Health-related quality of life during and after stem cell transplantation

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ABSTRACT

Hematopoietic stem cell transplantation (HSCT) is an established treatment for a variety of malignant diseases, as well as a small proportion of non-malignant disorders. The treatment before the HSCT (called conditioning) can be either myeloablative (MAC) or given with reduced intensity (RIC). MAC is associated with high toxicity due to high doses of chemotherapy with or without total body irradiation (TBI), and is used in both autologous and allogeneic HSCT. In autologous HSCT the patient is the donor, and in allogeneic HSCT the donor is a sibling or an unrelated donor. RIC regimens are associated with reduced toxicity and are only for patients undergoing allogeneic HSCT. Both autologous and allogeneic HSCT have a strong effect on the patients’ health-related quality of life (HRQL). The two studies in this thesis were initiated when RIC was introduced at a hematological department in south-east Sweden in 2001. The overall purpose was to evaluate HRQL in patients undergoing HSCT. The studies covered the whole inpatient period and the following three years in order to have a comprehensive assessment of the patients’ HRQL over time. HRQL was assessed 13 times from baseline up to three years after HSCT with the instrument EORTC QLQ-C30. The instrument consists of 30 items divided into three major domains: functional status, symptom status, and global health/QoL. Almost all functional scales, global health status/QoL, symptom scales and single items were significantly affected in the two studies during the first two to three weeks from baseline. The symptoms that patients estimated to be the most severe in the studies were nausea and vomiting, loss of appetite, fatigue, and diarrhea. Two months after HSCT nearly all functional scales, global health status/QoL, symptom scales and single items in Study I had returned to the same value as at baseline in patients undergoing autologous HSCT. It took up to two years for patients undergoing allogeneic HSCT in Study II to return to the same value as at baseline. For patients in Study I, role-, emotional-, and social function, fatigue and dyspnea had significantly improved at the 3-year follow-up compared to baseline, whereas role function was the only function that had improved in Study II. Patients with lymphoma in Study I experienced significantly worse HRQL in week 2 and appetite loss at month 2 than patients with multiple myeloma (MM). Patients treated with MAC in Study II had significantly worse fatigue and nausea and vomiting at baseline and pain, sleep disturbance, appetite loss and diarrhea at weeks 3 and 4 than patients treated with RIC. Patients with extensive chronic Graft versus Host Disease (GvHD) in Study II reported significantly impaired physical function, role function, and global health status/QoL than patients with limited or no chronic GvHD. These results provide a good overview of patients’ symptoms and HRQL during and after HSCT and indicate when they require increased support from healthcare professionals. The results also demonstrate the importance of close follow-ups during the first year after HSCT in order to improve preventive interventions. The quick recovery of patients in Study I suggests that the extensive treatment is well tolerated.
This thesis is based on the following papers, which will be referred to in the text with their Roman numerals (I and II):


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APPENDIX

EORTC QLQ C-30 (English translation). To use the instrument, contact the Quality of Life Department (http://groups.eortc.be/qol/eortc-qlq-c30).
ABBREVIATIONS

