promote addressing sexuality and discussing the issues that matter to the patient/survivor. Additionally, they are appropriate to evaluate the support that is given.

Implications for future studies

Overall, there is little information about the exact impact of HM treatment on sexual functioning of survivors. Even though assessing the role of associated factors (e.g. sociodemographic and clinical characteristics, physical and psychological functioning) on sexual function was not an aim of this review, we came across similarities (association of increasing age and sexual problems)[27,28,38,42,43,45] but also inconsistencies (association of gender and sexual problems) [25,38,42,45].

To conclude, in order to obtain a better understanding of how often various sexual problems occur among all adult patients treated for HM, a standardized approach to investigate the extent and severity of the sexual problems among HM patients is needed. Longitudinal prospective cohort studies focusing on the effect of HM diagnosis and treatment and associated factors on sexuality are required. Moreover, because sexual problems are common in the general population, sexual outcomes of HM patients need to be compared with reference data from an age-matched control population.

However, the SexFS and the EORTC SHQ-22 seem well designed screening tools, further research on the validity of these patient-reported outcome measures in HM patients is recommended.

Conclusion

In conclusion, it seems that 18-50% of AL, HL and NHL, HM patients report sexual problems. Unfortunately, the reported methods and results varied widely between the 24 included studies in this systematic review and the exact impact of the influence of HM diagnosis and treatment on sexual function

remains to be answered. Longitudinal studies focusing on the effect of HM diagnosis and treatment on sexuality by using a validated questionnaires and comparison with normative data are hugely needed.

Conflict of interest

The authors declare no competing interests.

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Appendix 1: Search Strategies

Search strategy for PubMed (11 November 2020)

Search	Query	Results
#6	(#1 AND #5) OR #4	3,004
#5	("EORTC"[tiab] AND ("hdc"[tiab] OR "high dose chemotherap*"[tiab])) OR "nccn distress"[tiab] OR "distress thermometer*"[tiab] OR "functional assessment of cancer therap*"[tiab] OR "leukemia bmt"[tiab]	2,906
#4	(#1 AND #2) NOT #3	2,593
#3	((("Adolescent"[Mesh] OR "Child"[Mesh] OR "Infant"[Mesh] OR "adolescen*"[tiab] OR "child*"[tiab] OR "schoolchild*"[tiab] OR "infant*"[tiab] OR "girl*"[tiab] OR "boy"[tiab] OR "boys"[tiab] OR "boyhood"[tiab] OR "teen"[tiab] OR "teens"[tiab] OR "teenager*"[tiab] OR "youth*"[tiab] OR "pediatr*"[tiab] OR "paediatr*"[tiab] OR "puber*"[tiab]) NOT ("Adult"[Mesh] OR "adult*"[tiab] OR "man"[tiab] OR "men"[tiab] OR "woman"[tiab] OR "women"[tiab]))	2,134,382
#2	"Sexual Behavior"[Mesh:noexp] OR "Sexual Dysfunctions, Psychological"[Mesh] OR "Libido"[Mesh] OR "Coitus"[Mesh] OR "Sexuality"[Mesh:noexp] OR "Ejaculation"[Mesh] OR "Orgasm"[Mesh] OR "Penile Erection"[Mesh] OR "Sexual Dysfunction, Physiological"[Mesh] OR "sexual*"[tiab] OR "sex behavio*"[tiab] OR "sex disorder*"[tiab] OR "intercourse*"[tiab] OR "coital*"[tiab] OR "coitus"[tiab] OR "erecti*"[tiab] OR "dyspareuni*"[tiab] OR "orgasm*"[tiab] OR "ejaculati*"[tiab] OR "impoten*"[tiab] OR "vaginism*"[tiab] OR "libido"[tiab] OR "sex drive"[tiab] OR "sex interest*"[tiab] OR "sex desire*"[tiab] OR "sex arousal*"[tiab] OR "psychosexual*"[tiab] OR "sex aversi*"[tiab] OR "frigidit*"[tiab] OR "vaginal lubricati*"[tiab]	307,251
#1	"Hematologic Neoplasms"[Mesh] OR "Leukemia"[Mesh] OR "Lymphoma"[Mesh] OR "Multiple Myeloma"[Mesh] OR (("hematolog*"[tiab] OR "haematolog*"[tiab] OR "myeloproliferati*"[tiab] OR "myelodysplas*"[tiab] OR "myelofibro*"[tiab]) AND (cancer[sb] OR "neoplasm*"[tiab] OR "disease*"[tiab] OR "disorder*"[tiab] OR "syndrom*"[tiab])) OR "lymphoma*"[tiab] OR "myeloma*"[tiab] OR "hodgkin*"[tiab] OR "nonhodgkin*"[tiab] OR "leukemi*"[tiab] OR "leukaemi*"[tiab] OR "thrombocyt*"[tiab] OR "Bone Marrow Transplantation"[Mesh] OR "bmt"[tiab] OR "bone marrow graft*"[tiab] OR "bone marrow cell transplant*"[tiab] OR "bone marrow transplant*"[tiab] OR "Stem Cell Transplantation"[Mesh] OR "stem cell transplant*"[tiab] OR "hct"[tiab] OR "hsct"[tiab] OR "mud"[tiab] OR "ric"[tiab] OR "Bone Marrow Diseases"[Mesh] OR "anemi*"[tiab] OR "anaemi*"[tiab] OR "polycythemi*"[tiab] OR "polycythaemi*"[tiab]	970,295

Search strategy for Ebsco/CINAHL (11 November 2020)

#	Query	Results
S5	S1 AND S4	523
S4	S2 OR S3	103,798
S3	TI("EORTC HDC" OR "EORTC high dose chemotherapy" OR "NCCN distress" OR "Functional Assessment of Cancer Therap*" OR "leukemia bmt" OR "distress thermometer") OR AB("EORTC HDC" OR "EORTC high dose chemotherapy" OR "NCCN distress" OR "Functional Assessment of Cancer Therap*" OR "leukemia bmt" OR "distress thermometer")	1,618
S2	MH "Sexual Dysfunction, Female+" OR MH "Sexual Dysfunction, Male+" OR MH "Psychosexual Disorders" OR MH "Coitus" OR MH "Sexual Satisfaction" OR MH "Sexuality" OR MH "Sexuality (Omaha)" OR MH "Attitude to Sexuality" OR MH "Sexual Dysfunction, Male" OR MH "Sexual Dysfunction, Female" OR MH "Sexual Counseling" OR MH "Sex+" OR TI(sexual* OR "sex behavio*" OR "sex orientati*" OR "sex disorder*" OR intercourse* OR coital* OR coitus OR erecti* OR dyspareuni* OR orgasm* OR ejaculati* OR impoten* OR vaginism* OR libido OR "sex drive" OR "sex interest*" OR "sex desire*" OR "sex arousal*" OR psychosexual* OR "sex aversi*" OR frigidit* OR "vaginal lubricati*") OR AB(sexual* OR "sex behavio*" OR "sex orientati*" OR "sex disorder*" OR intercourse* OR coital* OR coitus OR erecti* OR dyspareuni* OR orgasm* OR ejaculati* OR impoten* OR vaginism* OR libido OR "sex drive" OR "sex interest*" OR "sex desire*" OR "sex arousal*" OR psychosexual* OR "sex aversi*" OR frigidit* OR "vaginal lubricati*")	102,244
S1	(MH "Hematologic Neoplasms+") OR (MH "Leukemia+") OR (MH "Leukemia, Lymphocytic+") OR (MH "Leukemia, Lymphocytic, Chronic+") OR (MH "Leukemia, Myeloid+") OR (MH "Leukemia, Myeloid, Acute+") OR (MH "Lymphoma, T-Cell, Cutaneous+") OR (MH "Lymphoma, T-Cell+") OR (MH "Lymphoma, B-Cell+") OR (MH "Lymphoma, Non-Hodgkin's+") OR (MH "Lymphoma+") OR (MH "Multiple Myeloma") OR TI(lymphoma* OR myeloma* OR hodgkin* OR nonhodgkin* OR leukemi* OR leukaemi*) OR AB(lymphoma* OR myeloma* OR hodgkin* OR nonhodgkin* OR leukemi* OR leukaemi*) OR (TI(hematolog* OR haematolog* OR myeloproliferati* OR myelodysplas* OR myelofibro* OR AB(hematolog* OR haematolog* OR myeloproliferati* OR myelodysplas* OR myelofibro*) AND ((MH "Neoplasms+") OR TI (adenoma* OR anticarcinogen* OR blastoma* OR cancer* OR carcinogen* OR carcinom* OR carcinosarcoma* OR chordoma* OR germinoma* OR gonadoblastoma* OR hepatoblastoma* OR lymphangioma* OR lymphangiomyoma* OR lymphangiosarcoma* OR lymphom* OR malignan* OR melanom* OR meningioma* OR mesenchymoma* OR mesonephroma* OR metasta* OR neoplas* OR	102,672

	<p>neuroma* OR nslc OR oncogen* OR oncolog* OR paraneoplastic OR plasmacytoma* OR precancerous OR sarcoma* OR teratocarcinoma* OR teratoma* OR tumor* OR tumour* OR disease* OR disorder* OR syndrom*) OR AB (adenoma* OR anticarcinogen* OR blastoma* OR cancer* OR carcinogen* OR carcinom* OR carcinosarcoma* OR chordoma* OR germinoma* OR gonadoblastoma* OR hepatoblastoma* OR lymphangioma* OR lymphangiomyoma* OR lymphangiosarcoma* OR lymphom* OR malignan* OR melanom* OR meningioma* OR mesenchymoma* OR mesonephroma* OR metasta* OR neoplas* OR neuroma* OR nslc OR oncogen* OR oncolog* OR paraneoplastic OR plasmacytoma* OR precancerous OR sarcoma* OR teratocarcinoma* OR teratoma* OR tumor* OR tumour* OR disease* OR disorder* OR syndrom*)) OR MH "Bone Marrow Transplantation+" OR MH "Hematopoietic Stem Cell Transplantation" OR MH "Myeloproliferative Disorders+" OR MH "Bone Marrow Diseases+" OR TI(thrombocyt* OR bmt OR “bone marrow graft*” OR “bone marrow cell transplant*” OR “bone marrow transplant*” OR “stem cell transplant*” OR hct OR hsct OR mud OR ric OR polycythem* OR polycythaemi*) OR AB(thrombocyt* OR bmt OR “bone marrow graft*” OR “bone marrow cell transplant*” OR “bone marrow transplant*” OR “stem cell transplant*” OR hct OR hsct OR mud OR ric OR polycythem* OR polycythaemi*)</p>	
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Search strategy for Ebsco/APA PsycINFO (11 November 2020)

#	Query	Results
S5	S1 AND S4	268
S4	S2 OR S3	187,926
S3	TI (“EORTC HDC” OR “EORTC high dose chemotherapy” OR “NCCN distress” OR “Functional Assessment of Cancer Therap*” OR "leukemia bmt" OR “distress thermometer”) OR AB (“EORTC HDC” OR “EORTC high dose chemotherapy” OR “NCCN distress” OR “Functional Assessment of Cancer Therap*” OR "leukemia bmt" OR “distress thermometer”)	787
S2	DE "Psychosexual Behavior" OR DE "Erection (Penis)" OR DE "Orgasm" OR DE "Female Orgasm" OR DE "Male Orgasm" OR DE "Sexual Abstinence" OR DE "Sexual Arousal" OR DE "Sexual Function Disturbances" OR DE "Dyspareunia" OR DE "Erectile Dysfunction" OR DE "Female Sexual Dysfunction" OR DE "Inhibited Sexual Desire" OR DE "Premature Ejaculation" OR DE "Priapism" OR DE "Vaginismus" OR DE "Sexual Intercourse (Human)" OR DE "Sexuality" OR DE "Sexual Satisfaction" OR DE "Endocrine Sexual Disorders" OR DE "Hypogonadism" OR DE "Sex Drive" OR DE "Libido" OR TI (sexual* OR “sex behavio*” OR “sex orientati*” OR	187,174

	<p>“sex disorder*” OR intercourse* OR coital* OR coitus OR erecti* OR dyspareuni* OR orgasm* OR ejaculati* OR impoten* OR vaginism* OR libido OR “sex drive” OR “sex interest*” OR “sex desire*” OR “sex arousal*” OR psychosexual* OR “sex aversi*” OR frigidit* OR “vaginal lubricati*”) OR AB (sexual* OR “sex behavio*” OR “sex orientati*” OR “sex disorder*” OR intercourse* OR coital* OR coitus OR erecti* OR dyspareuni* OR orgasm* OR ejaculati* OR impoten* OR vaginism* OR libido OR “sex drive” OR “sex interest*” OR “sex desire*” OR “sex arousal*” OR psychosexual* OR “sex aversi*” OR frigidit* OR “vaginal lubricati*”)</p>	
S1	<p>DE "Leukemias" OR TI (lymphoma* OR myeloma* OR hodgkin* OR nonhodgkin* OR leukemi* OR leukaemi*) OR AB (lymphoma* OR myeloma* OR hodgkin* OR nonhodgkin* OR leukemi* OR leukaemi*) OR (TI (hematolog* OR haematolog* OR myeloproliferati* OR myelodysplas* OR myelofibro* OR AB (hematolog* OR haematolog* OR myeloproliferati* OR myelodysplas* OR myelofibro*) AND (DE "Neoplasms" OR DE "Benign Neoplasms" OR DE "Breast Neoplasms" OR DE "Endocrine Neoplasms" OR DE "Leukemias" OR DE "Melanoma" OR DE "Metastasis" OR DE "Nervous System Neoplasms" OR DE "Terminal Cancer" OR DE "Liver Disorders" OR DE "Oncology" OR TI (adenoma* OR anticarcinogen* OR blastoma* OR cancer* OR carcinogen* OR carcinom* OR carcinosarcoma* OR chordoma* OR germinoma* OR gonadoblastoma* OR hepatoblastoma* OR lymphangioma* OR lymphangiomyoma* OR lymphangiosarcoma* OR lymphom* OR malignan* OR melanom* OR meningioma* OR mesenchymoma* OR mesonephroma* OR metasta* OR neoplas* OR neuroma* OR nslc OR oncogen* OR oncolog* OR paraneoplastic OR plasmacytoma* OR precancerous OR sarcoma* OR teratocarcinoma* OR teratoma* OR tumor* OR tumour* OR disease* OR disorder* OR syndrom*) OR AB (adenoma* OR anticarcinogen* OR blastoma* OR cancer* OR carcinogen* OR carcinom* OR carcinosarcoma* OR chordoma* OR germinoma* OR gonadoblastoma* OR hepatoblastoma* OR lymphangioma* OR lymphangiomyoma* OR lymphangiosarcoma* OR lymphom* OR malignan* OR melanom* OR meningioma* OR mesenchymoma* OR mesonephroma* OR metasta* OR neoplas* OR neuroma* OR nslc OR oncogen* OR oncolog* OR paraneoplastic OR plasmacytoma* OR precancerous OR sarcoma* OR teratocarcinoma* OR teratoma* OR tumor* OR tumour* OR disease* OR disorder* OR syndrom*))) OR TI (thrombocyt* OR bmt OR “bone marrow graft*” OR “bone marrow cell transplant*” OR “bone marrow transplant*” OR “stem cell transplant*” OR hct OR hsct OR mud OR ric OR polycythem* OR polycythaemi*) OR AB (thrombocyt* OR bmt OR “bone marrow graft*” OR “bone marrow cell transplant*” OR “bone marrow transplant*” OR “stem cell transplant*” OR hct OR hsct OR mud OR ric OR polycythem* OR polycythaemi*)</p>	8,029

Appendix 2.

Fig.2. Overview of quality assessment of the methodology of the 24 studies

	Chapman et al.,1979 [26]	Specht et al.,1984 [33]	Fobair et al.,1986 [41]	et Kreuser et al.,1987 [29]	Kornblith et al.,1990 [36]	Hannah et al., 1992 [40]	Bloom et al.,1993 [39]	Van Tulder et al.,1994 [31]
1. Was the research question or objective in this paper clearly stated?	Y	Y	Y	Y	Y	Y	Y	Y
2. Was the study population clearly specified and defined?	N	Y	Y	Y	Y	N	Y	Y
3. Was the participation rate of eligible persons at least 50%?	NR	Y	Y	NR	Y	NR	Y	Y
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	NR	Y	Y	NR	Y	N	Y	Y
5. Was a sample size justification, power description, or variance and effect estimates provided?	N	N	N	N	N	N	N	N
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	Y	N	N	N	N	N	N	N
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	Y	N	N	N	N	Y	N	N
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	N	N	N	N	N	N	N	N
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Y	Y	Y	Y	Y	N	Y	Y
10. Was the exposure(s) assessed more than once over time?	N	N	N	N	N	N	N	N
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	N	N	N	N	N	N	N	Y
12. Were the outcome assessors blinded to the exposure status of participants?	N	N	N	Y	Y	N	N	Y
13. Was loss to follow-up after baseline 20% or less?	NR	NA	NA	NA	NA	NA	NA	NA
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	N	N	N	N	Y	N	N	Y
calculated overall quality score	4	5	5	4	7	2	5	8

Y,yes; N,no; CD, cannot determine; NA, not applicable; NR, not reported

Fig.2. (Continued)

	Abrahamsen et al.,1998 [34]	Brierley et al.,1998 [47]	Kornblith et al.,1998 [35]	Watson et al.,1999 [24]	Homewood et al.,2003 [25]	Messerer et al.,2008 [27]	Aksoy et al.,2008 [46]	Kiserud et al.,2009 [43]
1. Was the research question or objective in this paper clearly stated?	Y	Y	Y	Y	Y	Y	Y	Y
2. Was the study population clearly specified and defined?	Y	Y	Y	Y	Y	N	Y	Y
3. Was the participation rate of eligible persons at least 50%?	Y	Y	Y	Y	Y	NR	NR	Y
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	Y	Y	Y	Y	Y	N	Y	Y
5. Was a sample size justification, power description, or variance and effect estimates provided?	N	N	N	N	N	N	N	N
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	N	N	N	N	N	N	N	N
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	N	N	N	Y	Y	N	N	N
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	N	N	N	N	N	N	N	N
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	N	Y	Y	N	Y	N	N	N
10. Was the exposure(s) assessed more than once over time?	N	N	N	N	N	N	N	N
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	N	N	N	N	N	N	Y	Y
12. Were the outcome assessors blinded to the exposure status of participants?	Y	Y	Y	Y	Y	Y	Y	Y
13. Was loss to follow-up after baseline 20% or less?	NA	NA	NA	NA	NA	NA	NA	NA
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	N	N	Y	Y	Y	Y	N	N
calculated overall quality score	5	6	7	7	8	3	5	6

Y,yes; N,no; CD, cannot determine; NA, not applicable; NR, not reported

Fig.2. (Continued)

	Recklitis et al.,2010 [38]	Beckjord et al.,2011 [42]	Eclink et al.,2013 [30]	Behringer et al.,2013 [28]	Greaves et al.,2014 [23]	Geyer et al.,2016 [44]	Kim et al.,2017 [45]	McFarland et al.,2018 [37]	Eclink et al.,2020 [32]
1. Was the research question or objective in this paper clearly stated?	Y	Y	Y	Y	Y	Y	Y	Y	Y
2. Was the study population clearly specified and defined?	Y	Y	Y	Y	Y	Y	Y	Y	Y
3. Was the participation rate of eligible persons at least 50%?	Y	Y	NR	Y	Y	Y	Y	Y	NR
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	Y	Y	N	Y	Y	Y	Y	Y	N
5. Was a sample size justification, power description, or variance and effect estimates provided?	N	N	N	N	N	N	N	N	N
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	N	N	N	Y	N	N	N	N	N
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	N	Y	N	Y	N	Y	N	Y	N
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	N	N	Y	Y	N	N	N	N	Y
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Y	Y	Y	Y	N	N	Y	N	Y
10. Was the exposure(s) assessed more than once over time?	N	N	N	N	N	N	N	N	N
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	N	Y	Y	N	Y	Y	Y	Y	Y
12. Were the outcome assessors blinded to the exposure status of participants?	Y	Y	Y	Y	Y	Y	Y	Y	Y
13. Was loss to follow-up after baseline 20% or less?	NA	NA	NA	N	NA	NA	NA	NA	NA
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	Y	Y	N	N	N	Y	Y	Y	N
calculated overall quality score	7	9	6	9	6	8	8	8	6

Y, yes; N, no; CD, cannot determine; NA, not applicable; NR, not reported

Chapter 3

Fertility and sexual Function in female Hodgkin lymphoma survivors of reproductive age



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Abstract

Aims and objectives To assess the perceived fertility status, and to determine the association between perceived fertility status and sexual function, as reported by young female Hodgkin lymphoma survivors.

Background Young female Hodgkin lymphoma survivors are at risk of infertility and impaired sexual function. However, little is known about their awareness of infertility and its association with sexual functioning.

Design A descriptive questionnaire survey.

Method In this cross-sectional study, a survey was completed by female Hodgkin lymphoma survivors (< 40 years). Outcome measures included self-reported fertility status and sexual problems, and the internationally validated Female Sexual Function Index.

Results In total, 36 survivors were included (mean age 32 years, SD=4). Eighteen females (50%) thought themselves fertile. Eight survivors (22%) who perceived themselves as being infertile were more often treated with alkylator-based chemotherapy, and 63% reported sexual dysfunction. Ten survivors (28%) were not aware as to whether they were fertile or not; seven of these would like to have children. The reported fertility status was related to age and chemotherapy regimen. Regarding sexuality, 14 (39%) of the female Hodgkin lymphoma survivors reported one or more sexual problem and none reported recovery. Female sexual dysfunction according to the Female Sexual Function Index was reported by 11 (31%) survivors.

Conclusion Almost 30% of Hodgkin lymphoma survivors do not know whether they are fertile or not. Overall sexual dysfunction is common in Hodgkin lymphoma survivors and comparable to the general population. However, a lack of desire was significantly more often reported in female Hodgkin lymphoma survivors.

Relevance to clinical practice To prevent assumed infertility and unintended childlessness by postponing parenthood in young female survivors, awareness of fertility status is needed. There is also a need to routinely assess sexual function and provide adequate interventions to improve arousal and lubrication problems.

Introduction

Over the last decades survival rates of patients with Hodgkin lymphoma (HL) have improved tremendously, due to intensified chemotherapy often combined with involved-field radiotherapy. Before 1960, every HL patient died of progressive disease, while nowadays cure can be as high as 80-90% [1].

Hodgkin lymphoma treatment in general may affect various aspects of quality of life including physical condition, fatigue and psychosocial function [2]. Some chemotherapy regimens containing alkylating agents, such as procarbazine and cyclophosphamide, can cause premature ovarian failure (POF) by affecting primordial follicles and thereby lowering the follicle reserve [3-5]. POF is defined as a loss of ovarian function before the age of 40 [6]. POF is also described as a late medical effect that can occur after a median follow-up of 15 years after cancer treatment in women younger than 25 years of age at the time of treatment [7]. Women vary in the number of follicles they have at birth. When their remaining follicles reach a certain threshold (about 1000, at a median age of 51), a woman's fertile period ends and menopause starts [8]. Alkylating agents can accelerate this process. Women who retain normal menses after alkylating agents are still at risk of POF [6,7,9]. Earlier studies revealed that in more than 80% of the women treated with alkylating-based chemotherapy, POF, and thereby infertility, occurs [3,4,10]. Only after the medical assessment of primordial follicles can one roughly predict POF [7,11]. Before commencing chemotherapy, all female patients with HL are told that their fertility could be affected by the treatment. However, fertility is hardly a discussion topic at this stage of treatment [12] and as a result, little is known about the awareness of young female patients with HL regarding their fertility status – before or after treatment. Thus, what do the female survivors know what their fertility status is after treatment has finished? Therefore, the primary aim of this study is to assess the perceived fertility status of female HL survivors.

Premature ovarian failure, cancer and cancer treatment can lead to a disruption of the sexual response cycles [13,14]. Up until today, only a few cross-sectional studies have reported on sexual problems among female HL survivors with 65% reporting decreased sexual activity and 56% decreased sexual interest (Recklitis et al. 2010). In patients with HL, sexual function is associated with POF [16-19] and psychological distress and changes in role and social functioning [20-22]. The younger the women, the more severe and complex the impact of POF can be on sexual functioning [18]. The consequences of (perceived) infertility such as distress, depression, anxiety, reduced self-esteem, reduction of sex hormones and psychological reactions of couples facing infertility can increase sexual dysfunction [17,18]. The alkylating agents used in some chemotherapy regimens can result in primary hypogonadism, which can

cause a decreased sexual desire. Also, POF itself can result in loss of sexual desire, vaginal dryness and dyspareunia.

As the incidence of HL is the highest in younger adults (of reproductive age), special attention is needed regarding the effect of the disease and its treatment on fertility and sexuality [14,19]. Our secondary aim is to determine the associations between the perceived fertility and sexual function in this young HL population.

Background

Since the 1960s, most women in Western societies are able to control their own reproduction. As a result of this, more women are delaying pregnancy [23]. The average age of first childbirths was 29 years in 2008 [23]. With regard to the high incidence of HL at young age, many young cancer patients may not have completed their families by the time of cancer diagnosis [12].

Sexual dysfunction is a common problem in the general population. About 40–45% of adult women have at least one sexual dysfunction [24]. Sexual dysfunctions are broadly defined as the inability to fully enjoy sexuality [25]. Following the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and World Health Organization International Classifications of Diseases (ICD-10), female sexual dysfunction is divided into four sexual disorders that cause personal distress, briefly defined as a desire disorder, arousal disorder, orgasm disorder and pain disorder. A desire disorder is a persistent absence of desire for sexual activity. An arousal disorder is a persistent inability to attain or maintain sufficient sexual excitement. An orgasm disorder is a persistent difficulty, delay or absence of orgasm after sufficient stimulation. Finally, a pain disorder, which is a persistent genital pain, is associated with sexual intercourse or stimulation.

Increasing age seems to be an important risk factor for developing a sexual dysfunction [24,26]. Other common risk factors are decreases in general health status, the presence of chronic diseases like diabetes mellitus or cardiovascular disease, psychiatric or psychological disorders and socio-demographic factors such as having no committed partner [24] and infertility [18]. However, large epidemiological studies on women's physical aspects of sexual dysfunction are still lacking [24].

There are published data of small studies available to compare sexual function between HL survivors with several control groups of similar age: (1) women with a diagnosis of infertility [18] and (2) women without sexual complaints [27].

Aims

The primary aim of this study is to assess the perceived fertility status as reported by female HL survivors at reproductive age. The secondary aim is to determine the association between the perceived fertility status and sexual function as reported by this population. Results may contribute to improve patient education and counselling targeting fertility and sexuality in female HL survivors.

Methods

Design

This was a descriptive questionnaire survey design. This study reports on questionnaire data that formed part of two larger surveys designed to evaluate infertility and sexual functioning in malignant lymphoma survivors.

