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Bedürfnisse, Belastungen und Ressourcen bei Patient*innen mit schwerer, persistierender GvHD nach allogener Stammzelltransplantation

Needs, burden and resources of patients with severe, persistent GvHD after allogeneic stem cell transplantation

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Diese Dissertation ist den Patient*innen der qualitativen Interviewstudie gewidmet.

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Abkürzungsverzeichnis / List of abbreviatons

aGvHD	Acute graft-versus-host disease
allo-SCT	Allogeneic stem cell transplantation
BMT	Bone marrow transplant
cGvHD	Chronic graft-versus-host disease
GI	Gastrointestinal tract
GvHD	Graft-versus-host disease
HAP	Human activity profile
HCP	Health care providers
HGS	Hand grip strength
HLA	Human leucocyte antigen
HRQoL	Health-related quality of life
HSCT	Haematological stem cell transplantation
MCS	Mental Component Summary
NIH	National Institutes of Health
PC	Specialist palliative care
PCS	Physical Component Summary
PROMs	Patient-reported outcome measures
QoL	Quality of life
SF-36	Medical outcomes short form 36
Sp-WB	Spiritual well-being
WHO	World Health Organisation
2MWT	2-minute walk test
6MWT	6-minute walk test

1.1 Zusammenfassung

Patient*innen, die nach allogener hämatopoetischer Stammzelltransplantation (allo-SCT) an einer schweren akuten oder chronischen Graft-versus-Host-Erkrankung (GvHD) leiden, können durch diese lebensbedrohlich erkranken – trotz des eigentlich kurativen Behandlungsansatzes der hämatoonkologischen Grunderkrankung. Aus klinischer Erfahrung heraus benötigt diese Patient*innengruppe aufgrund ihrer hohen Krankheitslast viel Unterstützung und oft eine palliativmedizinische Behandlung. Dies ist bisher jedoch kaum erforscht worden und wird nicht standardisiert angewendet. Patient*innen mit schwerer GvHD sind in Studien zur GvHD häufig unterrepräsentiert. Es ist das übergeordnete Ziel dieser Dissertation, die klinische Versorgung von Patient*innen mit schweren Formen von GvHD zu verbessern, indem ihre Belastungen, Ressourcen und Bedürfnisse untersucht werden und entsprechend auf diese eingegangen werden kann. Der erste Teil dieser Dissertation umfasst eine umfangreiche Literaturrecherche in der Datenbank PubMed, deren Ergebnisse in einem Review veröffentlicht wurden. Es zeigt sich, dass es keine Studien gibt, die sich explizit auf Patient*innen mit schweren Formen der GvHD beziehen. Einige wenige Studien können jedoch zeigen, dass die Lebensqualität als auch die physische Funktionsfähigkeit bei durch eine GvHD schwer betroffenen Patient*innen stärker eingeschränkt ist als bei Patient*innen mit milderen Formen der GvHD. Generell zeigt sich durch den Review ein großer Forschungsbedarf, da es aufgrund der sehr begrenzten Studienlage nicht möglich war, ein umfassendes Bild der Patient*innengruppe mit schwerer GvHD zu zeichnen. Auch gibt es keine Daten, inwieweit palliativmedizinische Therapien bei dieser Patient*innengruppe eingesetzt werden. Daher besteht der zweite Teil dieser Dissertation in der Durchführung einer qualitativen Interviewstudie mit 13 Patient*innen, die an schweren Formen der GvHD leiden. Aus Patient*innen-Sicht wurden Daten über deren Belastungen, Bedürfnisse und Ressourcen im Zusammenhang mit der GvHD gesammelt und diese anschließend mittels qualitativer Inhaltsanalyse nach Kuckartz ausgewertet. Die bereits im Review erwähnte eingeschränkte physische Funktionsfähigkeit und die verminderte Lebensqualität wurden von den Teilnehmenden bestätigt. Hervorzuheben ist jedoch das hohe Ausmaß an körperlicher Schwäche, welches zu zeitweise ausgeprägter Hilfsbedürftigkeit führt. Weiterhin nahm keine*r der Teilnehmenden an, jemals wieder die vor der allo-SCT bestehende Lebensqualität erreichen zu können. Die Teilnehmenden fühlten sich durch die Unvorhersehbarkeit des Verlaufs der GvHD und die langen, oft unvollständigen Genesungsprozesse belastet und isoliert. Bei fast allen Teilnehmenden traten depressive Symptome auf, und die Mehrheit äußerte Formen von Todeswünschen unterschiedlicher Ausprägung. Dies ist im Zusammenhang mit der GvHD noch nicht untersucht worden und

bedarf weiterer Forschung. Die qualitative Interviewstudie zeigt die starke Gesamtbelastung der Teilnehmenden. Es bestand die Meinung, dass die derzeitigen therapeutischen und unterstützenden Maßnahmen des deutschen Gesundheitssystems (insbesondere alleinstehende) Patient*innen mit schweren Formen der GvHD nicht ausreichend unterstützen. Des Weiteren tendierten die Teilnehmenden dazu, Palliativmedizin als End-of-life care zu sehen oder wussten nicht genau, was der Begriff bedeutet. Da palliativmedizinische Therapien bei hämatoonkologischen Erkrankungen trotz eines eindeutig bestehenden Bedarfs seltener eingesetzt werden, als bei soliden Tumorerkrankungen, stellt es eine wichtige Forschungsfrage dar, inwieweit die Integration der Palliativmedizin die Versorgung von Patient*innen mit schweren Formen der GvHD verbessern kann. Auch der Zeitpunkt, wann Palliativmedizin am besten in die Behandlung integriert werden sollte, ist unklar. Die genannten Ergebnisse der qualitativen Interviewstudie sollten genutzt werden, um neue Forschungsfragen zu stellen und diese in quantitativen Studien weiter zu untersuchen.

1.2 Summary

Patients who suffer from severe forms of acute or chronic graft-versus-host disease (GvHD) after having received an allogeneic hematopoietic stem cell transplantation (allo-SCT) may find themselves in a life-threatening situation despite being cured from the underlying haemato-oncological disease. According to our clinical assessment, these patients often need special support and require palliative care due to their high level of suffering, but this has hardly been researched so far. Furthermore, they are often underrepresented in studies on GvHD. The overall aim of this dissertation is to improve the clinical care for patients with severe forms of GvHD by investigating their burdens, resources and needs and to address those accordingly. Therefore, the first part of this dissertation was an extensive literature search in the database PubMed, the results of which were compiled in a literature review. It became apparent that no studies explicitly included only patients with severe forms of GvHD. However, few studies were able to show that the quality of life and physical functions were worse in severely affected patients than in patients with milder forms of GvHD. The very limited number of studies did not allow a comprehensive picture of patients with severe forms of GvHD to be drawn. Due to the lack of data it was not possible to evaluate the extent to which palliative care is used among this patient group. Further research is required in this field.

Therefore, in the second part of this dissertation a qualitative interview study with 13 patients suffering from severe forms of GvHD was conducted. Information on the burden, needs and resources from the patient's perspective were gathered and then evaluated by qualitative content analysis. The in the literature review already mentioned reduced physical functions and the reduced quality of life were confirmed by the participants. Outstanding was, however, the high extent of physical weakness, causing dependency on others and that none of the participants expected to be able to ever again reach the pretransplant level of quality of life. The participants felt burdened by the unpredictability of the course of GvHD and long and incomplete recovery processes which caused isolation. Symptoms of depression were apparent in nearly all of the participants and a majority reported a desire to die in varying degrees. This has not yet been investigated in the context of GvHD and requires further research. The qualitative interview study revealed the severe overall burden of the participants and their opinion, that current measures of the German health care system do not sufficiently support (particularly single / unmarried) patients with severe forms of GvHD. In this context, the participants tended to see palliative care as end-of-life care or did not know precisely what the term meant. Although palliative care is still less frequently used in haemato-oncological diseases than in solid tumour diseases, even though a clear need is seen, it could be an important research question to what extent the integration of palliative care can improve the care of patients with severe forms of GvHD. When should it best be integrated in the course

of GvHD? The mentioned findings of the qualitative interview study should be used to raise new research questions and should be further investigated in quantitative trials.

2. Introduction

Allogeneic hematopoietic stem cell transplantation (allo-SCT) is a curative approach for a variety of benign and malignant hematological diseases. It allows for recovery after receiving high-dose therapy and includes a graft-versus-tumor effect in which malignant cells can be recognized as foreign by immune cells in the graft [1]. One of its major complications is graft-versus-host disease (GvHD), in which immune cells of donor origin cause damage to host tissues in the recipient. This makes GvHD an important cause of morbidity and non-relapse mortality among recipients of allo-SCT [2]. Patients suffering from GvHD may have a variety of symptoms in one or more affected organs. This often requires immunosuppressive treatment that can cause side effects and patients often suffer from infections [3]. Physical impairments and a reduced quality of life (QoL) have been frequently observed in this patient group [4–7]. In our medical center, the University Hospital of Cologne, particularly patients with objectively and subjectively severe forms of their GvHD were perceived to need special support and to suffer from a very high overall symptom burden, long inpatient stays and sudden death. While an early integration of specialist palliative care (PC) has become an integral part of standard cancer care, PC services are less frequently used in patients with hematological malignancies. More invasive therapies, even shortly before death and less information about near death are received by these patients. With regard to allo-SCT, the integration of PC into the transplant trajectory has barely been investigated [8,9].

The described deficiencies raised interest in improving the multimodal treatment concept for patients with severe forms of GvHD, which is the overall aim of this dissertation. Its focus lays on needs, burdens and resources of patients with severe forms of GvHD. The first part comprises the performance of a focused literature search to obtain a present state of research regarding these issues. The second part deals with the conduction of a qualitative study, to directly interview affected patients in order to form a detailed picture of their needs, burdens and resources.

In the following chapter 2.1 the theoretical background of this dissertation will be described. In chapter 2.2, the research question and methodology will be introduced, followed by the presentation of the results in form of two publications in chapter 3. Their findings will be discussed in chapter 4.

2.1 Theoretical Background

2.1.1 Graft-versus-host Disease

Definition and Clinical Manifestation

Graft-versus host disease (GvHD) is the major complication of allogeneic stem cell transplantation (allo-SCT) which is a curative treatment for various benign and malignant hematologic diseases. It can occur in various clinical settings when tissues containing T cells are transferred from one person to another who is not able to eliminate those cells. It arises when donor T cells, primed by host or donor antigen-presenting cells, respond to genetically defined proteins on host cells. Patients whose immune system is suppressed and who receive a stem cell graft which includes white blood cells from a donor are especially at high risk for GvHD [10]. GvHD is mainly categorized into an acute (aGvHD) and a chronic (cGvHD) form, which are defined by clinical features [11]. Treatment of both forms depends on the clinical severity and the respective organ manifestations in the setting of GvHD and can consist of (high-dose) systemic or topical steroids and other immunosuppressive agents [10].

aGvHD is a systemic, inflammatory disease and the currently valid definition of the National Institute of Health (NIH) distinguishes between a classic aGvHD up to day 100 and a late-onset form, which is defined as presence of symptoms and signs of aGVHD after more than 100 days after allo-SCT. It can be categorized into a de novo form (if early aGvHD has been absent), a recurrent form (if a prior resolved early aGvHD reoccurs after more than 100 days) and a persistent form (if early aGvHD symptoms and signs persist after more than 100 days) [12,13]. Following activation of donor T cells by conditioning-induced tissue damage in the host, a cascade involving cellular and humoral factors leads to damage of the affected organs [14,15]. aGvHD predominantly involves three organs. The skin is its initial and most frequent manifestation in the form of a maculopapular exanthema or dermatitis which is often accompanied by pruritus. Predilection sites are light-exposed skin areas. The gastrointestinal tract (GI) is frequently the most severely affected organ with painful abdominal cramps and diarrhea being important symptoms. Vomiting, malabsorption and a poor nutritional status are commonly perceived among these patients. Due to hypovolemia and translocation of intestinal bacteria patients are at risk for sepsis. Liver involvement is least frequently observed and is mostly detected by an icterus or abnormal liver function test with hyperbilirubinemia [13,14].

cGvHD mostly occurs within the first year after allo-SCT [16]. It often follows aGvHD, but it is not its simple evolution [11,16]. Classic cGvHD is defined as absence of aGvHD features. If symptoms of both, aGvHD and cGvHD are present, this is defined as overlap syndrome [16].
The pathophysiology of cGvHD is poorly understood but most likely involves acute and chronical inflammation that leads to tissue injury and dysregulated immunity and to fibrosing

processes due to aberrant tissue repair [17]. Similar to autoimmune diseases, nearly every organ can be damaged. Skin, mouth, eyes, gastrointestinal tract, liver, lungs, joints and fascia, and the genital tract are mainly affected and included in the scoring system that is predominantly used (*see "Diagnostics and Classification"*). The affected number of organs can vary; about half of affected people have three or more involved organs [18].

Epidemiology

The risk of getting an *aGvHD* after allo-SCT varies widely within the literature between 35-72% [19,20], with about 14% suffering from severe forms of aGvHD (commonly described as grade III / IV) [21].

Incidence rates of *cGvHD* range from 30-70% after allo-SCT [18,21].

Diagnostics and Classification

aGvHD is predominantly a clinical diagnosis that should be histologically confirmed [20]. Besides the determination of histological degrees of severity of the affected organs, organ specific scores based on clinical symptoms of the skin, GI and liver are used which then can be integrated into overall severity levels from 0 (no GvHD) – IV (very severe GvHD). This has primarily been implemented by Glucksberg et al. in 1974 and was then modified in 1995 [22,23]. A similar classification system has been established by Harris et all [19].

cGvHD is commonly diagnosed by scores developed in 2005 by the NIH Consensus Group which have been updated in 2014. Organ specific severity scores (for the skin, mouth, eyes, GI, liver, lungs, joints and fascia, and the genital tract) can be integrated into a global score that distinguishes between mild, moderate and severe cGvHD. It includes the number of affected organs or sites and the organ-specific severity scores. The NIH scores are clinical scores but the NIH Consensus Group recommends the use of further testing e.g. histological confirmation to confirm the diagnosis of cGvHD if the clinical manifestation is ambiguous and to exclude other causes for it, such as drug reaction or infections. The NIH global score has been confirmed to predict overall survival and non-relapse mortality [11,16].

Severe forms of GvHD

Several factors have been identified to contribute to the severity of *aGVHD*, including degree of donor–recipient human leucocyte antigen (HLA) matching, intensity of conditioning regimen, older age, previous donor alloimmunization, and GvHD prophylactic regimen [24]. Severe

aGvHD is treated with systemic immunosuppressive therapy; mostly corticosteroids. Generally, only 50% of patients with aGvHD are likely to respond to their first-line treatment with corticosteroids [25]. The second-line treatment of aGvHD is heterogeneous. Patients with severe forms of aGvHD (grades III / IV) frequently need higher doses of immunosuppressive treatment than patients with milder forms of aGvHD [26] while aGvHD and its immunosuppression increase the risk and incidence for fulminant infections such as blood stream infections and treatment side effects [27,28]. Severe aGvHD (grade III / IV), particularly if steroid-refractory, remains a major threat to survival after allo-SCT [20,29].

Following the 2014 NIH Consensus Criteria, severe cGvHD has been characterized by a significant impairment of organ function. At least one of the relevant organs (skin, mouth, eyes, GI, liver, lungs, joints or fascia, or genital tract) is scored as severely affected (score of 3), or there is a lung score of 2 or 3. It can occur in form of classic cGvHD or in form of an overlap, which seems to be associated with a poorer overall survival [16,30]. The first line therapy of severe forms of cGvHD includes a systemic immunosuppression with a corticosteroid or a primary combination immunosuppression in order to reduce the need for steroids in the medium to long term. Similar to findings in aGvHD, more severe forms of cGvHD require more immunosuppressive medication than milder forms of cGvHD. In about half of the cases, cGvHD is steroid-refractory. Second-line medications then remain, for which until now there is no marketing authorisation for this indication [31]. Most death of patients with cGvHD are due to infection - associated with profound immune dysfunction [32]. The more severe the cGvHD, the higher is the non-relapse mortality [33].
cGvHD is a protective factor in context of relapse due to its graft-versus-malignancy effect. A higher severity of cGvHD is not associated with a better outcome in terms of a decreased relapse risk [32].

2.1.2 Supportive Care and Palliative Care in Patients with GvDH

Supportive Care

Supportive Care (SC) is a widely used term in the oncology setting. Its consensus definition is missing [34], but the Multinational Association of Supportive Care in Cancer (MASCC) suggests the following definition of SC:

"Supportive care in cancer is the prevention and management of the adverse effects of cancer and its treatment. This includes management of physical and psychological symptoms and side effects across the continuum of the cancer experience from diagnosis through treatment to post-treatment care.

Supportive care aims to improve the quality of rehabilitation, secondary cancer prevention, survivorship, and end-of-life care" [35]. Hui proposes to divide SC into three levels, based on

the specialisation level of the attending health care providers (HCP). He describes *primary SC* that is delivered by oncologists and HCP in the front line. *Secondary SC* involves specialized teams such as psychiatry or palliative care teams and *tertiary SC* provides SC in complex situations in tertiary care settings, such as palliative care units [34].

Supportive Care in GvHD

SC measures have recently been integrated in aGvHD and cGvHD treatment guidelines [16,31,36,37]. Following the definition of Hui, those measures mostly apply to primary SC and often concentrate on managing organ specific complications. Secondary SC measures, predominantly addressed in context of cGvHD, are: *physiotherapy, strength training, occupational therapy, nutritional therapy, rehabilitation medicine consultation, referral to specialist opinions, neuropsychological testing, cognitive-behavioral interventions, psychotherapy, palliative care* [36,38–40].

Palliative Care

The World Health Organization (WHO) published the following definition of PC:
"Palliative care is an approach that improves the quality of life of patients (adults and children) and their families who are facing problems associated with life-threatening illness. It prevents and relieves suffering through the early identification, correct assessment and treatment of pain and other problems, whether physical, psychosocial or spiritual" [41].
The major aim of PC is to preserve the best possible QoL. It can be delivered by primary care providers (*general PC*) or by specialized PC professionals (*specialist PC*), depending on the complexity of the situation [42,43]. General PC is required for a wide range of diseases. The most common ones are chronic diseases such as cardiovascular diseases (38.5%), cancer (34%), chronic respiratory diseases (10.3%), AIDS (5.7%) and diabetes (4.6%) [41]. Breathlessness, pain, fatigue, sleep-related disorders / nocturnal restlessness, nausea and vomiting, constipation, malignant wounds, anxiety and depression are examples for important symptoms / problems that are faced in PC [44].