ATG  Antithymoglobulin  
Auto-SCT  Autologous stem cell transplantation  
BEAM  Bezenun, etoposide, cytarabine, melphalan  
BuM  Busulphan, melphalan  
BuCy  Busulphan, cyclophosphamide  
CEC  Cyclophosphamide, etoposide, carboplatin  
EBMT  European group for Blood and Marrow Transplantation  
FAM  Fludarabine, cytarabine, melphalan  
FC + ATG  Fludarabine, cyclophosphamide and ATG  
FCM  Fludarabine, cyclophosphamide and melphalan  
FLAMSA-Cy-TBI  Fludarabine, amsacrine, cytarabine, cyclophosphamide + TBI  
FluBu  Fludarabine, busulphan  
G-CSF  Granulocyte colony-stimulating factor  
GvHD  Graft versus host disease  
GvL  Graft versus Leukemia (implies that specific cells of the immune system, especially T-cells, attack and destroy remaining leukemia cells)  
HLA  Human leukocyte antigen.  
HRQL  Health-related quality of life  
HSCT  Hematopoietic stem cell transplantation  
MAC  Myeloablative conditioning  
MM  Multiple myeloma  
QoL  Quality of life  
RD  Related donor  
RIC  Reduced intensity conditioning  
TBI  Total body irradiation  
URD  Unrelated donor  
ZAM  Idarubicin, cytarabine, melphalan
INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is an established treatment for a variety of malignant diseases as well as a small proportion of non-malignant disorders (1, 2). Patients receive various conditioning treatments before HSCT to prepare for the transplanted stem cells and to eliminate the disease. The conditioning can be myeloablative (MAC), which means high-dose chemotherapy with or without total body irradiation (TBI). This conditioning is associated with high toxicity (3, 4). The treatment can also be given with reduced intensity (RIC) (5, 6). RIC regimens are associated with a reduced toxicity that allows older people and those with compromised health to benefit from HSCT (7, 8). The choice of conditioning treatment depends on several factors such as diagnosis and type of HSCT. The most common side effects after conditioning treatment are nausea and vomiting, appetite loss, dryness of the mouth, taste changes, mucositis, diarrhea, fatigue, hair loss, sleeping disturbance (9-11), fever, and infections (12, 13). Later complications after HSCT, such as infertility and secondary malignancies, may be consequences of the conditioning treatment (14). Whether the patient is cured and survives following HSCT depends on several factors, such as diagnosis, age and type of HSCT (15). The experience of undergoing HSCT has a strong impact on the patients’ health-related quality of life (HRQL) (10, 11).

When the current study on patients undergoing allogeneic HSCT was initiated at a hematological department in south-east Sweden in 2001, most studies on quality of life (QoL) by other researchers had a retrospective and cross-sectional design (16-18). The results from the few studies with a longitudinal and prospective design showed that fatigue had a significant impact on daily functioning and QoL (19). Poor health and functioning had a negative impact on QoL, whereas the family had a positive impact on QoL (20). Measurements of HRQL during and after HSCT are therefore important to highlight specific areas that affect patients’ lives and to understand the patients’ experiences so that healthcare professionals can improve their daily care (21, 22). HRQL have become increasingly prevalent in clinical practice as well as in research, where it lately has been considerate as the primary efficacy endpoint in drug development. The knowledge about the patient’s HRQL during and after HSCT also gives the healthcare professional an opportunity to inform the patient about what to expect, which helps the patient to prepare for the HSCT (23). The overall purpose of this thesis was to evaluate HRQL in patients undergoing autologous and allogeneic HSCT. The studies covered the whole inpatient period and the following three years in order to arrive at a comprehensive assessment of the patients’ HRQL over time. The aim was also to identify symptoms that the patients experience during treatment, how they develop over time, and how long they persist after HSCT.
BACKGROUND

Hematological Malignancies
Hematological malignancies are a heterogeneous group of diseases which affect only 1–2% of cancer cases in the Swedish population. Together, leukemia, lymphoma, and myeloma represent the majority of hematological malignancies in Sweden (24). The main hematological malignancies studied in this thesis are lymphoid malignancy, including Hodgkin lymphoma, non-Hodgkin lymphoma, acute lymphatic leukemia, and multiple myeloma (MM), together with myeloid malignancies including acute myeloid leukemia, myelodysplastic/myeloproliferative neoplasm, and chronic myeloid leukemia.