Sample

We merged the data from two earlier cross-sectional studies of survivors who were treated for HL at our University Medical Centre for HL between January 1 1995 and December 31 2007. The first cohort study (n = 62), performed in 2008, was designed to give insight into gonadal toxicity resulting in infertility, hormonal disturbances and possibly effecting sexual function in male and female HL survivors. The second study (n = 56), performed in 2010, was designed to investigate the incidence of chemotherapy-related POF in female patients who had been treated for a malignant lymphoma (HL and nonHL). The response rates were 86 and 82%, respectively.

All survivors were informed by phone. After agreeing to participate, the patient information letter, informed consent form and questionnaire were sent by regular mail. All questionnaires were collected via regular mail. Written informed consent was obtained from all survivors.

The data of female HL survivors meeting the following inclusion criteria were selected for this study: (1) age between 18 and 40 years at the time of the data collection and (2) chemotherapy consisting of different types of drugs with or without adjuvant radiotherapy.

To be able to compare sexual functioning, we used the following samples: a control group consisting of 108 women without a sexual complaint (mean age 27.1 years) [27] and a group of 99 healthy fertile women (mean age 32.6 years) [18].

Questionnaire

Patients completed a questionnaire on fertility status and sexual problems specifically developed for this study. The survey included items regarding socio-demography (date of birth, marital status), date of HL diagnosis, self-reported fertility status (yes, no, do not know), use of contraception or hormone replacement therapy. Additionally, participants were asked whether or not they had a sexual problem and to define problems regarding sexual desire, arousal or lubrication, vaginal dryness, dyspareunia, sexual unattractiveness and whether this problem had improved, unchanged, resolved or worsened since treatment.

Sexual function was evaluated using the Female Sexual Function Index (FSFI). The FSFI is currently the most widely used questionnaire to assess female sexual function, also in oncological trials [28]. FSFI is an internationally validated 19-item self-report measure of sexual function [29]. The FSFI contains six domains: desire (two items), arousal (four items), lubrication (four items), orgasm (three items), satisfaction (three items) and pain (three items). All items have ordinal, Likert-type response formats and are scored from 0 (or 1)–5. Higher subscale or total scores indicate better sexual function. The FSFI total score is the sum of the six domains and has a maximum score of 36. A total score of ≤ 26.0 has been validated for diagnosing female sexual dysfunction [30]. A cut-off of <26.55 (total FSFI score) is proposed as a criterion for impaired sexual function in the Dutch general population [27].

Ethical approval

Approval for the using the questionnaire on sexual functioning has been given by the Ethics Committee of the VU University Medical Centre, Amsterdam, the Netherlands.

Statistical analyses

All statistical analyses were performed using SPSS, version 16.0 statistical software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were generated for all outcome measures. Associations between perceived fertility (fertile, not fertile, unknown) and sexuality (total FSFI score) as dependent variables and age (younger than 30 vs. 30 years and older), chemotherapy (with vs. without alkylating agent), radiotherapy (yes vs. no), child wish (yes vs. no), use of contraception (yes vs. no) and sexual dysfunction (dichotomous (yes vs. no) based on FSFI cut-off score) as independent variables were tested by chi-squared tests (fertility status) and t- tests (FSFI scores). To compare FSFI scores for female HL survivors in this study with a Dutch population (ter Kuile et al. 2006), Cohen's d effect sizes were computed for the six different domains

of the FSFI. An effect size of 0.2 was considered as a poor positive or negative effect (depending on the sign of the effect size) of HL on the FSFI scores, of 0.5 as a moderate effect and of 0.8 as a strong effect [31].

Results

Study cohort

An overview of patient characteristics is provided in Table 1. Thirty-six females participated in this study [mean age 32 years (SD = 4)]. The median time since treatment was 70 months: 16 women <5 years after treatment and 20 longer than 5 years after treatment. Regarding treatment regimens, 11 survivors were treated by adriamycin, bleomycin, vinblastine and dacarbazine (ABVD); 17 by four to eight cycles standard or dose-escalated dosages of bleomycin, etoposide, adriamycin, cyclophosphamide, oncovin, procarbazine and prednisone (BEACOPP); four with a combination of ABVD and BEACOPP; and four by mechlorethamine, oncovin, procarbazine, prednisone, adriamycin, bleomycin and vinblastine (MOPP-ABV). Adjuvant radiotherapy (involved field) was given to 22 patients, of whom one survivor has been irradiated on the pelvis. All patients were in complete remission at the time of the survey.

Fertility

Eighteen women (50%) considered themselves as being fertile, eight as being infertile (22%) and 10 did not know (28%). Patient-reported fertility status was tested for differences regarding age, type of chemotherapy, radiotherapy, use of contraception, child wish and sexual dysfunction (Table 2). Patients who considered themselves as not being fertile were all treated by alkylator-based chemotherapy ($p = 0.02$), and they more often (63%) reported sexual dysfunction ($p = 0.07$). Patients who did not know whether they were fertile or not were more often younger than 30 years of age (60%) ($p = 0.01$). Radiotherapy, use of contraception, and child wish were not significantly related to fertility status.

The majority (63%) of the patients who considered themselves as being infertile used contraception (63%), and some of them had a child wish (38%). Of the patients who did not know whether they were fertile or not, most used contraception (80%) and had a child wish (70%).

Fertility outcome in HL survivors was also significantly associated with age. Of the female survivors, 67% younger than 30 years of age and 15% older than 30 years were not aware as to whether they were fertile or not.

Sexuality

According to the FSFI scores, 31% of HL survivors reported a sexual dysfunction (Table 2). The FSFI score in HL survivors was not significantly associated with age, treatment modality, use of contraception or child wish (Table 2). Female survivors older than 30 years of age who perceived themselves as infertile reported the lowest FSFI scores (median 21.78 SD 8.70) ($p = 0.07$; Table 3), indicating sexual dysfunction.

Focussing on the sexual disorders and compared with other populations, female HL survivors reported more problems with sexual desire, arousal, lubrication, satisfaction and pain compared to women with no sexual complaints ([27]; Table 4).

With regard to the open-ended questions, 14 (39%) HL survivors reported one or more sexual problems (Table 5). A lack of desire followed by having problems with getting aroused was the sexual problems most perceived. Regarding the development of the sexual problem, none of the patients reported recovery.

Table 1 Demographic characteristics of study participants

Age at diagnosis (years)		
Mean (SD)	24 (5)	
Age at the time of study (years)		
Mean (SD)	32 (4)	
Time since treatment (months)		
Median (range)	70 (27–217)	
Relationship status		
Committed relationship	<i>n</i> = 35	97%
No committed relationship	<i>n</i> = 1	1%
Involved-field radiotherapy		
Yes	<i>n</i> = 22	61%
No	<i>n</i> = 14	39%
Chemotherapy including alkylating agents		
BEACOPP	<i>n</i> = 17	47%
BEACOPP and ABVD	<i>n</i> = 4	11%
MOPP-ABV	<i>n</i> = 4	11%
Chemotherapy without alkylating agents		
ABVD	<i>n</i> = 11	31%

SD, standard deviation; ABVD, adriamycin, bleomycin, vinblastine, and dacarbazine; BEACOPP, bleomycin, etoposide, adriamycin, cyclophosphamide, oncovin, procarbazine, and prednisone; MOPP-ABV, mechlorethamine, oncovin, procarbazine, prednisone, adriamycin, bleomycin, and vinblastine.

Table 2 Patient-reported fertility and sexuality outcomes

Variable	Fertility								<i>p</i> -value	Total score FSFI		
	Total		Yes		No		Don't know			Mean	SD	<i>p</i> -value
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%				
Alkylator-based chemotherapy									0.02*			0.40
Yes	25	69	13	72	8	100	4	40		27.82	7.26	
No	11	31	5	28	0	0	6	60		25.40	8.75	
Radiotherapy									0.34			0.72
Yes	22	61	10	56	4	50	8	80		27.51	6.71	
No	14	39	8	45	4	50	2	20		26.56	9.16	
Age at the time of study (years)									0.01*			0.28
<30	9	25	2	11	1	13	6	60		29.73	5.13	
30+	27	75	16	89	7	88	4	40		26.36	8.19	
Use of contraception									0.29			0.91
Yes	22	61	9	50	5	63	8	80		27.25	8.69	
No	14	39	9	50	3	38	2	20		26.96	6.14	
Child wish									0.37			0.37
Yes	19	53	9	50	3	38	7	70		28.21	7.17	
No	17	47	9	50	5	63	3	30		25.85	8.26	
Total score FSFI*									0.07			
<26.55	11	31	3	17	5	63	3	30		17.87	6.92	
>26.55	24	69	15	83	3	38	6	60		31.38	2.52	

FSFI, Female Sexual Function Index.

*missing values *n* = 1.

p < 0.05.

Table 3 FSFI domain characteristics

	Perceived fertility status					
	Infertile		Fertile		Not aware	
	<i>n</i>	Mean ± SD	<i>n</i>	Mean ± SD	<i>n</i>	Mean ± SD
Age						
<30 years	1	34.4	2	31 ± 1.97	6	28.28 ± 6.02
≥ 30 years	7	21.78 ± 8.70	16	27.87 ± 7.59	4	28.35 ± 8.67
Mean overall	8	23.36 ± 9.21	18	28.22 ± 7.22	10	28.30 ± 6.80
FSFI score						

FSFI, Female Sexual Function Index.

Table 4 Comparison of FSFI scores for female HL survivors with a Dutch population (ter Kuile *et al.* 2006) and results of effect size (Cohen's d)

	HL survivors <i>n</i> = 35 Mean ± SD	Dutch population <i>n</i> = 108 Mean ± SD	Cohen's d
FSFI subscales			
Desire	5.4 ± 2.1	6.7 ± 1.3	-0.85
Arousal	15.0 ± 5.2	17.6 ± 2.8	-0.74
Lubrication	16.9 ± 4.6	19.0 ± 3.2	-0.59
Orgasm	12.1 ± 3.6	12.8 ± 2.8	-0.23
Satisfaction	11.8 ± 3.6	13.4 ± 2.1	-0.63
Pain	12.00 ± 4.8	14.2 ± 1.9	-0.77

FSFI, Female Sexual Function Index; HL, Hodgkin lymphoma.

Table 5 Patient-reported sexual problems and outcome

Sexual problem	Total		Recovered <i>n</i>	Improved <i>n</i>	Unchanged <i>n</i>	Worsened <i>n</i>
	<i>n</i>	%				
Lack of desire	10	28	0	2	6	2
Problem getting aroused/lubricated	3	8	0	1	1	1
Vaginal dryness	3	8	0	0	2	1
Sexual unattractiveness	2	6	0	0	2	0
Vaginal infections	2	6	0	1	1	0
Pain or fear for pain	2	6	0	1	0	1
Does not want to be touched	1	3	0	1	0	0
Grief due to infertility	1	3	0	0	1	0

Discussion

To avoid unintended childlessness, young female HL survivors who are at risk of POF need to be aware of their fertility status. In this study, 10 patients (28%) were not aware whether they were fertile or not, of whom six were younger than 30 years and seven had a child wish. To educate and counsel young female HL survivors regarding sexuality, an understanding of the perceived problems is needed.

In line with the literature, HL survivors who considered themselves as not being fertile were all treated by alkylator- based chemotherapy, and a majority reported sexual dysfunction [3, 9,10,15-17,32]. It is remarkable that the majority (63%) of the patients who considered themselves as being infertile in our study still used a form of contraception, because contraception is only registered for the indication to prevent

pregnancy. Did they assume that they were fertile? As fertility had not been assessed in any of our survivors, it is not known whether these survivors were fertile or not.

Of our studied survivors younger than 30 years of age, 60% did not know whether they were fertile or not. To prevent this unawareness in patients at risk of POF, it is suggested to offer shared decisionmaking regarding the increased risk of infertility and the choices to be made [33]. The incidence of POF in this subpopulation will increase in time. According to previous studies, HL survivors aged above 30 years are at a greater risk of developing POF, and most of the younger women treated with alkylating agents will also eventually develop POF. Although POF cannot be accurately predicted, an indication of a reduced number of primordial follicles can be obtained by ultrasound imaging of the ovaries to measure volume and antral follicle counts or testing levels of anti-Müllerian hormone [7,11]. In the case of wishing to have a child, the medical assessment of primordial follicles may be advised.

If POF or the risk on POF in women treated for HL is not discussed nor evaluated, assumed infertility and unintended childlessness by postponing parenthood can occur. For that reason, we should not limit the estimation of fertility loss only to the young female survivors who have mentioned their child wish but offer this routinely to all survivors (<40 years) who are at risk of chemotherapy-induced infertility. Infertility has also a profound psychosocial impact: cognitive problems, high levels of distress and sleep disturbances [13,16,17,34,35]. Assumed fertility loss seems also to be a burden long after treatment, and survivors have problems coping with this [12]. Therefore, appropriate information provision should be offered to guide young HL survivors before and repeatedly during treatment.

From the patients' perspective, cancer patients and survivors are interested in being asked about their sexuality, and the impact the disease and treatment can have on the sexual relationship instead of questioning sexual functioning [36]. Although a sexual dysfunction can adversely impact on the patients' relationship and/or quality of life, it does not necessarily lead to a (sexual) problem. From nurses' perspective, it is for that reason important to find out whether there is a sexual problem instead of merely a sexual dysfunction. Although the number of patients in our study was limited, our data show that when the survivor experiences a sexual problem in almost all cases, there is also a sexual dysfunction according to a validated questionnaire.

Female survivors older than 30 years of age who perceived themselves as infertile reported the lowest FSFI scores meaning worse sexual functioning. Millheiser et al. (2010) investigated the effect of infertility on sexual dysfunction in 119 infertile and 99 healthy women aged between 18 and 45 years. Forty

per cent of the infertile women reported lower sexlife satisfaction and worse sexual functioning (arousal and desire) compared to 25% in women without infertility. The prevalence of overall sexual dysfunction among the subpopulations of female HL survivors in this study was comparable to both groups studied by Millheiser et al. (2010). This is in line with the published data of Recklitis et al. (2010) who found no differences in sexual functioning of HL survivors compared with a noncancer control group. However, compared to a Dutch population [27], the HL survivors significantly more often reported a lack of desire. A lack of desire might be caused due to primary hypogonadism, young age or the potential distress of impaired fertility.

According to the open-ended questions on sexual problems, HL survivors also reported arousal and lubrication problems. It is obvious from our data that survivors do not recover from these problems without appropriate treatment. By offering routine assessment and adequate interventions, such as vaginal estrogens, moisturisers or lubricants, there is not only a chance that we can improve arousal and lubrication problems but also that we can prevent patients from suffering pain and less sexual satisfaction [35].

As this single centre survey was conducted on a very small sample, the generalisation of these results is limited. However, with regard to perceived fertility, we think that there will be other haematological centres who recognise themselves in discussing fertility at the time of diagnosis and not thereafter [3].

Conclusion

Based on the information on possible infertility given before treatment and the fact that infertility is not routinely assessed, it is possible that female HL survivors assume they are infertile. Almost 30% of HL survivors do not know whether they are fertile or not. Overall sexual dysfunction is most common in HL survivors who perceive themselves as infertile. In general, sexual functioning is comparable to the general population. However, a lack of desire was significantly more often reported in female HL survivors.

Relevance to clinical practice

To prevent assumed infertility and unintended childlessness by postponing parenthood, female HL survivors should be counselled on their increased risk of infertility during treatment and follow-up. There is also a need for routine assessment of sexual function and providing adequate interventions to improve arousal and lubrication problems.

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Conflict of interest

None declared.

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Chapter 4

Self-reported sexual function in sexually active male Hodgkin lymphoma survivors



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Abstract

Introduction Unambiguous data on sexual dysfunction after Hodgkin lymphoma (HL) treatment are scarce.

Aims To form a baseline in this area, we compared patient-reported sexual function in sexually active male HL survivors in complete remission with a sexually active, age-matched, male Dutch sample population. Furthermore, we explored whether sociodemographic and clinical factors were associated with sexual dysfunction in HL survivors and investigated whether reporting to perceive sexual problems was indicative for sexual dysfunction.

Methods This cross-sectional study included male patients with HL who were treated with chemotherapy and age-matched sexually active males.

Main outcome measures Outcome measures included the internationally validated International Index of Erectile Function (IIEF) and self-reported sexual problems by adding 3 items to the study-specific questionnaire.

Results Erectile dysfunction (ED) occurred in 23.3% of the HL survivors vs in 23.0% of controls: respectively 13.3% and 12.3% had moderate to severe ED. However, more HL survivors positively answered the question whether they did perceive sexual problems than controls (20.0% vs 7.0%; $P .087$). More patients treated with bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone (BEACOPP) had sexual problems 33.3% vs 8.3% who were treated with doxorubicin, bleomycin, vinblastine, and dacarbazine ($P .057$). Importantly, we found that the mean IIEF score for erectile function was 15.7 in HL survivors who reported to perceive sexual problems (moderate ED) vs 28.3 (normal) in those without perceiving sexual problems.

Conclusion In general, sexual function of male HL survivors is comparable to that of matched normal controls. Perceiving sexual problems was associated with lower sexual function measured by the IIEF. None of the HL survivors who were treated with doxorubicin, bleomycin, vinblastine, and dacarbazine perceived sexual problems. However, one-third of HL survivors who were treated with BEACOPP did, including ED in one-third of the cases. This is an important consideration for daily clinical practice as BEACOPP is increasingly used as standard therapy in advanced-stage HL.

Introduction

During the past few decades, more effective therapy has led to better survival rates among patients with Hodgkin lymphoma (HL), and cures can presently be as high as 80-90% [1,2]. Nevertheless, treatment-related toxicity is still a major concern, and while long-term follow-up has revealed much detailed information, unambiguous data on sexual dysfunction after HL treatment are scarce.

Overall, sexual dysfunction may consist of a loss of sexual desire, arousal, difficulties reaching orgasm, pain with erection or orgasm, sexual satisfaction, or discontinuation of sexual activity [3-11]. Among men treated for cancer, the most common sexual problems are a loss of sexual desire and erectile problems [12]. Sexual dysfunction can have a variety of causes such as testicular damage, especially due to alkylating treatment agents and radiotherapy [13,14]. As a result, subnormal testosterone levels (hypogonadism) may lead to problems with sexual function [5-11]. In addition, cancer and its treatment can have negative effects on physiological, as well as psychological and interpersonal factors, which subsequently may impact on sexual function and satisfaction [3-5,7,9-11].

The fact that sexual dysfunction can be a problem in HL has been shown in a series of reports with 24 male HL survivors by Hannah et al, (1992)[15] to 1,826 male HL survivors by Behringer et al (2013)[16]. Even so, the exact extent of the problem is unknown, and reported results vary widely from 20% to 63% [16-23]. In addition, there are heterogeneous reports on these effects which compare patients to the general population, again with a large variation in results [16,22].

A problem with any new avenue of retrospective research is the lack of stable reporting scenarios against which comparisons can be made. To start with, the aforementioned variation might simply be explained by differences in the definitions of sexual dysfunctions. These are often subjective ranging from reporting “decreased sexual enjoyment” to actual “erectile dysfunction.” In addition, various (non)standardized and (non)validated questionnaires have been used [3], and when comparing new findings, only a limited number of prior studies took the sexual dysfunction rate in the general male population into consideration [8,16,22,23]. Critically, none of these studies used the International Index of Erectile Function (IIEF)[24,25] questionnaire which has presently been adopted as the “gold standard” for efficacy assessment in clinical trials investigating erectile dysfunction and when measuring male sexual function in male cancer populations [4]. In the largest series describing the outcome of 1,826 male HL survivors reported by the German Hodgkin Study Group, the European Organisation for Research and Treatment of Cancer sexual

function scale was used, based on 3 questions, and being validated in patients with testicular cancer only[16].

There is little doubt that as patients live longer, sexual issues will become more important. To help form a base line for this research area, we compared self-reported sexual function in sexually active male HL survivors with that of a sample drawn from sexually active, age-matched, Dutch males. We used the standardized and validated IIEF questionnaire. To support early detection of sexual dysfunction in HL survivors in the future, we also investigated whether sociodemographic factors and treatment regimen were associated with sexual dysfunction. Finally, we investigated whether reporting to perceive sexual problems was indicative for sexual dysfunction.

Material and methods

Study Design and Participants

This cross-sectional survey study was conducted in the VU University Medical Center in 2008. From a cohort of 112 HL survivors, patients who were treated between September 2002 and December 2007 were identified. The recruitment of the sample is presented in Figure 1. Patients who were treated with either ABVD regimen—doxorubicin, bleomycin, vinblastine, and dacarbazine (baseline and/or escalated)—or BEACOPP regimen—bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone, with or without adjuvant involved field—were also identified. Patients had to be in complete remission at the time of the study. Patients with severe physical or mental comorbidity, or who were not sexually active at the moment of the questionnaire, were excluded. Eligible patients were contacted and informed by telephone. After showing an interest to participate, the patient information letter, informed consent form, and questionnaire were sent by regular mail.

Control Population

In 2014, adult male members of a Dutch internet panel (www.panelclix.nl), representative of the general Dutch population, were asked if they might participate in a digital survey on sexual function for which a fee of 5 Euro per person was paid. Panelclix is an International Organization for Standardization (ISO)-certified European online recruitment agency. An online study-specific questionnaire was developed whereby information on age, marital status, and sexual activity was obtained. In addition, the IIEF questionnaire (discussed in the following sections) was used.

A total of 205 male participants completed the survey from which sexually inactive males were excluded (n= 13). This resulted in a database of 192 sexually active males. Each HL survivor (n = 30) was age-matched with 2 controls, randomly selected from the control population. 3 HL survivors could only be matched to one control, which resulted in a total of n =57 controls.

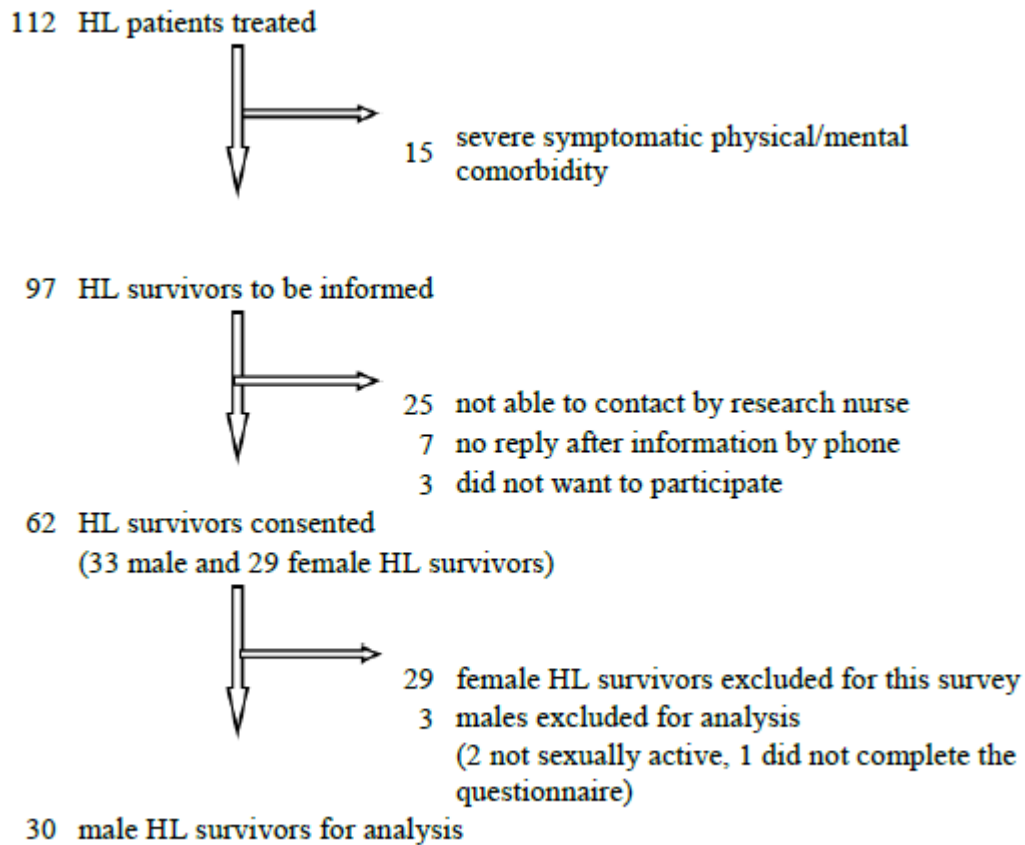


Fig.1. Flow of patients

Procedure

Sexual Function

Sexual function was evaluated by means of the IIEF. The IIEF is a validated, 15-item self-report questionnaire for the evaluation of male sexual function [25]. The IIEF comprises 5 subscales, including erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction. For grading erectile dysfunction, the cutoff scores as defined by Cappelleri et al [24] have been used. For all other domains, no standard reference cutoffs have been identified; a higher score indicates better sexual function [24,25].

Sexual Problems

In addition, perceived sexual problems were evaluated in the study-specific questionnaire by adding 3 items to it: (i) Do you perceive a sexual problem? (ii) If yes, please define the problem(s); (iii) Did the problem(s) improve, remain unchanged, resolve, or worsen since the treatment for HL began?

Sociodemographic and Clinical Characteristics

In addition, items on sociodemographic variables (age, committed relationship) were assessed in the study-specific questionnaire. Disease-specific items (date of HL diagnosis, stage of disease, treatment, time since treatment) were derived from medical records. Time in remission was calculated from date of complete remission until the date of questionnaire. Follow-up time (in months) was calculated from diagnosis until the date of questionnaire.

Ethical Consideration

The study was approved by the Ethics Committee of the VU University Medical Center, Amsterdam, the Netherlands. The study was conducted according to the Declaration of Helsinki, International Conference on Harmonisation Good Clinical Practice Guidelines, and the EU directive for Good Clinical Practice (2001/20/EG).

Data Analysis

All statistical analyses were performed using SPSS version 22 (IBM Corp, Armonk, NY). Dichotomous variables are described by frequency and percentage. All subscales and the total score of the IIEF are described by mean and standard deviation, and all other continuous normally distributed variables by mean and standard deviation and continuous nonnormally distributed variables by median and range. Reporting the presence of a sexual problem and erectile dysfunction according to the IIEF and the scores of the subscales and total score of IIEF were compared between the HL survivors and the controls using the Fisher's exact test for dichotomous outcomes and the Mann-Whitney U test for continuous subscales. Relations between clinical or sociodemographical factors and sexual function in HL survivors were assessed via the Fisher's exact test (for dichotomous factors), independent samples t-test (for the continuous factor age), and Mann-Whitney test (for the IIEF subscales and other nonnormal continuous factors). P values < .05 were considered to be significant.