Palliative Care in GvHD

The WHO explicitly recognizes PC under the human right to health [41] and it was introduced as standard care for patients with advanced cancer in the last years [45]. However, the majority of research in this area focuses on solid tumors and hematological malignancies have hardly been included. Patients with hematological malignancies might suffer from individual and unpredictable disease trajectories and a high symptom burden, resulting in specific PC needs such as physical and psychological symptom burden, impairments of QoL, social isolation,

informational needs, neurocognitive dysfunction, frequent hospital readmissions or late effects as a result of cancer therapy [46].

Only two randomized controlled trials by El-Jahwari et al. examined the integration of PC into the transplant trajectory in context of hematological stem cell transplantation (HSCT). It was shown that early integration of specialist PC during the transplant period resulted in less impaired QoL two weeks after transplantation, in lower depression and anxiety symptoms and in a less increased symptom burden compared with reception of standard transplant care [47]. Six months after HSCT a decline in depression symptoms and post-traumatic-stress disorder symptoms was found in patients who received specialist PC during transplant period, compared to patients who did not [48].

Occurrence of GvHD has recently been identified as an important need of PC [40,49]. However, there seems to be a significant research gap in this regard and no studies, focusing on this topic, were identified.

Connection between Supportive Care and Palliative Care

Improving the holistic needs of patients with advanced illness is the goal of both SC and PC. The distinction between SC and PC can be challenging in the clinical setting and both terms might be integrated differently in different health care systems. The European Society for Medical Oncology (ESMO) proposed to use the term of *patient-centered care* to unite the two concepts and to emphasize their common objective [50]. Hui describes SC services to be or not to be palliative in nature. But following his definition, all PC programs are providing SC for patients with advanced cancer [34]. In the German health care system and in the University Hospital of Cologne, specialist PC plays the major role in providing and organizing secondary and tertiary SC as well as end-of-life care for patients with advanced illness. Therefore, its integration should be further assessed in a multimodal concept of care for patients with severe forms of GvHD.

2.1.3 Definition of Quality of Life and Health-related Quality of Life

The WHO defines QoL as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns [51]. The term QoL makes an universal claim and cannot be assigned to just one discipline. While it includes more than just health, health is a very important component and condition of QoL. A lack of health reduces the quality of life on a broad scale. Therefore, in the medical context the term of Health-Related Quality of Life (HRQoL) is used [52]. However, there is no clear definition of this term, so the following one by Torrence is only mentioned to give an impression: HRQoL includes only those factors that are part of an

individual's health while non-health aspects of QoL, for example economic / political circumstances, are not included in HRQoL [53].

2.1.4 Definition of Physical Functioning

It is well documented that physical functioning is highly predictive of important clinical outcomes, such as mortality and morbidity. Physical functioning is of critical importance in QoL. Unfortunately, there is a great variation in terminology, definitions, and measures of physical functioning that can lead to confusion over which measures are most appropriate for particular situations.

One approach to defining physical functioning by Painter et al. is to differentiate simple physical movements from more complex activities. Physical movements or actions can be termed essential if they are needed to maintain independence in living [54]. Measuring physical functioning often refers to an individual's ability to carry out some pre-defined activities [55]. In the GvHD setting these are predominantly a 6-minute or 2-minute walk test (6MWT, 2MWT) or hand grip strength (HGS) [56]. Despite that patient-reported outcome measures (PROMs) can be used to objectify physical functioning, which will be described in the following chapter.

2.1.5 Patient-reported Outcome Measures

Measuring QoL, physical functioning or other subjective physical and psychological perceptions require special tools that enable comparability. Standardised measurement methods mostly in form of standardized questionnaires are therefore used; so-called patient-reported outcome measures (PROMs). These collect health outcomes directly from the people who experience them. PROMs can be applicable in a more generic way, while selected condition-specific PROMs are also used and validated for certain clinical conditions [57].

Frequently used PROMs in GvHD

There is currently no consensus on which PROMs to select when addressing QoL, symptom burden, or severity in the GvHD setting [58]. Nevertheless, the most commonly used PROMs that are relevant to this dissertation because they were used in the studies on which the literature review is based on are briefly presented in this section. They were also identified in two reviews by Kilgour et al. (systematic review) and Shaw [58,59].

Generic PROMs

- *Medical outcomes short form 36 (SF-36)*: The SF-36 is a 36-item self-report questionnaire. It yields an eight-subscale profile of scores (physical functioning, bodily pain, role limitations due to physical or emotional health problems, emotional well-being, social functioning, energy, and

perceptions of general health) as well as two physical and mental health summary measures (Physical Component Summary (PCS) and the Mental Component Summary (MCS)). Higher scores indicate better health status and QoL. The SF-36 is the most often used PROM in the GVHD population [58,60].

- *Human Activities Profile (HAP):* The HAP is a 94-item self-reported assessment of physical activity and symptoms. It contains a list of 94 specific activities ranked according to the energy expenditure required to perform the task. It is mostly used in patients with chronic diseases, particularly chronic obstructive pulmonary disease. Higher scores indicate greater activity and therefore preservation of function. Multiple methods of scoring are available, including primary scores, maximum activity score, and adjusted activity score [58,61].

Bone-marrow-transplant specific PROMs

- *Functional Assessment of Cancer Therapy-Bone Marrow Transplantation (FACT-BMT)*: The FACT-BMT is based on the Functional Assessment of Cancer Therapy (FACT-G) questionnaire, which was developed to assess QoL in cancer patients. It contains five subscale domains (Physical Well-Being, Social / Family Well-Being, Emotional Well-Being, Functional Well-Being, BMT Subscale) The additional 18-item BMT-specific subscale, focuses on concerns of allo-SCT patients such as worry of transplant failure, effects of treatment, sexuality, and reproduction. A higher score on the BMT subscale indicates better well-being [58,62].

cGvHD specific PROMs

- *Lee Symptom Scale (LSS)*: The LSS was developed to measure (GvHD specific) symptom burden in adult outpatients with cGvHD. The scale contains 30 items grouped in seven subscales (skin, eye, mouth, lung, nutrition, energy, and psychological). Patients report how “bothered” they feel about each symptom over the previous month using a five-point Likert scale from “not at all” to “extremely”. Subscales range from 0 to 100, with a higher score indicating worse symptoms. Subscales may be scored if at least 50% of items are answered, and subscales are averaged to calculate the summary score [63].

In *cGvHD* the use of PROMs gains more and more relevance. The NIH Chronic GvHD Consensus Response Criteria Working Group names the SF-36, the HAP and the FACT-BMT as cGvHD non-specific ancillary measures that are strongly encouraged in cGvHD trials. The LSS is named as a cGvHD specific core measure [64].

Trials specifically investigating PROMs in *aGVHD* are very limited and there exists no aGvHD specific PROM until today [65].

2.2 Aim and objectives of this dissertation

The starting point for this dissertation was the perception that more attention and support should be given to patients with severe forms of GvHD, who were considered particularly vulnerable and overlooked in the context of everyday clinical practice in the German health care system. The resulting overall aim of this work is therefore to improve treatment strategies of these patients by identifying their burdens, needs and resources. An initial literature search revealed a major research gap regarding this topic, which resulted in the following two objectives for this dissertation:

The objective of the first part is to conduct a focused literature review in the PubMed database, to provide a comprehensive overview of the state of research on burdens, resources and needs of patients with severe forms of GvHD.

The objective of the second part is to identify the burdens, needs and resources of patients with severe forms of GvHD by conducting a qualitative interview study.

3. Publications

In the following chapter, copies of the two publications that answer the two research objectives of this dissertation (see 2.2) will be displayed.

Literature Review

The original publication of the literature review was published online on 30/05/2021 at https://www.mdpi.com/2072-6694/13/11/2697.

Qualitative interview study

The original publication of the qualitative interview study was published online on 27/02/2025 at https://www.cambridge.org/core/journals/palliative-and-supportive-care/article/burden-resources-and-needs-of-patients-with-severe-graftversushost-disease-a-qualitative-study/9B902B5084FA3BDCD2D7E221BCD11A80.

Each of the two PubMed-listed publications describe and set out the corresponding chapters of *material and methods* and *results*. The aforementioned chapters will be replaced by the subsequent publications, meeting the criteria for a cumulative dissertation.

Data material (interview guide, transcription guide, codebook) which were produced for the qualitative content analysis based on Kuckartz (2018) for the qualitative interview study can be found in the appendix (chapter 7)[66].

3.1 Literature review

Wenzel, F.; Pralong, A.; Holtick, U.; Scheid, C.; Herling, M.; Simon, S.T. Burden and Needs of Patients with Severe GvHD from the Supportive and Palliative Care Perspective-A Literature Review. Cancers (Basel) 2021, 13, doi:10.3390/cancers13112697.

cancers

MDPI

Review

Burden and Needs of Patients with Severe GvHD from the Supportive and Palliative Care Perspective—A Literature Review

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Simple Summary: Patients who have been treated with an allogeneic, hematopoietic stem cell transplantation can develop severe graft-versus-host disease. This complication may place patients in a life-threatening situation, in which a curative goal of care can no longer be achieved and needs to be changed into a palliative one. In our clinical experience, this patient group is very heterogenous, with a high disease burden and special needs that are often overlooked. In this review, we summarize the current literature on the needs and burdens of patients with severe forms of graft-versus-host disease from a supportive and palliative care perspective to draw a comprehensive picture of this patient group. Despite a fundamental lack of studies, the findings suggest that the more severe the GvHD, the worse the quality of life and physical functioning. The relative void of data highlights the need for research on this special issue in order to optimize the treatment and care of patients with severe graft-versus-host disease.

Abstract: Graft-versus-host disease (GvHD) is a frequent, and often life-threatening, complication after an allogeneic, hematopoietic stem cell transplantation (allo-SCT). It can appear in an acute or a chronic form and presents different grades of severity. Particularly, the severe forms of GvHD are often responsible for a change of the curative intent for allo-SCT into a palliative goal of care. For this non-systematic review, we conducted a focused literature search in the MEDLINE database via PubMed to examine whether patients with severe forms of GvHD might have special needs and burdens from a supportive and palliative care perspective. To draw a comprehensive picture of this patient group, we included findings on quality of life (QoL) and physical symptoms and function as well as psychological and spiritual well-being. In most domains, patients with severe forms of GvHD showed greater impairment and a higher symptom burden compared to patients with milder forms of GvHD. However, we could not identify any studies that specifically investigated patients with severe forms of GvHD. Further research in this field is necessary to guarantee the highest standard of care for this very special patient group.

Keywords: graft-versus-host disease; palliative care; supportive care; hematopoietic stem cell transplantation; quality of life; physical function

Citation: Wenzel, F.; Pralong, A.; Holtick, U.; Scheid, C.; Herling, M.; Simon, S.T. Burden and Needs of Patients with Severe GvHD from the Supportive and Palliative Care Perspective—A Literature Review. *Cancers* **2021**, *13*, 2697. https://doi.org/10.3390/cancers13112697

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1. Introduction

Graft-versus-host disease (GvHD; transplant-versus-recipient reaction) is an immunological reaction that can occur as a result of an allogeneic bone marrow or blood stem cell transplantation (allo-SCT). Acute (a) GvHD is characterized by a rapid onset of clinical manifestations, usually within the first 2 months after allo-SCT, and mainly affects the skin, gastrointestinal tract (GI) and liver [1]. In addition, a distinction is made between late onset aGvHD, occurring after day +100 post-allo-SCT, and recurrent, or persistent, aGvHD [2]. In aGvHD, cells of the innate immunity and donor-specific lymphocyte subpopulations react against tissue-specific structures of the recipient [3].

In chronic (c) GvHD, persistent alloimmune processes lead to tissue and organ inflammation and as a result, to varying degrees of fibrosis and sclerosing processes in various organ systems [4]. Clinically, skin changes as well as mouth and liver affection dominate [2]; however, nearly every organ including the upper and lower gastrointestinal tracts, eyes, lungs, joints or fascia and the genital tract can be affected [5].

GvHD is the leading cause of no-relapse mortality after an allo-SCT [6]. aGvHD affects 40–72% of patients after allo-SCT. cGvHD is found in 30–70% of patients [7]. The clinical courses of both aGvHD and cGvHD are defined according to severity scores. Glucksberg et al. divide aGvHD into four grades, I-IV, of increasing clinical severity [8]. cGvHD is staged into 3 degrees of severity (mild, moderate, severe) as defined by the NIH Consensus Development Project, dated 2004 and 2014 [5,9], and multiple studies seem to prove the benefits of this score [10,11].

Clinical literature on GvHD predominantly focuses on prophylactic strategies, treatment modalities, or organ complications. Systematic analyses of the challenges, i.e., the physical and psychological symptoms patients are faced with, are scarce. To our knowledge, published data on aspects of supportive and palliative care, particularly in patients with severe aGvHD or cGvHD, have not been reviewed.

1.1. Severe Acute GvHD, as Defined by Grades III and IV

About 14% of patients that undergo allo-SCT suffer from aGvHD (grade III/IV), which we define as "severe aGvHD" for the scope of this review [12]. This definition includes all patients with severe symptoms affecting the skin, liver and (upper/lower) GI tract that correspond to a scoring system primarily used by Glucksberg et al. [8,13,14]. There are different risk factors for developing an aGvHD, with human leucocyte antigen disparity being implicated as the most important one [1,15,16]. Patients with more severe aGvHD often require higher doses of therapeutic immunosuppression [17]. With an increasing aGvHD grade, the response to immunosuppressive therapy tends to decrease, while organ involvement expands [15,18]. Furthermore, the predicted risk for and the development of aGvHD with the involved immunosuppressive prophylaxis and treatment significantly enhance the risk for fulminant and life-threatening viral and bacterial infections [19]. Severe aGvHD causes increased mortality [20], with a 30% probability of long-term survival for grade-III aGvHD and a long-term survival of less than 5% for grade-IV aGvHD [16].

1.2. Severe, Chronic GvHD

Following the 2014 NIH Consensus Criteria, severe cGvHD has been characterized by significant impairment of organ function. At least one of the relevant organs (skin, mouth, eyes, GI tract, liver, lungs, joints or fascia, or genital tract) is scored as severely affected (score of 3), or there is a lung score of 2 or 3. It can occur as a characteristic of cGvHD or as overlap syndrome of both aGvHD and cGvHD, with the latter being associated with a worse prognosis [5]. cGvHD, in its severe form, has a 2-year cumulative incidence that ranges from 8.3% to 27.6% [21]. It is a major cause of non-relapse mortality in patients surviving more than 2 years after allo-SCT. An increasing severity of cGvHD [6] and a progressive onset type of cGvHD [22] are associated with higher non-relapse mortality rates and lower overall survival as compared to milder forms of cGvHD [21]. Most cGvHD-related deaths are due to infection (60–85% of deaths in patients with cGvHD) or organ

failures [6,23]. There are different risk factors for developing cGvHD, with prior aGvHD being the most important one [22,24]. The use of peripheral blood stem cells instead of bone marrow grafts is associated with a higher incidence of severe cGvHD [6,20]. The appearance of cGvHD might reduce the risk of relapse [22], but importantly, increased severity is not associated with a decreased relapse risk [6].

Patients who are usually allo-transplanted with a curative intent, but who are affected by severe GvHD, may suddenly find themselves in a life-threatening situation, potentially with a subsequent palliative trajectory [25]. This is a challenging situation for patients, their informal caregivers and health care professionals because all those involved in the allo-SCT procedure pursue a curative goal of care, with the expectation of long-term survival through this treatment modality [26]. The aim of this review is to summarize the current literature regarding the question whether patients with severe GvHD—as defined by aGvHD grade III/IV or severe cGvHD (according to NIH criteria)—might have special needs and burdens from the perspective of supportive and palliative care that require further investigation and treatment. To address these issues, outcomes like physical symptoms, quality of life (QoL) and psychological well-being are covered here. Since the integration of specialist palliative care in recipients of allo-SCT is currently under investigation and broadly supported [27], this review will additionally discuss the question if and at what point specialist palliative care should be included in standard-of-care procedures in patients with severe GvHD.

2. Materials and Methods

For this review, a focused, non-systematic literature search in the MEDLINE database via PubMed was performed in July 2020 with an update in October 2020. The following key words were searched for and combined with each other: gvhd, (severe) graft versus host disease, graft versus host reaction, palliative care, palliative care/medicine, palliative treatment, palliation, end of life care, hospice care, supportive care, advance care planning, psychooncology, psychological oncology, psychosocial oncology, long term survivors, quality of life (QoL), spiritual well-being, breathlessness, distress, pain. No restrictions on study design were applied and original articles as well as reviews were considered, based on their full text. Only publications in the English language were included. Further publications were identified by citation tracking, by means of the PubMed link 'similar articles' and cross-referencing from relevant publications.

For aGvHD, studies using the severity score of Glucksberg et al., or scoring systems based on it were included [8]. To distinguish between the different forms of severity of cGvHD, only studies that applied the 2004 and 2014 NIH Consensus Criteria were included [5,9]. Given the rarity of reports that specifically addressed supportive or palliative care needs in patients with GvHD, we also screened publications that more generally addressed aGvHD or cGvHD without specific distinction of severity grades. References to this kind of study are made clear in the subsequent text.

3. Results

We included 12 studies on acute or cGvHD that made a distinction between the different grades of severity of GvHD. Out of the 12 publications, only 1 focused on aGvHD. We did not identify any study that specifically examined patients with severe forms of GvHD.

3.1. Physical Symptoms and Functional Capacity

When considering symptoms in acute or cGvHD without differentiation of severity grade, it appeared that aGvHD was a risk factor for fatigue and sleep disturbance [28]. Active cGvHD seemed to be correlated with pain syndromes. Furthermore, cGvHD was a risk factor for fatigue and sexual dysfunction [29].

With regard to severe GvHD, the current literature does not provide sufficient information to describe possible unmet physical symptoms that are specifically related to a high severity of the disease. Only one cross-sectional study was identified, in which Im et al.

examined the association between fatigue and severity of cGvHD in 263 patients (70.7% of study participants had severe GvHD) by use of the Lee Symptom Scale (LSS). This was a 30-item measure that was validated for evaluating adverse effects in cGvHD [30]. The authors did not find any negative association between the severity of GvHD and fatigue, although the symptom was prevalent in 84% of the included participants with cGvHD. Only a higher number of prior therapies for cGvHD showed a trend for an association with an increased incidence of fatigue [31].