Treatment for Hematological Malignancies
Chemotherapy remains the foundation in the treatment of hematological malignancies; however, combinations with new targeted therapies such as monoclonal antibodies (rituximab) for B-cell lymphomas(25, 26), proteasome inhibitors (bortezomib), and immunomodulatory agents (lenalidomid) (27) for patients with MM represent a new era in the treatment of hematological malignancies. Other targeted monotherapies, such as tyrosine kinase inhibitors for chronic myeloid leukemia have improved responses and outcomes for hematological malignancies (28). In spite of the success in past decades in the treatment options for hematological malignancies, many patients fail to respond to the therapy and require HSCT to survive (15).

HSCT
Research on HSCT began with the first atomic bomb and the radiation damage it caused. Bone marrow was given intravenously in 1951 to irradiated mice and guinea pigs. The experiment showed that the transplantation protected against lethal irradiation injury, but it was not until the mid-1950s that scientists found out that stem cells were responsible for the protection. These findings made it possible to treat patients with hematological diseases. The results of the clinical trials were often negative: either there was no engraftment, which means that the transplanted stem cells do not begin to reproduce new blood cells or, if the stem cells were engrafted, the patients developed fatal graft versus host disease (GvHD) (29). In 1957 Thomas et al. (2) attempted to treat patients with supralethal irradiation and bone marrow, but the only successful transplantations were in patients with leukemia who received stem cells from an identical twin. The success with HSCT came in the 1970s after the human leukocyte antigen (HLA) system had been discovered and the development of supportive treatments (blood and platelet transfusions and antibiotics), chemotherapies, and control of severe side effects had begun. The first bone marrow transplantation in Sweden was performed at Huddinge Hospital in 1975 (30). The Department of Hematology in Linköping started with autologous HSCT in 1991 and
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allogeneic HSCT in 1996. In a report on the number of HSCTs within the European group for Blood and Marrow Transplantation (EBMT) between 1990 and 2010, Passweg et al. (31) reported that HSCT had increased from 4234 patients in the first survey in 1990 to 33,362 patients in 2010. The survey is based on 37 countries in Europe and eight affiliated countries. HSCTs at the Department of Hematology in Linköping increased during the last six years to 20 allogeneic HSCTs and 46 autologous HSCTs per year. For the distribution of the most common diagnoses among transplanted patients from 1991 to 2012, see Table 1.

Table 1. Diagnoses of transplanted patients at the Department of Hematology in Linköping 1991-2012

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma cell disorders</td>
<td>320</td>
<td>37%</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>231</td>
<td>27%</td>
</tr>
<tr>
<td>Acute leukemia</td>
<td>158</td>
<td>18%</td>
</tr>
<tr>
<td>Chronic leukemia</td>
<td>57</td>
<td>7%</td>
</tr>
<tr>
<td>Solid tumors</td>
<td>52</td>
<td>6%</td>
</tr>
<tr>
<td>Myelodysplastic/Myeloproliferative</td>
<td>37</td>
<td>4%</td>
</tr>
</tbody>
</table>

Characteristics of stem cells are that they are capable of self-renewal and can be differentiated into different blood cells through an active process with different growth factors through hematopoietic regulators and receptors. The stem cells are responsible for maintaining the production of blood cells during a person’s lifetime and, in human adults, stem cells are primarily located in the bone marrow (32). The definition of HSCT is “any procedure where hematopoietic stem cells of any donor type and source are given to a recipient with the intention of repopulating and replacing the hematopoietic system in total or in part” (15).

There are two kinds of HSCT: autologous HSCT, where the patient is the donor, and allogeneic HSCT, where the donor is a sibling or an unrelated donor. The stem cell can be derived from the bone marrow, peripheral blood, or cord blood (15, 33).

The indication for autologous and allogeneic HSCT varies, depending on the diagnosis and disease status, and follows the recommendation given by the European School of Hematology and the EBMT (15). The main diagnosis for allogeneic HSCT in 2010 in Europe was acute leukemia and, for autologous HSCT, plasma cell disorders, followed by lymphoma (31).