Table 1 Demographic characteristics of HL survivors

	N=30	
	N	%
Age at diagnosis (years)		
Mean (SD)	36 (10)	
Age at time of study (years)		
Mean (SD)	39 (10)	
Time in remission (months)		
Median (range)	38 (9-83)	
Follow-up time (months)		
Median (range)	47 (14-89)	
Relationship status		
Committed relationship	27	90.0
No committed relationship	3	10.0
Stage of disease		
I+II	18	60.0
III+IV	12	40.0
BEACOPP regimen (%)	18 (60.0)	
8 cycles BEACOPP escalated	8	44.4
8 cycles BEACOPP	2	11.1
6 cycles BEACOPP escalated	4	22.2
4 cycles BEACOPP escalated + 4 cycles BEACOPP	3	16.7
2 cycles BEACOPP escalated + 2 cycles ABVD	1	5.6
ABVD regimen	12 (40.0)	
4 cycles ABVD	7	58.3
2-4 cycles ABVD like	5	41.7
Involved Field radiotherapy		
No	15 (50.0)	
BEACOPP regimen	15	100.0
ABVD regimen	0	0.0
Yes	15 (50.0)	
BEACOPP regimen	3	20.0
ABVD regimen	12	80.0

HL Hodgkin Lymphoma; SD, standard deviation; BEACOPP, bleomycin, etoposide, adriamycin, cyclophosphamide, oncovin, procarbazine, and prednisone; ABVD, adriamycin, bleomycin, vinblastin, and dacarbazine

Results

Patient Sociodemographic and Clinical Characteristics

In total, 30 HL survivors were analyzed. Sociodemographic and clinical characteristics of male HL survivors are presented in Table 1. The median age of the HL survivors was 38 years (range: 22-63), and 90% were in a committed relationship. All survivors (n=30) had been treated with combination chemotherapy, 12 survivors had been treated with 2-4 cycles ABVD, and 17 survivors with 4-8 cycles standard or dose-escalated BEACOPP. One survivor had been treated with a combined regimen of BEACOPP and ABVD. Adjuvant radiotherapy (involved field) was given to 15 patients, of whom 3 were treated with BEACOPP regimen. All 15 patients who did not receive radiotherapy received a BEACOPP regimen. 2 patients underwent pelvic irradiation, one in combination with ABVD and one in combination with BEACOPP. 2 patients had received autologous stem cell transplantation because of recurrent disease, both patients had a stage II disease, one received ABVD in combination with adjuvant radiotherapy, and the other patient received 8 cycles of BEACOPP in combination with adjuvant radiotherapy.

The median time of remission was 38 months (range: 9-83 months). The median follow-up time since treatment was 47 months (range: 14-89 months). In the medical records, no notes on provided sexual support were found.

Differences in Sexual Functioning

The IIEF questionnaire revealed no differences in sexual function between HL survivors and controls (Table 2). Also the degree of erectile dysfunction was comparable between HL survivors and controls: 23.3% of HL survivors reported mild to severe erectile dysfunction and 23.0% in controls (odds ratio 1.03) (Table 2).

Differences in Sexual Problems

HL survivors perceived more sexual problems than controls, although this was not statistically significant (20.0% vs 7.0%; $P = .087$) (Table 2). The following problems were reported by HL survivors: lack of sexual desire (n = 3), problems with getting aroused (n = 2), no firm erection (n = 2), problem getting too aroused (n = 1), erection not possible (n = 1), self-perceived sexual unattractiveness (n = 1), and lack of condition (n = 1). Sexual problems were not present before the start of therapy but developed during or after treatment. None of the problems disappeared.

Table 2 Comparison of main outcome measures of HL survivors and age-matched controls

	Score Range	HL survivors		Age-matched controls		<i>p-value</i>
		N=30		N=57		
IIEF subscales		Mean	SD	Mean	SD	
Erectile Function	1-30	25.8	7.3	26.1	6.1	0.60
Orgasmic Function	0-10	9.2	2.0	9.4	2.0	0.42
Sexual Desire	2-10	7.2	1.9	7.7	1.6	0.24
Intercourse Satisfaction	0-15	10.2	4.2	10.3	4.4	0.73
Overall Satisfaction	2-10	8.5	2.3	7.9	2.3	0.11
IIEF total	5-75	60.8	15.1	61.3	12.8	0.87
Erectile Function score		N	%	N	%	
no erectile dysfunction	26-30	23	76.7	44	77.0	0.68
mild erectile dysfunction	22-25	1	3.3	2	3.5	
mild to moderate erectile dysfunction	17-21	2	6.7	4	7.0	
moderate erectile dysfunction	11-16	1	3.3	5	8.8	
severe erectile dysfunction	1-10	3	10.0	2	3.5	
Perceiving a sexual problem						0.087
Yes		6	20.0	4	7.0	
No		24	80.0	53	93.0	

HL Hodgkin Lymphoma; IIEF, International Index of Erectile Function; SD, standard deviation

Differences in sociodemographic and clinical characteristics

Table 3 presents the associations of sociodemographic and clinical factors with sexual function in HL survivors. Differences were observed between survivors treated by BEACOPP and those treated by ABVD, although these were not statistically significant. Overall satisfaction was found to be lower in survivors treated with BEACOPP (mean 7.8 ± 2.7 vs 9.5 ± 0.8 survivors treated with ABVD, $P = .065$). Accordingly, more HL survivors who were treated with a BEACOPP regimen perceived sexual problems than those who were treated with ABVD ($6/18$ [33.3%] vs $0/12$ [0.0%], $P = .057$).

Table 3 Associations of sociodemographic and clinical factors with sexual function in HL survivors

	International Index of Erectile Function						Erectile Dysfunction		Perceiving a sexual problem	
	Erectile Function	Orgasmic Function	Sexual Desire	Intercourse Satisfaction	Overall Satisfaction	Total Score IIEF	yes	no	yes	no
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	N (%)	N (%)	N (%)	N (%)
Relationship status										
Committed relationship	26.3 ± 6.6	9.6 ± 0.9	7.4 ± 1.8	10.6 ± 3.9	8.7 ± 2.0	62.6 ± 12.5	6 (22.2)	21 (77.8)	5 (18.5)	22 (81.5)
No committed relationship	21.0 ± 13.0	5.7 ± 5.1	5.3 ± 2.1	6.7 ± 5.9	6.0 ± 3.5	44.7 ± 29.4	1 (33.3)	2 (66.7)	1 (33.3)	2 (66.7)
Stage of disease										
I-II	27.4 ± 5.2	9.4 ± 1.1	7.1 ± 1.7	10.8 ± 3.3	9.1 ± 1.5	63.8 ± 10.5	3 (16.7)	15 (83.3)	3 (14.3)	15 (85.7)
III-IV	23.3 ± 9.4	8.8 ± 2.9	7.3 ± 2.1	9.3 ± 5.3	7.6 ± 2.9	56.4 ± 20.0	4 (33.3)	8 (66.7)	3 (25.0)	9 (75.0)
Chemotherapy										
ABVD regimen	28.3 ± 2.6	9.2 ± 1.3	7.7 ± 1.5	11.5 ± 2.1	9.5 ± 0.8 ¹	66.2 ± 5.6	1 (8.3)	11 (91.7)	0 (0.0) ²	12 (100.0)
BEACOPP regimen	24.1 ± 8.9	9.2 ± 2.4	6.8 ± 2.0	9.4 ± 5.0	7.8 ± 2.7	57.3 ± 18.4	6 (33.3)	12 (66.7)	6 (33.3)	12 (66.7)
Involved Field radiotherapy										
no	24.3 ± 8.7	9.1 ± 2.6	6.9 ± 2.0	9.6 ± 4.8	7.8 ± 2.7	57.7 ± 17.9	5 (33.3)	10 (66.7)	4 (26.7)	11 (73.3)
yes	27.3 ± 5.6	9.3 ± 1.2	7.4 ± 1.7	10.9 ± 3.6	9.1 ± 1.6	64.0 ± 11.5	2 (13.3)	13 (86.7)	2 (13.3)	13 (86.7)
Age at time of study (years)							Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
							44.4 ± 13.8	38.0 ± 9.0	46 ± 13	38 ± 9
Time since start treatment (months)							Median(range)	Median(range)	Median(range)	Median(range)
							29 (18-74)	48 (14-89)	51 (29-74)	46 (14-89)
Time since remission (months)							22 (9-60)	44 (9-83)	31 (22-60)	41(9-83)

¹p=0.065, ²p= 0.057; SD, standard deviation; HL Hodgkin Lymphoma; BEACOPP, bleomycin, etoposide, adriamycin, cyclophosphamide, oncovin, procabazine, and prednisone; ABVD, adriamycin, bleomycin, vinblastin, and dacarbazine

Association Between Sexual Functioning According to IIEF vs Perceiving a Sexual Problem

Finally, we investigated whether reporting perceived sexual problems was indicative for sexual dysfunction as measured by the IIEF. All domains of the IIEF were found to be associated with perceiving sexual problems, except for orgasmic function (Table 4). In patients perceiving sexual problems, IIEF scores were lower, indicating less sexual function. In addition, in patients perceiving sexual problems, the mean IIEF score for erectile function was 15.7, indicative for moderate erectile dysfunction, whereas in patients without perceiving sexual problems, the mean IIEF score for erectile dysfunction was 28.3 being normal.

Table 4 Comparison of main outcome measure between HL survivors with versus without a sexual problem

IIEF subscales	Score Range	HL survivors with a sexual problem		HL survivors without a sexual problem		p-value
		Mean	SD	Mean	SD	
Erectile Function*	1-30	15.7	10.2	28.3	3.5	0.005*
Orgasmic Function	0-10	7.7	3.9	9.6	0.97	0.21
Sexual Desire	2-10	5.7	2.2	7.5	1.6	0.05*
Intercourse Satisfaction	0-15	5.5	5.0	11.4	3.1	0.005*
Overall Satisfaction	2-10	5.5	3.2	9.2	1.2	0.003*
IIEF total	5-75	40.0	20.9	66.0	7.3	0.001*

* p< 0.05; HL Hodgkin Lymphoma

Discussion

This retrospective study was performed to form a baseline for research into sexual functioning among male HL survivors. Patients were compared to an age-matched male control population (Table 1) and, on average, had been treated with standard best of our knowledge, this is the first study to compare the IIEFF scores with an age-matched male control population.

In general, sexual function of male HL survivors was found to be comparable to that of matched normal controls, with respect to all IIEF subscales comprising function, desire, and satisfaction. Furthermore, the degree of ED was comparable between HL survivors and controls: 23.3% in HL survivors and 23.0% in control—respectively 13.3% and 12.3% had moderate to severe erectile dysfunction. This has been reported previously and indicates that no additional care is needed in male HL survivors [16,22].

However, the prevalence of sexual problems in our population of HL survivors was remarkably lower than that recorded in another which used the validated Global Sexual Satisfaction Index from the Derogatis Sexual Functioning Inventory [22]. In this latter study, 54% of HL survivors (>7 years after treatment) reported decreased sexual activity, and 41% reported a decreased interest in sex. This may be due to the fact that our sample included a heterogeneously treated population, with 40% of early stage patients treated with ABVD and 60% of higher risk patients treated with BEACOPP. We found that although none of the HL survivors who were treated with ABVD perceived sexual problems, 33.3% of HL survivors who were treated with BEACOPP did. Behringer et al [16] reported that only survivors with early stages of HL reached the same levels of sexual functioning after therapy compared with controls, while survivors with higher stages of HL were more likely to develop long-term sexual problems. This is probably explained by the fact that the BEACOPP schedule includes 2 alkylating agents, namely procarbazine and cyclophosphamide, while the ABVD regimen has only one, namely dacarbazine.

Alkylating agents can lead to damage of the gonads, a well-known cause of sexual dysfunction [6-11,13,14,16]. Apart from these drugs, gonadal effects also depend on cumulative doses and combinations that have been applied [26]. Given the type of sexual problems reported by HL survivors who received the BEACOPP regimen, in particular, the lack of desire and problems with arousal, hypogonadism probably plays a role.

Furthermore, we found that patients perceiving themselves the presence of sexual problems were associated with them having a lower sexual function measured by the IIEF. This is in line with our previous study on the sexual functioning of young female HL survivors [27].

It appears that sexual dysfunction can easily be detected by early screening of sexual problems using just 3 questions. This would allow early specific intervention in the affected domain, as intervention strategies have been shown to minimize sexual dysfunction [5,28]. We recommend monitoring these patients for perceiving a sexual problem, to prevent clinical symptoms [29].

There are some limitations with the study to be acknowledged. First, many HL survivors have been excluded because of severe physical or mental comorbidity. In retrospect, it would have been better to have informed all patients instead of excluding on own interpretation. Second, our study design does not allow conclusions to be drawn on the evolution of sexual dysfunction over time, especially as early-onset sexual problems may be overlooked because of the 4-year median time between diagnosis and treatment. Moreover, it is possible that the previous treatment is not the sole influencer of the sexual dysfunction. Nevertheless, we feel the strength of our study is the identification and reporting of persistent sexual problems, which can now be addressed; after all, it has been previously reported that an improvement in sexual function is not to be expected for 2 years after hematopoietic stem cell transplantation [30]. As late effects on gonadal function due to alkylating agents are present both after transplantation and after treatment for HL lymphoma, a similar pattern is to be expected in this patient population. Another possible criticism is that the control population consisted of paid members of an online panel, so bias might have been induced. However, we expect that men with sexual dysfunction are more willing to participate in a survey as opposed to men without problems, overrating the incidence in the normal population. In addition, we could only match for age, as other factors such as comorbidities, which affect sexual function, could not be corrected for. However, as our survivor population is young with a median age of 38, we suppose such influence is limited. Finally, owing to its introductory nature, this study concerns a relatively small number of participants. Even so, we found a (near) statistical significance. In our opinion, this work creates a baseline for further research and monitoring as we believe that increasing the number of patients will only strengthen our conclusions.

Conclusions

We found that sexual function of male HL survivors, as measured by the IIEF, is comparable to that of matched normal controls. However, the type of treatment seems important; while none of the HL survivors who were treated with ABVD perceived sexual problems, one-third of HL survivors who were treated with BEACOPP did, including erectile dysfunction in one-third of cases. Eliciting perceived sexual problems revealed by using just 3 questions was associated with lower sexual function measured by the IIEF. The use

of screening for perceiving sexual problems using a simple tool to identify patients who might have sexual dysfunction should be further explored. The IIEF questionnaire to identify and quantify the nature and extent of sexual problems should be used in cases where patients report issues, permitting early intervention in affected domains and potentially improving quality of life. This is an important consideration for daily clinical practice as BEACOPP is increasingly used as standard therapy in advanced-stage HL.

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Conflicts of Interest

The authors report no conflicts of interest.

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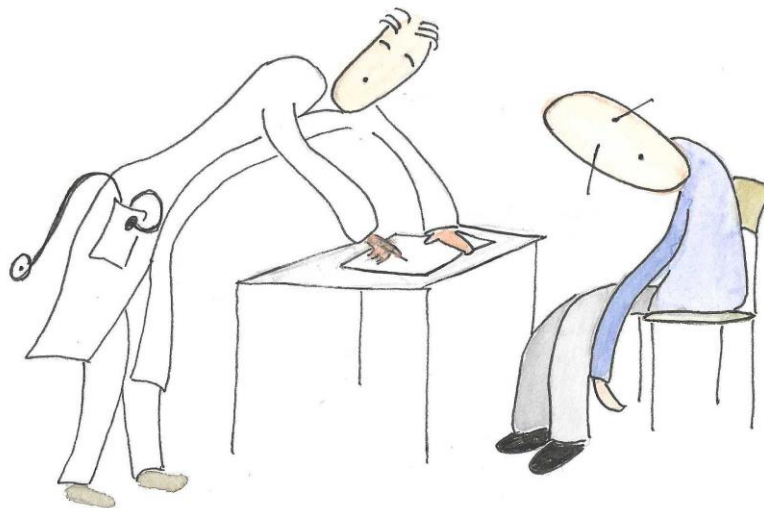
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Part II

Addressing sexuality in clinical practice

Chapter 5

**Perceived need for information of patients with hematological malignancies:
a literature review**



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Abstract

Aims and objectives To provide insight into the perceived need for information of patients with haematological malignancies.

Background Providing timely and accurate information to patients diagnosed with a haematological malignancy is a challenge in clinical practice; treatment often has to start promptly, with little time to inform patients.

Design Literature review.

Methods A comprehensive literature search was conducted from all available literature to May 2013 in the databases: Cumulative Index to Nursing and Allied Health Literature, PsycINFO and PubMed (Medline). Relevant studies were reviewed regarding the perceived need for information on various topics, sources of information and satisfaction with information provided.

Results The initial search revealed 215 articles, fourteen of which were relevant. Patients need basic information on the disease (diagnosis and diagnostics), treatment (various treatment options, side effects and duration), prognosis (curability and prolonging life) and all other topics (recovery, self-care and psychosocial functioning). Need for detailed information varied between studies. Patients expressed a higher need for medical than for psychosocial information. Patients preferred to receive information from their doctors the most, followed by nurses. Most studies described patients' satisfaction with the information provided.

Conclusion Based on the limited number of data available, medical information is for patients of higher priority compared to psychosocial information. Patients need basic information on diagnosis, treatment, prognosis and all other topics. Need for detailed information varied between studies. Patients were satisfied with the provided information, preferably offered by doctors and nurses.

Relevance to clinical practice The perceived need for information and satisfaction with the information provided differs strongly between patients. In clinical practice, more attention is needed for information tailored to the patient, taking into account important moderating factors such as age, type of cancer, time since diagnosis, treatment modality and coping style.

Introduction

In the past years, there has been growing attention concerning the need for information and sources of information among patients with cancer in general [1,2]. Unfulfilled information needs may cause anxiety, depression, reduced ability to cope with the disease, difficulties in gaining control, non-compliance and sexual problems [2-5]. On the other hand, benefits of enhanced provision of information include increased patient involvement in decision-making, realistic expectations, greater satisfaction with treatment choices and a better quality of life [2,4,6-8]. Moreover, patients' recall of information is often hampered because they are overwhelmed by the diagnosis [9-13].

Providing timely, efficient and accurate information is especially for patients diagnosed with a haematological malignancy, a challenge in clinical practice. These patients often have a substantial chance of cure, even though the diseases are almost always disseminated at diagnosis. However, intensive therapy has to be started early in order to be effective; especially in case of acute leukaemia, aggressive lymphoma or multiple myeloma (MM) treatment has to start at the day of diagnosis, to prevent more severe illness, permanent organ failure and complications. On the other hand, patients are subject to imminent and daily danger of serious and even fatal infections and bleeding due to the disease and the treatment, especially in case of high-dose chemotherapy and autologous or allogeneic stem cell transplantation. Moreover, the impact of the disease and treatment on quality of life is substantial. Worldwide, on an annual base, more than 850000 patients are diagnosed with a haematological malignancy [14]. In spite of the large number of patients, detailed information on the information needs of patients with haematological malignancies is not readily available. It is essential to understand the need for information of this specific group of patients, because there are large differences between the behaviour, treatment and outcome of haematological malignancies and solid tumours. Furthermore, because of the shift of tasks from doctors to clinical nurse specialists, clinical nurse specialists are the new professionals with whom patients with cancer regularly come into close contact, giving them a vital role in patient information provision.

Aims

The purpose of this literature review was to provide an overview of the studies investigating the information needs of patients with a haematological malignancy. Furthermore, we aim to examine the associated factors related to the need for information, the information sources used and the extent to which patients are satisfied with the information provided. The results will contribute to a better understanding of the perceived need for information by patients with haematological malignancies and may help to improve existing

sources of information, develop new ones and help doctors and (specialist) nurses with more patient-targeted information provision.

Methods

Search strategy

A literature search was conducted in the following databases: Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsycINFO and PubMed (Medline). A collection specialist performed the search at June 2013. The following search terms were used as key word, free text word and words in title and abstract: haematologic neoplasms, leukaemia, lymphoma, MM, combined with the search terms: information need, information needs, patient information, patient education, health education.

Selection criteria

A study was eligible for inclusion if it (1) reported on the perceived need for information by patients with haematological malignancies and (2) was written in English or Dutch. No restrictions were made regarding the year of publication. Studies were excluded if they (1) described the development or implementation of a survey instrument, (2) reported on information needs of family members and carers of patients with cancer, (3) reported on patients below 18 years of age, (4) reported on coping or quality of life of patients with haematological malignancies, (5) evaluated the effectiveness of information courses for haematology patients, their family members or health-care professionals, (6) describing various treatment-related topics of patients with haematological malignancies and (7) reported on patients with solid tumours. The reference lists of all selected studies were screened for studies not identified in the database search. This yielded no additional articles.

Study selection

Studies were selected in two steps. First, independent from each other, an initial selection was made, using the inclusion and exclusion criteria, based on titles and abstracts. In case of ambiguity, the full text of articles was read. Second, studies that possibly met the inclusion criteria, studies without an abstract and studies that could not clearly be excluded based on title and abstract were retrieved in full text and scrutinised more extensively for eligibility, by the two reviewers (JR and CE), independently of each other. Studies of uncertainty were discussed with a third researcher (PH) until consensus was reached.

Search and article selection

The initial search in CINAHL, PubMed (Medline) and PsycINFO revealed 211 articles. Four articles were found by personal communication. Based on title and abstract, we excluded 189 articles that did not meet our inclusion criteria. Of the remaining 26 potentially relevant articles was read the full text, of which finally fourteen articles were relevant to our review [15-28] (See Fig. 1).

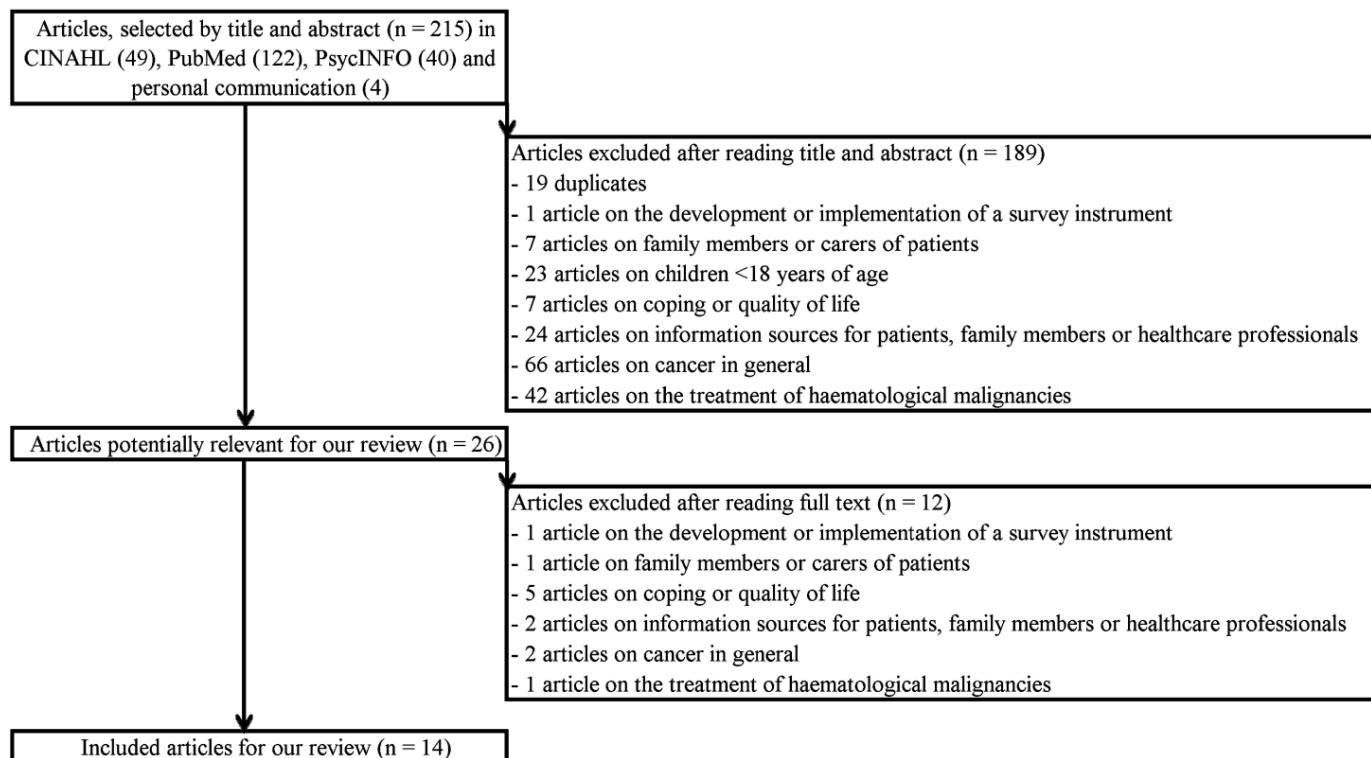


Figure 1 Flow chart of article selection.

Quality assessment

The quality of the studies was reviewed by the first author (JR) and verified by a second reviewer (CE), using for quantitative or mixed method studies suitable topics of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist [29], the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement checklist [30], and the Meta-analysis of Observational Studies in Epidemiology (MOOSE) statement [31]. In order to assess the quality of the qualitative studies, we used the quality framework for social research [32]. Each item that matched our criteria was assigned as one point. The maximum score on quantitative/mixed studies was 33 points; the maximum score on qualitative studies was seventeen points. Studies scoring two-thirds or more of the maximum points were assessed as adequate quality. All 14 studies met the assessment and were of adequate

quality. However, none of the studies reported details on how was dealt with missing data, and most studies did not describe details about possible bias of the studies. In all studies, the sample size was described, but none of the studies described the rationale of this chosen sample size. The quality of the four qualitative studies was also of adequate quality according to the framework of quality research [32].

Characteristics and quality assessment of the included studies

Twelve articles were published <10 years ago, and seven articles recently (less than four years ago). All articles originated from Western countries. Three were retrospective studies, nine were cross-sectional studies, one study both cross-sectional and retrospective and one was a longitudinal study. Most articles reported on a small sample size (less than 70 patients). Age of patients, type of haematological malignancy and time since diagnosis and treatment modality varied substantially among the studies. To assess the need for information, eight studies used questionnaires, four studies used interviews and two studies used a combination of both. Table 1 gives an overview of all characteristics of the reviewed articles.

Data abstraction

Data of the studies were abstracted by JR, using a data abstraction form in Excel, and were verified by CE. The data that were abstracted included: design of the study, aim of the study, diagnosis, time since diagnosis, number of patients, median/mean age of the patients, questionnaire used and participating hospitals. Based on a systematic review describing the need for information of patients with cancer in general, the included studies were analysed regarding the need for information on various important themes:(1) the diagnosis cancer, (2) treatment, (3) prognosis, (4) rehabilitation, (5) coping, (6) social functioning, (7) surveillance and health, (8) financial or legal issues, (9) the medical system and (10) body image/sexuality [1].

Furthermore, included studies were analysed regarding (11) various sources of information and (12) satisfaction with the information provided. Data of the included studies were analysed by the two researchers JR and CE, independently of each other. By means of a consensus meeting, we came to a common judgement.