With regard to physical function, a significant decrease of this parameter was shown in patients with aGvHD of all severity grades in a retrospective study by Hamada et al. However, compared to less severely affected patients, patients with severe aGvHD (15% of 76 study participants) had a longer time to recovery, which resulted in longer hospitalization. At discharge, physical functions in these patients were not fully restored, which was examined by measuring the knee extensor strength and performance of a 6-min walk test [32].

As for physical functions in cGvHD, Baird et al., in their cross-sectional natural history study, found worse outcomes in nearly all functional measures for patients with severe cGvHD (66% of 189 study participants) as compared to patients with milder forms of cGvHD [10]. To examine physical functioning, they used various patient-reported outcome measures (PROMs) such as LSS or the Short-Form-36 (SF-36), which is a 36-item survey with focus on mental and physical health and functioning. It includes a physical component summary measure (PCS) that combines the categories of physical functioning, role-physical and bodily pain [10,33]. PROMs allow to better measure the subjective outcomes of patients and to relate them to the NIH global score [34].

Their findings are in accordance with those by Pidala et al., who found that particularly the PCS was negatively affected in patients with severe cGvHD (39% of 567 study participants) [35]. In a multicenter, observational cohort study, they reported a significant association of an impaired 2-min walk test (2MWT) with higher symptom burden (measured by LSS), greater functional disability and more severe cGvHD (according to NIH global score) as well as more severe patient-reported cGvHD [35]. The 2MWT is an indicator for physiologic reserve and vulnerability, and its usefulness has been confirmed by Pavletic et al. in patients with cGvHD [36].

In addition, an association between a lower Karnofsky performance status (impaired functioning) of patients with cGvHD and higher cGvHD disease severity in several NIH sub-scores was shown. The Karnofsky performance status is a tool to measure disease burden and function [37].

In their systematic review with focus on QoL and functional capacity in patients with cGvHD, Agh et al. concluded that patients with more severe cGvHD had significantly lower functional capacities (measured by various PROMs) than patients with less severe cGvHD. In their opinion, GvHD symptoms could be seen as a predictor for functional capacity [38]. In contrast to most findings above, Mitchell et al. reported in a cross-sectional study with 100 study participants (50% with severe GvHD) that severity of cGvHD was not a predictor of functional performance [39].

An overview of the main results of our review on physical symptoms and physical functions in patients with severe GvHD is presented in Table 1.

Table 1. Publications identified by the PubMed search on physical symptoms and functions in patients with GvHD, with specific results on severe GvHD.

First Author, Year, Country	Study Design	Form of GvHD	Patient Population	Main Outcomes	Main Results on Severe GvHD
Im, 2016, USA [31]	Cross-sectional	cGvHD	263 study participants; 70.7% had severe cGvHD	Fatigue in patients with moderate to severe cGvHD	84% of participants endorsed fatigue in different forms, but no correlation was found between the prevalence of fatigue and NIH cGvHD severity.
Hamada, 2019, Japan [32]	Retrospective chart review	aGvHD	76 study participants; 15% had aGvHD grades III and IV	Effect of the severity of aGvHD on physical function	A decline in physical functions was shown for all participants who developed aGvHD, but participants with aGvHD grades III and IV showed worse recovery of physical functions compared to participants with milder forms.
Baird, 2013, USA [10]	Cross-sectional	cGvHD	189 study participants; 66% had severe cGvHD	Assessment of the validity of the NIH criteria as determinants in severely affected patients	Participants with more severe cGvHD showed worse outcomes in nearly all functional measures compared to milder forms of cGvHD.
Pidala, 2013, USA [35]	Prospective cohort	cGvHD	584 study participants; 39% had severe cGvHD	Assessment of physical functions in patients with cGvHD by HGS and 2MWT and its relation to PROs	A significant association of an impaired 2MWT with higher symptom burden (measured by LSS), greater functional disability and more severe cGvHD was shown.
Agh, 2019, Hungary [38]	Systematic Review	cGvHD	n.a.	Systematic overview of HRQoL and functional capacity of patients with cGvHD	More severe cGvHD was correlated with worse physical functions.
Mitchell, 2009, USA [39]	Cross-sectional	cGvHD	100 study participants; 50% had severe cGvHD	Assessment of determinants of functional performance in patients with cGvHD	cGvHD severity was no significant predictor of functional performance.

aGvHD: acute graft-versus-host disease; cGvHD: chronic graft-versus-host disease; HGS: hand grip strength; HRQoL: health-related quality of life; LSS: Lee symptom scale; 2MWT: 2-min walk test; n.a.: not applicable; NIH: National Institutes of Health; PROs: patient-reported outcomes.

3.2. Psychological and Spiritual Well-Being in Patients with Severe GvHD

3.2.1. Psychological Well-Being

cGvHD, in general, is seen as a risk factor for persistent distress as well as for depression [29]. One-third of patients with cGvHD were reported to show significant depression or anxiety in a longitudinal observational study by Jacobs et al. In addition, the authors examined coping in patients with cGvHD, which was seen as an important factor for handling of stressful situations. They found task-oriented coping to be associated with fewer symptoms of depression and higher QoL over time in cGvHD. Avoidance in the form of social diversion also allowed better coping with cGvHD and showed better QoL as compared to other coping strategies. In this trial with 52 study participants, 71.2% had moderate, and 28.8% had severe cGvHD [40].

Little is known about the psychological well-being of patients with severe cGvHD. We identified only one secondary analysis of a prospective cohort that distinguished between the different grades of cGvHD, examining psychological distress by depression and anxiety. El-Jawahri et al. found that approximately 19.3% of 482 study participants with cGvHD suffered from depression, 22.8% had anxiety, and 14% showed symptoms of both, which was comparable with the findings of Jacobs et al. [40,41]. They could not find any association between the incidence of depression and the severity of cGvHD (40% had severe cGvHD), but patients with self-reported symptoms of depression showed a higher symptom burden of their cGvHD. Patients with self-reported anxiety had impairments in QoL and in physical functioning and also showed a higher GvHD symptom burden [41].

3.2.2. Spiritual Well-Being

In a prospective longitudinal study that did not differentiate between cGvHD severity grades, Wong et al. named cGvHD to be the only important factor that significantly reduced spiritual well-being (Sp-WB) after allo-SCT in comparison to patients that did not suffer from cGvHD after allo-SCT [42].

Harris et al. could not find any effect of the severity of cGvHD on the level of spiritual well-being (Sp-WB) in a cross-sectional study. However, the longer patients suffered from cGvHD, the poorer Sp-WB was found to be. Sp-WB was assessed by the FACIT-Sp, which is a 12-item scale that measures meaning and purpose, harmony and peace, and closeness to God or to a higher power [43]. In this study, higher Sp-WB was positively associated with higher QoL. Out of the 51 participants included in this study, 4% had mild, 65% had moderate and 31% had severe cGvHD [43].

3.3. Quality of Life in Severe GvHD

In a multicenter, observational, prospective study, Pidala et al. were the first to evaluate whether severity of cGvHD, as defined by NIH criteria, was related to QoL as measured by the tools of SF-36 and the Functional Assessment of Cancer Therapy-Bone Marrow Transplant (FACT-BMT) [44]. They found disease severity to be the most significant determinant of impaired QoL independently of most other examined covariates such as other diseases or sociodemographic variables. In their study cohort of 298 participants, 10.4%, 58.7% and 30.9% had mild, moderate and severe cGvHD, respectively [44]. Baird et al. also found the NIH global severity score to significantly correlate with nearly all QoL PRO measures (including LSS, SF-36 PCS, FACT-BMT etc.). Furthermore, involvement of joints/fascia, sclerotic skin and lung disease showed the most significant impact on QoL [10]. Two additional cross-sectional studies examined the relation between QoL and NIH global severity and found similar results. In both, worse QoL was associated with worse NIH global severity of cGvHD. The first study had 1140 participants, with 9% suffering from severe cGvHD [45]. The second one included 264 participants, and 19.3% had severe cGvHD [46].

Pidala et al. further evaluated if changes in cGvHD severity by NIH global criteria were associated with changes in QoL, which could not be confirmed. Patient-reported changes in severity of cGvHD showed a much greater association with changes in all QoL

measures as compared to clinician-reported changes and changes in GvHD severity as assessed by the NIH criteria. Apart from the global severity score, higher organ-specific severity grades also had a negative impact on QoL in patients with cGvHD [47]. According to Pidala et al., the organ-specific GI score and elevated bilirubin were also related to patient-reported QoL [48]. Agh et al. underlined higher severity of cGvHD to be a very important factor that negatively determined QoL in this patient group [38].

Hamilton et al. reported on the lower socioeconomic status of patients being associated with higher patient-reported severity of cGvHD and a reduced QoL, but they did not examine an association between severity of cGvHD, as objectified by the NIC global severity score, and socioeconomic status [49]. As for cGvHD without specification of severity, Jacobs et al. identified patients with cGvHD and lower perceived social support to experience poorer QoL [40]. An overview of the main results of our review on QoL in patients with severe GvHD is presented in Table 2.

Most of the retrieved data focuses on cGvHD, but Lee et al. found a measurable decline of QoL in patients with aGvHD in the first 6 months after allo-SCT, which improved within the first year post-transplantation, unless patients developed cGvHD [50].

Table 2. Publications identified by the PubMed search on quality of life in patients with GvHD with specific results on severe cGvHD.

First Author, Year, Country	Study Design	Form of GvHD	Patient Population	Main Outcomes	Main Results on Severe GvHD
Pidala, 2011, USA [44]	Cross-sectional	cGvHD	298 study participants; 30.9% had severe cGvHD	Association of patient-reported QoL and the severity of cGvHD	Severe cGvHD was associated with worse patient-reported QoL compared to milder forms of cGvHD.
Baird, 2013, USA [10]	Cross-sectional	cGvHD	189 study participants; 66% had severe cGvHD	Assessment of the validity of the NIH criteria as determinants in severely affected patients	Participants with more severe cGvHD showed worse outcomes in nearly all QoL measures compared to milder forms of cGvHD.
Kurosawa, 2017, Japan [45]	Cross-sectional	cGvHD	1140 study participants; 9% of patients had severe cGvHD	Association of patient-reported QoL and the severity of cGvHD	Severe cGvHD was associated with worse patient-reported QoL compared to milder forms of cGvHD.
Mo, 2013, China [46]	Cross-sectional	cGvHD	264 study participants; 19.3% had severe cGvHD	Association of patient-reported QoL and the severity of cGvHD	Severe cGvHD was associated with worse patient-reported QoL compared to milder forms of cGvHD.
Pidala, 2011, USA [47]	Prospective cohort	cGvHD	336 study participants; 27% had severe cGvHD at the beginning of the study	Association of changes in cGvHD severity (measured by NIH criteria by the clinician as well as patient-reported)	Changes in NIH-assessed cGvHD severity did not have an impact on changes in QoL, but changes in patient-reported cGvHD severity were associated with changes in QoL measures.
Agh, 2019, Hungary [38]	Systematic review	cGvHD	n.a.	Systematic overview of HRQoL and functional capacity of patients with cGvHD	Four of five included studies that assessed the impact of cGvHD severity on HRQoL found significantly worse HRQoL in patients with more severe cGvHD.

cGvHD: chronic graft-versus-host disease; HRQoL: health-related quality of live; n.a.: not applicable; NIH: National Institutes of Health; QoL: quality of life.

4. Discussion

The appraisal of available literature for this review revealed a fundamental lack of large and representative studies describing supportive and palliative care needs of patients with severe GvHD. Publications that made clear assertions regarding aGvHD grade-III/IV or severe cGvHD were rare. However, we were able to extract some findings from general studies on GvHD, allowing us to draw first conclusions on palliative and supportive issues of patients suffering from the severe form of GvHD.

The literature findings suggest that patients with more severe GvHD suffer from worse physical functioning [10,32,35,38] and show a more impaired QoL as compared to those with less severe forms of GvHD [10,38,44–46]. With regard to physical symptoms, it was not possible to gather sufficient data to show if specific symptoms were especially burdensome in the severe forms of GvHD and if so, which ones those were. Nevertheless, the findings reported here indicated that special attention and treatment for those patients should be considered. Since psychological well-being can be impaired in patients with cGvHD [41], it is important to enhance research on the particular subset of patients suffering from severe GvHD following allo-SCT. The question should be addressed as to how these patients perceive their situation, what helps them to cope and which form of support should best be offered to them by whom (profession/discipline).

A main question is about the role that specialist palliative care (PC) can play for patients with severe aGvHD or cGvHD because severe GvHD may result in high symptom burden and a life-threatening situation [51]. In her review, Mitchell reports that severe GvHD could function as a longitudinal sentinel for the integration of specialist PC into standard care along the transplant trajectory [27]. In the large retrospective chart review, Han et al. found that the occurrence of GvHD after allo-SCT might be related to more frequent PC use [52]. El-Jawahri et al. surveyed transplant physicians about PC. Most of them named GvHD as a substantial unmet PC need after allo-SCT [53]. However, beyond these studies on PC after allo-SCT in general, we did not identify trials that specifically focused on the integration of specialist PC into the standard care of severe GvHD. This was quite surprising for us because patients who are treated in our medical center for severe forms of GvHD show a high level of burden and needs, requiring effective supportive and palliative care.

Due to our findings such as the high symptom burden, the loss of QoL and the highly impaired physical functions, as well as impaired psychological and spiritual well-being, we see the integration of PC into the care of patients with severe forms of GvHD as a main issue for clinical practice and for research [41]. Moreover, further important topics of PC such as communication about prognosis and end-of-life matters, prognosis perception, quality of end-of-life care and advance care planning also need to be considered. Research in this field is highly warranted.

We can only hypothesize about the reasons for the lack of such data on severe GvHD because at least in our medical center we perceive this patient group to have a high level of suffering and very special needs, which warrants intensified research. The burden of disease could, in fact, be a great impediment that might cause this shortage of systematic data because it might be difficult to include patients with severe GvHD in studies due to their instable medical condition and reduced physical and cognitive function [35]. Since severe GvHD causes high morbidity, patients might die prior to completion of a study [54] or before a study even takes place. Those circumstances require special study designs in this area, and to examine this patient group, studies should focus on severe GvHD patients directly.

Furthermore, rating the severity of GvHD only by taking into consideration the NIH global severity score might be insufficient. Although some trials show a good correlation of the scores and outcomes such as QoL, patients with GvHD form a very heterogenous population and might undergo rapid changes in morbidity. For this reason, integration of PROMs as an integral endpoint into research and treatment of GvHD is of high interest. Such PROMs allow the evaluation of issues that go beyond the clinician's perspective of severity and should also be considered for our patient group with severe GvHD [55,56].

5. Conclusions

This review shows a fundamental lack of representative studies to describe the burden and needs of patients with severe GvHD after allo-SCT and the role of supportive and palliative care for this patient group. Findings in patients with severe GvHD, such as a more impaired QoL and reduced physical functioning as compared to patients with less extensive and less severe GvHD, indicate that research in this field is highly warranted. Aiming to integrate specialist PC early, it is important to examine at what point specialist PC should be integrated into the allo-SCT trajectory, particularly from the patient's point of view. We consider this review to promote awareness and act as a primer for such initiatives. Further research is needed to be able to draw a comprehensive and differentiated picture of the burden, needs and resources of affected patients and to optimize their treatment with a multidisciplinary approach.

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3.2 Qualitative interview study

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Burden, resources, and needs of patients with severe graft-versus-host disease – A qualitative study

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Abstract

Objectives: Severe forms of acute and chronic graft-versus-host disease (GvHD) are life-threatening complications after adjusted to allogeneic hematopoietic bone marrow or peripheral blood stem cell transplantation (allo-HSCT) and are a major cause of non-relapse mortality. Little is known about the burden, needs, and resources of this specific patient group. This qualitative interview study aimed to explore the experiences of patients with severe forms of GvHD and their perception of palliative care (PC).

Methods: Semi-structured interviews were conducted among 13 participants at a tertiary university hospital and were evaluated by qualitative content analysis.

Results: The participants described a high psychological and physical symptomatic burden resulting in severely impaired physical function up to loss of independence, which all substantially limited their quality of life (QoL). Frequent long-term hospitalizations highly impacted their social life including the ability to work. A desire to die was frequently experienced, particularly when participants suffered from peaks of burden and uncertainty about the future. Dying was either feared or perceived as relief. Not all participants received PC and the term was sometimes associated with fear or remained unclear to them.

Significance of results: Patients with severe forms of GvHD described a multifactorial, high overall burden, and permanently impaired QoL, which needs special support. Next to depressive symptoms, the frequently reported desire to die has not yet been thoroughly studied and requires further research. The infrequent use of PC in this context implicates a need for structural improvement and education in the German healthcare system.

Introduction

Graft-versus-host disease (GvHD) is a major complication of allogeneic hematopoietic bone marrow or peripheral blood stem cell transplantation (allo-HSCT). It represents a main reason for non-relapse morbidity and mortality (Lee et al. 2003; Zeiser and Blazar 2017). It may manifest as acute GvHD (aGvHD) that is characterized by a rapid and dynamic onset of clinical manifestations and predominantly affects the skin, the gastrointestinal (GI) tract, and liver (Harris et al. 2013). There is also a late-onset form of aGvHD that occurs after day + 100 post-allo-HSCT, and recurrent or persistent forms have been defined (Jagasia et al. 2015). Its prevalence ranges from 40% to 72% in the context of allo-HSCT (Harris et al. 2016).

GvHD can further appear in a chronic form (cGvHD), which is the result of complex allogeneic immune-mediated tissue and organ inflammation, leading to fibrosis and sclerosing processes in various organ systems. About 30–50% of patients suffer from cGvHD after an allo-HSCT (Hamilton 2021).

aGvHD and cGvHD are defined according to severity scores, which are mostly based on organ-specific criteria. Glucksberg et al. categorized aGvHD into 4 severity grades (Glucksberg et al. 1974), which was updated by Harris et al., introducing the MAGIC grading system (Harris et al. 2016). cGvHD is mostly divided into 3 degrees of severity (mild, moderate, and severe), as defined by the NIH Consensus Development Project (Filipovich et al. 2005; Jagasia et al. 2015).