Besides the stage of the disease, other factors that may affect the outcome of HSCT must be considered in the decision regarding HSCT, i.e., age, the time interval from diagnosis to HSCT, along with donor/recipient histocompatibility and the gender combination of the donor/recipient for patients undergoing allogeneic HSCT (15).
The Collection Procedure

Today the standard way to collect hematopoietic stem cells is through peripheral blood, so-called peripheral blood stem cells. Normally, there are few stem cells in the blood, so to increase the number of stem cells for patients undergoing autologous HSCT, the patients are given chemotherapy and granulocyte colony-stimulating factor (G-CSF) whereas the donors receive only G-CSF. G-CSF is a growth factor normally found in the body which stimulates the proliferation and differentiation of the neutrophil cells. The stimulation leads to a rapid division of stem cells leading to bone marrow releases of the stem cells so they can migrate into the blood stream (34). Stem cells are then harvested using apheresis technology. The stem cells are either frozen (when used in autologous HSCT) for use at a later stage or given back directly to the patients after the stem cell collection (normally used in allogeneic HSCT) (Figure 1).

Figure 1. The autologous and allogeneic processes

The autologous process

1. Mobilization: patient treated with chemotherapy and G-CSF
2. About 10 days after the stem cell collected from the peripheral blood stream through apheresis technology
3. Whole blood enters the centrifuge (1) and separates into plasma (2), leukocytes (3), and erythrocytes (4). Selected components are then drawn off (5).
4. The stem cells are then processed in a laboratory and frozen until the patients reinfusion of stem cells
5. HSCT: Patients treated with chemotherapy before the reinfusion of stem cells
6. Reinfusion of stem cells

The allogeneic process

1. Patients start their conditioning treatment
2. The donor is mobilized with G-CSF for 4 days
3. On the fifth day the stem cell collected from peripheral blood stream through apheresis technology
4. The stem cells are then processed in a laboratory
5. The stem cells are then administered to the patient
6. The stem cells are then given back directly to the patient

(Images from clipart, images 3 from Wikipedia, released under the GNU Free Documentation License, image 6, autologous process from private archive)
The Conditioning Regimens
The aim of the conditioning regimen (treatment given before the HSCT) is to create space for the transplanted stem cells, to induce immunosuppression, and to eliminate the disease (35, 36). The conditioning can be myeloablative, which means that high doses of chemotherapy (with or without TBI) are given to the patient, and is used in both autologous and allogeneic HSCT. This conditioning is associated with high toxicity (3, 4). Another form of conditioning treatment, given with reduced doses, so-called reduced intensity conditioning, is only used for patients undergoing allogeneic HSCT (5, 6). The development of RIC regimens came after the importance of the graft-versus-Leukemia (GvL) effect was detected (37). RIC regimens are associated with reduced toxicity so as to allow older people and those with compromised health to benefit from HSCT (7, 8).

Treatment Procedure and Practice during HSCT
Before HSCT the patients are subjected to a comprehensive medical history investigation, a physical examination, and additional testing to ensure that they can cope with the treatment. The patient is admitted to the department one day before the conditioning treatment starts. The conditioning regimens suppress in particular the production of all cells in the bone marrow, which leads to decreased white blood cells, platelets, and erythrocytes. Extremely low white blood cells lead to these patients being extremely sensitive to infections and increased risk of life-threatening infections. To avoid life-threatening infections, the patients are isolated when the white blood cells decrease to < 1.0 x 10^9/L. The isolation period lasts until the white blood cells increase > 1.0 x 10^9/L, which takes approximately 10–12 days. A low platelet count means that the patient can easily start bleeding from, for example, the gingival, nasal cavity, or hemorrhoids. A low erythrocyte count leads to anemia, which results in weakness and tiredness.