Table 1. Characteristics of the studies

Author	Year	Diagnosis	Time since diagnosis	Age	Patients	In or out-patients	Country	Method	Question-naire EORTC QLQ-INFO25	Study design	Participating hospitals
Oerlemans	2012	NHL,HL, MM	mean 3.7 y	mean 61,6	1135	out	NL	survey semi-structured interviews		cross	ten
Tariman	2011	MM	at diagnosis	mean 67,5	20	out	USA	survey	INQ	cross	two
Friedman	2010	NHL,HL, MM	mean 4.7 y	mean 64,2	67	out	USA	survey in-depth interview ranking priorities	selfmade	cross	one
Gansler	2010	leukemia, lymphomaMM	all stages	adults	29	nr	USA	interview	nr	cross	nr
Grinyer	2010	HL	5-34y	23-45	3	out	UK		nr	retro	nr
Mohamedali	2010	AML NHL,HL, MM,AML,ALL,C	at diagnosis, 1 mo and 5-6 mon after diagnosis	18-59 and >60	35	out	Canada	survey	CPS, Decision regret scale, SWD	cross	one
Parry	2010	ML, CLL	mean 20 mo since treatment	mean 50,3	51	out	USA	in-depth interview	nr	cross	nr
Lobb	2009	NHL,HL, MM, leukemia	mean 8 mo since treatment	mean 54	66	out	Australia	survey	CaSUN CPS, Decision regret scale, SWD	cross	two
Yogaparan	2009	AML	at diagnosis	mean 64,2	31	nr	Canada	survey in-depth interview	TINQ, BC,PLNS, PINQ	cross	one
Broeren	2008	MM	>9y	median 60	15	out	NL	interview	nr	retro	nr
Hammond	2008	NHL	2-5y	adults	250	out	USA	survey	adapted version UCLA/RAND sexual module, Groningen sexual question	cross	nr
Jonker-Pool	2004	NHL,HL	median 7.6 y at diagnosis, 2-5 mo after diagnosis	median 42	50	out	NL	survey	naire	cross+ retro	one
Friis	2003	AML	median 8 y since treatment	adults	21	in/out	Denmark	in-depth interview	nr	long	one
Turner	1996	HL	median 8 y since treatment	median 36	165	out	UK	survey	nr	retro	nr

NHL=non Hodgkin lymphoma, HL=Hodgkin lymphoma, MM=Multiple Myeloma, AML=acute myeloid leukemia, ALL=acute lymphatic leukemia, CML=chronic myeloid leukemia, CLL=chronic lymphatic leukemia, y=year, mo=month, nr=not reported, cross=cross-sectional, retro=retrospective, long=longitudinal

Results

Perceived need for information

Cancer-specific information

The theme cancer-specific information was reported in 8 of 14 (57.1%) included articles. Almost all patients wanted basic information about their diagnosis, such as the diagnosis and the curability [21,25]. However, the need for detailed information, such as different subtypes of their disease, varied between studies [21,25]. Patients with acute myeloid leukaemia (AML) seemed to have a low need for detailed information at diagnosis [21]. A low information need for details was present, especially in the older MM and AML patients [21,25]. In contrast, one other study on patients with AML aged fifty and older reported that these

patients wanted to know details about their diagnosis [19]. (For details on all information needs, see Table 2a,b.)

The priority of information needs varied, but overall, medical topics such as cancer-specific information and treatment-related information seemed to have more priority than psychosocial information [17,22,23]. Regarding the phase of the disease, the need for information was highest in the diagnostic and early treatment phase, at least in patients with MM [25]. For disease-specific information, the priorities at the time of diagnosis were cancer type, diagnostics and risk factors for haematological malignancies [17]. Survivors of lymphoma and MM wanted to have more information about the cause of the disease [27].

Treatment and decision-making

The most cited category was treatment and decision-making, described by eleven of fourteen included studies (78.6%). Patients wanted basic information on treatment options, possible short- and long-term side effects and the duration of treatment [17,22,25]. Also, general information about stem cell transplantation was highly appreciated [25]. Information on clinical trials and recent advances in research was another important subject [17]. In the first week after diagnosis, relevant information for patients with acute leukaemia was related to practical and individual problems during treatment, such as the psychological and physical impact of the treatment and how to deal with various side effects [21].

After the completion of treatment, information on problems related to treatment or on the development of secondary malignancies was very important [16,18,23,27]. Other important topics were an overview of anticancer treatments, screening options for the recurrence of cancer and health problems due to cancer treatment [23].

Patients who did not reach cure expressed different needs for information. These patients were more interested in treatment plans, such as palliative treatment and supportive care. In one study, patients valued information about nutrition, vitamins and complementary medicine as relevant [21], but other studies reported information concerning complementary and alternative therapies as not very important [23,25].

The need of detailed information concerning treatment varied between the studies, similar to diagnosis-specific information. In the study by Yogaparan, patients with AML older than 50 considered details about treatment as important; almost all patients wanted to know the most important treatment options (94%), the possible side effects (97%) and how treatment works (97%) [19]. In contrast, admitted

patients with AML and patient with MM did not attach importance to details about the therapy, such as the composition of chemotherapy, medications and how the treatment affects the immune system [21,25].

Most patients were not actively involved in treatment decision-making. Less than half of the patients with MM wanted to contribute to decision-making for their treatment plan. These patients trusted their doctor in offering the best treatment options [25]. This is consistent with a study on 165 patients with Hodgkin lymphoma (HL), which reported that the doctor made all treatment decisions in 62% of the cases. In this study, 58% of the patients considered themselves as much involved as they wanted to be. These percentages were not influenced by the treatment outcome [24]. Patients considered early temporary side effects as more important in treatment decision-making than late morbidity [24]. Most patients with acute leukaemia also preferred and played a collaborative or passive role in treatment decision-making [19,28]. In contrast, Tariman et al. reported that most patients (95%) diagnosed with MM wanted shared and active roles in decision-making, possibly moderated by the higher education and income level of the patients in this study [22]. Various factors influenced the patients' attitude in decision-making, such as gender, age and health status. Males played a more passive role than females [19]. Older patients and physically ill patients with AML also were more likely to leave matters in the hands of the doctor [21], but in another study with patients with AML, no differences were found regarding age [28]. Furthermore, members of a patient association had a higher need for general information and detailed information and showed a higher involvement in decision-making [25].

Prognosis and follow-up

Information concerning prognosis and follow-up was mentioned in 5 of 14 studies included (35.7%). Overall, basic information concerning prognosis was important for patients. Of the patients with AML older than 50, 94% wanted to know the chances of prolonging life with treatment [19]. Moreover, patients with all kinds of haematological malignancies wanted to know the risks and treatment of recurrence of the disease [16,17]. But detailed survival information, such as remission rates, was not important for admitted patients with AML, similar to diagnosis and treatment-related information [21].

Rehabilitation

One of the least mentioned themes is rehabilitation information with a score of 3 of 14 (21.4%). Patients mostly appreciated information about recovery in the home situation after the completion of therapy, for example stem cell transplantation and information concerning care routines and home modifications [25].

Older patients with MM considered information on self-care as third priority, possibly due to the wish to stay independent [22]. Other important issues were information about physical and psychosocial recovery and nutrition [16].

Coping

Another not frequently mentioned theme is information concerning coping, mentioned in 4 of 14 studies (28.6%). Several studies reported reasons why patients avoided information, such as the fear of losing hope or lack of energy [21,25]. While other studies showed that patients wanted information about other patients and about the impact of the illness on their daily life ([15-17,21]. However, other studies showed that a majority of the patients were not interested in contact with other patients [17,25].

Social functioning

Information on social functioning was mentioned in 6 of 14 articles (42.9%). It was considered as important, but seems to have a low priority [17,23,25]. Other important items were support for their partners, how the disease could affect their family situation and how to tell the children about the disease [25]. In most studies, only a minority of the patients were interested in information on psychosocial care for themselves or for their partners [15,25,27]. Social support and how to talk with physicians were rated as the least important information needs [17,23].

Surveillance and health

The least frequently mentioned theme was surveillance and health information, cited in 2 of 14 articles (14.3%). Information on health-care services was mentioned in two studies. Lobb reported that 68% of the patients with haematological malignancies needed information on available local health-care services [15]. After treatment, patients younger than sixty considered a plan for monitoring overall health-care service and mental health important. However, mental health-care service was valued as one of the least important information issues [23].

Financial and legal issues

Financial and legal information was mentioned in 3 of 14 articles (21.4%). Information about insurance and financial information related to the disease was important for survivors [16,17,23]. This was especially important in the phase after initial treatment [17]. Some patients expressed a need for information on financial compensation for home adjustments [25].

Body image/sexuality

Body image and sexuality-related information was discussed in 5 of 14 articles (35.7%). Although sexuality and fertility was one of the least important issues [22,23], a need for information was expressed especially by young males with malignant lymphoma [20,23,26]. Males rated fertility and sexuality information as more important than women [23,26]. Patients with MM wanted information concerning the influence of medication on the fertility and the reaction of the body after Stem cell transplantation (SCT) [25].

Sources of information

Sources of information were discussed in 53% of the reviewed articles [15,16,19,21,22,24,25,28](see Table 3). The most important information patients received came from their doctors [16,19,25,28], followed by nurses [19,21,22,28]. Another important information source was printed material [16,19,21,22,24,25,28]. Patients found that information leaflets provided control over the degree and the timing of absorbing information about their condition. They found it useful to know that the information was in their possession, so they would have access to it at a later stage, for example for questions that might arise at home [19,24]. One study found that printed information about leukaemia in general was glanced at, but that the patients were rarely able to recall much of the content two months after diagnosis [21].

Most patients found information via the Internet useful [16,22,25]. Some reported that the information was not up to date, and some patients said that the information was too overwhelming and confronted them too much with the possible course of the disease. For some patients, this was a reason for not seeking information on the Internet. Others valued information on the Internet supplemental to the information provided by their doctor [25]. Meeting other patients with the same disease was also mentioned as a source of information [15,22,25].

Satisfaction with information

Satisfaction with the received information was discussed in 8 of the 14 reviewed articles [18-21,24-27](see Table 4). Satisfaction with the information received varies widely, ranging from 52–67% [20,24,27].. Results of five studies revealed that patients were satisfied with the information received by their doctor [19,21,24,25,27]. Patients found the doctors good judges of the amount of information the patients wanted [19,25]. Those who wanted little information about their condition appreciated the fact that the information was not forced on them [25]. Friis reported that some patients with AML said they often received information they did not ask for [21].

Table 2 (a) Details of medical information needs per topic; (b) Details of psychosocial information needs per topic

Author	Cancer-specific information	Treatment-related and decision-making information
(a)		
Broeren	<p>Almost all patients want information about their diagnosis. Most important information is how to tackle the disease. Only a few patients want information concerning procedures or tests</p>	<p>Almost all patients want information about the best treatments and possible side effects. They are not interested in detailed treatment information. Less than half of the patients are actively involved in decision-making. They are interested in different treatment options. After completion of treatment, patients rate a summary of the anticancer treatments as important. An alternative medicine technique is rated as least important information. After the completion of treatment, patients rate a plan to screen for possible return of the cancer and health problems due to the cancer treatment as important</p>
Friedman	<p>Medical issues are rated as more important than psychosocial issues</p>	<p>Patients in partial remission want to have information about palliative treatment and supportive care, such as information about nutrition, vitamins and complementary medicine. In the first week after diagnosis, relevant information seemed to be related to practical and individual problems during treatment, for instance how to deal with various side effects. At diagnosis, the most important information is treatment options and long-term side effects of treatment. Patients also would like to have information on clinical trials and recent advances. After initial treatment, during relapse, remission or the maintenance of therapy, most important information is prognostic information such as follow-up tests to detect recurrence. Medical information is more important compared to psychosocial and coping information. During treatment, information about treatment options, long-term side effects and coping with side effects is important for patients</p>
Friis	<p>Apart from basic information such as the diagnosis, the curability and the duration of the treatment, patients are rarely interested in details of the diagnosis, prognosis and therapy</p>	<p>Patients lack information on the late effects of mantle field radiotherapy on the arise of secondary malignancies. This information was not easy to access</p>
Gansler	<p>At diagnosis, cancer type, diagnostics and risk factors for cancer are the priorities for cancer-specific information</p>	
Grinyer Hammond Jonker-Pool Lobb	<p>66% of the patients want understandable information; 62% of the patients want up-to-date information about their disease</p>	
Mohamedali		<p>52% of the patients preferred to play a collaborative decision-making role. 37% preferred a passive role and 11 % an active decision-making role</p>

Table 2 (Continued)

Author	Cancer-specific information	Treatment-related and decision-making information
Oerlemans	29% of the patients wanted more information. One topic, on which patients would like to have more information, was the course and cause of the disease (24–59% of the patients). Patients without comorbidity, using the Internet for information or the hospital of treatment was associated with receiving more disease-related information	Patients want more information concerning late effects of treatment (30–50% of the patients). Receiving more information on treatment was associated with a younger age, less comorbidity, having a treatment of chemotherapy and the hospital of treatment. Receiving more information on medical tests was associated with less comorbidity, higher education level and the use of Internet. I-non-Hodgkin lymphoma patients and multiple myeloma patients under active surveillance had a lower perceived level of received information concerning treatment
Parry	Patients lack medical and psychosocial information after treatment. They do not know where to find this information	Patients want to know the risks of developing secondary malignancies and their treatment
Tariman		Patients at diagnosis rate the different types of treatment and the advantages and disadvantages of these treatments as most important information
Turner		In deciding choice of therapy, 61% of the patients thought that short-term, temporary side problems as development of secondary malignancies and relapse of disease are more important. In 62% of the patients, the doctor makes all treatment decisions. Of all patients, 58% were as much involved, as they wanted. These percentages were not influenced by the treatment outcome
Yogaparan	97% of the patients (absolutely) want to know the specific medical name of the illness	94, 97 and 97% of the patients (absolutely) want to know, respectively: the major treatment options, the possible side effects and how treatment works. Most patients preferred and played a collaborative or passive role in treatment decision-making. Males played a more passive role than females

Table 2 (Continued)

Author	Prognostic information	Body image and sexuality information
Broeren	Only a few patients asked for their prognosis themselves; others read written information concerning prognosis. Patients want honest and straightforward information about their prognosis	Patients want information concerning the influence of medication on their fertility. Information about the reaction of the body after SCT was also important
Friedman		Sexuality and fertility is one of the least important issues
Friis	Many patients do not want specific information about their prognosis	
Gansler Grinyer Hammond		13% of the patients want more information about fertility. This is related to a younger age, nonwhite ethnicity, less comorbidity, a better physical function and a less-than-excellent perceived quality of care. 28% of the patients want more information about sexual functioning. This is related to male gender and a treatment of SCT
Jonker-Pool		27% of the patients need information concerning sexuality; this is related to a younger age
Lobb Mohamedali Oerlemans		
Parry	Patients want to know the risks and treatment for recurrence of the disease	
Tariman	The second priority of information is the likelihood of cure	The lowest information priority for patients is feelings about the body and sexual attractiveness
Turner Yogaparin	94% of the patients want to (absolutely) know the chances of prolonging life with treatment	

Table 2 (Continued)

Author	Rehabilitation information	Coping information	Social information	Surveillance and health information	Financial and legal information
(b)					
Broeren	Information concerning the recovery in the home situation is highly appreciated, especially in patients receiving SCT	Only a few patients need information concerning psychosocial support for themselves or partners. The majority of the patients are not interested in contact with fellow patients	Few patients wanted information concerning how the disease could affect family situations		Some patients need an advisor for financial help for supportive instruments
Friedman			Psychosocial information is rated as less important than medical information. Social support is rated as one of the least important information needs	Mental healthcare service is rated as one of the least important information priorities	
Friis		Several patients want information about other patients and the impact of the illness on their life. One of the reasons for not seeking information is the fear of losing hope			
Gansler		Patients are interested in ways to be involved with other cancer patients. One of the least important information priorities during all treatment phases is support groups	How to talk with physicians is one of the least important information priorities		Financial and insurance information is most important for patients in the phase after initial treatment
Grinyer					

Table 2 (Continued)

Author	Rehabilitation information	Coping information	Social information	Surveillance and health information	Financial and legal information
Hammond Jonker-Pool Lobb		59% of the patients need to talk to others who have experienced cancer	73% of the patients want support in concerns about return of the disease 55% of the patients need information for their partner or family	68% of the patients would like to have information about available local healthcare service	
Mohamedali Oerlemans			Psychosocial aftercare was a topic survivors wanted more information about (10–30% of the patients)		
Parry	Patients want to know information about the physical and psychosocial recovery		Patients lack psychosocial information after treatment. They also want information about where to go for support groups and help with nutrition		Patients want information about financial and insurance issues
Tariman	For patients, the third information priority is caring for their self at home				
Turner Yogaparin					

Table 3 Sources of information

Author	Sources of information
Broere	Most important information came from doctors. Most information was sought from sources inside the health care. Other information came from the Internet and a patient association
Friedman	
Friis	Patients sought information by asking nurses and fellow patients. Printed information was glanced at, but patients could not recall this information
Gansler	
Grinyer	
Hammond	
Jonker-Pool	
Lobb	Talk to others who experience cancer was one of the unmet needs of patients with haematological malignancies
Mohamedali	Physicians, followed by nurses, were the most useful sources of information
Oerlemans	
Parry	The most preferred information sources were healthcare professionals, support groups, the Internet, telephone or printed material
Tariman	Patients have different sources of information; the Internet, doctors, family and friends, books, pamphlets, nurses, other patients and support groups
Turner	90% of the patients would appreciate written information
Yogaparin	Most common sources of treatment information were doctors, nurses and written material. The most uncommon sources were family and friends and other patients and the Internet

Table 4 Information satisfaction

Author	Satisfaction with the information received
Broere	Overall, patients are very satisfied with the information received by their specialist. The majority are satisfied with the information concerning prognosis, rehabilitation and treatment. Some patients lacked information about side effects of treatment.
Friedman	
Friis	Patients were satisfied with the information received.
Gansler	
Grinyer	Patients lacked information concerning the risks of secondary malignancies after radiotherapy for non-Hodgkin lymphoma (NHL).
Hammond	13 and 28% of the patients two to five years after diagnosis with NHL would have more information concerning, respectively, fertility and sexuality.
Jonker-Pool	50% of the patients thought that the information about sexuality was (absolutely) insufficient.
Lobb	
Mohamedali	67% of the patients were satisfied with the information received. Satisfied patients received more information concerning disease, medical tests, treatment and other service.
Oerlemans	Satisfied patients found that the information received was more useful compared with dissatisfied patients. Patients with Hodgkin lymphoma were more satisfied than I-NHL survivors. The satisfaction with information was positively associated with having treatment of chemotherapy and negatively with comorbidity.
Parry	
Tariman	
Turner	48% of the patients felt they had not had enough information; 51% had as much information as they needed. 52% of the patients were satisfied with the information; this was associated with a greater satisfaction with the involvement in decision-making. Treatment outcome did not influence this.
Yogaparin	The majority of patients felt that they were given adequate information to make their treatment decision.

Discussion

This literature review shows that there are few and contrasting data on the need for information in patients with a haematological malignancy [15-28]. This is in contrast with the large number of data on the information needs of patients with cancer in general, which was described in a review of 112 studies [1]. The results of the present review showed that patients with haematological malignancies need basic information on the disease (diagnosis and diagnostics), treatment (various treatment options, side effects and duration), prognosis (curability and prolonging life) and all other topics (recovery, self-care and psychosocial functioning). Need for detailed information varied between the included studies. Patients expressed a higher need for medical than for psychosocial information. Most studies reported a passive

involvement in treatment decision-making. Patients preferred to receive information from their doctors the most, followed by nurses. Most studies described patients' satisfaction with the information provided.

These results of the present review show that the need for information seems similar in patients with a haematological malignancy and in cancer patients with solid tumours, but there are some important differences. Regarding the need for information on the disease and treatment, patients with cancer in general want as much information as possible, good as well as bad news [33-35], and they prefer to receive detailed, but tailored information [35]. Patients with haematological malignancies show a need for general information, but not for so much detailed information on their diagnosis, treatment and side effects [19-21,34,25,26]. The lower need of detailed information in patients with haematological malignancies may be explained by the fact that a substantial number of these patients are initially in an acutely life-threatening situation and are often hospitalised at the moment of their diagnosis [21]. Similar to patients with cancer in general, they showed a higher need for information on medical issues than on psychosocial issues [1,17,22,23,36,37]. This also may reflect the often acute life-threatening situation in patient with haematological malignancies, which may trigger the need to be informed on diagnosis and treatment, whereas a need for information on practical and long-term consequences of the disease is expressed at a later stage. A study on the quality of life of patients after allogeneic stem cell transplantation revealed similar results. Across their transplant trajectory, treatment influenced the first period, the physical-related quality of life in particular, and thereafter treatment effects other quality of life dimensions including psychological and role functioning [38].

It seems that older patients have a lower need for information, are less interested in details and are more passive in decision-making than younger patients, both among patients with solid tumours and among patients with haematological malignancies [13,21,25,34,35,39,40]. A possible explanation for the differences in degree of detailed information in the studies of Friis and Yogaparan may be the hospitalisation in the first study and possibly also the different methods of the studies [19,21]. Considering the higher cure rate in younger patients with haematological malignancies, information on sexuality and fertility is important [20,23,26].

Besides age, factors such as gender, socio-economic status, educational level and coping style may also influence the need for information in patients with cancer in general [34,35,41-43]; little mention of these factors could be found in the studies reviewed. Despite the fact that demographic factors was in none of the reviewed articles, a primary or secondary objective, this review on haematologic cancer patients found

no evidence that differences in gender [21,25], education level [21,25,43], partner status or income [22], might be possible moderating factors. In one study, membership of a patient association influenced the need for information [25]. Regarding gender and need for information on fertility and sexuality, Hammond et al. (2008) and Friedman et al. (2010) reported that men with NHL had higher needs than women. [23,26]. It may be possible that a different style of coping with the disease is a moderating factor [21,25].

According to the literature, satisfaction with the information received is important, because information satisfaction, fulfilled information needs and fewer information barriers are related to a better quality of life [7,8]. Among patients treated for haematological malignancy, satisfaction with the information received varies widely, ranging from 52–67% [20,24,27].

Providing information could improve the treatment decision-making process [44]. A recent study reported that out of all the information sources, the treatment staff influences the treatment decision most [45]. Regarding shared decision-making, patients with cancer in general want to share responsibility for decision-making, while this seems less evident in patients with haematological malignancies [19,21,24,25,34]. There are some factors that may explain this difference, such as coping style and physical condition. Coping style may be related to shared decision-making and the need for information: some patients may actively search information, while others tend to avoid getting information [21,22,25]. A possible explanation for a lower need for detailed information in patients with cancer might be the coping style by avoidance [46]. Furthermore, patients with haematological malignancies are often sick or hospitalised during their illness trajectory. As regards the factor age, which is known to have an influence on decision-making in patients with cancer in general; older patients are more likely to prefer the doctor to make treatment decisions [6,34,40], which may be related to the fact that older patients are more familiar with a paternalistic style of making treatment decisions [6,40]. However, this does not explain the more passive form of decision-making in haematology patients, because the age distribution of haematology patients is in line with the age distribution in patients with cancer in general [47].

In the results of this review, we focussed on the information needs of patients. It is important to realise that patients can have a different perception of importance of information than doctors and nurses. Doctors attached importance to medical technical information such as the meaning of remission [21]. Concordance on the importance of medical technical information seems to be high between doctors and patients, but this is not the case for psychosocial information [23]. Remarkably, patients' preferences for decision-making, information and understanding of this information are rarely discussed between doctors

and patients with haematological malignancies [48]. Doctors proved to be the most important source of information for patients with cancer in general as well as for patients with haematological malignancies [1,19,21,25,33,49-52]. However, nurses are also important in providing information [19,21,28,51]. An emerging information source is the Internet [25,52-54]. Older patients and less educated patients use the Internet less often [19,45,50], probably because this age group is less familiar with the Internet as an information source.

Methodological considerations

The findings in this literature review may have been influenced by a number of factors: first, the fourteen selected studies varied substantially regarding study design and outcome measures. Different methods involved different (study-specific) surveys (validated and not validated), interviews and questions and thereby different answers. This makes it difficult to compare results of the different studies. The purpose of qualitative studies [16-18,21,22,25] was to investigate the need for information in depth by interviewing a small sample of patients until data satisfaction is reached. Results of qualitative studies are often used as input for the development of questionnaires to be used in quantitative studies. More than a quarter of the articles reviewed were retrospective studies [18,20,24,25] with the consequence of recall bias. Moreover, in the selected articles, information was often lacking on the characteristics of nonparticipants and how missing data were dealt with.

Most studies focused on patients who had received diagnosis or treatment several years before, which implies that they probably had different information needs than patients at diagnosis. Another limitation is response bias by more participation of patients in a better physical condition. Finally, most studies did not distinguish between patients with different haematological malignancies, who may have different needs for information due to the different nature of their diseases.

Despite these drawbacks, we presented as clear as possible an overview of the literature currently available on the perceived need for information among patients with haematological malignancies. It is clear that there is a lack of knowledge, especially on information needs of patients at the time of diagnosis and of severely ill patients who are treated as inpatients. Besides, there is a lack of insight into the long-term effects of treatment, in particular for newly developed treatments. Consequently, not all information needs can be fulfilled.

Conclusion

Based on the limited number of data available, patients with haematological malignancies need basic information on diagnosis, treatment, prognosis and other topics. Need for detailed information varied between studies. Medical information is for patients of higher priority compared to psychosocial information. The majority of the patients are satisfied with the information received, preferably offered by doctors and nurses. Providing information and shared decision-making may be improved towards a personalised approach. A large-scale study is required to better assess the need for information during the entire trajectory, from diagnosis to survivorship or decease, taking into account important moderating factors such as age, type of cancer, treatment modality and coping style.

Relevance to clinical practice

Haematologists and nurses both have their own central role in providing patients with basic information concerning diagnosis, treatment options, short- and long-term side effects and prognosis of the disease. Although psychosocial aspects often have less priority according to this review, it is important to pay attention to the psychosocial aspects of diagnosis and treatment such as implications for work and social life, and rehabilitation. Nurses and other health-care professionals can provide additional information on specific topics, if needed. Because of the shift of tasks from doctors to clinical nurse specialists, clinical nurse specialists are the new professionals with whom patients with cancer regularly come into close and long-term contact, giving them a central role of responding to the perceived need for information. It is essential to verify whether patients completely understand and are satisfied with the information that is provided. It is also important to identify whether and when there is a need for additional information and there is a desire for shared decision-making. In addition to oral information, other sources of (multimedia) information may include brochures, websites or apps that should be offered to patients in a personalised manner.

Future research

To obtain a better understanding of the perceived need for information among patients across the disease span, future studies are needed, with a qualitative as well as a quantitative approach, using a uniform assessment for all information categories, including sufficient inpatients and outpatients for each of the haematological malignancies in different phases of the disease. Furthermore, more insight is needed into the knowledge and attitude of haematologists, nurses and other health-care professionals regarding the perceived need for information by patients, enabling to improve adequate and personalised information provision.

Disclosure

The authors have confirmed that all authors meet the ICMJE criteria for authorship credit (www.icmje.org/ethical_1author.html), as follows: (1) substantial contributions to conception and design of, or acquisition of data or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be published.