Patients with severe GvHD usually show a high symptomatic burden, which for cGvHD is commonly evaluated by using the Lee Symptom Scale (Teh et al. 2020). Probably due to their

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impaired health condition, the group of patients with severe GvHD is still underrepresented in such analyses (Lee et al. 2018). Thus, in this qualitative study the primary aim was to explore the challenges that those patients face from their own perspective, including their burdens, resources, and needs to give them a voice.

In a previous review, we concluded that special care in the form of multimodal treatment concepts can be helpful for patients with severe forms of GvHD (Wenzel et al. 2021). An important part of this might be the integration of palliative care (PC), since transplant physicians reported GvHD symptoms to be an important indication for the use of PC (El-Jawahri et al. 2018a). Nowadays seen as an integral part of standard cancer care, there is only few data on the role and utilization of PC in the context of allo-HSCT. This indicates that integrating PC into the allo-HSCT procedure likely contributes to achieve the best possible symptom control, to help to better cope with the illness and its prognosis, and to optimize the quality of life (QoL) of affected patients (Simon et al. 2021). Therefore, exploring how the study participants perceive PC was another aim of this study.

Materials and methods

Using a qualitative approach in the form of a content analysis (Kuckartz 2018), we conducted semi-structured, face-to-face in-depth interviews. Ethical approval was obtained from the Ethics Committee of the Faculty of Medicine of the University of Cologne (Reference Number 20-1253). The reporting of this study follows the guidelines of the Consolidated Criteria for Reporting Qualitative Studies (Tong et al. 2007).

Recruitment

Patients were recruited face-to-face or via telephone by F.W. (female, medical student) in the form of purposive sampling from October 2020 to March 2021 and were eligible for this study if diagnosed with persistent, severe acute or chronic GvHD after an allo-HSCT. We defined *severe aGvHD* as grade III or IV, following the scoring system by Glucksberg et al. (1974) and *severe cGvHD* by the NIH Consensus Criteria (Jagasia et al. 2015). Patients were further eligible if they were ≥18 years old, treated in the out- and inpatient bone marrow transplantation (BMT) unit at the University Hospital of Cologne (UHC), with no cognitive impairment (according to clinical assessment) and sufficient German language skills. Verbal and written informed consent for participation in this study was obtained.

Data collection

Demographic data and clinical information were retrieved from the patient's health records of the UHC. The interviews were conducted once by one interviewer (F.W. – trained by S.T.S., male, consultant in PC, senior clinical research fellow) following a semi-structured interview guide (Table 1). The participants did not know the interviewer prior to study commencement. They were informed that the interviewer was working on her doctoral thesis and was not involved in their treatment and that the interviews would be anonymized. The interviews were conducted individually between 2 months and 7 years after transplantation. Whether patients had received PC during the allo-HSCT process varied. Psychological support was offered after every interview if participants felt burdened.

Table 1. Topics of the semi-structured interview guide

- Specific symptoms and symptomatic burden of GvHD
- Physical and psychological burden
- Thoughts about the end of life
- Use of palliative care
- Patient's resources
- Unmet needs and wishes of patients

Data analysis

Descriptive analysis was performed for demographic and clinical data of the participants. For analyzing the audio-recorded interviews, the qualitative content analysis by Kuckartz (2018) was used. In this qualitative thematic analysis, categories are formed within a category system (Kuckartz 2019). After verbatim transcription (Institut für Kulturanthropologie und Europäische Ethnologie 2022), the interviews were read several times to get an overview of their contents. The transcripts were not returned to the participants for feedback. By using the software MAXQDA 2020®, the main categories were built deductively, following the semi-structured interview guide. These main categories were coded in all interviews and then divided into subcategories (Table 2), which was performed by 2 researchers (F.W. and Isabel Düster (I.D.); female, research assistant, and medical student – both trained by S.T.S.) and then compared and standardized by developing a description of the coding tree. The following 3 interviews were coded by both researchers to verify the category system. Findings were interchanged regularly among the research team (F.W., Isabel Düster (I.D.), S.T.S.) and modifications were taken to form a final category system. All interviews were then coded. Every code was summarized and integrated into thematic summary tables, which allowed to compare and contrast statements of different participants (Kuckartz 2019).

Results

Seventeen patients were approached, of whom 2 were not interested in participating, 1 felt too ill, and 1 consented, but died before the interview. Thirteen patients (female $n = 5$, male $n = 8$, median age 49 years) were included in the study, until content saturation was assumed (see Table 3 for participant demographics). Two interviews were conducted at the participant's homes, 2 were conducted during inpatient stays, and 9 were conducted ambulatory. They lasted 38–72 min and during 2 interviews a family member was present.

Burden associated with specific forms of severe GvHD

Severe GvHD of the GI tract

The majority of the participants suffered from a severe aGvHD of the GI tract and named diarrhea and pain as the 2 major burdensome symptoms.

> I had only been laying on the couch, because, I had partly … to go to the toilet twice per hour. And this continuously, during day and night-time. (P10, Pos. 15)

The frequency and persistence of diarrhea led to great exhaustion, involving bedriddenness, and unpredictably long hospital stays with dependence on healthcare providers (HCPs) or patient's social network. Commonly experienced fecal incontinence caused distress and insecurity, leading to avoidance of social contact.

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Table 2. Category system – overview of the main categories with first subcategories

1 Special aspects of the course of the disease
2 Burden
2.1 Due to the general course of the disease
2.2 Specifically due to GvHD
3 Comprehensive consequences of the illness and its burdens
3.1 Coping with everyday life
3.2 Social environment
3.3 Being aware of the disease
3.4 Decrease in quality of life
3.5 Other
4 Perception/experiences during medical care
4.1 Negative experiences during medical care
4.2 Medical care perceived positively
4.3 Other
5 Resources/coping factors
5.1 Structural support
5.2 Mental resources/relief
5.3 Social resources/relief
5.4 Building a feeling of security
5.5 Spiritual resources
6 Dying/death
6.1 Confrontation with threat to live/death
6.2 Palliative care
7 Needs
7.1 Needs in context of therapy
7.2 Social needs
7.3 Psychological needs
7.4 Physical needs
7.5 Structural needs
8 Other/individual aspects

Suffering from nocturnal diarrhea was mentioned as an important reason for insomnia. In the course of GvHD, many participants experienced a decrease of its frequency, but none ever regained normal digestive functional states.

Pain was experienced as a continuous or intermittent symptom and could usually only be relieved with high doses of analgesics.

> It feels as if you had a mucositis, and the skin is gone … and then food rides over it. (P3, Pos. 79)

Some participants did not suffer from pain at all.

Moreover, the participants often suffered from a lack of appetite or nausea, followed by a significant weight loss, which caused great distress. Some participants felt an inner barrier, making them unable to eat.

> You can't eat. Or you eat a little bit and that was it. It is not possible. That's all, you cannot describe it. (P12, Pos. 95)

Table 3. Demographic data of participants

Characteristics	Participants ($N = 13$)
Gender	
Female	5
Male	8
Median age (years)	49
18–39	3
40–59	8
>60	2
Primary disease	
Acute myeloid leukemia	9
Acute lymphoblastic leukemia	1
Chronic lymphocytic leukemia	1
Myelodysplastic syndrome	1
Myeloproliferative disorder	1
Characteristics of GvHD	
Acute: overall grade 4	6
Main organ site: lower gastrointestinal tract	6
Chronic: NIH grade severe	7
Main organ site: lung	1
Lower gastrointestinal tract	4
Skin	1
Fasciitis/tendinitis	1
Family status	
Married/long-term relationship	8
Single/widowed	5
Having children	
Non-adult	6
Adult (≥18 years)	3
None	4
Occupation (if have worked before allo-HSCT)	
Full-time	1
Part-time	3
None	8
Time post-allo-HSCT (years)	
0–2	5
2–4	3
4–6	4
6–7	1
Overall duration of cumulative inpatient stay(s) prior to the time of interview (days)	
30–60	2
61–90	4
91–120	2
120–200	5

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Severe GvHD of the skin

Severe skin GvHD caused restlessness due to pain and pruritus. It was associated with visual stigmatization, hence insecurity in public, which caused a feeling of shame and disgust toward oneself.It was perceived as onerous that therapies could not bring immediate relief due to the delayed effects of topical therapies. For the application, the participant felt dependant on HCPs.

Severe GvHD of the lung

One participant suffered from pulmonary GvHD, which manifested as a pronounced weakness due to chronic breathlessness. The participant reported about the permanent limitation of his everyday life, needing daily assistance by family members and a wheelchair when leaving the house. The GvHD compromised recovery from the allo-HSCT procedure.

Further forms of GvHD

Contributing to the overall burden of the participants, various – although often scored as milder – organ affections of GvHD (liver/bile, joints/fascia, eyes, and oral/genital mucosa) were endured by the participants. These were predominantly perceived as bothersome and another side to be taken care of, but less dangerous than the severe forms of GI, skin, and pulmonary GvHDs.

Overall burden associated with severe GvHD

Weakness

The constant presence of weakness limited the participants' activities of daily living (ADLs) and made participants feel helpless.

> I couldn't really do anything that would build up my body because I was always short of air. (P11, Pos. 32)

Particularly muscle weakness was limiting as patients had difficulties judging whether strength was sufficient for certain ADLs. They described a tendency to fall, inability to get up after falling, incapability to stand, walk, or climb stairs, or a limitation of these functions.

Isolation

During in-hospital stays, isolation and loneliness were mentioned as a decisive burden, particularly on the BMT ward, where patients are more isolated for protective measures, as compared to regular wards. Since most of the participants were hospitalized for a long time, they often only saw 1 or 2 authorized visitors and missed their social network. Participants imagined this to be particularly burdensome for patients without family support.

> I have seen those people. Young people that have died. Because they have just been so lonely. They have lived alone. (P12, Pos. 101)

The persisting high symptomatic load after hospital discharge, e.g., weakness or fecal incontinence, isolated the participants from their social environment and limited their participation in public life. Changes of social relations were noted and the loss of former close relationships saddened many participants.

Dependence on others

Feeling dependant on others and needing assistance with ADLs was uncomfortable for the participants and made them feel embarrassed and vulnerable, particularly if being cared for by HCPs and not family members.

> So, when you lay in bed and realize, okay, I have to go to the toilet, but you cannot manage it at all. And then you have to be washed, by people who are actually strangers to you. This has been the worst for me. (P11, Pos. 10)

A feeling of losing control emerged as well as the concern of being a burden, while not being able to fulfill the (expected) social function.

Mental strain due to GvHD

The participants had not expected to get such severe GvHD and had difficulties to mentally cope with it. It was straining not to be able to participate properly in life for such a long time and sometimes the extent to which the allo-HSCT can be considered curative was questioned.

> It was a disaster, or still is. I still can't cope with it at all. Um, apart from the fact that the question always is what does it mean to be cured of the underlying disease? Is that really the case? I have no idea. (P10, Pos. 35)

Depressive symptoms and existential distress

Symptoms of depression often occurred when participants were in very poor physical conditions, felt overwhelmed by new complications, or realized health limitations could become chronic. Particularly a lack of prospect of recovery caused hopelessness and made the participants feel desperate, powerless, and demoralized. Further triggers were pain, exhaustion, loneliness, feeling locked away, reduced ADL, and reduced working abilities. Some participants were diagnosed with depression and several were treated with antidepressants.

Most participants experienced tiredness of living or a desire to die when the above-mentioned triggers peaked. These thoughts could be associated with fear, but had a liberating character in burdensome phases.

> This comes up sometimes and then I tell myself: Before living like this, I prefer not to live at all. (P13, Pos. 66)

In 2 cases, participants reported they had suffered from active suicidal ideation because of their GvHD burden.

Uncertainty and fear

The occurrence of the GvHD made the participants aware of the unpredictability of their prognosis. This generated uncertainty and fear, such as the fear of persistence or recurrence of GvHD symptoms or the recurrence of the underlying disease.

> I think I was even more afraid of that than of dying. That I would somehow have to be … yes … cared for all my life or something. (P7, Pos. 55)

At a certain point, the treatment options were also perceived as unclear and "only trial and error" (P10, Pos. 57), which next to uncertainty caused fear of limited treatment options.

Other important fears included the uncertainty of managing life independently, becoming permanently dependant on others, getting complications which cause rehospitalization, or the permanent need of medication with harmful side effects.

Perception of the threat to life

Apart from life-weary thoughts, which we classified as an expression of psychological distress, all participants reported to perceive the life-threatening character of their diagnosis, mainly during inpatient-stays, but in form of a dynamic process with individual peaks. Being confronted with the death of other transplant recipients increased anxiety and the feeling of being in a life-threatening situation.

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A minority of patients described having felt very close to dying at some point and described acceptance and a sense of letting go. But participants mostly did not feel close to dying.

> Well, I knew that all of this can be life-threatening, but I thought no, it won't be. (P5, Pos. 60)

Most participants described thoughts of the threat to life as phase-dependent, but one participant saw death as a constant threat, causing consistent fear and despair.

Cognitive impairment

A reduced ability to focus and to remember or difficulties in carrying out familiar work processes were described, which made participants feel easily overloaded. However, these impairments usually improved over time.

Resources/coping factors

Being cared for by family members and friends was seen as the most important resource to cope with burdens caused by GvHD.

A feeling of hope was given by doctors who expressed an optimistic attitude toward a positive recovery outcome.

> Yes, but Dr Y told me, everything will be fine, Miss X. and, when I heard that, I thought in this moment okay, then I will not give up. (P5, Pos. 2)

The participants perceived the offer of psychotherapy as relieving and it was seen as a good opportunity to speak freely, regardless of its use.

If being religious (all religious participants were of Christian faith), pastoral care seemed to serve the same function as psychotherapy. Faith was seen as a resource, but doubts were frequently experienced alongside hope, particularly in tough times.

A positive mind set was addressed as a very important coping factor, while establishing it was considered as a lengthy process that may not be possible during worst times.

> She told me, you have to make this disease your friend. … I did not understand this at all … but in the meantime … in the meantime I think I understand what she meant. That is the only possibility to somehow get into a light-hearted life. By accepting and living with the disease. Whether I make it my friend … (person laughs out loud), this is still difficult. But I understand where one has to get to. (P1, Pos. 78)

Many participants described that the resource of setting future goals was important, but only possible in an improved state of health. During symptom peaks, participants stated that they often did not think about the future and lived from day to day.

Support needs

The participants had a great need for medical information. Due to the unpredictability of the disease course, they felt very insecure and longed to be able to assess their health status and to gain control over their situation.

Structural needs often related to ADLs after discharge, e.g., in form of domestic help. These were particularly expressed by patients without family support.

The course of disease

The disease courses of the participants were heterogenous and unpredictable, but all characterized by long inpatient stays and frequent hospital readmissions due to complications.

> Directly in the BMT Ward, um. One or two months, I think. But then I had several complications and … I believe altogether it was about a year that I was here. (P8, Pos. 18)

After discharge, none of the participants could live without assistance, which caused despair and the feeling of being a burden. Activity levels were extremely reduced and it took months or even years to return to an autonomous life.

> At the beginning, I couldn't do much, I have to say. …. During the day I just laid here on the sofa. …. And then last year we walked up and down the street a bit. That's all I managed to do. (P2, Pos.13)

Resuming work

Return to work took place at least 2 years after transplantation, when the participants felt more stable. The majority of participants considered themselves not (fully) able to work.

Quality of life

For none of the participants, the QoL reached the level before the diagnosis of the underlying disease and most suspected this would not happen anymore, which was unexpected and difficult to accept. QoL was worst during hospitalization and while experiencing high symptomatic burden.

> At zero. I don't have any quality of life. You don't have that with diarrhea. And when you can't participate in life, not at all. (P3, Pos. 84)

Perception of PC

Most participants did not know what the term PC meant. In case they knew about it, PC was mostly perceived as end-of-life care. In this case, the question of whether they had received PC evoked irritation or defensiveness.

Only some of the participants were aware of having received specialist PC, which was positively associated with pain-relieving therapy. Most participants were not sure about having received specialist PC or could not distinguish between specialist PC and other specialties.

Discussion

Our qualitative study emphasizes burden, resources, and needs of patients with severe GvHD. Next to specific symptoms of the severely affected organs, the participants suffered from long and mostly incomplete recovery processes, riddled with occurrences of somatic distress, complications, and frequent hospitalizations.

We want to highlight the unpredictability of the GvHD course in our cohort, which was perceived as particularly burdensome among the patients, causing a constant threat and a feeling of demoralization. They had not expected such a severe complication and felt shocked how much it suddenly dominated their lives. This corroborates with another qualitative study, which explored QoL after GvHD in the UK and named the unpredictability as burdensome, leading to uncertainty about the future (de Vere Hunt et al. 2021).

Participants named prolonged isolation as an important source of suffering. This came from protective isolation within prolonged hospital stays, which is known to cause loneliness and psychological distress, and poor post-discharge health, and is consistent with our findings (Biagioli et al. 2017; Tecchio et al. 2013). The participants in our study felt very dependent on their HCPs, but also on family members. This was linked to extreme physical weakness, which impaired their ability for self-care. While

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reduced physical functioning is a known restriction for patients with GvHD (Agh et al. 2019; Baird et al. 2013; Pidala et al. 2013), we would like to emphasize its high extent among our cohort, resulting in all of them requiring comprehensive assistance after discharge. Having been interviewed at different stages of survivorship, most participants described a protracted, undulating, but progressive recovery process. All of them described a persistently reduced QoL and did not anticipate that the pretransplant level could ever be reached again, what we consider to be a central message of this study. This is supported by several studies, which found severe cGvHD to be associated with very poor QoL (Baird et al. 2013; Kurosawa et al. 2017; Mo et al. 2013; Pidala et al. 2011).

Regarding returns to their occupational work, a long sick leave of at least 2 years was remarkable among the participants if a return to work was possible at all and most of the participants then worked part time. An association between suffering from aGvHD or cGvHD and taking full-time sick leave for 1 year after transplantation has been already described (Bhatt et al. 2021; Eriksson et al. 2021). An investigation of the correlation between the grade of severity of GvHD and the average time of sick leave would be informative.