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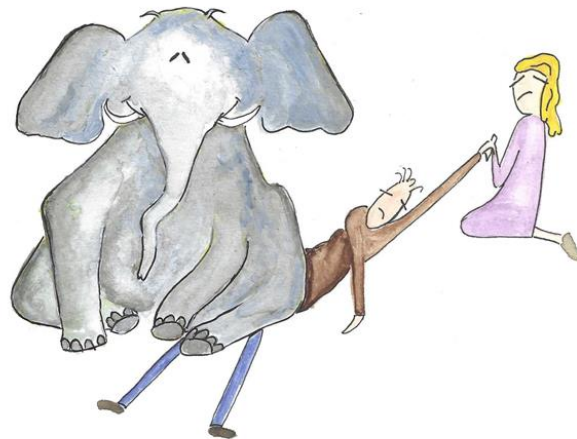
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Chapter 6

**Discussing sexuality in cancer care:
towards personalized information for cancer patients and survivors**



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To the Editor,

We have read with interest the manuscript “Discussing sexuality in cancer care: towards personalized information for cancer patients and survivors” by Albers et al. [1]. In a cross-sectional survey among members of cancer patient organizations, the authors investigated the patients’ need for information about sexuality and how to improve communication and aimed to identify “who really wants to know.” The authors concluded that 65% of members had a need for information regarding sexuality. Younger patients, patients with a self-reported negative effect of cancer on sexuality, and patients who were diagnosed less than 2 years ago reported a greater need for information. Most participants were treated for solid cancers.

Although we applaud Albers’ work, we believe that we should address the needs of the patients’ partners as well; therefore, we performed a multicenter longitudinal survey to measure the need for information not only among patients with hematological malignancies (HM) during the first 18 months of treatment but also among their partners. To identify information needs on sexuality, six questions were developed for this study. In addition to the results of Albers et al., we here report not only cross-sectional data but also longitudinal data of information needs on sexuality of patients and their partners as the need for information might well change over time.

This prospective survey was conducted in the Netherlands between 2013 and 2015. Adult patients (n =344) diagnosed with HM and their partners were invited to participate directly after diagnosis (T0), 3 months (T1), 6 months (T2), 1 year (T3), and 18 months after diagnosis (T4). With regard to sexuality, the Sexual and Fertility Information Need Questionnaire (SFINFOQ) is comprised of 6 items on information needs regarding (1) changes in sexuality (3 items), (2) support for sexual difficulties (2 items), and (3) precautions that need to be taken (1 item). The response format of the items was a 5-point Likert scale (range: not important to extremely important). The responses “very important” and “extremely important” were identified as an informational need at that time. Furthermore, the survey included items on possible factors that might influence information needs. Except for age (categorized in clinically relevant blocks: adolescents and young adults < 36 years, adults 36–69 years, older adults \geq 70 years), education (low, middle, and high), and diagnosis (per disease), all other sociodemographic and health status variables were dichotomized. A multivariable model was built with a forward selection procedure using generalized estimating equations, to account for the longitudinal data collection (p value for entry < 0.05). All data were analyzed using IBM SPSS 26 statistics. The study was approved by the Ethics Committee of the VU

University Medical Center, Amsterdam, the Netherlands. Written informed consent was obtained from all patients.

In total, the survey was completed by 266 patients and 134 partners at one or more time points. The mean age of the patients at time of diagnosis was 58 years (SD 14.9). Over 18 months from diagnosis, range 42 (at T0) to 48% (at T3) of patients expressed a need for information regarding changes in sexuality, 40 (T1) to 44% (T3) expressed a need for support for sexual difficulties, and 41 (T3) to 46% (T0) expressed a need for precautions that need to be taken. Multivariable analyses (Fig. 1) revealed that information needs of patients regarding changes in sexuality and precautions to be taken were associated with younger age, male sex, and a monitoring cognitive coping style. A need for support was associated with younger age and a monitoring coping style.

Regarding their partners, 34% (T4) to 52% (T3) expressed a need for information regarding changes in sexuality, 39% (T1) to 50% (T0) expressed a need for support for sexual difficulties, and 34% (T4) to 53% (T0) expressed a need for precautions that need to be taken. For their partners, multivariable analyses revealed that information needs regarding changes in sexuality and precautions to be taken were associated with younger age. A need for support was associated with seeking information on the Internet. In contrast to the patients, information needs were not associated with gender of the partner.

It was known already that patients have a need for information for longer time following the diagnosis of cancer. This mainly comes from cross-sectional studies, as in the study of Albers [1]. These data might be biased by the fact that patients experiencing sexual problems are more likely to reply than those who are not. In our longitudinal study, the response rates of both patients and partners were high (77% and 73%, respectively). The patients were recruited from five different hospitals, both academic cancer centers as well as regional hospitals. Therefore, we feel our population is representative for patients and partners seen in general practice.

The persistent high need for information on sexuality might well be explained by late sexual dysfunction as a consequence of both the disease and the treatment [2]. Alkylating agents can cause premature menopause [3–5] and hypogonadism in men [2, 6], resulting in vaginal dryness and discomfort in women and problems with sexual interest/desire in men when testosterone levels change. Neurotoxic agents can cause autonomous neuropathy [2, 7] and consequently arousal problems such as erectile dysfunction or lubrication. Irradiation of the pelvic area might also affect gonadal function in the same way as alkylating

agents [2, 6], while it can impair the peripheral nerves and pelvic blood flow. As also observed in cancer patients, sexual problems in HM patients may be enhanced by psychological and social factors [8].

As a result of all of the aforementioned, partners can experience sexual problems as well [9]. When living with a partner with cancer, priorities like an active and satisfying sex life are easily set aside. Some partners find it inappropriate to have sex with their ill partner, while for others the sexual relationship changes because of a shift in common roles [10].

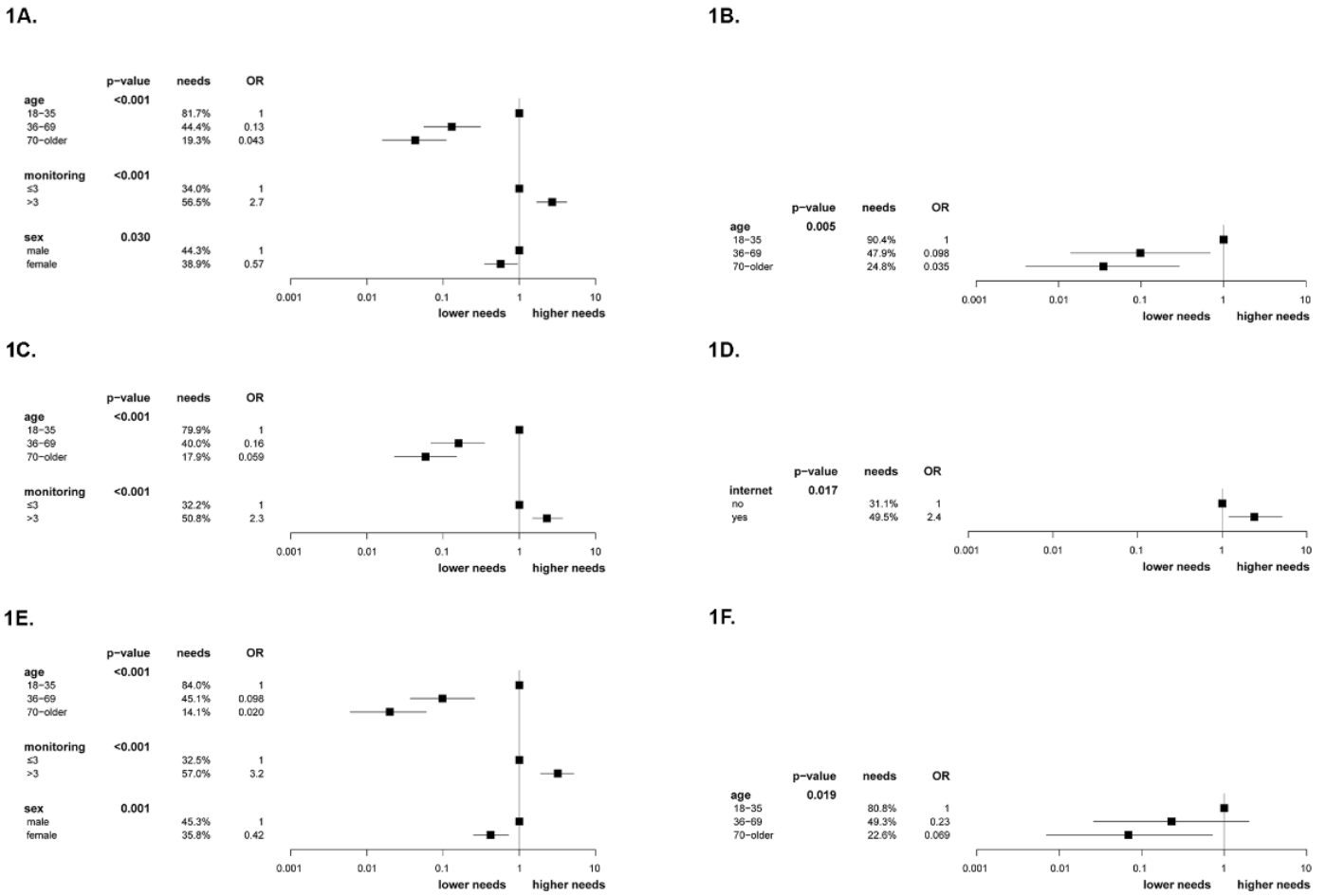
We have demonstrated that partners, like patients, have a persisting high need for information about sexuality. Therefore, we believe that information needs of intimate partners should be acknowledged and appropriate education about the impact on sexuality should be offered to all patients and their partners. Data Availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Compliance with ethical standards

Conflict of interest

The authors declare that they have no conflict of interest.

Figure 1. Forest plots of multivariable analyses for information needs regarding changes in sexuality (A, B), support (C, D) and precautions (E, F) among patients (A, C, E) and their partners (B, D, F). The percentage of patients/partners with information needs are reported within each subgroup. OR=odds ratio.

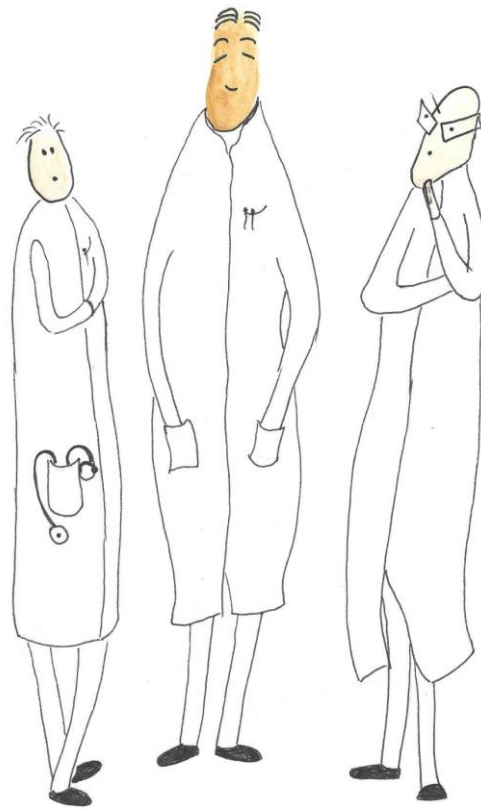


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Chapter 7

Health-care professionals' perspective on discussing sexual issues in adult patients after hematopoietic cell transplantation



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Abstract

The majority of adult patients have sexual concerns after post-haematopoietic cell transplantation. Even so, health-care professionals (HCP) do not routinely discuss these problems. We, therefore, surveyed all the members of the European Society for Blood and Marrow Transplantation to evaluate the barriers and facilitators to discussing sexual issues. The 73- item web-survey was completed by 166 registered nurses (RNs) and 126 medical doctors (MDs). Sixty-eight percent reported that they seldom discussed sexual issues. Younger MDs ($p < 0.001$) and those who work in non-western European countries ($p = 0.003$), RNs with probably less sexual education themselves ($p = 0.002$), MDs and RNs who have limited knowledge about sexual complications ($p < 0.001$) and MDs and RNs who feel uncomfortable discussing sexual issues ($p < 0.001$) are all less likely to discuss these matters. The major perceived barriers were that patients might be embarrassed if sexual issues were discussed in the presence of a relative (60% RNs, 67% MDs) and that professionals prefer patients to raise sexual issues themselves (54% RNs, 44% MDs). The most important perceived facilitator was for the patient to initiate discussion ($\geq 90\%$ for RNs and MDs). Overall, haematopoietic cell transplantation survivors may not be receiving the support on sexual issues they probably need.

Introduction

Haematopoietic cell transplantation (HCT) is often the only curative option for many malignant and non-malignant haematological diseases. However, high-dose radiation, and the use of alkylating agents in treatment, can cause premature menopause [1–3], hypogonadism [2, 4, 5], polyneuropathy [6], and graft versus host disease [7–9]; all of which can result in alterations to the patient's sexual functioning and satisfaction [10–12]. Disruption of sexual function is one of the most common long-term side-effects following both allogeneic and autologous HCT [13–18] and, according to the most extended longitudinal study report, 46% of male and 80% of female patients have sexual problems 5 years post-transplantation [16]. Long-term sexual complications include changes in sexual function [17, 8] and changes, which could impact on sexuality [15, 17, 8, 19–21]. The impact of disrupted sexual function usually becomes evident 1 year after HCT, during the recovery and reintegration phases [22, 23].

Because sexuality is an important aspect of overall health and quality of life, and because many HCT patients are at risk of developing sexual problems, it is important to discuss sexual issues with patients to promote their recovery and well-being. Unfortunately, there is much evidence that cancer patients are disappointed by the information they receive regarding sexual issues. Health-care professionals (HCP) rarely routinely discuss this subject [14, 15, 17, 21, 24–26]. For instance Humphreys et al. [15] reported that nearly half of patients questioned received no information about the possible consequences of treatment on sexual function before bone marrow transplantation. This seems important as patients who did receive information reported they experienced better sexual function after transplantation [15]. Other studies have reported that only 13–33% registered nurses (RNs) [27, 28] and 25%–38% medical doctors (MDs) [27–29] discussed sexual issues with cancer patients, with many barriers to addressing patients' sexuality in oncological settings being identified. Physicians put forward a perceived lack of time as well as a lack of knowledge as the most important reasons for their not addressing such issues [27–33]. Nurses reported their own lack of comfort on the subject as well as feelings of embarrassment as being significant barriers [27, 28, 31–43]. To examine this question in more detail, we designed and distributed an online survey among the medical staff involved with such patients. Our main aim was to investigate how often HCP throughout Europe discuss sexual issues with their adult patients. In addition, barriers and facilitators to discussing sexual issues with patients were determined.

Subjects and methods

Design

Cross-sectional survey

Subjects

Between March and July 2014, we sent an online questionnaire to all 3127 members (physicians, principal investigators, nurses) of the 193 centres of the European Society for Blood and Marrow Transplantation (EBMT). The centres were requested to further distribute the questions to those caring for HCT patients.

Study-specific questionnaire

A self-administered questionnaire, previously devised by Moore et al. [37] for use among oncology nurses of men diagnosed with testicular cancer, was adapted for use with HCT staff [39]. The adapted questionnaire (available as Supplemental Material) consisted of 73 items divided into seven sections namely:

1. Demographics (gender, age, religion, country)
2. Work experience, additional education/training following registration, plus previous education specifically taken in the field of sexuality
3. Discussing sexual issues with patients (frequency of discussing sexual issues)
4. Perceived barriers to discussing sexual issues with patients
5. Perceived facilitators to discussing sexual issues with patients
6. Self-reported knowledge about sexual issues and comfort level relating to discussing sexual issues and
7. Comments (free text).

The response format of the items in Sections 4 and 5 was a 5-point Likert scale (range: strongly agree—strongly disagree, or very comfortable—very uncomfortable). Current clinical practice surrounding the discussion of sexual issues with patients was evaluated by means of a single item added to the study-specific questionnaire: “In the last 6 months, how frequently have you informed patients that you were available to discuss their sexual concerns?” (never/occasionally or frequently/very frequently/with all patients).

The perceived knowledge and comfort when discussing sexual issues were evaluated with 11 items; barriers to discussing sexual issues were evaluated using 28 items, subdivided into environmental barriers

(6 items), patient barriers (11 items), and other potential barriers (11 items). Facilitators for discussing sexual issues with patients were evaluated with 10 items. To obtain insight into which factors are the most relevant, we compared perceived knowledge of sexual issues, comfort when discussing sexual issues, and barriers and facilitators to discussing sexual issues among HCP who rarely discussed sexual issues, with those who discussed sexual issues routinely.

The questionnaire was available in French, German, Dutch, Italian and English languages.

Statistical analyses

All statistical analyses were performed using SPSS version 21 (IBM Corp. Armonk, NY). Demographics are described using frequencies and percentages and comparisons between groups (i.e., complete responders versus incomplete responders and frequency of discussing sexual issues) via Chi-square or Fisher's exact tests. Except for age (categorised in clinically relevant blocks) and sexual education (categorized in hourly blocks), all other variables were dichotomised as follows:

1. Geographic distribution (western European/ non- western European)
2. Religion (religious/not religious or not practising)
3. Academic qualification (received post graduate education (yes/no))
4. Time working in HCT (more/less than 5 years)
5. Current clinical setting (only inpatient/other)
6. Barriers and facilitators ((strongly) agree/neutral or (strongly) disagree)
7. Questions about the frequency of discussing sexual health (none or occasionally/(very) frequently or with all patients)
8. Self-reported knowledge levels ((strongly) agree/ neutral or (strongly) disagree)
9. Self-reported comfort levels ((very) comfortable/neutral or (very) uncomfortable).

Chi-square tests or Fisher's exact tests were used to examine statistically significant differences between groups.

P-values < 0.05 were considered to be significant, p- values < 0.1 were considered to indicate a trend.

Results

Demographic data

In total, 426 EBMT members responded (14% response rate). Responses from 59 RNs and 44 MDs were

excluded because of incomplete or missing data. Thirty-one HCP (16 RNs, 15 MDs) who only worked with children or adolescents did send completed data but, as sexual issues were rarely or never discussed (94% of RNs and 80% of MDs) these responses were excluded from the factor analysis. The final analyses were carried out on the remaining 292 responses (equivalent to 9% response rate).

The study population, therefore, consisted of 166 RNs and 126 MDs, from 34 countries. The majority of RNs and MDs came from European countries; the Netherlands (RNs 36 (22%), MDs 14 (11%)), Belgium (RNs 35 (21%), MDs 6 (5%)), United Kingdom (RNs 23 (14%), MDs 18 (14%)) and Italy (RNs 19 (11%), MDs 23 (18%)). The demographic data are described in Table 1.

We compared the demographic data of respondents who completed the questionnaire and respondents from whom responses on barriers and facilitators were missing (Table 1). Differences between HCP who did complete the questionnaire with those who did not, included self-reported religious affiliation; RNs 44%/71%, $p = 0.001$; MDs 57%/84%, $p = 0.003$, and a lack of post graduate education; (RNs 23%/42%, $p = 0.006$; MDs 7%/ 38%, $p < 0.001$).

Frequency and associated factors related to discussing sexual issues

The majority of RNs and MDs did not, or only occasionally, discussed sexual issues with individual patients; RNs (68%), MDs (68%), see Table 2, perceived knowledge and comfort are shown in Table 3. about the long-term sexual complications of HCT ($p < 0.001$), or feel uncomfortable discussing sexual issues ($p < 0.001$) or work with a paediatric / teenage population are all less likely to discuss sexual issues.

Perceived knowledge on sexual issues

RNs and MDs who infrequently discussed sexual issues reported a significantly lower knowledge level in 8 of the 11 areas related to the impact of HCT on sexual issues (Table 3). Seven out of 8 areas were concordant between RNs and MDs. RNs only differed from MDs in that RNs who never/occasionally discussed sexual issues perceived less knowledge to talk to patients about concerns regarding fertility ($p = 0.016$), whereas MDs who never/occasionally discussed sexual issues reported less knowledge talking to patients about the impact of HCT on patients' body image ($p = 0.036$).

Table 1. Demographics characteristics of the study population who did and did not complete the questionnaire

	Registered Nurses				<i>p</i> - <i>value</i>	Medical Doctors				<i>p</i> - <i>value</i>
	completed (N=166)		not completed (N=52)			completed (N=126)		not completed (N=37)		
	n	%	n	%		n	%	n	%	
Gender					0,33					0,75
Male	21	12,7	4	7,7		61	48,4	19	51,4	
Female	145	87,3	48	92,3		65	51,6	18	48,6	
Religion					0.001*					0.003*
Religious	73	44,0	37	71,2		72	57,1	31	83,8	
Not practising or not religious	93	56,0	15	28,8		54	42,9	6	16,2	
Academic qualification					0.006*					<0.001*
registration	38	22,9	22	42,3		9	7,1	14	37,8	
post graduate education	128	77,1	30	57,7		117	92,9	23	62,2	
Years working in HSCT#					0,77					0,38
0-5 years	35	21,1	10	19,2		13	10,3	6	16,7	
more than 5 years	131	78,9	42	80,8		113	89,7	30	83,3	
Current practice area#					0,26					0.029*
hematology inpatient	91	55,2	24	46,2		37	29,4	18	48,6	
in and/or out patient	74	44,8	28	53,8		89	70,6	19	51,4	
Sexual Health Education pre- and or post graduate					0,50					0,088
none/unsure	58	34,9	25	48,1		54	42,9	26	70,3	
0-1 hour	23	13,9	7	13,5		19	15,1	4	10,8	
1-5 hour(s)	52	31,3	14	26,9		28	22,2	5	13,5	
6-10 hours	18	10,8	2	3,8		11	8,7	1	2,7	
11-15 hours	5	3,0	1	1,9		4	3,2	0	0	
> 15 hours	10	6,0	3	5,8		10	7,9	1	2,7	

*p<0.05, # missing values

Table 2. Discussing sexual issues in relation to characteristics of the Registered Nurses and the Medical Doctors

	Registered Nurses (N=166)				<i>p-value</i>	Medical Doctors (N=126)				<i>p-value</i>
	never/occasionally		(very) frequently/all my patients			never/occasionally		(very) frequently/all my patients		
	n	%	n	%		n	%	n	%	
<i>In the last 6 months, how frequently have you informed patients that you were available to discuss their sexual concerns?</i>	112	67,5	54	32,5		85	67,5	41	32,5	
Age in years#					0,81					<0.001*
20-35	32	71,1	13	28,9		9	81,8	2	18,2	
36-55	69	65,7	36	34,3		68	75,6	22	24,4	
55+	11	68,8	5	31,3		8	32,0	17	68,9	
Gender#					0,93					0,14
Male	14	66,7	7	33,3		45	73,8	16	26,2	
Female	98	67,6	47	32,4		40	61,5	25	38,5	
Geographic distribution					0,17					0,003*
western European	103	66,0	53	34,0		69	62,7	41	37,3	
non-western European	9	90,0	1	10,0		16	100,0	0	0,0	
Religion#					0,80					0,58
Religious	50	68,5	23	31,5		50	69,4	22	30,6	
Not practising or not religious	62	66,7	31	33,3		35	64,8	19	35,2	
Academic qualification#					0,35					0,72
registration	28	73,7	10	26,3		7	77,8	2	22,2	
post graduate education	84	65,6	44	34,4		78	66,7	39	33,3	
Years working in HSCT#					0,33					0,55
0-5 years	26	74,3	9	25,7		10	76,9	3	23,1	
more than 5 years	86	65,6	45	34,4		75	66,4	38	33,6	
Current practice area#					0,21					0,66
hematology inpatient	65	71,4	26	28,6		26	70,3	11	29,7	
in and/or out patient	46	62,2	28	37,8		59	66,3	30	33,7	
Sexual education received					0.002*					0,078
none	43	74,1	15	25,9		36	66,7	18	33,3	
0-1 hour	18	78,3	5	21,7		14	73,7	5	26,3	
1-5 hour(s)	34	65,4	18	34,6		23	82,1	5	17,9	
6-10 hours	14	77,8	4	22,2		7	63,6	4	36,4	
11-15 hours	1	20,0	4	80,0		1	25,0	3	75,0	
> 15 hours	2	20,0	8	80,0		4	40,0	6	60,0	

*p<0.05, # missing values

Younger MDs ($p < 0.001$) and those who work in non-western European countries ($p = 0.003$), plus RNs who have received less sexual education ($p = 0.002$), as well as MDs and RNs with limited knowledge

Comfort in discussing sexual issues

RNs/ MDs who infrequently discussed sexual issues felt significantly less comfortable in 10 and in 6 of the 11 areas, respectively (Table 3). Averages were calculated and showed that 44% of RNs who rarely discussed sexual issues felt comfortable in all areas, compared to 81% of RNs who routinely discussed these subjects ($p < 0.001$). For MDs these percentages were 59% and 74%, respectively, ($p < 0.001$). Six areas were concordant between RNs and MDs; RNs only differed from MDs in that RNs who never/ occasionally discussed sexual issues felt significantly less comfortable compared with RNs who routinely discussed sexual issues, in all areas except for the impact of HCT on body image.

Barriers

The main barrier perceived by HCP (>50%) who never/ occasionally discussed sexual issues was the perception that patients would feel embarrassed if these subjects were discussed in the presence of a family member (RNs 60%/MDs 67%); this was significantly higher than among HCP routinely discussing sexual issues; (RNs 39% ($p = 0.011$)/ MDs 39% ($p = 0.003$)) (Table 3). Furthermore, 54% of RNs and 44% of MDs who never/occasionally discussed sexual issues, felt that patients would prefer the HCP to wait until the patient initiates the discussion and/or raises a concern. This was in contrast to 35% of RNs and 17% of MDs who routinely discussed sexual issues ($p = 0.026$ and $p = 0.004$, respectively). In HCP routinely discussing sexual issues, none of the barriers were present in >50% of responses. Fifteen of 28 barriers were found to be significantly different between RNs who rarely discussed sexual issues and RNs who routinely discussed sexual issues. Significantly different barriers, reported by > 30% of respondents who never/occasionally discussed sexual issues were; a heavy workload/lack of time (31%/15%), a lack of services to refer the patient to (36%/15%), the perception that patients would feel embarrassed discussing sexual issues either alone (33%/9%), or in the presence of a third person (60%/39%), that patients do not want to discuss sexual issues (30%/15%) and that patients prefer nurses to wait for the patient to initiate the discussion (54%/35%). For MDs, significantly different barriers reported by those > 30% of respondents who never/occasionally discussed sexual issues were: a heavy workload/lack of time (39%/20%), a lack of services to refer the patient to (44%/20%), the perception that the patients' time in (outpatient) clinic was too short (32%/5%), that patients would feel embarrassed discussing sexual issues in the presence of a third person (67%/39%), that patients would prefer doctors to wait for the patient to initiate the discussion (44%/20%) and an awareness by the physician that the patient is suffering from a mental health issue (33%/15%).

Facilitators

The majority of RNs and MDs felt that almost all facilitators were helpful, often in more than 80% of the respondents. “Having observed a team member discussing sexual issues with a patient” was perceived as a significant facilitator in 49%/41% of RNs/MDs who rarely discussed sexual issues compared to 33%/24% of RNs/MDs, respectively, who routinely discussed sexual issues (Table 3).

Two perceived facilitators were found to be significantly different between RNs who rarely, and those who regularly, discussed sexual issues. Those who rarely discussed sexual issues reported more often that “Having a private environment to discuss sexual issues” as helpful (96%/83%), while “Having standard operating procedures/policies on how to address sexual issues significantly” was reported as a facilitator much less often (52%/70%).

There were three facilitators showing significant differences between MDs who rarely, and those who routinely, discussed sexual issues namely: being prompted by a care plan (74%/55%), having sufficient time to sit and talk to patients (92%/79%), and having knowledge of the sexual difficulties HCT patients experience (86%/69%). These were all reported more frequently by MDs who never or only occasionally discussed sexual issues.

Table 3. Percentage of Registered Nurses and Medical Doctors who reported to never / occasionally discussed sexual issues, compared with those who reported to frequently discuss them. Results also presented for competence barriers, perceived comfort, potential barriers, and facilitators to discussion.

	Registered Nurses (N=166)					Medical Doctors (N=126)				
	never/ occasionally		(very) frequently/with all my patients		<i>p-value</i>	never/ occasionally		(very) frequently/with all my patients		<i>p-value</i>
	n	%	n	%		n	%	n	%	
<i>In the last 6 months, how frequently have you informed patients that you were available to discuss their sexual concerns?</i>	112	67,5	54	32,5		85	67,5	41	32,5	
Knowledge										
<i>I have the knowledge to talk to patients about</i>										
the impact of HSCT on the patient's body image	94	83,9	50	92,6	0,12	69	81,2	39	95,1	0.036*
the impact of HSCT on the patient's male sexual function	64	57,1	44	81,5	0.002*	59	69,4	38	92,7	0.004*
the impact of HSCT on the patient's female sexual function	65	58,0	45	83,3	0.001*	60	70,6	40	97,6	<0.001*
the option of preservation of fertility	63	56,3	38	70,4	0,081	75	88,2	38	92,7	0,44
the impact of vaginal dryness/atrophy	48	43,2	42	77,8	<0.001*	52	61,2	35	85,4	0.006*
the impact of an erectile dysfunction.	75	67,0	49	90,7	0.001*	60	70,6	36	87,8	0.034*
the impact of low sexual desire	65	58,0	49	90,7	<0.001*	53	63,1	36	87,8	0.004*
concerns regarding fertility	73	65,2	45	83,3	0.016*	73	85,9	36	90,0	0,52
concerns regarding future sexual relationships	69	62,2	45	83,3	0.006*	47	55,3	36	87,8	<0.001*
concerns to talking to their partner about sexual function	58	52,3	44	81,5	<0.001*	40	47,1	36	87,8	<0.001*
responding to a patient who misinterprets the intentions of my questions	69	61,6	41	75,9	0,068	53	62,4	25	61,0	0,88
Comfort										
<i>I am comfortable talking to patients about</i>										
the impact of HSCT on the patient's body image	86	76,8	49	90,7	0.031*	60	71,4	33	80,5	0,28
the impact of HSCT on the patient's male sexual function	35	31,3	39	72,2	<0.001*	48	56,5	31	77,5	0.023*
the impact of HSCT on the patient's female sexual function	40	37,0	46	88,5	<0.001*	48	57,8	29	76,3	0.050*
the option of preservation of fertility	54	48,6	42	77,8	<0.001*	70	83,3	32	78,0	0,47
the impact of vaginal dryness/atrophy	37	33,6	38	70,4	<0.001*	45	52,9	30	73,2	0.030*
the impact of an erectile dysfunction.	39	35,1	46	85,2	<0.001*	44	51,8	27	67,5	0,098
the impact of low sexual desire	43	38,7	46	85,2	<0.001*	39	45,9	29	70,7	0.009*
concerns regarding fertility	62	55,9	47	87,0	<0.001*	70	82,4	34	82,9	0,94
concerns regarding future sexual relationships	47	42,0	44	83,0	<0.001*	41	48,8	31	75,6	0.004*
concerns to talking to their partner about sexual function	46	41,4	42	80,8	<0.001*	44	51,8	32	78,0	0.005*
responding to a patient who misinterprets the intentions of my questions	43	38,4	35	64,8	0.001*	41	48,2	21	53,8	0,56

HSCT, hematopoietic stem cell transplantation; GVHD, graft versus host disease

*p<0.05

Table 3. (Continued)

	Registered Nurses (N=166)					Medical Doctors (N=126)				
	never/ occasionally		(very) frequently/with all my patients		<i>p-value</i>	never/ occasionally		(very) frequently/with all my patients		<i>p-value</i>
	n	%	n	%		n	%	n	%	
Environmental barriers										
<i>I do not talk to patients about their sexual concerns because....</i>										
of a heavy workload and a lack of time	34	30,6	8	14,8	0,029*	32	38,6	8	20,0	0,040*
there is no private environment	37	33,3	11	20,4	0,085	21	25,3	9	22,5	0,73
there is a lack of support from colleagues/managers	18	16,2	0	0,0	0,002*	11	12,9	2	4,9	0,16
there is a lack of services to refer patients to	40	35,7	8	14,8	0,005*	37	43,5	8	20,0	0,011*
patients are only in hospital/outpatient clinic for a short period so there is no time to discuss sexual issues	17	15,2	5	9,4	0,31	27	31,8	2	4,9	0,001*
patients sexual concerns are too private to document in the notes	27	24,1	2	3,7	0,001*	16	18,8	3	7,3	0,091
Other potential barriers										
<i>I would be reluctant to discuss sexuality concerns because....</i>										
patients would get embarrassed/offended if I initiated a conversation about the impact of cancer on their sexuality	37	33,0	5	9,3	0,001*	26	30,6	7	17,1	0,11
patients would get embarrassed/offended if I initiated a conversation about the impact of cancer on their sexuality if a family member or relative were present	67	59,8	21	38,9	0,011*	57	67,1	16	39,0	0,003*
patients might misinterpret my questions as a sexual advance or a seductive gesture	2	1,8	0	0,0	0,32	5	5,9	1	2,4	0,40
patients would refuse to answer my questions if I asked them about their worries about the impact of the cancer on their sexuality	18	16,1	0	0,0	0,002*	9	10,6	1	2,5	0,12
patients do not want to talk to nurses/doctors about sexual concerns as they consider it is their role	26	23,2	1	1,9	<0,001*	12	14,1	1	2,4	0,043*
other colleagues would think I was infringing in the patients right to privacy if I raised a discussion on sexual issues	5	4,5	0	0,0	0,11	6	7,1	1	2,4	0,29
the patients family/significant others would not want nurses/doctors* to talk to patients about their sexual concerns	12	10,7	4	7,5	0,52	12	14,1	4	9,8	0,49
patients do not want to talk about sexual issues, as it is the furthest thing from their minds when they have just been through HSCT	34	30,4	8	14,8	0,031*	25	29,4	4	9,8	0,014*
patients prefer nurses/doctors to wait until they raise their concerns	60	53,6	19	35,2	0,026*	37	43,5	7	17,1	0,004*
patients would get emotionally distressed if I initiated a conversation about the impact of HSCT on their sexuality	18	16,2	5	9,3	0,23	30	35,3	9	22,5	0,15
talking to patients about the impact of HSCT on sexuality is the role of the specialist	34	30,4	16	29,6	0,92	27	31,8	16	39,0	0,42

HSCT, hematopoietic stem cell transplantation; GVHD, graft versus host disease

**p*<0,05

Table 3. (Continued)

	Registered Nurses (N=166)					Medical Doctors (N=126)				
	never/ occasionally		(very) frequently/with all my patients		<i>p</i> -value	never/ occasionally		(very) frequently/with all my patients		<i>p</i> -value
	n	%	n	%		n	%	n	%	
Patient barriers										
<i>I would be reluctant to</i>										
talk to a patient younger than me about the impact of HSCT on their sexuality	18	16,1	2	3,7	0,022*	6	7,1	4	9,8	0,60
talk to a patient older than me about the impact of HSCT on their sexuality	16	14,4	2	3,8	0,045*	7	8,3	3	7,3	0,84
talk to a patient about the impact of HSCT on their sexuality if they were single	13	11,6	2	3,7	0,096	6	7,1	4	9,8	0,60
talk to a patient about the impact of HSCT on their sexuality if they have a different sexual orientation	29	26,1	3	5,6	0,002*	15	17,6	6	14,6	0,67
raise a discussion about the impact of HSCT on their sexuality with a patient who is of a different culture	34	30,4	3	5,6	<0,001*	19	22,4	6	14,6	0,31
raise a discussion about the impact of HSCT on their sexuality with a patient who is of a different religion	31	27,7	12	22,2	0,45	20	23,5	10	24,4	0,92
raise a discussion about the impact of HSCT on their sexuality with a patient who I know has a mental health problem	27	24,3	6	11,3	0,052	28	32,9	6	14,6	0,030*
raise a discussion about the impact of HSCT on their sexuality with a patient who I know is anxious	24	21,4	10	18,5	0,66	20	23,8	9	22,0	0,82
raise a discussion about the impact of HSCT on their sexuality with a patient who I know has a progressive disease	23	20,5	5	9,3	0,069	25	29,4	6	14,6	0,071
raise a discussion about the impact of HSCT on their sexuality with a patient who I know has GVHD	13	11,6	3	5,6	0,22	11	12,9	5	12,2	0,91
talk to patients of the opposite gender about the impact of HSCT on their sexuality	15	13,4	1	1,9	0,018*	15	17,9	4	9,8	0,24
Facilitators										
<i>The following would facilitate me to talk to patients about their sexual concerns.</i>										
Being told by another professional that the patient had concerns	90	81,1	48	88,9	0,20	70	83,3	28	70,0	0,088
Being asked questions by the patient regarding their sexuality	109	98,2	53	98,1	0,98	81	96,4	36	90,0	0,15
Being prompted by a care plan	66	59,5	35	64,8	0,51	62	73,8	22	55,0	0,036*
Having standard operating procedures/ policies on how to address sexual issues	78	70,3	28	51,9	0,021*	48	57,1	18	45,0	0,21
Having received relevant communication workshops/ training	98	89,1	46	85,2	0,47	58	69,0	28	70,0	0,91
Having a private environment to have such discussion	90	82,6	52	96,3	0,014*	71	84,5	32	82,1	0,73
Having sufficient time to sit and talk to patients	93	85,3	51	94,4	0,088	77	91,7	30	78,9	0,048*
To have known the patient for 2-3 weeks and have developed a good rapport	89	80,2	38	70,4	0,16	72	85,7	31	77,5	0,25
Having observed an example of a teammember talking to patients about sexual issues	53	48,6	18	33,3	0,061	34	40,5	9	23,7	0,072
Having knowledge on the sexual difficulties HSCT patients experience	99	90,0	47	87,0	0,57	72	85,7	27	69,2	0,032*

HSCT, hematopoietic stem cell transplantation; GVHD, graft versus host disease

Discussion

It is generally recognised that many patients have sexual problems following HCT and it is also probable that adequate information helps or even improves sexual function. Even so, talking to those staff involved suggests that sexual issues are still not routinely discussed among the HCP community.

We, therefore, performed a survey supported by the EBMT of its members, to determine the number of RNs and MDs who routinely discuss sexual issues with their patients and to explore the potential barriers and facilitators to discussions among those who do not have such conversations.

An analysis of this survey indicates that two-thirds of respondents rarely discuss sexual issues with their patients. A lack of knowledge, and being uncomfortable with the topic, both contribute to HCP

avoiding such talks. Many factors are leading to these problems, such as a reluctance to do so by MDs working in non-western European countries, or of MDs being younger, while a lack of training as to the long-term sexual complications of HCT influenced RNs. Furthermore, HCP who never, or only occasionally, discussed sexual issues with their patients reported their own lack of knowledge about sexual issues as being relevant. In addition, feeling uncomfortable while talking about sexual issues appeared important. Factors influencing comfort are unknown, however, the fact that younger and non-western European MDs, plus RNs with less sexual education, tended not to discuss sexual issues, suggests that cultural differences and experience play an important role. Moreover, it was noted that fewer respondents who reported themselves as religious, completed the questionnaires. This suggests that barriers to discussing sex might be linked to religious beliefs.

Further analyses of the barriers and facilitators involved, showed that the most frequent barrier, even for HCP who did routinely hold such discussions, was the perception that patients would become embarrassed if sexual issues were discussed especially if a relative was present during the consultation. These feelings of embarrassment have been previously described in relation to HCP caring for gynaecological and colorectal patients [31, 36, 38, 39, 44]. Moreover, in the recent literature, the presence of a third party during consultation was mentioned by HCP as causing embarrassment [39, 40].

Many HCP felt that it would be more appropriate if the patients themselves initiated the discussion on sexual issues. Indeed, the patient initiating discussion of the topic was the major facilitator for nearly all HCP. Leaving the initiative to the patient is understandable, as for some patients knowing that sex and reproduction are affected is sufficient, and they do not always want help for their sexual problems [39]. Nevertheless, patients need to be informed about the impact that HCT can potentially have on both sexuality and sexual function and they need to know whether treatment or support is available. Additionally, patients would surely benefit from knowing that sexual issues are common problems. In fact, having this confirmation is sometimes sufficiently helpful. However, without preparatory information it is more difficult for the patient to initiate discussions (for instance on such issues as the possible effect on (new) sexual relationships) [24]. Earlier work has shown that education is an important factor in this arena and Humphreys et al. [15] reported that patients who received information regarding the consequences of treatment on sexual function before bone marrow transplantation reported better sexual function post-transplantation. Crucially, sexual problems need to be identified in order to obtain adequate support [41].

Our study is limited by the low response rate, which is not uncommon for large surveys and we realise that the results might, therefore, not be representative of a larger cohort. Participation bias is also a

possible limitation, which is difficult to exclude. Overall, it is also possible there was an overrepresentation from HCP interested in the subject matter and, as a consequence, fewer RNs and MDs who do not routinely discuss sexual issues in clinical practice responded. Even so, this would indicate that the problem of not discussing sexual concerns may have been underestimated.

In spite of these limitations, this survey clearly shows that there is a lack of routine clinical assessment of this subject and it seems obvious that better support information would be useful. A questionnaire assessing sexual function, followed up by discussions of the results appears to be an effective intervention/strategy for promoting patient- physician communication [43, 45–47]. Furthermore, the routine implementation of a simple validated screening tool used at scheduled time-points, could determine the need for such a discussion. The Brief Sexual Symptom Checklist for Men/Women is one such checklist that consists of four simple questions, and addresses not only patients' level of satisfactions with sexual function but also assesses duration, identification of the type of sexual problems, and importantly, the willingness of the patient to discuss the problem with an HCP [39, 48–50]. If the patient has concerns and is willing to talk about problems, the use of the step based model (PLISSIT model) can be useful to properly intervene, from providing information to referral to a dedicated specialist [51]. Furthermore, although previous studies have reported that more education does not necessarily lead to improved ability to incorporate discussions surrounding sexuality into usual care, it has also been shown that additional sexuality-related education does help HCP to feel more comfortable discussing this subject [21, 34, 52, 53]. The results presented here would appear to further validate this theory. Therefore, in our opinion, appropriate education about the impact of HCT on male and female sexuality should be included in education programmes for HCP who follow-up patients after HCT [54].

In conclusion, this study shows that while many HCT survivors experience sexual problems, the majority do not routinely discuss them with staff and advisors. Embarrassment, or at least a discomfort about discussing sexual concerns, and a lack knowledge and relevant education on the side of the medical staff side, are major barriers for HCP initiating such discussions; the discomfort is such that initiation of discussions on this topic usually originates from the patient.

Future research

Research to develop a more detailed understanding of patients' requirement for information regarding sexual concerns, and how best to communicate them, would complement the work presented in this paper. Future investigations might also consider the training needs of HCP to facilitate comfortable and competent discussions, manage patient expectations, provide information and deal with issues when they

arise, and allow referral where appropriate.

Finally, this study has highlighted the fact that children and teenagers are rarely included in discussions about sexuality and sexual problems. This is of concern as, while the topic may not be relevant today, it will be later in the patient's life. We plan to address this in future studies.

Compliance with ethical standard

Conflict of interest The authors declare that they have no conflict of interest.

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Supplemental Material original questionnaire for oncology nurses by Moore et al. (2012) and adapted questionnaire for hematology staff		
The aim of this questionnaire is to investigate the Barriers and Facilitators to Oncology Nurses Discussing Sexuality Concerns with Men diagnosed with Testicular Cancer.	adapted	The aim of this questionnaire is to investigate the Barriers and Facilitators to Hematology Staff Discussing Sexuality Concerns with People following Hematopoietic Stem Cell Transplantation.
1. What is your gender?		1. What is your gender?
male/female		male/female
2. What is your age?		2. What is your age?
20-25		20-25
26-30		26-30
31-35		31-35
36-40		36-40
41-45		41-45
46-50		46-50
51-55		51-55
55+		55+
3. What is your religion?		3. What is your religion?
Roman Catholic		Roman Catholic
Church of Ireland	adapted	Church of England/protestant
Presbyterian	adapted	Jewish
Methodist		Methodist
Islam		Islam
Other, please specify.....		Other, please specify.....
	supplemented with	4. What country are you from?.....
4. What is your current position?	adapted answers	5. What is your current position?
Staff Nurse		Senior Nurse
CNM1		Research Nurse
CNM2		Registered Nurse
CNS		Clinical Nurse Specialist/ ANP
ANP		Physician

Other, please specify.....		Specialised Physician (Hematologist)
		Other, please specify.....
5. What is your highest academic qualification to date?	adapted answers	6. What is your highest academic qualification to date?
Certificate in Nursing		Nursing Registration
Certificate in Midwifery		specialist nursing training in Oncology/hematology
Diploma in Nursing		Masters Degree
Bachelors Degree in Nursing		PhD
Higher Diploma in Oncology		medical degree
Masters degree		specialist medical training, please specify.....
PhD		
Other, please specify.....		
6. How long have you been working in Oncology?	adapted	7. How long have you been working in Hematology?
0-1 year		0-1 year
1-5 years		1-5 years
6-10 years		6-10 years
11-15 years		11-15 years
16-20 years		16-20 years
21-25 years		21-25 years
26-30 years		26-30 years
30 years +		30 years +
7. What is your current practice area?	adapted answers	8. What is your current practice area?
Oncology In Patient		Hematology, inpatient
Oncology Day Unit		Hematology, Day Unit
Oncology Outpatients		Hematology, Outpatient Clinic
Other, please specify.....		Research
		Other, please specify.....
8. How much lecture content on 'Sexual Health' was included in your pre registration nursing education?		9. How much lecture content on 'Sexual Health' was included in your pre registration education?
None		None
0-1 hour		0-1 hour

1-5 hours		1-5 hours
6-10 hours		6-10 hours
11-15 hours		11-15 hours
15 hours +		15 hours +
unsure		unsure
9. How much lecture content on ‘Sexual Health’ was included in your post graduate nursing education?		10. How much lecture content on ‘Sexual Health’ was included in your post graduate education?
0-1 hour		0-1 hour
1-5 hours		1-5 hours
6-10 hours		6-10 hours
11-15 hours		11-15 hours
15 hours +		15 hours +
unsure		unsure
10. In the last 6 months, how frequently have you informed patients that you were available to discuss their sexual concerns?		11. In the last 6 months, how frequently have you informed patients that you were available to discuss their sexual concerns?
Never		Never
Occasionally		Occasionally
Frequently		Frequently
Very frequently		Very frequently
With all patients		With all patients
11. In the last 6 months, how frequently have you responded to your patients’ sexual concerns and discussed them with them?		12. In the last 6 months, how frequently have you responded to your patients’ sexual concerns and discussed them with them?
Never		Never
Occasionally		Occasionally
Frequently		Frequently
Very frequently		Very frequently
With all patients		With all patients
12. In the last 6 months, on average, how many patients have wanted to discuss their sexual concerns with you?		13. In the last 6 months, on average, how many patients have wanted to discuss their sexual concerns with you?
None		None
1-5		1-5

6-10		6-10
11-15		11-15
16-20		16-20
20+		20+
I DO NOT TALK TO PATIENTS ABOUT THEIR SEXUAL CONCERNS BECAUSE:(ranging from strongly agree to strongly disagree)		I DO NOT TALK TO PATIENTS ABOUT THEIR SEXUAL CONCERNS BECAUSE:(ranging from strongly agree to strongly disagree)
of a heavy workload and a lack of time		of a heavy workload and a lack of time
there is no private environment		there is no private environment
there is a lack of support from colleagues/managers		there is a lack of support from colleagues/managers
there is a lack of services to refer patients to		there is a lack of services to refer patients to
patients are only in hospital for a short period so there is no time to discuss sexual issues	adapted	patients are only in hospital/outpatient clinic for a short period so there is no time to discuss sexual issues
patients sexual concerns are too private to document in the nursing kardex	adapted	patients sexual concerns are too private to document in the notes
PERCEPTIONS OF BARRIERS FROM PATIENTS/OTHERS (ranging from strongly agree to strongly disagree)		PERCEPTIONS OF BARRIERS FROM PATIENTS/OTHERS (ranging from strongly agree to strongly disagree)
patients would get embarrassed / offended if I initiated a conversation about the impact of cancer on their sexuality		patients would get embarrassed / offended if I initiated a conversation about the impact of cancer on their sexuality
patients would get embarrassed / offended if I initiated a conversation about the impact of cancer on their sexuality if a family member or relative were present		patients would get embarrassed / offended if I initiated a conversation about the impact of cancer on their sexuality if a family member or relative were present
patients might misinterpret my questions as a sexual advance or a seductive gesture		patients might misinterpret my questions as a sexual advance or a seductive gesture
patients would refuse to answer my questions if I asked them about their worries about the impact of the cancer on their sexuality		patients would refuse to answer my questions if I asked them about their worries about the impact of the cancer on their sexuality
patients do not want to talk to nurses about sexual concerns as they consider it the doctor's role	adapted	patients do not want to talk to nurses/doctors* about sexual concerns as they consider it the doctor's/nurses* role

other colleagues would think I was infringing on the patients right to privacy if I raised a discussion on sexual issues		other colleagues would think I was infringing on the patients right to privacy if I raised a discussion on sexual issues
the patients family/significant others would not want nurses to talk to patients about their sexual concerns		the patients family/significant others would not want nurses to talk to patients about their sexual concerns
patients do not want to talk about sexual issues, as it is the furthest thing from their minds when they have just been diagnosed with testicular cancer	adapted	patients do not want to talk about sexual issues, as it is the furthest thing from their minds when they have just been through HSCT
patients prefer nurses to wait until they raise their concerns	adapted	patients prefer nurses/doctors* to wait until they raise their concerns
patient would get emotionally distressed if I initiated a conversation about impact of cancer on their sexuality	adapted	patients would get emotionally distressed if I initiated a conversation about impact of HSCT on their sexuality
talking to patients about impact of cancer on sexuality is the role of the Clinical Nurse Specialist	adapted	talking to patients about impact of HSCT on sexuality is the role of the Specialist
I HAVE THE KNOWLEDGE TO TALK TO PATIENTS ABOUT (ranging from strongly agree to strongly disagree)		I HAVE THE KNOWLEDGE TO TALK TO PATIENTS ABOUT (ranging from strongly agree to strongly disagree)
the impact of an orchidectomy (removal of testes) on the patient's body image	adapted	the impact of HSCT on the patient's body image
the impact of cancer/treatment on the patient's male sexual function	adapted	the impact of HSCT on the patient's male sexual function
the option of sperm banking	adapted	the option of fertility preservation
the option of prosthesis	not adopted	
	supplemented with	the impact of HSCT on the patient's female sexual function
the impact of an erectile dysfunction		the impact of an erectile dysfunction
the impact of impotence	not adopted	
	supplemented with	the impact of vaginal dryness/atrophy
ejaculatory difficulties	not adopted	
	supplemented with	the impact of reduced sexual desire
their concerns regarding fertility		their concerns regarding fertility
how to carry out a testicular self examination	not adopted	

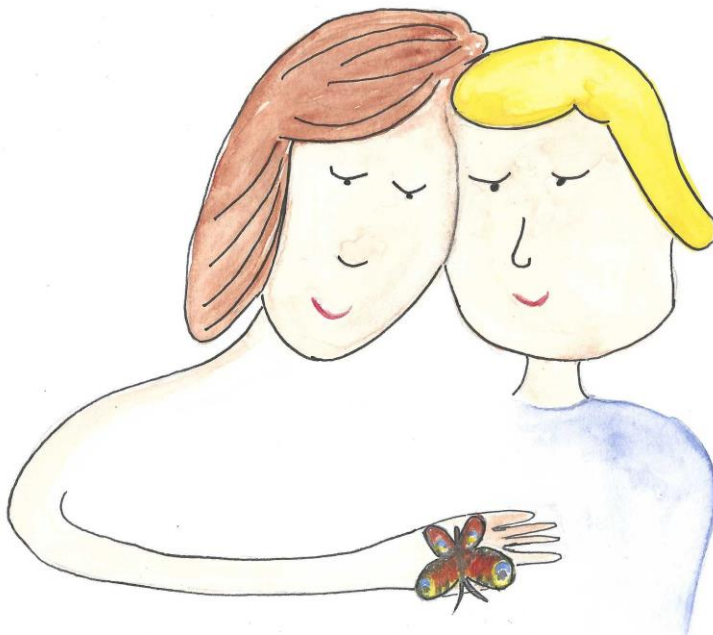
their concerns regarding future sexual relationships		their concerns regarding future sexual relationships.
their concerns to talking to their partner about sexual function		their concerns regarding talking to their partner about sexual function.
I have the capability to talk to patients who misinterpret the intentions of my questions		I have the capability to talk to patients who misinterpret the intentions of my questions
I AM COMFORTABLE TALKING TO PATIENTS ABOUT:(ranging from very comfortable to very uncomfortable)		I AM COMFORTABLE TALKING TO PATIENTS ABOUT:(ranging from very comfortable to very uncomfortable)
the impact of an orchidectomy (removal of testes) on the patient's body image	adapted	the impact of HSCT on the patient's body image
the impact of cancer/treatment on the patient's male sexual function	adapted	the impact of HSCT on the patient's male sexual function
the option of sperm banking	adapted	the option of fertility preservation
the option of prosthesis	not adopted	
	supplemented with	the impact of HSCT on the patient's female sexual function
the impact of an erectile dysfunction		the impact of an erectile dysfunction
the impact of impotence	not adopted	
	supplemented with	the impact of vaginal dryness/atrophy
ejaculatory difficulties	not adopted	
	supplemented with	the impact of reduced sexual desire
their concerns regarding fertility		their concerns regarding fertility
how to carry out a testicular self examination	not adopted	
their concerns regarding future sexual relationships		their concerns regarding future sexual relationships.
their concerns to talking to their partner about sexual function		their concerns regarding talking to their partner about sexual function
I have the capability to talk to patients who misinterpret the intentions of my questions		I have the capability to talk to patients who misinterpret the intentions of my questions
I WOULD BE RELUCTANT TO:(ranging from strongly agree to strongly disagree)		I WOULD BE RELUCTANT TO:(ranging from strongly agree to strongly disagree)
talk to a patient younger than me about the impact of testicular cancer on their sexuality	adapted	talk to a patient younger than me about the impact of HSCT on their sexuality

talk to a patient older than me about the impact of testicular cancer on their sexuality	adapted	talk to a patient older than me about the impact of HSCT on their sexuality
talk to a patient about the impact of testicular cancer on their sexuality if they were single		talk to a patient about the impact of HSCT on their sexuality if they were single
		talk to a patient about the impact of HSCT who is of a different sexual orientation
to raise a discussion about the impact of testicular cancer on their sexuality with a patient who is of a different culture	adapted	to raise a discussion about the impact of HSCT on their sexuality with a patient who is of a different culture.
raise a discussion about the impact of testicular cancer on their sexuality with a patient who is of a different religion		raise a discussion about the impact of HSCT on their sexuality with a patient who is of a different religion.
to raise a discussion about the impact of testicular cancer on their sexuality with a patient who I knew had a mental health problem	adapted	to raise a discussion about the impact of HSCT on their sexuality with a patient who I know has a mental health problem
	supplemented with	to raise a discussion about the impact of HSCT on their sexuality with a patient who I know is anxious
	supplemented with	to raise a discussion about the impact of HSCT on their sexuality with a patient who I know has a progressive disease
	supplemented with	to raise a discussion about the impact of HSCT on their sexuality with a patient who I know has GVHD
talk to patients of the opposite gender about the impact of testicular cancer on their sexuality	adapted	talk to patients of the opposite gender about the impact of HSCT on their sexuality
THE FOLLOWING WOULD FACILTATE ME TO TALK TO PATIENTS ABOUT THEIR SEXUAL CONCERNS:(ranging from strongly agree to strongly disagree)		THE FOLLOWING WOULD FACILTATE ME TO TALK TO PATIENTS ABOUT THEIR SEXUAL CONCERNS:(ranging from strongly agree to strongly disagree)
being told by another professional that the patient had concerns		being told by another professional that the patient had concerns
being asked questions by the patient regarding their sexuality		being asked questions by the patient regarding their sexuality
being prompted in the nursing care plan		being prompted in the nursing care plan

having clinical policies on how to address sexual issues	adapted	having standard operating procedures/ policies on how to address sexual issues
having received communication workshops that involved role play which would help to develop skills	adapted	having received relevant communication workshops/ training
having a private environment on the ward	adapted	having a private environment to have such discussions
having sufficient time to sit and talk to patients		having sufficient time to sit and talk to patients
to have known the patient for 2-3 weeks and have developed a good rapport		to have known the patient for 2-3 weeks and have developed a good rapport
having observed the CNS talking to patients about sexual issues	adapted	having observed an example of a team member talking to patients about sexual issues
having knowledge on the sexual difficulties testicular patients experience	adapted	having knowledge on the sexual difficulties HSCT patients experience
COMMENTS TO DISCUSSING SEXUALITY WITH TESTICULAR CANCER PATIENTS	adapted	COMMENTS TO DISCUSSING SEXUALITY with HSCT recipients
Please add any further comments you may have on discussing sexuality with testicular cancer patients	adapted	Please add any further comments you may have on discussing sexuality with HSCT recipients

Chapter 8

Recommended patient information sheet on the impact of haematopoietic cell transplantation on sexual functioning and sexuality



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Abstract

Sexual concerns are common after haematopoietic cell transplantation (HCT). Exposure to total body irradiation (TBI), alkylating agent and graft versus host disease (GvHD) can all affect sexual function, leading to problems in sexual desire, arousal and the orgasm phase of the sexual response cycle. In high-risk haematological malignancies, such as acute leukaemia and myelodysplastic syndromes, HCT often offers the highest chance for long-term survival. In addition, these haematological diseases and HCT can have an impact on body image, self-esteem, (sexual) relationship and psychosocial factors, all of which are able to affect sexuality and sexual function. Five years post HCT, 80% of the female survivors and 46% of the male survivors report sexual dysfunction.