Almost all of the participants reported symptoms of depression and the majority felt tired of living during the peaks of symptomatic burden. Two studies found that approximately 1/5–1/3 of patients with cGvHD suffer from depressive symptoms and that its appearance may be linked to a higher burden of cGvHD (El-Jawahri et al. 2018b; Jacobs et al. 2019). We hypothesize that severe GvHD could be considered a trigger for psychological distress, as it prolongs the course of allo-HSCT, is often unexpected in its dimension, and must be managed in an already health-reduced state. Research on the desire to die in the context of GvHD does not seem to exist yet. But research on the broad term of "desire to die" has intensified in recent years for people suffering from life-limiting progressive diseases. A first definition published in the German Palliative Care Guideline describes "desire to die" as a continuum ranging from acceptance of death (satiety of life) to acute (consciously planned) suicidality. Between these 2 poles, the pressure to enact the desire increases, hoping to die soon or wishing to accelerate the dying phase (Kremeike et al. 2021). The statements of the participants in this study are reflected in the above definition. Further research in this field is indicated.

Among the participants, it was common to associate the term PC with end-of-life care. They were not sufficiently informed about this specialty, which aims to improve QoL not only near the end of life, but also more generally in serious health-related suffering due to severe illness (Radbruch et al. 2020). Furthermore, not all participants were given the opportunity to receive a PC treatment. This fits with the current state of research, according to which the use of PC in allo-HSCT is scarcely investigated and practiced (Pralong et al. 2023; Simon et al. 2021).

As for many patient groups, social resources were very important to the participants (Applebaum et al. 2014; Nørskov et al. 2021). Alarmingly, they considered the services provided by the German health care system as not sufficient for patients without a supportive social system, which also had been pointed at in another qualitative study from Germany, examining the needs after allo-HSCT (Parisek et al. 2021).

Finally, a need for medical information was frequently addressed due to the unpredictability of the course of disease and the wish to gain control over the situation.

Limitations

The majority of the participants suffered from severe GvHD of the GI, which means that the sample is not representative of all manifestations of severe GvHD. In addition, there may be a participation bias as some patients were too ill to participate in the study and a recall bias if interviewed several years after allo-HSCT. Furthermore, some topics such as sexual dysfunction might not have been addressed by the participants. It might be associated with shame. In 2 interviews, family members were present, which could have restricted the unbiased verbalizations by those 2 participants. It should be noted that this study lacks racial diversity as all participants were Caucasian in Germany. Furthermore, it was conducted in a European care setting and may not be transferable to other settings.

Conclusion

This qualitative study provided an overview of the complexity and burden that participants have to endure due to severe GvHD, further complications, and the unpredictability of their course. The frequently addressed desire to die in the context of severe GvHD has not yet been described in this detail and represents an important field of future research.

Participants' definition of the term of PC as an end-of-life care suggests that the meaning of PC in the German society remains misinterpreted or is unknown. This study appears to be the first to make statements on PC in the context of GvHD in the German healthcare system, which shows a lack of research on its local use. Since our findings support that GvHD symptoms represent an important need for timely PC involvement, further research in this field is highly warranted.

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Ethical approval. This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Commission of the Faculty of Medicine of the University of Cologne (Reference Number 20-1253). Informed consent was obtained from all individual participants included in the study.

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4. Discussion

4.1 Key findings of the dissertation

The aim of this dissertation is to examine the burdens, needs and resources of patients with severe forms of GvHD with the overall aim to improve treatment strategies for this highly suffering and often overlooked patient group.

By conducting a comprehensive literature review, a broad overview of the state of research on this topic was provided [30]. It was shown, that patients with severe forms of GvHD suffer from more impaired physical functions and from more impaired QoL compared to patients who suffer from milder forms of GvHD. Psychological distress particularly in form of depressive symptoms and impaired spiritual well-being (Sp-WB) were prevalent in patients with cGvHD, while no connection between the corresponding prevalences and the severity of cGvHD was discovered. No information could be found regarding the occurrence of possible unmet physical symptoms and their relation to the severity of the disease. The literature review revealed a fundamental lack of large and representative studies describing SC and PC needs of patients with severe forms of GvHD. Matching studies predominantly focused on cGvHD; severe forms of aGvHD seem to be even more underrepresented [30].

The aim of the subsequent qualitative interview study was to draw a detailed picture on the burdens, needs and resources of 13 participants treated in the University Hospital of Cologne and suffering from severe forms of GvHD, to provide a first insight of where further research is needed to support this patient group [67]. Therefore, semi-structured, face-to-face in depth interviews were performed and evaluated following content analysis by Kuckartz [66].

A key result of the qualitative interview study was the permanently reduced QoL described by all participants while an improvement up to the pre-transplant level was not expected in the long term.

This was generated by severe physical symptoms, which never completely regressed. The unpredictability of the course of GvHD was an important burden in this context, which caused a constant feeling of distress and anxiety. In addition, there was often the issue of social isolation and dependence on health care providers (HCP) or people from the participants' social environment. The participants were unable to work for at least two years. In some cases, this was permanent and participants were otherwise only able to work part-time. Psychologically, the participants were very negatively affected and almost all reported depressive symptoms. If particularly afflicted by GvHD symptoms or complications, a desire to die was reported, predominantly in the form of tiredness of living associated with thoughts of no longer having to endure the suffering. But active suicidal thoughts due to the overall burden of the GvHD have also been addressed.

Frequently mentioned needs were the requests for more medical information and more structural support particularly after discharge. Most important were social resources in form of family support.

This qualitative interview study points out the extreme overall burden that patients with severe forms of GvHD must endure. In this context the participants have been asked about their perception of PC. Alarmingly, they were either unfamiliar with the term or categorised it as end-of-life care, which evoked negative associations. This qualitative interview study appears to be the first study to examine the complex disease situation for patients with severe forms of GvHD. It is also the first in the German health care system and shows that further research and more support for patients with severe forms of GvHD are needed.

The use of PC seems to be a reasonable approach here, but it is not yet sufficiently applied. Research should therefore focus on PC in the context of GvHD, and the current health care system should be improved [67].

4.2 Comparison of the main findings of the literature review with results of the qualitative interview study

- Can the findings of the qualitative interview study complement the results of the literature review?

Physical functions

In the literature review five out of six included studies / reviews examining physical functions in patients with GvHD (section 3.1) found more impaired physical functions in patients with severe forms of GvHD compared to patients with milder forms of GvHD. Only one of these studies included participants with aGvHD. Only Mitchell et al. could not find an association between cGvHD severity and the level of functional performance [30,68]. Most of the included studies used PROMs for examining physical functions such as the LSS or the (PCS of the) SF-36 score [30]. While these have not been applied in the qualitative interview study, its findings support the durable impairment of physical functions in this patient group. Weakness was mentioned as often constantly present and particularly muscle weakness limited the participants in fulfilling their activities of daily living [67].

Specific physical symptoms

In the literature review aGvHD was seen as a risk factor for fatigue and sleep disturbances [69] while cGvHD seemed to be correlated with pain syndromes, fatigue and sexual dysfunction [30,70]. While no distinction between symptoms in aGvHD and cGvHD in the qualitative interview study has been made, specific symptoms were mostly associated with the dominating organ

manifestation of the participants. Pain was associated with GvHD of the GI and GvHD of the skin. Sleep disturbances were associated with GvHD of the GI (due to diarrhoea) and GvHD of the skin (due to restlessness and pruritus). The specific term of “fatigue” had not been addressed during the interviews with the participants [67].

Its definition by the German Fatigue Society is: *“Fatigue in cancer means tiredness and exhaustion that can occur in connection with cancer and its treatment. Fatigue is often not directly related to previous physical or mental exertion or strain. Fatigue is usually not only physical, but also emotional and mental. It is typical of fatigue that the feeling of fatigue is not significantly improved by periods of rest.”* [71].

Several aspects of this definition were frequently mentioned by the participants of the qualitative interview study (e.g. exhaustion involving bedriddenness, persisting (muscle-) weakness, reduced activity levels) but no statement can be made whether the participants would characterise their symptoms as fatigue. Furthermore, the symptom of sexual dysfunction had not been addressed in the qualitative interview study [67].

Further symptoms mentioned particularly by participants with GvHD of the GI were a lack of appetite or nausea followed by significant weight loss. Malnutrition and weight loss are known complications in patients with GvHD (of the GI) and associated with poor prognosis in patients after HSCT, while it seems that this has not yet been explicitly examined in patients with severe forms of GvHD. In their cross-sectional study Bassim et al found 29% of study participants with moderate or severe cGvHD to be malnourished. Particularly participants with cGvHD of the GI, lung and mouth were affected [72–74]. Furthermore, pruritus caused suffering in severe skin GvHD and chronic breathlessness limited in severe GvHD of the lung [67].

Depressive symptoms and anxiety

While cGvHD is seen as a risk factor for depression, only one secondary analysis of a prospective cohort in the literature review could be identified, that examined self-reported depressive symptoms and self-reported symptoms of anxiety in participants with cGvHD. While 19,3% of the participants of this study by El-Jawahri et al. suffered from depressive symptoms, no association between the incidence of depressive symptoms and the severity of cGvHD was found [30,75]. Interestingly, in the qualitative interview study almost all of the participants reported depressive symptoms and several were diagnosed with depression and treated with antidepressive medication [67] which significantly exceeds the results of the literature review. This difference is striking and suggests that severe forms of GvHD are associated with the development of depressive symptoms, which should be analyzed more closely. 22.8% of the participants in the study by El-Jawahri suffered from anxiety [30,75]. In the qualitative interview study fear and anxiety were also prevalent. Important types of fear included the fear of persistence or recurrence of GvHD symptoms / of the underlying disease, the fear of limited

treatment options, the uncertainty of managing life independently, becoming permanently dependant on others, getting complications which cause re-hospitalization, or the permanent need of medication with harmful side effects. Despite that, the participants reported to be aware of the life-threatening character of their diagnosis and anxiety could increase phase-dependently while suffering from a high symptom burden [67].

QoL

Findings of a decline of QoL for severe forms of GvHD appear to have only been investigated for severe forms of cGvHD so far [30].

Pidala et al. described the severity of cGvHD to be the most important factor in decline of QoL independently of other examined covariates such as further diseases or sociodemographic variables [7]. Furthermore, various other studies confirmed the finding of more reduced QoL in patients with severe forms of cGvHD, compared to milder forms of cGvHD [5,30,76,77].

All participants included in the qualitative interview study described a strongly reduced QoL or stated to not have any QoL anymore. For none of the participants QoL reached pre-transplant levels. The worst QoL was described during inpatient stays and when suffering from a high symptom load of GvHD [67]. Baird et al. found organ involvement of joints / fascia, sclerotic skin and lung disease to show the most significant impact in QoL [5,30]. However, in the qualitative interview study the dominantly affected organs with its specific symptoms caused the greatest reduction of QoL (GI, skin, lung), while other organ affections (liver / bile; joints / fascia; eyes; oral / genital mucosa) were perceived as bothersome but not as dangerous [67].

4.3 Further important results of the qualitative interview study that raise research questions

The results of the qualitative interview study clearly show the high overall burden of participants with severe forms of GvHD at all levels (physical, psychological, social, occupational).

Even though the sample size and the study design do not allow any quantitative statements to be made, it is striking that certain aspects, such as the significantly reduced QoL or the occurrence of depressive symptoms, were reported by (almost) all participants and seem to be very relevant in this patient group. In this section relevant findings, that have not already been mentioned in section 4.2, will be discussed [67].

The need for more support

The participants of the qualitative interview study named the need for medical information as an important unmet need to gain more control and self-empowerment over their situation. The unforeseeable occurrence of GvHD in such a severe form as well as the unpredictability of its

trajectory generated anxiety symptoms and a feeling of being in an uncontrollable situation [67]. This should be taken as an incentive to critically assess and, if necessary, improve the care of patients with severe forms of GvHD in the inpatient and outpatient setting in the German medical system. In addition, structural and social support was not considered sufficient for patients without family support, in particular after discharge. This need can be better comprehended if one considers the long period of isolation that the participants mentioned both as inpatients and post-inpatients, along with their dependence on HCPs or people from their social environment. Some of the participants even made assumptions that co-patients without social support had a worse course of disease or died earlier [67]. This appears not to have been investigated in relation to severe forms of GvHD. In one prospective, multi-center observational study by Hamilton et al. having a partner was positively associated with better LSS scores in cGvHD [78]. There is no data considering the wider social environment which plays an important role for the participants in the qualitative interview study [67]. Regarding allo-SCT there have been studies investigating the impact of marital status / a stable relationship on the outcome after allo-SCT (non-relapse mortality, relapse, occurrence of aGvHD / cGvHD). So far most studies have found no positive association between patients in a stable relationship and better outcomes [79–81].

The need for more support should be investigated in further detail and, if necessary, support should be increased.

Desire to die

The majority of the participants of the qualitative interview study reported a tiredness of living or a desire to die when in very poor physical conditions or if triggered by further aspects of their disease, described in the qualitative interview study. However, only a minority of participants truly felt that they were close to death [67].

As already mentioned, a desire to die in patients with GvHD and generally after allo-SCT does not seem to have been investigated yet. In a cross-sectional study by Wilson et al. in patients with palliative cancer 18.3% acknowledged occasional transient thoughts on a desire to die, and 12.2% reported an apparently genuine desire to die [82]. Despite a possible desire to die, many patients also retain their will to live throughout the course of their illness. In some studies, both phenomena were found to be negatively correlated, yet simultaneous expressions of both a high wish to hasten death and a high will to live are possible [83]. Currently, the definition of desire to die is not yet standardized, which complicates (quantitative) research. Since the various forms of it can be placed on a continuum of increasing suicidality, as well as changes in the intensity of the desire to die over time can occur, addressing this issue as well as proactively addressing the will to live is important for patients and their physicians [84]. The qualitative interview study provides first evidence of triggers for a desire to die in patients with

severe forms of GvHD. A central research question arising from its results is to investigate these in more detail and to analyze the occurrence of a desire to die / a will to live in patients with (severe forms of) GvHD qualitatively and quantitatively [67].

Palliative Care for patients with severe forms of GvHD

In the qualitative interview study the participants associated the term PC with end-of-life care and were not sufficiently informed about this specialty. Some of them had never heard of it and not all participants were given the opportunity to receive a PC treatment. While GvHD has been named as an important indication for the integration of PC into patient's care, its use in patients with GvHD has not yet been investigated [49,67]. It has also hardly been examined in hematological malignancies, while obstacles to early PC interventions in this field include an overestimation of survival with underestimation of PC needs and difficulties balancing curative goals and therapy risks while attempting to convey patients' hopes [85,86]. In a qualitative approach HCP named time constraints as the main barrier to palliative care integration. Another barrier is that PC is often perceived as end-of-life care, which was also reflected in the qualitative interview study [67]. In addition, structural problems such as difficulties in regular contact and communication between transplant physicians and PC specialists sometimes result in PC not being available [9,87]. In the previously mentioned two RCTs by El-Jawahri et al. which focused on symptom control, the effectiveness of a consultative model on improving symptoms and quality of life after allo-SCT was confirmed [42,47,48]. Integrating specialist PC early in the course of the allo-SCT procedure likely contributes to achieve the best possible symptom control, to help patients and HCP to better cope with the illness and its prognosis, and to optimize QoL [9]. It seems urgent to further investigate the benefits of PC for patients with GvHD and how PC can best be integrated into the treatment of this patient group.

4.4 Methodological strengths and limitations

An extensive literature search for the review was conducted. It was not systematic; only research results in English that were freely available on PubMed were included. Yet it showed a significant lack of representative studies describing the burden and needs of patients with severe GvHD after allo-SCT. The role of SC and PC has not yet been adequately investigated [30]. In the subsequently conducted qualitative interview study patients were interviewed in order to form a detailed picture of their needs, burden and resources in the context of their GvHD. Since the majority of the participants suffered from severe GvHD of the GI, the sample was not representative for all manifestations of severe GvHD. There may be a participation bias as some patients were too ill to participate in the study [67]. Participants were actively approached by HCP if they matched the inclusion criteria. Therefore, only patients who were currently treated in the University Hospital of Cologne are included in the study (single center study).

The results may not be transferable to other health care settings. A recall bias could have been present if the participants were interviewed several years after allo-SCT. In two interviews, family members who were on site could have restricted the unbiased verbalizations of two of the participants. It should be noted that this study lacks racial diversity as all participants were Caucasian in Germany [67]. The qualitative study design included a small patient cohort compared to quantitative research. Nevertheless, by conducting semi-structured in-depth interviews and evaluating them with qualitative content analysis, a detailed picture of the needs and burdens of patients with severe forms of GvHD was drawn. It can be used as a primer for further quantitative research.

5. Conclusion

This dissertation project aims to support patients with severe forms of GvHD. Its first part focused on describing the current state of research by understanding the needs, burdens and resources of this patient group. A large research gap was identified here and at the same time the few existing results (severely reduced QoL, reduced physical functions) showed a high need for further investigation. Accordingly, a qualitative interview study was conducted to obtain relevant information through direct patient contact. It should be emphasized that the participants were impaired and heavily burdened in almost all domains of their daily life. In addition to distinctive physical symptoms, severe GvHD also caused significant psychological distress and appears to act as a trigger for depression. In the majority of the participants, this peaked in a desire to die, which was described in this form for the first time. Another central message is that none of the participants expected to ever regain their pre-transplant level of QoL. Thus, the results of the qualitative interview study support the assumption that severe GvHD symptoms are important PC needs. Since PC was commonly perceived as end-of-life care by the participants, the extent to which its meaning remains misunderstood in the German society should be further investigated and measures should be improved to help people understand the correct meaning of PC and facilitate access towards it. The results gained in the literature review and the qualitative interview study represent a broad overview of the burdens, needs and resources of patients with severe GvHD and provide approaches for further qualitative research.

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7. Anhang / Appendix

Zusätzliches Material der qualitativen Arbeit

7.1 Interview-Leitfaden / Interview guide

7.2 Transkriptions-Leitfaden / Transcription guide

7.3 Codebuch / Codebook

7.1 Interviewleitfaden / Interview guide

Vor dem Interview:

- *Vorstellung:*
  Wir haben ja bereits Kontakt gehabt, ich stelle mich trotzdem noch einmal kurz vor. Ich bin Freya Wenzel, Medizinstudentin und Doktorandin ich freue mich, heute mit Ihnen das Interview führen zu dürfen.
- *Bedanken:*
  Ich möchte mich bereits jetzt ganz herzlich für Ihre Teilnahme bedanken. Sie helfen uns damit sehr!
- *Studienziel:*
- Zur Erinnerung: Das Ziel des heutigen Interviews sind Ihre Erfahrungen mit der GvHD. Wir möchten gerne Ihre Bedürfnisse, Wünsche, Belastungen als auch Dinge die Ihnen Kraft schenken, erfragen. So soll die Behandlung für Patient*innen mit schwerer Abstoßungsreaktion verbessert werden.
- *Beantwortung:*
  Ich werde Ihnen im Folgenden offene Fragen stellen. Ich freue mich, wenn Sie ausführlich antworten, nehmen Sie sich so viel Zeit, wie Sie brauchen. Die Antworten sind sehr persönlich, und es gibt kein Richtig oder Falsch, wir interessieren uns für alle Themen, die Sie bewegen.
- *Datenschutz:*
  Alle hier besprochenen Themen werden unter Berücksichtigung der Datenschutzrichtlinie pseudonymisiert behandelt.
- *Fragen:*
- Haben Sie noch Fragen?