It has been shown that these patients cope better after having discussed sexual health. While health-care providers (HCPs) have the responsibility to address sexual issues, it has been demonstrated that 48%–82% HCT recipients reported not having discussed sexual issues with their HCPs and that only one-third of the HCPs routinely discussed sexual issues with their patients. HCPs describe a lack of knowledge and being uncomfortable with the topic as the most important reasons for not addressing sexual functioning. Even so, it would help >90% HCPs if the patient initiated discussing sexual issues. However, to empower patients addressing sexual issues, adequate comprehensive patient information is needed. In an effort to better meet the patients' need, a patient information sheet: 'Information for patients undergoing Hematopoietic Cell Transplantation: the impact of the disease and treatment on sexual function and sexuality', has been created.

In this review, we describe what is known about the impact of HCT on sexual function and briefly the management of sexual problems.

Introduction

Recent improvements in the treatment of haematological malignancies have increased survival rates and life expectancy. This raises the important question whether and to what extent future (sexual) life is hampered by the side effects of cancer treatment, as sexual dysfunction is of importance for the quality of life of patients [1–3]. Sexual dysfunction is common in the general population, with 40%–45% of adult women, and 20%–30% of adult men, reporting at least one sexual dysfunction [4]. Apart from cancer-treatment-induced sexual dysfunction, risk factors for developing sexual dysfunction are older age, inferior general health status, the presence of comorbidities (e.g. diabetes mellitus, cardiovascular disease, urinary tract infections, psychiatric or psychological disorders) and socio-demographic factors such as being female and having no committed partner [5, 6]. The pathophysiology of sexual dysfunction is heterogeneous, ranging from biological (e.g. vascular, hormonal, neurological, urological, iatrogenic, psychiatric, obesity or poor health) and psychological (e.g. emotional problems, depression and anxiety) to social causes (e.g. sexual abuse, alcohol/tobacco/opioids/ recreational drug abuse, marital problems, difficulty talking about the sexual relationship with the partner, no sexual partner, sexual dysfunction in the partner, low education and unemployment) [4, 7, 8]. Cancer treatment, especially haematopoietic cell transplantation (HCT), is known to affect all these domains, which will be discussed hereafter [9–15].

Patients and their partners want information regarding the effects of illness, treatment and disability on sexuality and intimacy [15, 16]. This (unfulfilled) information need and the attitude of the health-care providers (HCPs) towards addressing sexuality [13, 17, 18] have heightened the need for easy available information for patients and their partners. In an effort to better meet this need, a patient information sheet: ‘Information for patients undergoing Hematopoietic Cell Transplantation: the impact of the disease and treatment on sexual function and sexuality’, has been created. Topics cover aspects that may affect sexuality and intimacy. Our aim is to make the patient information on sexuality accessible and understandable to patients and their partners. It is hypothesised that this information may facilitate the patient in the discussion of expected sexual problems with their HCP, where necessary.

The impact of haematopoietic cell transplantation on sexual function

Sexual problems following autologous and allogeneic HCT are common. In high-risk haematological malignancies, such as acute leukaemia and myelodysplastic syndromes, HCT often offers the highest chance for long-term survival. In order to identify literature with respect to sexual function and HCT, a comprehensive search was carried out from the bibliographic databases PubMed and EMBASE from

inception till February 20, 2018. Search terms included controlled terms from MeSH in PubMed and Ebsco for CINAHL/PsycINFO. The full search can be retrieved from the corresponding author. To understand sexual dysfunction during and after HCT, we included only longitudinal studies, and three prospective studies were identified [12–14]. Humphreys et al [13] showed decreased sexual activity among HCT survivors at 1 and 3 years post HCT compared to pre-HCT. About 60% were sexually active before HCT and 40% at 3 years post HCT. Problems with sexual desire ranged between 33% and 78% and arousal difficulties between 22% and 78%. Women are more likely than men to report sexual difficulties [13]. In addition, Humphreys et al [13] examined sexual functioning and communication regarding this issue with their health-care provider in recipients of allogeneic stem cell transplantation from pre-transplant to 1 and 3 years post-transplant. In addition, those patients who discussed their condition with an HCP reported better sexual function.

In the prospective case-matched controlled study by Syrjala et al [12], the sexual function of 161 survivors was evaluated from pre-transplant up to 5 years post HCT. In addition, sexual function in this population was compared with controls from the general population. Five years after treatment, 80% of female survivors versus 61% of female controls and 46% of male survivors versus 21% of male controls reported sexual dysfunction. While the sexual function of female survivors was not improved at 5 years post HCT, the sexual function of the male survivors was improved at 2 years, however, not to the level of sexual function reported by controls. The aetiology is not exactly known; however, the fact that hypogonadism can recover in men, which is not very likely in women, may play an important role [19]. In addition, in general, women appear to report sexual difficulties more often [4].

Wong et al [14] found that chronic graft versus host disease (GvHD) in both genders contributed negatively to sexual dysfunction and dissatisfaction during the 3 years following HCT. Both men and women with chronic GvHD reported a negative impact on several domains of sexual function, and in addition, women with chronic GvHD reported significantly poorer sexual satisfaction.

In addition, other reports indicated that both disease and treatment can have an impact on body image, self-esteem, (sexual) relationships and psychosocial factors, all of which can negatively impact intimacy, sexuality and sexual function [7, 20].

The causes of sexual dysfunction in haematopoietic cell transplantation survivors

HCT is associated with acute and chronic side effects that can result in alterations in sexual functioning. Acute side effects of chemotherapy and total body irradiation (TBI; e.g. nausea, vomiting, hair loss and fatigue) can induce loss of sexual desire [21]. Several anti-cancer drugs are known to affect the biology of the gonadal function and in HCT survivors alkylating agents are suggested to be the main cause of sexual dysfunction. In 99% of female and 92% of male HCT survivors, premature menopause [22–24] and hypogonadism [23, 25, 26] are observed [27]. Problems with sexual interest/desire may be explained by the impact on testosterone—a driver of sexual desire. Premature menopause can lead to vaginal and/or vulvar atrophy, causing continuous discomfort and/or pain, and vaginal dryness during sexual activity, negatively affecting interest and desire. TBI is similarly toxic for gonadal function, but can also impair peripheral nerves and pelvic blood flow [28]. Physical sexual arousal (e.g. erectile function and vaginal lubrication) is mainly guided by circulation and good neural synapses. When one of these is disrupted, men can experience difficulties in developing or maintaining an erection during sexual activity while women can experience difficulty in becoming lubricated.

In the long term, GvHD [14, 29, 30] may also lead to sexual dysfunction with genital GvHD directly impacting sexual function. The first presentation of male genital GvHD is often dyspareunia (difficult or painful sexual intercourse) or urinary difficulties. Inflammatory and non-inflammatory genital skin changes with erectile dysfunction are significantly more frequent in patients with genital GvHD: 80% with genital GvHD versus 36% in patients with non-genital GVHD [30]. For women, the first complaint of genital GvHD is also dyspareunia or urinary difficulties often with similar symptoms (vulvovaginal dryness, pruritis, burning, pain, dysuria, dyspareunia and at times, bleeding) and genital atrophy due to oestrogen deficiency [20].

Communication about sexual issues

It is clear that HCT survivors cope better after having discussed sexual health [13]. In addition, early recognition and management of sexual dysfunction can lead to improved sexual function and quality of life for HCT survivors and their partners. HCPs have the responsibility to address sexual issues. Nevertheless, sexual dysfunction is an issue that HCPs, as well as patients, find difficult to discuss. A survey among HCPs of the European Society for Blood and Marrow Transplantation (EBMT) showed that a lack of knowledge and being uncomfortable with the topic contributed to avoiding discussions on sexual dysfunction. The majority of HCPs (>90%) were reluctant to discuss the topic feeling it would be more appropriate if the

patients themselves initiated the discussion regarding sexual issues [18]. Most HCPs felt they had not received appropriate training to address sensitive issues like sexual health [31], were often too embarrassed to ask about sexual concerns or thought that the decline of sexual function is a normal event. In general, sexual issues are not routinely discussed with HCT recipients with 48%–82% of the recipients reporting not having discussed sexual issues with their HCP [13, 17, 32]. Therefore, it is not surprising that many patients and their partners were disappointed by the lack of information, support and practical strategies provided by health-care professionals [15, 16].

It is not only important that survivors are informed about the impact that HCT might have on both sexuality and sexual function, information should also be tailored to the individual. For some, knowing that sex and reproduction are affected is sufficient, and they do not always need support in case of sexual dysfunction. However, other survivors need to know whether treatment or support is available. Apart from extensive patient information, HCT recipients should be questioned about urinary symptoms and sexual health. Part of the regular patient follow-up can identify patients with genital GvHD resulting in timely referral for adequate management [30].

Treatment strategies for sexual dysfunction

Treatment of sexual dysfunction is dependent on the cause(s). Although the main focus of this review article is supplying patient information, we provide a concise overview of management suggestions and interventions.

Within HCT, the efficacy of the majority of the biological interventions for sexual problems has not yet been demonstrated [14]. However, several treatment options for sexual dysfunction are said to be worth trying [21]. As most patients perceive some changes in sexuality and sexual function after HCT, they need to rebuild their sexual life. Consequently, when patients report sexual difficulties, it is important to ask about the partners' feelings and whether the couple are able to discuss this within the relationship. If necessary, communication about the sexual relationship with the partner should be promoted. In case of fatigue, pain or other complaints, the patient should be advised to rest or to use analgesia before sexual activity, or other appropriate advice regarding symptom management should be given.

In the case of sexual problems due to hypogonadism and erectile dysfunction, testosterone and phosphodiesterase type 5 inhibitor (PDE5 inhibitors) can improve sexual function [28, 33–35]. For treatment or prevention of postmenopausal vaginal atrophy, various options are available, such as hormonal

replacement therapy (systemic and topical) [36]. Vaginal lubricants and moisturisers are available to prevent or minimise dryness and pain during sexual activity in case of vaginal atrophy or decreased vaginal lubrication [36]. There are several health-care professionals and disciplines that may facilitate patient management.

- (a) Nurse practitioner, clinical nurse specialist.
- (b) Social worker or psychologist in case of relational difficulties.
- (c) Pelvic physiotherapy in case of dyspareunia or vaginal pain when having sexual intercourse and when vaginal lubricants do not give relief.
- (d) Male/female sexologist in case of need for intensive treatment after all specific suggestions have been tried.
- (e) Urologist, andrologist in case of ejaculation disorders or Peyronie's disease.
- (f) Patient group or patient organisation providing peer support.

In cases where there is a suspicion or clinical manifestation of genital GvHD (such as genital changes, urinary symptoms or sexual concerns), patients should be referred either to a gynaecologist, dermatologist, urologist or other clinicians trained in the assessment and management of genital GvHD, for assessment and management of genital GvHD [20].

Patient information

Assuming that HCPs can provide understandable patient information, many cancer patients cannot recall that sexual changes were discussed, while other patients are not satisfied with the information that was given [15, 16]. The majority of patients prefer verbal and written information [32]. Therefore, this combined approach is preferable.

Earlier work by Gamel et al [37] has shown that informational needs regarding sexuality vary across the treatment trajectory. Prior to treatment, the effects of HCT on sexuality should be explained so that, at the time of discharge post HCT, patients may know which sexual activities are restricted and for how long. Awareness of symptoms, monitoring and reporting to HCPs are also important. At the time of rebuilding their sexual life, suggested to be 1 year post HCT [17, 38, 39], patients should be informed about most

frequently occurring sexual dysfunction post HCT [37]. During the entire patient information process, patients should be advised that sexual changes are common and given reassurance.

Patients consider medical and treatment information in the context of haematological malignancies of higher priority than psychosocial information [40, 41]. Thus, for most people, sexuality is of minor importance compared to treatment-related issues and survival [40]. However, this only means that the impact of HCT on sexual function is less relevant at that time. As patients return to a 'normal life', sexual dysfunction might well become more pressing after the first year post HCT. Patients seem to report impairment of sexual function at earliest 1 year post HCT [17, 38, 39], therefore ideally, from this moment, HCPs should start routinely addressing sexuality.

Conclusion

The sexual dysfunctions that HCT survivors face are decreased sexual activity, less sexual desire, erectile dysfunction or decreased vaginal lubrication, sexual pain (dyspareunia), orgasm problems and genital changes. Five years post HCT, survivors still report sexual dysfunction. Sexual function of female survivors is not likely to improve without any intervention, whereas sexual function of male survivors might improve within the first 2 years without intervention. HCT survivors need to be informed about the impact that HCT can potentially have on both sexuality and sexual function, because survivors need to be aware of the changes and the support that is available. Patient education can prevent deteriorating sexual function but, without preparatory information, it is more difficult to initiate the required discussions.

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Conflicts of interest

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Appendix: patient information sheet for patients undergoing HCT: the impact of the disease and treatment on sexual function and sexuality

Sexual dysfunction is a common phenomenon throughout the general population. Often this is influenced by psychological or social factors, but certain chronic diseases can be a direct cause. It is certainly possible that HCT may have an impact on sexual function and related intimacy and sexuality. This may be reflected in negative feelings about one's body image, self-esteem and sexual relationship.

What are the acute side effects of the HCT that can affect sexuality?

During the treatment period, the acute side effects of chemotherapy, such as nausea, vomiting, hair loss and fatigue, will most probably lead to a reduction in the desire for sexual activity. Certain treatments, such as chemotherapy with alkylating agents or TBI, can suppress the function of the ovaries and testicles, causing a reduction in male or female hormone production. In men, the low testosterone level can cause problems with erectile function, while in women, premature menopause with vaginal dryness and pain during intercourse. TBI could impair peripheral nerves or pelvic blood flow, causing erectile dysfunction in men or vaginal dryness in women.

What are the long-term effects of the HCT that can affect sexuality?

Frequently reported problems with sexual function are reduction in sexual desire (often through a negative body-image or not feeling sexually attractive), arousal difficulties (erectile dysfunction in men or vaginal dryness in women), pain during intercourse and absence of orgasm. Chronic GvHD can lead to various sexual problems in men and women. The first presentation of genital GvHD is often painful sexual intercourse, urinary difficulties and genital skin changes (such as inflammatory and non-inflammatory lesions in men, vulvovaginal dryness/itching/pain/bleeding in women).

Should sex be avoided?

In order to maintain or rebuild a satisfactory sexual relationship between you and your partner, it is important that intimacy and sexual activity is not avoided. There is no medical reason to avoid sexual intercourse as long as this does not cause bleeding or pain. It is realistic that sexuality will change, try not to force but be gentle and use lubricants, especially when platelets are low. Pregnancies do occur after HCT; however, pregnancy should be avoided soon after the treatment. Therefore, it is advised to use contraceptive methods at least until you know what your fertility status is.

Should sexual problems be reported?

Yes, it is important to report sexual problems to your HCP because in some cases they may indicate medical problems which need to be referred to another medical specialist for treatment. In particular, genital changes or urinary symptoms may indicate GvHD.

How can sexual problems be managed?

It is important to pay attention to any difficulties as they strongly influence the recovery of the patient. There are several treatment options and several disciplines that can help to manage sexual problems. Some of the examples of treatments are as follows.

- (a) Testosterone and phosphodiesterase type 5 inhibitors [Viagra, Cialis] can improve sexual function in the case of hypogonadism and erectile dysfunction.
- (b) Hormone replacement therapy (HRT) can prevent postmenopausal vaginal atrophy, besides it can also help women experiencing lower desire, orgasmic difficulties and sexual pain. Topical oestrogen can also help vaginal health in addition to non-hormonal moisturisers and lubricants.
- (c) Vaginal lubricants and moisturisers can minimise dryness and pain.

The disciplines that are on hand to help from coping with the problems to actually manage these problems are: nurse practitioners, clinical nurse specialists, social workers, psychologists, psychosexual therapists, pelvic physiotherapists, gynaecologists, dermatologists, urologists, andrologists, sexologists, patient groups or patient organisations.

Sexual problems that occur after HCT are often caused by the disease or the treatment. Early recognition and management of sexual problems can lead to improved sexual function and quality of life for you and your partner. Tell us about it.

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Chapter 9

General Discussion



General Discussion

The main aim of this thesis is to obtain more knowledge on sexual (dys)function that patients with hematological malignant (HM) diseases may face during and after treatment, on the need for information on sexuality among HM survivors, and on the way health-care providers (HCPs) address sexuality in clinical practice. This knowledge is crucial to develop tailor-made guidelines for high quality information on sexuality for HM survivors in the future.

In order to provide solid evidence for future guidelines three topics were investigated;

1. To determine to what extent information on sexuality is needed, the prevalence of sexual problems among patients with HM diseases was determined. As prevalence is highly dependent on how 'sexual problems' are defined the different nomenclature to indicate the presence of sexual problems was described. In addition, the factors that could be associated with sexual problems, such as fertility status, sociodemographic and clinical characteristics were investigated.
2. To provide data that can be used to tailor information on sexuality, the information needs on sexuality were investigated, not only among patients with HM diseases but also among their partners. This information was obtained during the first 18 months of treatment.
3. Finally, it was investigated how often HCPs throughout Europe actually discuss sexual issues with HM patients, and what are the main barriers and facilitators for discussions on sexuality with patients.

Knowledge of the human sexual response cycle is fundamental to understand sexual (dys)function [1, 2]. The models that represent human sexual function distinguish four different phases of sexual function [1, 3, 4]. Changes in sexual function or actual sexual dysfunction according to Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [5] can occur after a disruption in one of these phases of the sexual response cycle: desire, arousal, and orgasm. In addition, sexual dysfunction can also occur as a result of pain upon penetration and overall difficulty having intercourse (dyspareunia). Lastly, changes in sexual function can impact the sexual relationship, as we know that an active and satisfying sex life is easily set aside when a serious illness is involved [6]. To measure changes in sexual function, at least all the phases of the sexual response cycle, dyspareunia and the impact on the sexual relationship should be assessed.

1. Sexual problems among patients with HM diseases; definition, prevalence and associated factors.

In a systematic literature review on sexual problems among patients with HM diseases (Chapter 2) we found in the high quality papers that sexual problems occur in 18-50% of Acute Myeloid Leukemia (AML), Hodgkin lymphoma (HL), and non-Hodgkin lymphoma (NHL) patients from diagnosis until 3.5 year after diagnosis [7-9]. Advanced-stage HL patients prior to treatment reported the highest prevalence of sexual problems [7]. Based on evidence from Chapter 3 and 4, prevalence of sexual dysfunction is estimated at 31% (females) to 20% (males) in HL survivors and comparable to the general population. Erectile dysfunction was estimated at 23% in both HL patients and controls. However, more HL males perceived sexual problems than controls (20.0% vs 7.0%; $P = .087$). Watson et al. and Beckjord et al. reported prevalence rates of 18-35% among respectively patients with AML and NHL after treatment [8, 9]. Nevertheless, there is not enough data yet to understand the exact impact of HM treatment on sexual functioning of HM patients. There are various aspects to consider to understand why (the prevalence of) sexual problems in HM patients is heterogeneously reported. The systematic literature review (Chapter 2) showed that only one study measured all the phases of the sexual response cycle, dyspareunia and the impact on the sexual relationship [8], and two studies measured frequency of sexual activity, desire, arousal and satisfaction [10-12]. All other studies assessed only three domains or even fewer. Evaluation of sexual function in men and women should at least include all phases of the sexual response cycle, painful intercourse and the impact on the sexual relationship [1-4]. In order to get complete insight into the prevalence and the character of sexual problems, the “gold standard” was used for measuring sexual function in cancer populations in Chapter 3 and 4. In the cross-sectional study among female Hodgkin lymphoma (HL) survivors (Chapter 3) the Female Sexual Function Index (FSFI) was used [13]. This validated questionnaire assesses six domains: desire, arousal, lubrication, orgasm, satisfaction, and pain, and provides an overall score for sexual function [14]. The validated International Index of Erectile Function (IIEF) used in a study among male HL survivors (Chapter 4) assesses five domains: desire, erectile function, orgasm, intercourse satisfaction, and overall satisfaction [15]. The IIEF quantifies the level of erectile dysfunction [16] and for the other domains no standard reference cut-offs are available; a higher score indicates better sexual function [15, 16]. In recent years, two promising tools for assessing sexuality in cancer survivors have been developed. The National Institutes of Health's Patient-Reported Outcomes Measurement Information System® (PROMIS®) Network developed the PROMIS Sexual Function and Satisfaction Measure (SexFS). This is an item bank which includes many different familiar and less familiar

domains. In total, there are 131 items in 18 domains [17-19]. A brief SexFS is available, including 8 items for males, and 13 items for females [19]. The European Organization for the Research and Treatment of Cancer (EORTC) has developed the 22-item Sexual Health Questionnaire (EORTC SHQ-22), a validated questionnaire for the assessment of physical, psychological, and social aspects of sexual health in cancer patients and survivors [20]. The SexFS and EORTC SQH-22 measure patients' perceptions of their sexuality by items that have been explicitly reported as relevant by patients themselves, and are meant to be used for all genders. However, no cut-off values are available (yet). All above mentioned outcome measures have advantages and disadvantages. Selection of an outcome measure highly depends on the aim of a project. It is highly likely that the use of different outcome measures at least partly explains the differences in reported prevalence of sexual problems in HM. In addition, while the majority of patients diagnosed with HM is over the age of 65, sexual outcomes were measured among a fairly young study population (age between 30 and 44 years old (range 18-90)). Furthermore, most of the studies (n= 22) were cross-sectional cohort studies (with assessment ranging from the first year to 25 years after diagnosis), which hampers thorough understanding of the evolution of sexual problems over time. Lastly, the impact of novel therapies (e.g. immunotherapies, methylating agents, and targeted therapies) on sexual problems in HM patients needs to be investigated. Novel therapies are increasingly used as standard treatment in HM. Nonetheless, it can be concluded that sexual problems often occur in patients with HM diseases, due to the disease as well as the treatment [21, 22]. Sexual concerns are especially common in patients with HM disease after Hematopoietic stem Cell Transplantation (HCT). Even five years post HCT, up to 80% of the female survivors and 46% of the male survivors report sexual dysfunction [23]. Exposure to total body irradiation, high dose alkylating agents, and graft versus host disease are known to affect sexuality after HCT [24-27].

Factors were investigated that could be associated with sexual problems, such as fertility status, sociodemographic and clinical factors. The systematic review in chapter 2 did not focus on fertility status. In the cross-sectional study on female HL patients in Chapter 3 overall sexual dysfunction was most common in females who perceived themselves as infertile), which is in line with the literature [28, 29].

With respect to sociodemographic and clinical factors, in male HL patients, type of treatment may be associated with sexual problems: 33.3% patients treated with BEACOPP (versus 8,3% without BEACOPP) reported more sexual problems ($p=0.57$), in particular a lack of desire and problems with arousal (Chapter 4). Given the type of these sexual problems, hypogonadism as a result of the gonadal effect due to the alkylating agents, probably plays a role [7, 21, 30-37]. This is important in daily clinical practice because of the increased use of BEACOPP as standard therapy in advanced stage HL. HCPs should be aware of

possible sexual problems after BEACOPP and, if needed, offer counseling regarding the increased risk for infertility and sexual problems during clinical consultation [2, 24, 38-41].

2. What are the information needs on sexuality among patients and partners within the first 18 months of treatment for HMs?