Interviewbeginn (Beginn der Audioaufnahme)

1. Erzählen Sie vom Verlauf Ihrer Erkrankung seit der Stammzelltransplantation.

2. Beschreiben Sie die Symptome, die Sie durch die Abstoßungsreaktion haben.

   -Welches Symptom belastet Sie am meisten?
   -Welches Symptom beeinträchtigt Sie am stärksten?

-Wodurch verspüren Sie Linderung?

3. Inwiefern fühlen Sie sich körperlich durch die GvHD belastet? / Beeinflusst die GvHD Sie bis heute?

   -Was fehlt Ihnen am meisten?
   -Benötigen Sie Hilfe im Alltag / Wer hilft Ihnen im Alltag?
   -Haben Sie Unterstützung außerhalb der Familie beantragt / erfahren?
   -Was sind Ihre Einschränkungen im Alltag?

4. Wie geht es Ihnen psychisch?

   -Würden Sie sagen, dass sie von der GvHD überrumpelt waren? Und von der einschränkenden Situation die durch sie entstanden ist?
   -Wie empfinden Sie die Situation, als von der Grunderkrankung geheilt zu gelten, und dann trotzdem so krank zu sein?
   -Wie würden Sie Ihre Lebensqualität einschätzen / beschreiben?

5. Wie sind sie aktuell ärztlich versorgt?

   -Wie gut fühlen Sie sich (zur Zeit der GvHD) betreut?
   -Wurden Sie schon mal palliativmedizinisch betreut?
   -Was bedeutet das Wort Palliativmedizin für Sie?

6. Wie stellen Sie sich Ihre Zukunft vor?

   -Was ist ihre größte Hoffnung / Wunsch?
   -Was ist ihre größte Sorge?

7. Wie sind Ihre Gedanken zum Thema Sterben und Tod?

   -Welche Gefühle kommen in diesem Zusammenhang auf?

   -Wie häufig denken Sie über den Tod nach?

   -Was ist ihre größte Sorge im Hinblick auf den Tod / das Sterben?

   -Haben sich Ihre Gedanken über den Tod durch die GvHD verändert?

   -Was gibt Ihnen Halt?

   -Hat mit Ihnen im Laufe Ihrer Behandlung jemals über das Thema geredet?

8. Hat sich das Verhältnis zu ihrem Umfeld durch die GvHD verändert?
   -Positiv?
   -Negativ?

9. Wer oder was gibt Ihnen im täglichen Leben Halt / Kraft?
   -Gibt es Momente in denen Sie Ihre Krankheit vergessen können?
   -Suchen Sie Halt im Glauben?

10. Was würden Sie Patient*innen raten, die rein fiktiv eine vergleichbare Situation wie Sie erleben würden?

11. Gibt es spezielle Themen, über die Sie noch erzählen möchten, die wir noch nicht angesprochen haben?

-Interviewende (Beendigung der Audioaufnahme)

12. **Machbarkeit Studienprozedere**

Nun noch eine Frage zum Ablauf der Studie insgesamt.

1. Wenn Sie nun nochmal an den Ablauf der Studie ganz allgemein denken, von dem Zeitpunkt an, als *wir* (Erstkontakt nachschauen!) Sie das erste Mal angesprochen haben, bis zu unserem heutigen Termin: Wie empfanden Sie den Ablauf der Studie insgesamt? (ggf.: An welchen Stellen hätten wir etwas anders oder besser machen können?)

Antwort:

Nach dem Interview:

- *Bedanken:*
  Vielen Dank, dass Sie sich die Zeit für die Teilnahme an dieser Studie genommen haben. Sie haben uns damit sehr geholfen.
- *Rückfragen:*
  Haben Sie noch Fragen an mich?
- *Kontakteinwilligung:*
  Dürften wir bei Rückfragen nochmals auf Sie zukommen?
- *Angebot:*
  Sollten Sie sich nach dem Interview emotional belastet fühlen, können Sie mich oder die anderen Betreuer der Studie jederzeit kontaktieren.

-Verabschiedung

Punkte, die in Finalerhebung auffällig waren:

- _____ - _____ - _____ - _____

7.2 Transkriptionsleitfaden / Transcription guide

Regelsystem zur Transkription

Modul	Regel	Beschreibung
Sprachglättung	Ausdrucksweise	
	Wörtlich	Es wird wörtlich transkribiert, also nicht lautsprachlich oder zusammenfassend. Vorhandene Dialekte werden nicht mit transkribiert, sondern möglichst genau ins Hochdeutsch übersetzt [66].
	Leicht geglättet	Sprache und Interpunktion werden leicht geglättet, d.h. an das Schriftdeutsch angenähert. Die Satzform, bestimmte und unbestimmte Artikel etc. werden auch dann beibehalten, wenn sie Fehler enthalten [66]. Bei Fremdsprachigkeit wird, falls zum Verständnis notwendig, stärker geglättet.
Pause	Intervallskalierte Pause (..), (…), (Pause)	Deutlich längere Pausen werden durch in Klammern gesetzte Auslassungspunkte (…) markiert. Entsprechend der Länge der Pause in Sekunden werden ein, zwei oder drei Punkte gesetzt [66]. Längere Pausen werden mit (Pause) beschrieben.
Lautäußerungen / nichtsprachliche Ereignisse	Lautäußerungen (seufzt); nicht: mmh	Zustimmende oder bestätigende Lautäußerungen der

	nicht sprachliche Ereignisse (Jemand betritt das Zimmer)	Interviewerin werden nicht mittranskribiert, sofern sie den Redefluss der befragten Person nicht unterbrechen. Lautäußerungen der interviewten Person, die die Aussage unterstützen oder verdeutlichen, werden in Klammern notiert[66]. Nichtsprachliche Ereignisse werden in Klammern gesetzt, sofern sie den Gesprächsfluss unterbrechen.
Interaktion	P: Das ist schlimm, ja. (I: Das ist wirklich schlimm) Ja.	Einwürfe der jeweils anderen Person werden in Klammern gesetzt.
Unsicherheit	(unverständlich) (unverständlich, ggf. Wut)	Unverständliche Worte oder Sätze werden mit unverständlich gekennzeichnet. Bei Vermutung auf Wortlaut ist dieser in Klammern ergänzt.
Formales	Absätze I: P:	Jeder Sprechbeitrag wird als eigener Absatz transkribiert. Sprecherwechsel zeigt sich durch eine Leerzeile[66]. Absätze der Interviewerin werden durch I: gekennzeichnet. Absätze der befragten Person werden durch P gekennzeichnet[66].

7.3 Codebuch / Codebook

Definitorischer Rahmen

Das Untersuchungsziel der vorliegenden Studie sind Erkenntnisse über die Bedürfnisse, Belastungen und Ressourcen bei Patient*innen mit schwerer, persistierender GvHD nach allogener Stammzelltransplantation. Die Auswertung erfolgt nach Kuckartz [66].

Auswahleinheit

Die Auswahleinheit umfasst 13 Interviews mit Patient*innen, die die im Rahmen der Studie „Bedürfnisse, Belastungen und Ressourcen bei Patient*innen mit schwerer, persistierender GvHD nach allogener Stammzelltransplantation – eine qualitative Interviewstudie“ bestehenden Einschlusskriterien erfüllen. Die Durchführung und Auswahl der Patient*innen erfolgte im CIO der Uniklinik Köln.

Es handelt sich um die folgenden Einschlusskriterien:

1. Zustand nach allogener Stammzelltransplantation sowie die Diagnose einer schweren, persistierenden, akuten oder chronischen GvHD (Grad 3,4)
2. Alter ≥ 18 Jahre
3. Die Patient*innen werden ambulant oder stationär durch die KMT-Station und Transplantationsambulanz behandelt
4. Es besteht eine kognitive Funktionsfähigkeit (nach klinischer Einschätzung durch die rekrutierenden Ärzte)
5. Es sind ausreichende Deutschkenntnisse vorhanden; schriftliche Texte in deutscher Sprache können gelesen und verstanden werden
6. Es liegt eine schriftliche Einwilligung in die Studienteilnahme nach erfolgter Aufklärung vor

Analyseeinheit

Die Analyseeinheit entspricht der Auswahleinheit, also den entsprechenden Interviews. Es wurde ein Kategoriensystem erstellt. Auf Basis des Interviewleitfadens wurden deduktiv Hauptkategorien gebildet. Es handelt sich dabei um folgende Codes:

-Besonderheiten im Krankheitsverlauf
-Belastungen
-Übergreifende Belastungs- und Krankheitsfolgen
-Wahrnehmung / Erlebnisse in der medizinischen Versorgung
-Ressourcen / Bewältigungsfördernde Faktoren
-Sterben / Tod

-Bedürfnisse
-Sonstiges / Individuelles

Beschreibung Vorgehensweise:
Mithilfe dieser Hauptcodes wurden drei zufällig ausgewählte Interviews codiert. Um eine Intercoder-Übereinstimmung zu erzielen wurden für die den Hauptcodes zugeteilten Interviewabschnitte von jeweils von zwei Personen (Freya Wenzel, Isabel Düster) auf zweiter Ebene Subcodes entwickelt. Diese wurden verglichen und Unstimmigkeiten wurden diskutiert, bis die Einigung auf ein gemeinsames Kategoriensystem gelang. Nun wurde konsensuell kodiert. Das bedeutet, dass Texte unabhängig voneinander kodiert und die Codierungen im Folgenden verglichen werden[66] (S. 210-212). In diesem Fall wurde das entstandene Kategoriensystem durch zwei Personen (Freya Wenzel, Isabel Düster) auf drei zufällig gewählte Interviews angewendet. Die Ergebnisse wurden diskutiert und das Kategoriensystem wurde in zusätzlicher Absprache mit Herrn Prof. Dr. Steffen Simon optimiert.
Alle 13 Interviews wurden im Folgenden mit dem endgültigen Kategoriensystem kodiert. Jeder Code wurde zusammengefasst und in thematische Summarys integriert, die es ermöglichten, die Aussagen der verschiedenen Teilnehmenden in Fallübersichten zu vergleichen und gegenüberzustellen[66].

Die Interviewtranskripte als auch die thematischen Summerys sind auf Nachfrage bei der Dissertantin dieser Promotionsschrift einsehbar.

7.3.1 Codesystem

1 Besonderheiten im Krankheitsverlauf
2 Belastungen
2.1 Durch allgemeinen Krankheitsverlauf
2.1.1 Soziale Belastungen
2.1.2 Körperliche Belastungen
2.1.2.1 Schlafprobleme / Erhöhte Müdigkeit
2.1.2.2 Einschränkungen durch Kraftlosigkeit / Schwäche
2.1.2.2.1 Verlängerte Erholungs- / Regenerationszeit
2.1.2.3 Nahrungsaufnahme eingeschränkt
2.1.2.3.1 Künstliche Ernährung
2.1.2.3.2 Subjektive Blockade
2.1.2.3.3 Erbrechen und Übelkeit
2.1.2.3.4 Appetitlosigkeit
2.1.2.4 Subjektiv belastendste Krankheitserlebnisse
2.1.2.5 Kognitive Einschränkungen
2.1.2.6 Körperliche Residuen
2.1.2.7 Weiteres
2.1.3 Psychische Belastungen
2.1.3.1 Schwierigkeiten mit der Krankheitsbewältigung
2.1.3.2 Todeswunsch
2.1.3.2.1 Lebensmüdigkeit
2.1.3.2.2 Suizidgedanken
2.1.3.3 Ängste
2.1.3.4 Depression
2.1.3.5 Kontakt zu Mitpatient*innen
2.1.3.6 Entwicklung von Aversionen
2.1.3.6.1 gegen Medikamente
2.1.3.6.2 gegen Krankenhaus (-aufenthalt)
2.1.3.7 Weiteres
2.1.4 Strukturelle Belastungen
2.1.4.1 Im häuslichen Umfeld
2.1.4.2 Stationäre / ambulante Versorgung
2.1.4.3 Weiteres
2.2 *Spezifisch durch GvHD*
2.2.1 Körperliche Belastungen (1)
2.2.1.1 Leber / Galle
2.2.1.2 Höchste Symptomlast (1)
2.2.1.3 Residuen der GvHD
2.2.1.4 Sehnen und Faszien

- 2.2.1.5 Lunge
- 2.2.1.6 Hautabstoßung
- 2.2.1.7 Augenabstoßung
- 2.2.1.8 Schleimhäute
- 2.2.1.9 Darmabstoßung
  - 2.2.1.9.1 Begleitproblematiken
  - 2.2.1.9.2 Durchfälle
  - 2.2.1.9.3 Weiteres
- 2.2.2 Psychische Belastungen (1)
  - 2.2.2.1 Ängste durch GvHD
  - 2.2.2.2 Mit Auftreten dieser GvHD (in dieser Form) nicht gerechnet
    - 2.2.2.2.1 Schwierigkeit mit der GvHD umzugehen
  - 2.2.2.3 GvHD unangenehm / peinlich / erniedrigend

3 Übergreifende Belastungs- und Krankheitsfolgen

- 3.1 Alltagsbewältigung
  - 3.1.1 Alltagsaktivitäten nicht mehr / schlechter bewältigen können
    - 3.1.1.1 Berufstätigkeit (nicht) in vollem Umfang möglich
- 3.2 Soziales Umfeld
  - 3.2.1 Selektion des Umfelds
  - 3.2.2 Berufliches Umfeld
  - 3.2.3 Familie
    - 3.2.3.1 Kinder
    - 3.2.3.2 Partner/in
    - 3.2.3.3 Weiteres soziales Umfeld
- 3.3 Präsenz der Erkrankung
- 3.4 Abnahme der Lebensqualität
- 3.5 Sonstiges

4 Wahrnehmung / Erlebnisse in der medizinischen Versorgung

- 4.1 Negative Erlebnisse in med. Versorgung
- 4.2 Betreuung als gut wahrgenommen
- 4.3 Weitere

5 Ressourcen / Bewältigungsfördernde Faktoren

- 5.1 Strukturelle Unterstützung
  - 5.1.1 häusliche Versorgung / Pflege
  - 5.1.2 ergänzende Therapieangebote / Heilmethoden
  - 5.1.3 Weiteres
- 5.2 Psychische Ressourcen / Entlastung
  - 5.2.1 Einnahme von Psychopharmaka
  - 5.2.2 Psychotherapie / Psychoedukation
  - 5.2.3 Innere Einstellung
    - 5.2.3.1 Ziele setzen

- 5.2.3.2 Kraft durch persönliche Einstellung
- 5.2.3.3 Akzeptanz
- 5.2.3.3.1 Integration der Krankheit in den Alltag
- 5.3 Soziales Umfeld Ressourcen / Entlastung
- 5.3.1 Medizinisches Personal
- 5.3.2 Kontakt zu Mitpatient*innen
- 5.3.3 Familie
- 5.3.3.1 Partner/in
- 5.3.4 Umfeld
- 5.4 Aufbau Sicherheitsgefühl
- 5.4.1 durch Besserung der Krankheit
- 5.5 Spirituelle Ressourcen
- 5.5.1 Glaube als Bewältigungsfaktor
- 5.5.1.1 Seelsorge
- 5.5.1.2 Abnahme des Glaubens
- 5.5.2 Glaube hat keinen Einfluss

6 Sterben / Tod

- 6.1 Auseinandersetzung mit Lebensbedrohlichkeit / Tod
- 6.2 Palliativmedizinische Betreuung
- 6.2.1 Behandlung erhalten
- 6.2.2 Behandlung nicht erhalten
- 6.2.3 Bewertung / Wahrnehmung der palliativmedizinischen Betreuung
- 6.2.3.1 Palliativmedizin als unterstützende Behandlung
- 6.2.4 Bedeutung des Wortes "Palliativmedizin"
- 6.2.4.1 Palliativmedizin als Sterbebegleitung
- 6.2.4.2 Palliativmedizin unbekannt
- 6.2.4.3 Weitere

7 Bedürfnisse

- 7.1 Therapieassoziierte Bedürfnisse
- 7.1.1 Erkrankung realistisch bewerten / einschätzen können
- 7.2 Soziale Bedürfnisse
- 7.2.1 Kontakt zu Mitpatient*innen
- 7.3 Psychische Bedürfnisse
- 7.3.1 Aufbau Sicherheitsgefühl
- 7.4 Köperliche Bedürfnisse
- 7.5 Strukturelle Bedürfnisse
- 7.5.1 Veränderungwünsche, Anregungen

8 Sonstiges / Individuelles

1 Besonderheiten im Krankheitsverlauf

In diesem Code sollen Textpassagen codiert werden, die sich auf den Krankheitsverlauf der Patient*innen beziehen und ggf. von anderen Krankheitsverläufen abweichen können.
Eine besondere Rolle spielt hier auch die Dauer, beispielsweise von Krankenhausaufenthalten.

2 Belastungen

Unter den Code "Belastungen" fallen alle Textpassagen, die vom Patient*innen als belastend wahrgenommen werden. Eine Unterteilung erfolgt dabei in körperliche Belastungen und in psychische Belastungen. Da es sehr oft schwierig ist, Belastungen zu filtern, die sicher spezifisch für die GvHD sind und klar beispielsweise von Medikamentennebenwirkungen abzugrenzen sind, gibt es hier eine zusätzliche Unterteilung. Spezifisch der GvHD zu zuordnende Belastungen sollen daher in den Untercode " Spezifisch durch GvHD" eingeteilt werden.

2.1 Durch allgemeinen Krankheitsverlauf

Dieser Code bezieht sich auf Belastungen im Krankheitsverlauf, die nicht spezifisch auf die GvHD zurückgeführt oder von dieser abgegrenzt werden können. Jedoch belasten sie den Teilnehmenden, der von diesen Komplikationen betroffen ist, im Gesamtkontext der Grunderkrankung.

2.1.1 Soziale Belastungen

Hier geht es um soziale Belastungen wie beispielsweise Isolation, Unverständnis etc.
Der Kontakt zu Mitpatient*innen als Belastung wird unter dem entsprechenden Untercode unter "psychische Belastungen" kodiert.

2.1.2 Körperliche Belastungen

Unter diesen Code fallen alle Textpassagen, in denen es um körperliche Belastungen der Patient*innen aufgrund des Krankheitsverlaufs geht. Abzugrenzen sind Belastungen, die spezifisch aufgrund der GvHD bestehen. Diese werden unter dem Code "Spezifisch durch GvHD" kodiert.

2.1.2.1 Schlafprobleme / Erhöhte Müdigkeit

Schlafprobleme multifaktorieller Genese, erhöhte Müdigkeit, Erschöpfung, erhöhtes Ruhe / Schlafbedürfnis

"Zum Beispiel es war auch schlimmer an manchen Tagen in der Woche. Ich konnte morgens nicht aufstehen. Ich konnte den ganzen Tag schlafen. Das, ich denke der Körper ist so geschwächt und der versucht, alle Funktionen abzuschalten. Das ist auch so, dass man schläfrig ist"

2.1.2.2 Einschränkungen durch Kraftlosigkeit / Schwäche

Aktivitäten nicht bewältigen können aufgrund von körperlicher Schwäche, Muskelabbau etc.

"Schwächegefühl total ne, also mein Mann trägt mich auch jetzt noch die Treppe hoch ne. Alles was unter 90 Grad ist in der Hüfte, ne komm ich alleine nicht hoch ne. Toilette haben wir extra ein bisschen hochgelagert zu Hause beim Renovieren. Schon vorher und äh, die ist mir trotzdem zu tief. Dann nutze ich ja noch das eigene Klo und da ist ein Heizungskörper an dem ich mich hochziehen kann. Ne, so ein Handtuchhalter. Wenn der nicht da wäre, müsste man mir sogar bei der Toilette helfen ne."

2.1.2.2.1 Verlängerte Erholungs- / Regenerationszeit

Die Teilnehmenden beschreiben aufgrund der empfundenen Schwäche verlängerte Erholungs- / Regenerationszeiten

2.1.2.3 Nahrungsaufnahme eingeschränkt

Multifaktoriell ist Essen nur eingeschränkt oder nicht möglich.

2.1.2.3.1 Künstliche Ernährung

Hier werden Textpassagen kodiert, bei denen Patient*innen angeben, künstlich ernährt worden zu sein.

2.1.2.3.2 Subjektive Blockade

Der Patient erlebt ein Gefühl, dass das Essen nicht möglich ist, beispielsweise nicht rutscht. Eine genaue Beschreibung bzw. ein genaues "Verstehen" dessen, ist schwierig.

„Pat: Wegen dem Essen..ähm...bei..wenn ich das Essen aufgemacht habe und da konnte ich zum Beispiel noch riechen, das war ja das Komische. Und das hochgemacht habe und mir kam der Geruch entgegen, hat bei mir alles dicht gemacht. Konnte ich nicht.“

2.1.2.3.3 Erbrechen und Übelkeit

Hier werden Textpassagen codiert, in denen Teilnehmende Erbrechen oder Übelkeit empfanden.

2.1.2.3.4 Appetitlosigkeit

Die Patient*innen geben Appetitlosigkeit als Grund für verminderte oder erschwerte Nahrungsaufnahme an.

"Ähm, ähm, die Abstoßung fing eigentlich erst ein paar Wochen später an. Ähm, durch, ja, Erbrechen und sowas. Das war, ähm, ja, man nimmt halt irgendwie, ja wie soll ich das sagen...ähm, man nimmt halt ab, weil man keinen Appetit mehr hat."

2.1.2.4 Subjektiv belastendste Krankheitserlebnisse

Hier werden alle Textpassagen codiert, in denen der Patient von Ereignissen im Krankheitsverlauf berichtet, die ihn sehr belastet haben. Dies kann beispielsweise auch ein akutes Nierenversagen sein.

2.1.2.5 Kognitive Einschränkungen

Der Patient gibt subjektiv kognitive Einschränkungen an.

2.1.2.6 Körperliche Residuen

Hier geht es darum, wie die Patient*innen die Verbesserung ihrer Symptomatiken beschreiben und das, was davon zum Interviewzeitpunkt übriggeblieben ist. Codiert werden können auch Textpassagen, die sich nicht spezifisch auf die GvHD konzentrieren

2.1.2.7 Weiteres

Hier geht es um körperliche Belastungen, die sich nicht in die oben genannten Untercodes kategorisieren lassen, aber relevant sein könnten.

2.1.3 Psychische Belastungen

Hierunter fallen insbesondere psychische Belastungen, die aufgrund der Gesamtbelastung entstehen.

2.1.3.1 Schwierigkeiten mit der Krankheitsbewältigung

Hier werden Textpassagen codiert, in denen beschrieben wird, dass der Umgang mit der GvHD schwierig ist oder es schwierig war, diese Komplikation zu akzeptieren.

2.1.3.2 Todeswunsch

Hier werden Textpassagen kodiert, die sich mit Gedanken über den Tod als Belastungsfolge beschäftigen. Abzugrenzen oder ggf. mehrfach zu kodieren sind hier bei Textstellen, die sich auch unabhängig von Belastungsfaktoren mit dem Thema Sterben und Tod beschäftigen.

2.1.3.2.1 Lebensmüdigkeit

Auftreten von Lebensmüdigkeit, öfter ausgedrückt durch: "keine Lust mehr haben". Abgrenzend zu Sterben und Tod drücken diese Codes oft die starke Belastung der Patient*innen aus und beschäftigen sich nicht explizit mit dem Tod oder dem Sterbeprozess.

„Und auch im Verlauf recht konstant oder gab es...?
Pat: ...Ähm es gab schon mal so Momente, wo ich gedacht habe, boa jetzt hast du keine Lust mehr. Aber, die waren eigentlich relativ wenig. Und, dann auch sehr kurz.“

2.1.3.2.2 Suizidgedanken

Auftreten von aktiven Suizidgedanken. Diese treten durch die Belastung der Krankheit auf, es geht jedoch hier nicht um ein Versterben als Folge von körperlichen Symptomen.

„Und das heißt, haben Sie dann manchmal über das Sterben oder so nachgedacht?
Pat: Ja, aber mehr in meiner depressiven Phase, wo ich mir gedacht habe, was willst du eigentlich, du fällst allen bloß auf den Geist und nimmst dir selber das Leben. Also die Phase hatte ich auch ja.“

2.1.3.3 Ängste

Temporäre oder begleitende Ängste.

„Ähm, ich weiß jetzt nicht, ob ich jetzt unbedingt ein paar Tage gerne alleine zu Hause sein möchte, weil ich dann auch äh, ein bisschen Angst habe. Wenn ich dann zum Beispiel koche oder sowas, dass ich das von der Luft her oder insgesamt vom körperlichen Zustand nicht hinkriege“

2.1.3.4 Depression

Der Patient beschreibt eigenständig eine depressive Phase im Zusammenhang mit der Erkrankung.

„das ist immer tagesformabhängig. Es gibt Tage, da möchte ich überhaupt nichts machen und es gibt Tage, da könnte ich denn, Bäume ausreißen aber...das war auch, um nochmal auf die ganzen negativen Eigenschaften zurück zu kommen. Nachdem ich dann erfahren hatte, dass ich berufsmäßig nichts mehr machen kann, kam eine tiefe Depressionsphase“

2.1.3.5 Kontakt zu Mitpatient*innen

Hier geht es um den Kontakt zu Mitpatient*innen als belastenden Faktor.
Der Code " Kontakt zu Mitpatient*innen" wird innerhalb dieses Codesystems bewusst mehrfach codiert. Er ist sehr komplex und hat je nach Kontext und Situation der Patient*innen sehr unterschiedliche Bedeutungen. Diese sollen später bewusst verglichen werden können.

2.1.3.6 Entwicklung von Aversionen

Die Patient*innen geben an, im Krankheitsverlauf verschiedene Arten von Abneigungen entwickelt zu haben. Dadurch kann auch ein Vermeidungsverhalten entstehen. Die Abgrenzung zu Ängsten ist teilweise nicht einfach. Jedoch geht es hier insbesondere auch um eine Art der Konditionierung, das Verbinden verschiedener Situationen / Handlungen mit negativen Erfahrungen.

2.1.3.6.1 gegen Medikamente

2.1.3.6.2 gegen Krankenhaus (-aufenthalt)

2.1.3.7 Weiteres

Hier geht es um Codes in denen es um psychische Belastungen geht, die sich jedoch nicht den entsprechenden Subcodes zuordnen lassen, aber relevant sein könnten.

2.1.4 Strukturelle Belastungen

Hier geht es um Strukturen, die einen im Rahmen der GvHD verstärkt belasten, wie zum Beispiel, eine Bettpfanne nutzen zu müssen vor Schwäche.

2.1.4.1 Im häuslichen Umfeld

Hier geht es um strukturelle Belastungen, die insbesondere im häuslichen Umfeld aufgefallen sind.

2.1.4.2 Stationäre / ambulante Versorgung

Hier geht es um Erfahrungen mit der Therapie der GvHD und im stationären Setting, beispielsweise von der pflegerischen Seite her. Es werden keine Veränderungswünsche kodiert, die unter dem Code „Veränderungen“ codiert werden.

2.1.4.3 Weiteres

Hier geht es um strukturelle Belastungen, die sich nicht in die entsprechende Subcodes eingruppieren lassen, aber relevant sein könnten.

2.2 Spezifisch durch GvHD

Unter diesem Code werden Belastungen kodiert, die durch die Teilnehmenden in direkten Zusammenhang mit ihren verschiedenen GvHD-Formen gebracht werden.

2.2.1 Körperliche Belastungen (1)

Hier geht es um alle körperlichen Belastungen die spezifisch mit der GvHD in Bezug zu setzen sind. Wenn sich Folgen aus den Belastungen ergeben, die direkt genannt werden, werden diese hier ebenfalls kodiert. Es kann daher sein, dass eine psychische Belastung, die sich aus körperlicher Belastung ergibt, doppelt hier und unter psychische Belastungen kodiert wird.

2.2.1.1 Leber / Galle

2.2.1.2 Höchste Symptomlast (1)

Falls abgrenzbar, nennt der Patient hier Dinge, die ihn am meisten beeinflusst haben oder die stärksten Symptome, die ihn belastet haben.

I: Aber was war jetzt so, wenn die Ärzte das sage ich mal auch Abstoßung genannt haben, was war so das Schlimmste für Sie? Das schlimmste Symptom, kann man das überhaupt so sagen?
Pat: Äh, das schlimmste an sich war glaube ich so dieses, dieses, man zwängt sich das Essen rein und der Körper, beziehungsweise der Körper stößt es wieder ab, weil der Darm einfach nicht mitmacht und sowas. Und, ähm, ja ständig dieses, dieses Gefühl zu haben, man ist einfach krank. Weil man dauerhaft Durchfall hat, öfter Erbrechen muss, das war so für mich das Schlimmste.“

2.2.1.3 Residuen der GvHD

Hier sollen Belastungen oder Symptome genannt werden, die aufgrund der GvHD entstanden sind und bis zum Interviewzeitpunkt als relevant wahrgenommen wurden.

2.2.1.4 Sehnen und Faszien

2.2.1.5 Lunge

2.2.1.6 Hautabstoßung

2.2.1.7 Augenabstoßung

2.2.1.8 Schleimhäute

2.2.1.9 Darmabstoßung

2.2.1.9.1 Begleitproblematiken

Die Patient*innen geben weitere Probleme aufgrund der Darm-GvHD bzw. des ständigen Durchfalls an, beispielsweise Gewichtsverlust.

"Das hatte dann als Begleiterscheinung noch Hämorrhoiden und Sonstiges. Das war alles eine ziemliche Katastrophe."

2.2.1.9.2 Durchfälle

Hier geht es um die Durchfallsymptomatik, Folgen und Einschränkungen, die sich daraus ergeben.

2.2.1.9.3 Weiteres

Hier geht es in Codes die der Darmabstoßung zugeordnet werden können, aber sich nicht den entsprechenden Subcodes zuordnen lassen.

2.2.2 Psychische Belastungen (1)

Unter diesem Code werden Textpassagen eingruppiert, die psychische Belastungen beschreiben, die direkten Zusammenhang mit der GvHD gebracht werden können.

2.2.2.1 Ängste durch GvHD

Hier geht um die Ängste, die aus der GvHD erwachsen sind, wie zum Beispiel die Angst vor erneutem Auftreten schwerer Symptome.

2.2.2.2 Mit Auftreten dieser GvHD (in dieser Form) nicht gerechnet

Mit Auftreten dieser GvHD nicht gerechnet.
Trotz Aufklärung hat Patient mit GvHD in der Art und Weise wie er sie erlitten hat, nicht gerechnet und wurde ggf. überrumpelt.

2.2.2.2.1 Schwierigkeit mit der GvHD umzugehen

Es ist schwierig, die GvHD haben zu müssen, sie zu akzeptieren oder anzunehmen. Dies kann eine verzweifelte Komponente haben.

I: „W*ie, also ich weiß, man kann das bestimmt nicht so gut trennen aber wie ging es Ihnen damit psychisch? Also auch dieses Wort Abstoßung, das löst ja manchmal vielleicht erstmal irgendwas aus.*

Pat: Das war schwer für mich. Weil ich das Gefühl hatte, eigentlich von Anfang an, dass mein Körper die Zellen von dieser Frau nicht möchte. Und ich habe da halt so viel, ich habe da halt auch ein paar andere Frauen kennen gelernt und von denen hatte niemand irgendetwas. Und ich hatte direkt zwei. Und irgendwie hat es sich nicht richtig angefühlt.“

2.2.2.3 GvHD unangenehm / peinlich / erniedrigend

Symptome der GvHD wie z.B. Durchfälle / Ausschläge sorgen für Scham und ein unangenehmes Gefühl, auch um Umgang mit dem Umfeld oder unbekannten Menschen.

"Nein. Das hatte ich jetzt, aber da war das jetzt nicht so, wie Durchfall, den man kennt. Das zog sich dann auch als ich zu Hause war, habe ich dann auch ein paar Mal in die Hose gemacht. Das ist halt peinlich und unangenehm."

3 Übergreifende Belastungs- und Krankheitsfolgen

Hier geht es um Folgen, die durch die greifbaren und zuteilbaren Belastungen auslöst werden können. Jedoch können hier auch Krankheitsfolgen eingruppiert werden, die nicht immer negativ sein müssen. Bsp: Änderung des Umfelds, manche Kontakte werden enger.

3.1 Alltagsbewältigung

Hier geht es um die körperlichen Folgen der Symptomatiken.

3.1.1 Alltagsaktivitäten nicht mehr / schlechter bewältigen können

Durch multifaktorielle Genese ist ein normaler Alltag nicht zu bewältigen, es besteht Hilfsbedürftigkeit. Die Patient*innen sind durch diese Einschränkungen oft örtlich gebunden.

„An der Darmabstoßung oder? (I: Ja, genau) Ja doch, dass man einfach unsicher geworden ist, irgendwo hinzugehen. Immer, alles planen musste; wo man hingeht, wo ist die nächste Toilette, was kann ich mir zutrauen, wenn ich irgendwo hingehe, was, wenn ich da irgendwo länger bin, was gibt es da zu Essen, muss ich mir selber was mitnehmen?“

3.1.1.1 Berufstätigkeit (nicht) in vollem Umfang möglich

Der Patient kann nicht arbeiten oder kann nicht im gewöhnten Ausmaß arbeiten

"Ne, man erstmal geht man nicht mehr arbeiten, damit geht es ja schon los."

3.2 Soziales Umfeld

Hier geht es um mögliche Änderungen in den Beziehungen der Patient*innen aufgrund der Erkrankung. Es kann beispielsweise zu einer Selektion des Umfelds kommen oder die Pflege der Beziehungen kann erschwert werden. Da diese Veränderungen verschiedene soziale Netzwerke betreffen, sind diese als Untercodes aufgegliedert.

Abgrenzung zum Code „Soziales Umfeld Ressourcen / Entlastung“: Dort ist Mensch / Soziales immer positiv bewertet.
Abgrenzung zum Code „Soziale Belastungen“: Belastungen sind immer in einem negativen Kontext zu sehen, eine Veränderung des sozialen Umfelds kann auch positive Veränderungen mit sich bringen

3.2.1 Selektion des Umfelds

Intensivierung mancher Kontakte, Wegfall anderer Kontakte, Realisieren der Personen, die in der Situation wichtig für einen sind.

"Und so zum erweiterten Umfeld, haben Sie das das Gefühl, dass Sie Verständnis erfahren, dass? Pat: Da hat sich das teilweise sehr geändert. Sowohl positiv wie negativ. Es gibt ein paar Leute, die so, wo ich eher gesagt hätte, so etwas entferntere Bekannte, wo ich ähm, sehr viel Hilfe bekommen habe und die mir sehr viel Hilfe damals angeboten haben und dann auch, dies gar nicht so sehr im Sinne von sie gehen für mich einkaufen oder so.“

3.2.2 Berufliches Umfeld

Alle Beziehungen die sich auf die berufliche Ebene beziehen. Beruf als Lebensbereich, der sich verändern und wegbrechen kann.
Beruf als plötzlich fehlender Lebensbereich.

"Hat sich die Beziehung zu ihrem Umfeld verändert?
Pat: Nein. Das Einzige, das Arbeitsumfeld ist weggefallen, aber das ist auch das Einzige."

3.2.3 Familie

Beziehung zur engeren oder erweiterten Familie und die Veränderung dieser durch die GvHD.

Abgrenzung „Soziales Umfeld / Ressourcen / Entlastung“: Hier geht es eher um die Änderung der Beziehung und den direkten Einfluss der GvHD diesbezüglich“. Bei „Soziales Umfeld / Ressourcen / Entlastung“ geht es um die Rolle als kraftgebenden Faktor.