The literature review on information needs in patients with HM (Chapter 5), showed that information needs regarding sexuality was underreported in patients with HM. Four of the fourteen included studies included sexuality. Two of these studies reported that sexuality was of low priority while the other two studies reported that patients had a need for information about sexuality. In addition, one study described that half of the patients evaluated the patient information about sexuality they received as insufficient. The literature review also showed that knowledge is lacking on the need for information among intimate partners, or whether the need for information about sexuality changes over time. Further research was conducted and examined patients with HM and their partners participating in a longitudinal cohort study on information needs (Chapter 6). During a time frame from diagnosis to 18 months follow-up, approximately half of the patients and their intimate partners expressed a persistent need for information on sexuality. The information they needed comprised changes in sexuality, support for sexual problems, and precautions to be taken. Although younger male patients and younger intimate partners with a monitoring coping style had the highest need for information, also patients and partners of 70 years and of female gender had informational needs. It can be concluded that all HM patients and their partners need to be informed about sexuality [24, 38, 42].

3. How often do HCPs throughout Europe discuss sexual issues with HM patients, and what are barriers and facilitators to communication?

We found that only one-third of HCPs routinely discussed sexual issues with their patients (Chapter 7). Earlier work has shown that a proactive approach to sexual health is not a part of routine oncological practice either [43-46]. In order to improve patient information about sexual dysfunction related to disease and treatment and to create awareness for sexual problems that may be encountered in clinical practice, we investigated what the reasons were for not discussing sexual issues. In line with the literature we found that a lack of training was one of the major barriers [47-51]. Despite the exact impact of the diagnosis and treatment of HM on sexual function is still unknown, when sexual problems occur after cancer therapy, they can be severe [22], and do not resolve without support (Chapter 3 and 4). Crucially, patients need to be informed about the sexual changes upfront because otherwise it is impossible for them to address the issue.

Besides, patients who received sexual education reported a significantly better sexual outcome after HM treatment [27, 52, 53]. Based on our findings, we advise HCPs to initiate sexuality by providing adequate information regarding sexuality to patients treated for HM and their partners, starting at the point of diagnosis and continuing at follow-up visits. However, awaiting results of future research to follow, it would help the conversation by starting with asking patients about their sexuality and learning where to refer patients with sexual problems. HCPs can learn by doing, eventually they will become more comfortable and knowledgeable about discussing sexual issues. The use of the Permission, Limited Information, Specific Suggestions, Intensive Therapy (PLISSIT) model may facilitate HCPs in providing tailored information [54, 55].

Strengths and limitations of this thesis

The strength of this thesis is that we have set a solid base on how to proceed. Firstly, by performing the first systematic review about the prevalence of various sexual problems in survivors of HM diseases we have found that extensive longitudinal prospective studies using validated questionnaires among the real life population HM patients that have been treated with current therapies have not yet been performed. Secondly, to start a baseline on self-reported sexual function in HL survivors we used the standardized and validated questionnaires to measure sexual function, and compared sexual function between HL survivors and controls. Thirdly, we have demonstrated that patients and their intimate partners have a constant high need for information about sexuality while a minority HCPs routinely raises the topic.

Several limitations should be taken into account when interpreting the findings of this thesis. An important limitation of both cross-sectional survey studies among HL survivors (Chapter 3 and 4) was that many survivors were not reached. There might be an overrepresentation of healthy HL survivors, and sexual problems among HL survivors may have been underestimated. In our study among European HCPs (Chapter 7) an overrepresentation of HCPs interested in discussing sexuality with their patients were more likely to participate in the study, and this might indicate that the problem of not discussing sexual concerns may have been underestimated.

Implications for clinical practice

In our opinion, appropriate training about the impact of HM on male and female sexuality and how to discuss this sensitive topic should be included in future education programs for HCPs. Until more results of

future studies are available we recommend the following algorithm for addressing sexual function in HM survivors [2].

It is essential that all patients and partners are informed about the changes in sexuality that may occur, safety of having sex during and after cancer treatment, and how to cope with the lack of sexual desire and arousal difficulties [24, 38-40]. There is evidence that the majority HCT patients prefer verbal and written information on sexuality [56]. Therefore, at least a patient education sheet materials about the impact of the disease and treatment on sexual function and sexuality should be offered (Chapter 8). In addition, practical suggestions for preventing or overcoming problems, present patient anecdotes and strategies to try as an individual or a couple are of importance [24, 56]. During the entire patient information process, patients should be advised that sexual changes are common and be given reassurance that further help is possible.

To identify a sexual problem during follow up, there is a need to assess sexual function regularly. HCPs are advised to initiate the topic by asking: “Many patients after cancer treatment and their partners have sexual health concerns, do you or your partner have any concerns?” In the meantime, assessment of the reproduction function of the patient by laboratory tests should be performed [39, 57, 58]. In both studies (Chapter 3 and 4) we detected sexual dysfunction by screening sexual problems using the following 3 questions; 1) Do you perceive a sexual problem?, 2) If yes, please define the problem(s), and 3) Did the problem(s) improve, remain unchanged, resolve or worsen since treatment for HL began? Initiating the topic can also be done by using the three questions, or by a patient reported outcome measure (PROM) [2, 59, 60] such as the validated brief PROMIS Sexual Function and Satisfaction Measure (SexFS) [19].

After patient information and regular assessment of sexual function, the actual conversation between patients and HCPs can begin. If the patient has concerns and is willing to talk about problems, the use of a communication frameworks with a multilevel approaches [61, 62] can be useful to properly intervene, from promoting communication to referral to a dedicated specialist. Numerous models are available for supporting communication about sexual health in medical settings, like the 5A's model (Ask, Advise, Assess, Assist and Arrange Follow-up) [63], the BETTER model (Bring up, Explain, Tell, Timing, Educate, and Record) [64] and the PLISSIT model (Permission, Limited Information, Specific Suggestions, and Intensive Therapy)[55]. El-Jawahri et al. demonstrated that HCPs who received a short training were competent to assess and address sexual health concerns of patients after HCT [27]. Experience within the author’s team shows that a chosen team member able to handle these referrals is desirable. It will encourage

HCPs to touch the topic and saves time and embarrassment and accelerates patients' satisfaction and knowledge.

In order to assist HM patients to cope with various sexual problems and the consequences for the sexual relationship, further research is needed to study whether the approaches which have been shown effective among HCT patients regarding patient-information and addressing sexual function are effective enough to prevent deterioration of sexual function also in HM patients without HCT.

Recommendations for future research

In order to develop guidelines for high quality information on sexuality for HM survivors in the future, further research on several areas is urgently needed. The field is important because the prognosis of patients with HM diseases has greatly improved [65], therefore as patients live longer, it is assumed that sexual issues will become even more important. Secondly, sexual problems might easily be prevented by routinely discussing sexuality [27, 52, 53]. So as to obtain a better understanding of how often sexual problems occur among all adult patients treated for HM within the first years after diagnosis, a longitudinal prospective approach is needed to investigate the extent and severity of the sexual problems. Although sexual problems are important to address irrespective of whether the prevalence is equal or higher than in the general population, from a scientific point of view it is important to compare data in a control group. Only this will learn which disease- or treatment-related factors are important in the pathogenesis of sexual problems in patients with HM. Furthermore, when designing future studies we recommend the following: 1) patients of all ages that reflect HM patients should equally be included, and 2) the impact of all the novel therapies in HM needs to be included. Adequate self-report measures of sexual function, that do include all important domains for sexual function, are the SexFS [17-19], and the EORTC SHQ-22 [20]. Both SexFS and EORTC SHQ-22 provide comparison to the general population. However, further research on the validity of the SexFS and the EORTC SHQ-22 of these patient-reported outcome measures in HM patients is recommended.

Conclusions

This thesis provides evidence that sexual problems occur in 18-50% of fairly young HM patients who have been treated with traditional treatments such as chemotherapy and radiotherapy. Although this may be comparable to the general population in certain patient groups, firstly we expect a higher incidence of sexual problems in a considerable number of patients indicating the need for special attention. Secondly, even if

comparable to the general population it is important to address the issue of sexual problems. Patients clearly have an ongoing need for information on sexuality and others found that sexual outcome is improved by discussing and sexual education. However, it appears that only one third of medical doctors and registered nurses working in Hematology in Europe discuss sexual issues with their patients. Barriers for effective communication according to these HCPs is discomfort, and a lack of knowledge and relevant education. The findings of this thesis contribute to develop guidelines for high quality information on sexuality tailored to HM survivors.

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Chapter 10

Summary

Samenvatting

Summary

Chapter 1 is the general introduction to this thesis. In recent years the prognosis of patients with a hematological malignancy (HM) has greatly improved due to an increasing treatment armamentarium. Consequently, the long-term impact of anti-cancer treatment is becoming increasingly important. Sexuality is one of the domains that is negatively affected not only during treatment but also following treatment. Many cancer survivors desire and deserve a “normal life”, and sexual gratification and emotion is seen as an integral part of this future life. However, it seems that health-care providers (HCPs) are often unaware of the sexual problems that patients experience, as not only patients feel reluctant to discuss these problems, also HCPs do not address sexuality for the same reason. In addition, detailed insight into sexual function as such and into the way HCPs and patients address sexual problems in routine care is scarce. The main aim of this thesis was to obtain more knowledge on sexual (dys)function that HM survivors may face during and after treatment, how health-care providers address sexuality in clinical practice, and on the need on information among HM survivors. This knowledge is crucial to develop high quality information on sexuality tailored to HM survivors in the future.

Chapter 2 consisted of a systematic review investigating the prevalence of various sexual problems among patients treated for HM to improve understanding of the impact on sexuality during treatment and survivorship period. We found 24 studies that met our criteria. Methods differed across studies, with 14 of the 24 studies lacking validity data, and only six studies comparing sexual problems with a general population. Based on the few high quality studies, it is estimated that sexual problems occur in 18-50% of Acute Leukemia, Hodgkin lymphoma, and non-Hodgkin lymphoma patients. Sexual problems may be common among HM patients, but unfortunately, the results doesn't really contribute to our understanding of the extent of the problem. Nevertheless, the outcomes were measured inconsistently making the results difficult to generalize. Moreover, we concluded that sexual dysfunction is either not reported or underreported in patients and survivors of most HM. Future studies are needed to gain more insight in the extent of sexual problems among HM patients.

Chapter 3 concerned a cross-sectional study in which we compared self-reported sexual function of young female Hodgkin lymphoma (HL) patients with a normative population. We determined the association between perceived fertility status (as reported by female HL survivors) and sexual function. We showed that 31% HL survivors reported a sexual dysfunction which is actually comparable to the general population. Patients who considered themselves as not being fertile more often (63%) reported sexual dysfunction ($p=0.07$). In addition, when focusing on the sexual domains, HL patient reported more often problems with sexual desire, arousal, lubrication, satisfaction and pain compared to the normative controls. Regarding the development of the sexual problem, none of the patients reported recovery.

Chapter 4, to form a baseline on sexual dysfunction following HL in sexually active male survivors, we performed a cross-sectional study in which we compared self-reported sexual function of male HL patients with age matched controls. In order to investigate who is at greatest risk for sexual dysfunction, we examined whether sociodemographic factors and treatment regimen were associated with sexual dysfunction. Lastly, we investigated whether reporting to perceive sexual problems was indicative for sexual dysfunction. The results showed that erectile dysfunction (ED) occurred in 23.3% of the HL survivors versus in 23.0% of controls: respectively 13.3% and 12.3% had moderate to severe erectile dysfunction moderate to severe ED. None of the HL survivors who were treated with ABVD perceived sexual problems. However, one third of HL survivors who were treated with BEACOPP did, they reported mainly problems with sexual desire and erectile dysfunction. Importantly, we found that HL survivors who reported to perceive sexual problems the mean International Index of Erectile Function (IIEF) score for erectile function was 15.7 (moderate erectile dysfunction) versus 28.3 (normal) in those without perceiving sexual problems. Therefore, sexual dysfunction can be easily detected early by screening on sexual problems using 3 questions only.

Chapter 5 described a literature review to provide insight into the perceived need for information of patients with haematological malignancies. We found fourteen studies that met our criteria. Overall, the perceived need for information and satisfaction with the information provided differs strongly between patients. Focusing on sexuality, this was addressed by four of the fourteen studies. Two of these studies reported that sexuality was of low priority while the other two studies reported that patients had a need for information about sexuality. In addition, one study described that half of the patients found the patient information about sexuality insufficient.

Chapter 6 described a Letter to the Editor to: “Discussing sexuality in cancer care: towards personalized information for cancer patients and survivors”. We performed a multicenter longitudinal survey to measure the need for information among patients with HM and their intimate partners during the first 18 months of treatment. To identify information needs on sexuality, six questions were developed for this study. Over 18 months from diagnosis, range 42 to 48% of patients (n=266) expressed a need for information regarding changes in sexuality, 40-44% expressed a need for support for sexual difficulties, and 41-46% expressed a need for precautions that need to be taken. Regarding their partners (n=134), 34-52% expressed a need for information regarding changes in sexuality, 39-50% expressed a need for support for sexual difficulties, and 34-53% expressed a need for precautions that need to be taken. Multivariable analyses revealed that information needs of patients regarding changes in sexuality and precautions to be taken were associated with younger age, male sex, and a monitoring cognitive coping style. A need for support was associated with younger age and a monitoring coping style. For their partners, multivariable analyses revealed that information needs regarding changes in sexuality and precautions to be taken were associated with younger

age. A need for support was associated with seeking information on the internet. In contrast to the patients, information needs were not associated with gender of the partner.

Chapter 7 described the results of the survey among the members of the European Society for Blood and Marrow Transplantation to evaluate the frequency and barriers and facilitators to discussing sexual issues. We investigated the barriers among health-care professionals to discussing sexual issues and the differences between complete responders versus incomplete responders and the frequency of discussing sexual issues. The study showed that one-third medical doctors (MDs) and registered nurses (RNs) routinely discussed sexual issues. The major perceived barriers were limited knowledge, feeling uncomfortable discussing sexual issues, the presence of a relative, and the preference of patients raising sexual issues themselves. Younger MDs and those who work in non-western European countries, plus RNs who have received less sexual education, as well as MDs and RNs with limited knowledge about the long-term sexual complications of hematopoietic cell transplantation (HCT). Follow-up studies are needed to assess patients' need for information on sexual concerns, as described in **Chapter 6**. Follow-up research should also provide insight into how sexuality best can be communicated.

Chapter 8 described the impact of HCT on sexual function, the pathophysiology, and briefly the management of sexual problems. For this, we extracted some of the findings of our systematic literature review (in relation to sexual function and HCT) (**Chapter 2**). In an effort to better meet the informational need of patients, a patient information sheet: “Information for patients undergoing Hematopoietic Cell Transplantation: the impact of the disease and treatment on sexual function and sexuality,” has been created.

Chapter 9 summarizes the results of this thesis, and describes the implications and gives recommendations for follow-up research. From the studies that have been done so far, too little is known to describe the actual impact of HM on sexuality. Half of patients and their intimate partners need this information. Unfortunately, the lack of knowledge about the long-term effects of treatment on sexuality among medical doctors and registered nurses prevents patients and their partners from getting the information they need. The chapter consists of 2 parts. The first part is to provide insight into what is known about sexual problems among HM patients as a result of the disease and/or treatment. The second part will discuss sexuality in clinical practice. This chapter also provides methods that can contribute to discussing sexuality.

Samenvatting

Hoofdstuk 1 is de algemene inleiding van dit proefschrift. In de afgelopen jaren is de prognose van patiënten met een hematologische maligniteit (HM) sterk verbeterd door de vele behandelingsmogelijkheden. Dit houdt in dat gevolgen van de behandeling op lange termijn steeds belangrijker worden. Zo kunnen onder andere seksuele problemen ontstaan, niet alleen tijdens de behandeling, maar ook na de behandeling. Veel overlevenden van kanker verlangen en verdienen een "normaal leven", en seksualiteit wordt gezien als een integraal onderdeel van dit toekomstige leven. Het lijkt er echter op dat zorgverleners zich vaak niet bewust zijn van de seksuele problemen die patiënten ervaren. Niet alleen patiënten zijn terughoudend om seksuele problemen te bespreken, ook zorgverleners zijn terughoudend. Daarnaast ontbreekt het de hulpverleners aan kennis van de seksuele problemen en de competentie hoe het gesprek aan te gaan. Het belangrijkste doel van het proefschrift was om meer kennis te verwerven over seksuele (dys)functie waarmee HM-patiënten tijdens en na de behandeling te maken kunnen krijgen, hoe zorgverleners seksualiteit in de klinische praktijk bespreken en over de informatiebehoefte van HM-patiënt. Deze kennis is cruciaal om in de toekomst patiënten informatie over seksualiteit te ontwikkelen die is afgestemd op de behoefte van de HM-patiënt.

Hoofdstuk 2 beschrijft een systematisch literatuuronderzoek naar hoe vaak seksuele problemen voorkomen bij patiënten die voor HM werden behandeld. Het doel was inzicht te krijgen van de impact op seksueel functioneren tijdens de behandeling en daarna. We vonden 24 studies die aan onze zoekcriteria voldeden. Methoden verschilden tussen studies, zo waren in 14 van de 24 studies niet-gevalideerde meetinstrumenten gebruikt, en slechts zes studies hadden seksuele problemen vergeleken met een algemene populatie. Op basis van slechts drie kwalitatief goed uitgevoerde studies kon geconcludeerd worden dat bij 18-50% van de acute leukemie, Hodgkin-lymfoom en non-Hodgkin-lymfoompatiënten seksuele problemen op treden. Over het algemeen waren de bevindingen inconsistent gemeten, waardoor resultaten niet generaliseerbaar zijn. Bovendien concludeerden we dat seksuele disfunctie niet of onder- gerapporteerd was bij patiënten en overlevenden van de meeste HM. Vervolgonderzoek is nodig om goed inzicht te krijgen in de omvang van seksuele problemen onder HM patiënten.

Hoofdstuk 3 beschrijft zelf-gerapporteerde seksuele functie van jonge vrouwelijke Hodgkin Lymfoom (HL) patiënten vergeleken met een algemene populatie. Een tweede doel was of er een verband was tussen vruchtbaarheidsstatus (zoals gerapporteerd door vrouwelijke HL patiënten) en seksuele functie. Van de HL patiënten meldden 31% een seksuele disfunctie, dit was vergelijkbaar met de algemene bevolking. Van de patiënten die zichzelf onvruchtbaar beschouwden rapporteerde 63% een seksuele disfunctie ($p=0.07$). HL patiënten meldden vaker problemen met seksueel verlangen, opwinding, lubricatie, tevredenheid en pijn in vergelijking met de algemene bevolking. Met betrekking tot het verloop van het seksuele probleem meldden geen van de patiënten herstel.

Hoofdstuk 4, om referentiewaarden te verzamelen voor seksueel functioneren na HL bij seksueel actieve mannelijke patiënten, voerden we een crosssectionele studie uit waarin we zelf gerapporteerde seksuele functie van mannelijke HL-patiënten vergeleken met op leeftijd gematchte controles. Om te onderzoeken wie het grootste risico loopt op seksuele disfunctie, onderzochten we of sociodemografische factoren en het behandelingsregime geassocieerd waren met seksuele disfunctie. Tot slot onderzochten we of het melden van seksuele problemen indicatief was voor seksuele disfunctie. De resultaten toonden aan dat erectie dysfunctie (ED) voorkwam bij 23,3% van de HL-overlevenden versus in 23,0% van de controles: en respectievelijk 13,3% en 12,3% hadden matige tot ernstige ED. Geen van de HL-patiënten die met ABVD waren behandeld rapporteerden seksuele problemen. Echter, een derde van de HL overlevenden die waren behandeld met BEACOPP meldden problemen met seksueel verlangen en ED. HL-patiënten die seksuele problemen meldden hadden een gemiddelde International Index of Erectile Function (IIEF) score voor erectiele functie van 15,7 (matige erectiestoornissen) versus 28,3 (geen erectiestoornissen) bij degenen zonder seksuele problemen. Het melden van seksuele problemen bleek indicatief voor seksuele disfunctie, en zo kan seksuele disfunctie vroeg worden gedetecteerd door seksuele problemen te screenen met slechts 3 vragen.

Hoofdstuk 5 beschrijft een literatuurstudie die tot doel had inzicht te geven in de behoefte aan informatie van patiënten met HM. Resultaten toonden dat de informatiebehoefte en tevredenheid over de verstrekte informatie sterk verschilt tussen patiënten. Uit dit literatuuronderzoek bleek ook dat de behoefte aan informatie over seksualiteit was bestudeerd door slechts vier van de veertien studies. Twee van deze studies meldden dat informatie over seksualiteit een lage prioriteit had, terwijl de andere twee studies meldden dat patiënten wel behoefte hadden aan informatie over seksualiteit. Bovendien beschreef een studie dat de helft van de patiënten de patiëntinformatie over seksualiteit onvoldoende vond.

Hoofdstuk 6 beschrijft een brief aan de redacteur: "Seksualiteit bespreken in de zorg voor kankerpatiënten: naar gepersonaliseerde informatie voor kankerpatiënten en overlevenden". We voerden een multicenter longitudinaal onderzoek uit om de behoefte aan informatie te meten bij patiënten met HM en hun partners tijdens de eerste 18 maanden van de behandeling. Om de informatiebehoefte over seksualiteit in kaart te brengen werden zes vragen ontwikkeld voor patiënten en hun intieme partners. Tot 18 maanden na de diagnose gaf 42 tot 48% van de patiënten (n=266) aan behoefte te hebben aan informatie over veranderingen in seksualiteit, 40-44% gaf aan behoefte te hebben aan ondersteuning bij seksuele problemen en 41-46% gaf aan behoefte te hebben aan voorzorgsmaatregelen die genomen moeten worden. Wat hun partners betreft (n=134), gaf 34-52% aan behoefte te hebben aan informatie over veranderingen in seksualiteit, 39-50% gaf aan behoefte te hebben aan ondersteuning bij seksuele problemen en 34-53% gaf aan behoefte te hebben aan voorzorgsmaatregelen die genomen moeten worden. Uit de multivariabele analyse bleek dat jongere patiënten, mannelijke patiënten en het hebben van een monitoring cognitieve coping stijl de hoogste

behoefte aan informatie over seksualiteit hadden. Terwijl de behoefte onder de intieme partners het hoogst was onder jongere partners en onder partners die meer hadden gezocht naar informatie op internet. In tegenstelling tot de patiënten werden de informatiebehoeften niet geassocieerd met het geslacht van de partner.

Hoofdstuk 7 beschrijft de frequentie en barrières en facilitators voor het bespreken van seksuele problemen met HM patiënten onder de leden van de European Society for Blood and Marrow Transplantation (EBMT). De studie toonde aan dat een derde van de artsen en verpleegkundigen routinematig seksuele problemen bespraken. De voornaamste barrières waren beperkte kennis, zich ongemakkelijk voelen bij het bespreken van seksuele problemen, de aanwezigheid van een familielid en het idee dat patiënten zelf seksuele problemen aan de orde zouden stellen. Seksualiteit werd minder vaak besproken door jongere artsen, en artsen die in niet-West-Europese landen werkten, en door verpleegkundigen die minder scholing over seksuele complicaties hebben gevolgd. Seksualiteit werd ook minder besproken door artsen en verpleegkundigen die aangaven te weinig kennis te hebben over de langdurige gevolgen van de behandeling op seksualiteit, of die zich ongemakkelijk voelen bij het bespreken van seksuele problemen. Vervolgonderzoek is nodig om de behoefte van patiënten aan informatie over seksuele zorgen in te kunnen schatten, hetgeen beschreven is in **Hoofdstuk 6**. Vervolgonderzoek moet ook inzicht geven in hoe seksualiteit het beste kan worden gecommuniceerd.

Hoofdstuk 8 beschrijft de impact van hematopoëtische stamceltransplantatie (HCT) op de seksuele functie, de pathofysiologie en kort de behandelingen van seksuele problemen. Hiervoor hebben we bevindingen van ons systematische literatuuronderzoek (met betrekking tot seksuele functie en HCT) geëxtraheerd (**Hoofdstuk 2**). In een poging te voldoen aan de informatiebehoefte van patiënten, is een informatiebrief geschreven: "Informatie voor patiënten die een hematopoëtische stamceltransplantatie ondergaan: de impact van de ziekte en behandeling op seksuele functie en seksualiteit."

Hoofdstuk 9 vat de resultaten van dit proefschrift samen, beschrijft de implicaties en geeft aanbevelingen voor vervolgonderzoek. Vanuit de studies die tot nu toe gedaan zijn is te weinig bekend om de daadwerkelijk impact van HM op seksualiteit te beschrijven. De helft van de patiënten en hun intieme partners hebben behoefte aan deze informatie. Helaas voorkomt het gebrek aan kennis over de langdurige gevolgen van de behandeling op seksualiteit onder artsen en verpleegkundigen dat patiënten en hun partners de informatie krijgen die zij nodig hebben. Het hoofdstuk bestaat uit 2 onderdelen. Het eerste onderdeel is het inzichtelijk maken van wat er bekend is over seksuele problemen onder HM patiënten als gevolg van de ziekte en/of behandeling. Het tweede deel beschrijft hoe het bespreken seksualiteit in de klinische praktijk aangepakt zou moeten worden. In dit hoofdstuk wordt tevens een werkwijze gegeven die kan bijdragen aan het bespreken van seksualiteit.

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Corien Eeltink

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Curriculum Vitae

Corien Eeltink werd geboren op 18 augustus 1961 te Edam. In 1978 behaalde zij haar HAVO-diploma waarna zij begon aan de opleiding verpleegkunde A in het Onze Lieve Vrouwe Gasthuis te Amsterdam. Na het behalen van het diploma in 1983 heeft zij gewerkt als verpleegkundige A in het Onze Lieve Vrouwe Gasthuis te Amsterdam, vanaf 1985 voor de afdeling hematologie in het Academisch Medisch Centrum te Amsterdam, en vanaf 1 januari 2000 voor de afdeling hematologie in VU Medisch Centrum te Amsterdam. In juni 2002 begon zij aan de opleiding Advanced Nursing Practice aan de Hanzehogeschool te Groningen. Sinds 2004 is zij werkzaam als verpleegkundig specialist. Na het behalen van de “Best nurses abstract 24th Meeting of the EBMT nurses group in Florence 2008: ‘Sexual dysfunctions during and after chemotherapy for hematological malignancy. Do patients want to know?’ startte ze met haar promotieonderzoek ‘Sexuality in patients with hematological malignancies; from a patient, partner and health-care professional perspective’. Tevens werd zij in 2008 lid van de research groep van de European Bone Marrow Transplantation (EBMT) nurses group. Vanaf 1 september 2021 is zij werkzaam als verpleegkundig specialist in het Dijklander Ziekenhuis. Zij is project coördinator bij het project ‘Gesprekken over Psychosociale behoeften, intimiteit en Seksualiteit’, een ZonMw gesubsidieerd project. Corien is getrouwd met Jan Kes. Zij hebben 2 zoons, Jan (30) en Barend (27).