Abgrenzendes Beispiel „Soziales Umfeld / Ressourcen / Entlastung“:

"Aber ich habe da so... (fängt an zu weinen) Wenn ich vorher hier hinmusste, dann ist ja mein Mann immer mitgefahren. Und jetzt..seitdem der nicht mehr da ist, da war ich noch nie alleine hier. Immer war eine Schwester oder mein Bruder. Ich war noch nie alleine hier. Ich werde so gut von denen gehalten, halt. Da kann ich mich immer in jeder Situation drauf verlassen. Und das ist so richtig gut"

3.2.3.1 Kinder

Alle Codes, die die Beziehung oder Beziehungsänderung, beispielsweise Entfremdung durch längere räumliche Trennung zu Kindern beschreiben.

„Haben Sie das Gefühl, dass es vielleicht ihre ältere Tochter auch irgendwie reifer hat werden lassen? Pat: Auf jeden Fall. Ich brauch gar nix sagen. Mama soll ich in den Keller gehen und Nudeln holen? Mama komm, ich helfe dir, ich halte dich fest, ne beim Treppe gehen. Ich ziehe dich hoch, ne.“

3.2.3.2 Partner/in

Beziehung speziell zur Lebenspartnerperson, falls vorhanden. Potentielle Belastung der Patnerperson, Rolle als ggf. vertrauteste Person im Leben der Patient*innen

"Und das geht halt alles jetzt gar nicht und ich erwarte dann auch viel zu viel von meinem Partner, ne. Dass er Sachen sieht, wo ich noch nicht mal was sagen müsste eigentlich ne. Aber das tut er nicht, weil er ja auch selber so seine Beschäftigung hat ne und doch selber auch müde ist, wenn er zu Hause ist. Und, ähm..ja da haben wir uns viel gestritten. Also das ist dann halt auch so psychisch auch sehr schwer."

3.2.3.3 Weiteres soziales Umfeld

Insbesondere Beziehung zu Freund*innen.

3.3 Präsenz der Erkrankung

Wie präsent ist die GvHD / Erkrankung im Alltag der Patient*innen?
Ist es den Patient*innen durch gewisse Umstände / Tätigkeiten / Ablenkung möglich, die Einschränkungen durch die Krankheit vergessen können?

3.4 Abnahme der Lebensqualität

Bewertung der subjektiven Lebensqualität durch den Patient*in nach dessen subjektiven Kriterien. Zeitlicher Verlauf oder Veränderungen dessen. Da die Abgrenzung zu mehreren, weiteren HC schwierig ist, muss ein entsprechend zugeordneter Code das Wort „Lebensqualität“ explizit enthalten -ist als Folge und sehr generell zu sehen

3.5 Sonstiges

4 Wahrnehmung / Erlebnisse in der medizinischen Versorgung

Hier geht es um die Wahrnehmung der medizinischen Versorgung und um Erlebnisse, die für die Patient*innen sowohl positiv als auch negativ einschneidend gewesen sein können.

4.1 Negative Erlebnisse in med. Versorgung

Erlebnisse, oft sehr individuell, die die Patient*innen beschäftigt / belastet haben.

4.2 Betreuung als gut wahrgenommen

Positive Erlebnisse im stationären oder ambulanten, medizinischen Setting.

4.3 Weitere

Hier geht es um Wahrnehmungen in der medizinischen Versorgung der Patient*innen, die sich nicht in einen der anderen Subcodes eingruppieren lassen.

5 Ressourcen / Bewältigungsfördernde Faktoren

Hier geht es um intrinsische sowie extrinsische Ressourcen, die den Patient*innen bei der Krankheitsbewältigung helfen können.

Hierbei ist eine Ressource als definiert „jedes Potential […], das die Verhaltensoptionen eines Systems erhöht und damit seine Lebens- und Problemlösefähigkeit verbessert“, wobei eine Ressource „materiell-wirtschaftlicher, sozialer, emotionaler oder intellektueller Natur“ sein kann. (nach Heiko Kleve; Mediation – Eine systemische Methode Sozialer Arbeit 1.
Der Text ist publiziert in: Pfeifer-Schaupp, Hans-Ulrich (Hrsg.) (2002): Systemische Praxis. Modelle – Konzepte
– Perspektiven. Freiburg/Br.: Lambertus, S. 156-176 sowie in: Kleve, Heiko (2003): Sozialarbeitswissenschaft,
Systemtheorie und Postmoderne. Grundlegungen und Anwendungen eines Theorie- und Methodenprogramms.
Freiburg/Br.: Lambertus, S. 170-191)

5.1 Strukturelle Unterstützung

Z.B. gute Betreuung

5.1.1 häusliche Versorgung / Pflege

Entlastung im Alltag durch Hilfe von außen z.B. Pflege / Betreuungsdienste / Reinigungskräfte etc.

*„Aber das heißt, Sie hatten jetzt von außen da nie Hilfe in sage ich jetzt mal Alltagsdingen?
Pat: Doch, es kam auch ein Pflegedienst. Aber wie gesagt, die größere Hilfe war eher meine Familie, die ja...(lacht) haben ja auch ein bisschen Vorkenntnisse gehabt dadurch und...“*

5.1.2 ergänzende Therapieangebote / Heilmethoden

Unterstützung der Patient*innen über die Gewährleistung der Pflege hinaus. Beispielsweise durch Physiotherapie, Musiktherapie.
Psychotherapie wird unter dem Punkt "Psychische Ressourcen / Entlastung" kodiert.

5.1.3 Weiteres

Strukturelle Belastungen die sich nicht in einen der oberen Subcodes einordnen lassen.

5.2 Psychische Ressourcen / Entlastung

Unter diesen Code fallen alle Dinge, die die Teilnehmenden im Hinblick auf psychische Belastung unterstützt haben. Das können sowohl medizinische als auch Gesprächsangebote sein. Seelsorge, die teilweise ebenfalls diese Funktion übernimmt, wird unter dem Hauptcode „Spirituelle Ressourcen“ kodiert.

5.2.1 Einnahme von Psychopharmaka

Hier werden Textstellen codiert, in denen Patient*innen berichten, Psychopharmaka einzunehmen.

5.2.2 Psychotherapie / Psychoedukation

Hier geht es um Inanspruchnahme von Psychotherapie. Seelsorge, die ähnliche Funktionen einnehmen kann, wird abgegrenzt und unter " Spirituelle Ressourcen" kodiert.

5.2.3 Innere Einstellung

Hier geht es um intrinsische Bewältigungsfaktoren.

5.2.3.1 Ziele setzen

Hier werden Textstellen kodiert, bei denen Teilnehmende konkrete Ziele formulieren und in welchem Kontext.

5.2.3.2 Kraft durch persönliche Einstellung

Aussagen die eine positive Einstellung und Herangehensweise als kräftigenden Faktor beinhalten. Dies hat teilweise auch mit Selbstdisziplin zu tun, der Patient möchte „das Beste“ aus der Situation machen.

„Und, was hat Ihnen in der Zeit Kraft gegeben?
Pat: Ja, viel meine Familie. Und einfach, ja, ähm...ja, wie soll ich das sagen. Die Lust am Leben ne. Ich wollte mein Leben nicht einfach schon so früh aufgeben. (I: mhh, ja). Ich bin ja noch relativ jung, und äh, ja das wäre einfach zu schade gewesen. So wenig vom Leben mitzubekommen.“

5.2.3.3 Akzeptanz

Annehmen der Erkrankung, Integration dieser in den Alltag

5.2.3.3.1 Integration der Krankheit in den Alltag

Alle Codes, die darauf zielen, mit der Krankheit zu leben und diese in den Alltag zu integrieren, bzw. den Alltag an die Krankheit anzupassen. Es erfolgt also zu einem gewissen Grad eine Annahme der Erkrankung. Hier wird auch interpretativ codiert.

„Und, das ist auch, das üben Sie auch voll aus? Also da sind sie 100% belastbar?
Pat: Ja, 40 Stundenwoche. (I: Ja). Wobei ich jetzt halt körperlich merke, dass ich das halt nicht mehr leisten kann, aber das hat damit ja nicht so was zu tun. Also, die in der Werkstatt wussten das. Dass ich dann öfter mal auf Toilette verschwinden könnte, aber das hat immer alles gut geklappt.“

5.3 Soziales Umfeld Ressourcen / Entlastung

"Das heißt, Kraft ist mehr über soziale Kontakte (Pat: Genau) und über das Arbeitsziel wieder (Pat: Genau, genau), wenn ich das richtig verstehe.
Pat: Über soziale Kontakte, Freunde, Familie. Ja"

5.3.1 Medizinisches Personal

Hier geht es darum, das medizinisches Personal, z.B. eine bestimmte Aussage eines Arztes den Patient*innen Hoffnung vermittelt. Allgemeine positive Erfahrungen sind unter dem Code "Wahrnehmung / Erlebnisse" in der medizinischen Versorgung zu kodieren.

5.3.2 Kontakt zu Mitpatient*innen

Hier geht es um die Wahrnehmung von Kontakt zu Mitpatient*innen als Ressource.
Der Code " Kontakt zu Mitpatient*innen" wird innerhalb dieses Codesystems bewusst mehrfach codiert. Er ist sehr komplex und hat je nach Kontext und Situation der Patient*innen sehr unterschiedliche Bedeutungen. Diese sollen später bewusst verglichen werden können.

5.3.3 Familie

Stärkender Faktor ist die engere Familie der Patient*innen

5.3.3.1 Partner/in

Lebenspartner* in wirkt als stärkender Faktor.

5.3.4 Umfeld

Freunde, Mitpatient*innen / Umfeld schenken Kraft.

5.4 Aufbau Sicherheitsgefühl

Für Patient*innen ist eine Stabilisierung und die Vermittlung von Sicherheit wichtig. Sie benötigen etwas, das sie hält /absichert oder auch Angehörige absichert. Diese Ressource hat auch den Faktor eines befriedigten Bedürfnisses.

Dieser Code ist schwierig vom Code "Akzeptanz" bzw. dessen Untercode " Integration in den Alltag" abzugrenzen. Jedoch ist der Aufbau eines Sicherheitsgefühls unabhängig von der Akzeptanz der Erkrankung für die Patient*innen essentiell und es geht nicht unbedingt nur um deren Integration in den Alltag, sondern auch um Sicherheit im stationären Alltag oder die Entwicklung von Routinen.

5.4.1 durch Besserung der Krankheit

5.5 Spirituelle Ressourcen

Alle Codes die im Zusammenhang mit Religion und Hilfestellung diesbezüglich stehen.

5.5.1 Glaube als Bewältigungsfaktor

Ein religiöser Glaube spielt in der Krankheitsbewältigung eine Rolle.
Hier kann Glaube Sicherheit vermitteln → Gott zeigt mir, dass es gut geht. Er kann aber auch eine Anlaufstelle für kraftgebende Gedanken und Reflexion sein

„Und, haben Sie dann über den Tod auch nachgedacht?
Pat: Sehr ja. Ich habe viel zu Gott gebetet ne und ich glaube auch an Gott ne. Und, äh, zuletzt jetzt bei der, äh, beim CMV ne. Da hatte ich Gott nicht mehr so gespürt ne, wie sonst. Deswegen dachte ich auch, jetzt geht es zum Ende hin, ne.“

5.5.1.1 Seelsorge“

Seelsorge als Bewältigungsfaktor setzt in der Regel den Glauben als Bewältigungsfaktor voraus.
Teilweise scheinen ähnliche Funktionen wie bei einer Psychotherapie zu bestehen.
Eine Abgrenzung besteht hier durch ein bewusstes Benennen der entsprechenden Therapieform.

5.5.1.2 Abnahme des Glaubens

Aufgrund von Krankheitssituation kommt es zu Zweifeln oder zur Abnahme des Glaubens.

„Und, haben Sie dann über den Tod auch nachgedacht?

Pat: Sehr ja. Ich habe viel zu Gott gebetet ne und ich glaube auch an Gott ne. Und, äh, zuletzt jetzt bei der, äh, beim CMV ne. Da hatte ich Gott nicht mehr so gespürt ne, wie sonst. Deswegen dachte ich auch, jetzt geht es zum Ende hin, ne.“

5.5.2 Glaube hat keinen Einfluss

Unabhängig einer bestehenden Religiosität hat der Glaube für die Patient*innen keine kraftgebende Rolle.

6 Sterben / Tod

Unter diesen Code fallen alle Textabschnitte, die sich mit Gedanken oder der Bedeutung des Sterbens oder des Todes auseinandersetzen. Eingeschlossen wird ebenfalls die Wahrnehmung von Palliativmedizin.
Abgegrenzt werden Gedanken über den Tod als Todeswunsch, beispielsweise Suizidgedanken. Diese werden unter dem Hauptcode "Belastungen" kodiert.

6.1 Auseinandersetzung mit Lebensbedrohlichkeit / Tod

Aussagen zu Gedanken oder Einstellungen gegenüber der Lebensbedrohlichkeit, der Möglichkeit, aufgrund der GvHD zu versterben.

Der Patient scheint teilweise das Gefühl zu haben, die Lebensbedrohlichkeit oder Gefahr zu Versterben spüren oder einschätzen zu können. Von außen wirkt dies teilweise auch verdrängend.

„Pat: Und dann habe ich gedacht, dass ich....es kann auch...muss nicht aber ne...lebensbedrohlich sein..aber ich meine, ich weiß nicht...es ist schwierig zu beschreiben..Also, ich wusste es, das kann alles lebensbedrohlich sein, aber ich dachte nee, das wird nicht sein.“

6.2 Palliativmedizinische Betreuung

Möglicher Erhalt von palliativmedizinischer Betreuung und Einstellungen, Gedanken diesbezüglich. Subjektives Verständnis des Begriffes Palliativmedizin.

6.2.1 Behandlung erhalten

Patient*innen die in irgendeiner Form palliativmedizinisch betreut wurden.

6.2.2 Behandlung nicht erhalten

Patient*innen die sich keiner palliativmedizinischen Mitbetreuung bewusst sind

I:“Wurden Sie durch die Palliativmedizin schon mal betreut?“
Pat: „Nee, möchte ich auch nicht.“

6.2.3 Bewertung / Wahrnehmung der palliativmedizinischen Betreuung

Empfinden der palliativmedizinischen Betreuung durch die Patient*innen

6.2.3.1 Palliativmedizin als unterstützende Behandlung

Palliativmedizin wird positiv, als Hilfe, wahrgenommen.

Das heißt, die haben Sie dann in den schlimmsten Phasen wahrscheinlich mitbetreut ne?

„Pat: Ja, auf jeden Fall, das schon. Ne..da hatte ich glaube ich auch immer einen Ansprechpartner und sowas. Das war...ja..das war eigentlich immer super. Da wurde immer schnell und so drauf eingegangen, alles gemacht.“

6.2.4 Bedeutung des Wortes "Palliativmedizin"

Die subjektive Bedeutung oder Definition von Palliativmedizin für die Patient*innen

6.2.4.1 Palliativmedizin als Sterbebegleitung

Direkte Wahrnehmung des Wortes Palliativmedizin im Zusammenhang mit Sterben / Tod.

„Was bedeutet das Wort Palliativmedizin für sie?
Pat: Ja, das ist...Therapie, wo man Patienten, die nicht mehr kurativ zu behandeln sind, hilft, mit den Schmerzen und Problemen die sie haben zurecht zu kommen, und die zu lindern und ihnen zu ermöglichen dann, einigermaßen beschwerdefreies Leben erstmal zu führen. Und auch letztendlich einigermaßen beschwerdefrei zu sterben ja..“

6.2.4.2 Palliativmedizin unbekannt

Bei der Frage nach Palliativdefinition sind die Patient*innen unsicher oder wissen nicht genau, was das bedeutet.

„Wurden Sie in der Zeit irgendwann mal palliativmedizinisch betreut? Gerade zu der Abstoßungszeit? Pat: „Was genau verstehen Sie jetzt darunter? Also ich habe eigentlich hier immer nur Kontakt gehabt zum Dr. H.“

6.2.4.3 Weitere

Hier geht es um weitere Bedeutungen des Wortes Palliativmedizin für die Patient*innen.

7 Bedürfnisse

Hier werden die Bedürfnisse der Teilnehmenden erfasst, die entweder explizit geäußert oder entsprechend interpretiert werden können.

7.1 Therapieassoziierte Bedürfnisse

Hier geht es um Bedürfnisse, die im Hinblick auf die medizinische Versorgung der Teilnehmenden geäußert werden.

7.1.1 Erkrankung realistisch bewerten / einschätzen können

Es handelt sich um ein informatives Bedürfnis, um Kontrolle und Einschätzungsvermögen im Hinblick auf die GvHD zu gewinnen.

*"Mir wäre es glaube ich lieber gewesen, ich hätte von vorneherein wirklich ganz klar gewusst, die Wahrscheinlichkeit, dass Sie wieder so fit sind wie vorher ist gegen Null. (**I:** Mhh.) Ähm...weiß ich nicht, vielleicht wäre es damals auch falsch gewesen, das kann ich nicht sagen. Das kann ich nur aus der momentanen Situation heraus sagen.“*

7.2 Soziale Bedürfnisse

Hier geht es insbesondere darum, seine neue soziale Rolle zu finden oder die vor der Erkrankung möglichst wieder einzunehmen

7.2.1 Kontakt zu Mitpatient*innen

Der Code " Kontakt zu Mitpatient*innen " wird innerhalb dieses Codesystems bewusst mehrfach codiert. Er ist sehr komplex und hat je nach Kontext und Situation der Patient*innen sehr unterschiedliche Bedeutungen. Diese sollen später bewusst verglichen werden können.

7.3 Psychische Bedürfnisse

Z.B. Sicherheit gewinnen, das Erkrankung nicht wieder kommt

7.3.1 Aufbau Sicherheitsgefühl

Hier geht es um ein Sicherfühlen auf verschiedenen Ebenen, beispielsweise Absicherung der Familie oder auch Kontrolle der Symptome
Das kein ein Bedürfnis sein oder auch (gleichzeitig) eine Ressource → Siehe Code Ressourcen / Bewältigungsfördernde Faktoren

7.4 Körperliche Bedürfnisse

Zu Kräften kommen etc.

7.5 Strukturelle Bedürfnisse

Hier geht es um strukturelle Bedürfnisse, Veränderungswünsche, die oft auch einen individuellen Charakter haben können

7.5.1 Veränderungswünsche, Anregungen

Bestehen oder Nichtbestehen von Wünschen nach völlig verschiedenen Veränderungen durch Patient*innen

8 Sonstiges / Individuelles

Diverse Interviewauszüge, die interessant sind, aber sich keiner bestehenden Hauptkategorie zuordnen lassen. Teilweise gibt es diesbezüglich einen individuellen Charakter, der nicht unbedingt auswertbar ist.