For optimal monitoring during the hospital stay, various bloods sampling, weight control, heart rate, blood pressure, and temperature control are performed each day. All food and fluid intakes are recorded, and urine and stool frequency, as well as consistency and appearance, is noted. Decreased fluid or calorie intake is compensated for by giving the patients intravenous nutrition. Transplantation rooms are equipped with locks and a special ventilation system to keep the circulating air as clean as possible. Hospitalization lasts for about 3–4 weeks for a patient undergoing autologous HSCT and 4–6 weeks for patients undergoing allogeneic HSCT. Depending on local guidelines, patients undergoing HSCT often have food and environmental restrictions up to three month after HSCT and longer for those undergoing allogeneic HSCT. After discharge, patients who have undergone autologous HSCT have no further visits to the outpatient clinic concerning HSCT, whereas patients who have undergone allogeneic HSCT have a much more comprehensive aftercare.
Complications after HSCT

The acute toxicity after conditioning treatment affects the patients in varying degrees, and the most common side effects are nausea and vomiting, appetite loss, dryness of the mouth, change in taste, mucositis, diarrhea, fatigue, hair loss, sleep disturbance (9-11), fever, and infections (especially bacterial infections) (12, 13). All patients are given preventive treatment for various agents that can cause infection (i.e. virus, fungal infection, and Pneumocystis jiroveci). Patients undergoing allogeneic HSCT are more vulnerable since their own immune system is depressed by immunosuppressive therapy and the immune reconstitution is not fully developed. This can lead to severe infection with increased morbidity and mortality (13, 38). GvHD is a common complication after allogeneic HSCT and is caused by several factors that trigger the activation of donor T-cells. The donor T-cell recognizes the patient as a foreign body host and therefore attacks different body organs. The targets for the T-cell in acute GvHD are the skin (varying degrees of skin rash), gastrointestinal tract (diarrhea), and the liver (increased liver values, particularly bilirubin). The risk of developing acute GvHD is 30–50% for patients with a related donor and may be higher with an unrelated donor (39). There are a number of factors which increase the risk for GvHD, for example, human leukocyte antigen disparity, older age, female donor to male recipient, prior allo-immunization and the used GvHD prophylaxis (40). Acute GvHD normally occurs within 100 days after HSCT (39, 40). It is graded from 1 to 4, where 1 is mild GvHD and 4 is a life-threatening condition involving all three organs. Chronic GvHD normally occurs 100 days after HSCT. The pathophysiology of chronic GvHD is still not fully understood, but it has similarities with acute GvHD (41). Chronic GvHD affects significantly more organs than acute GvHD and is divided into mild, moderate, and severe chronic GvHD, depending on the number of organs involved and the severity of the attack on the affected organs (in Study II the old definitions, limited and extensive, are used) (40).

Table 2. Acute GvHD grade and involvement (40)

<table>
<thead>
<tr>
<th>Grade of acute GvHD</th>
<th>Degree of organ involvement</th>
<th>Stage</th>
<th>Skin/Maculopapular rash</th>
<th>Liver/Bilirubin</th>
<th>Gi / Diarrhea</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Skin: + to ++*</td>
<td>+</td>
<td>&lt; 25% of body surface</td>
<td>34–50 mmol/L</td>
<td>&gt; 500 mL</td>
</tr>
<tr>
<td>II</td>
<td>Skin: + to +++</td>
<td>++</td>
<td>25–50% of body surface</td>
<td>51–102 mmol/L</td>
<td>&gt; 1000 mL</td>
</tr>
<tr>
<td></td>
<td>Gut and/or liver: +</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mild decrease in clinical performance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Skin: ++ to +++</td>
<td>+++</td>
<td>Generalized erythroderma</td>
<td>103–255 mmol/L</td>
<td>&gt; 1500 mL</td>
</tr>
<tr>
<td></td>
<td>Gut and/or liver: ++ to +++</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Marked decrease in clinical performance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Skin: +++ to ++++</td>
<td>++++</td>
<td>Generalized erythroderma with bullae formation and desquamation</td>
<td>&gt; 255 mmol/L</td>
<td>Severe abdominal pain with or without ileus</td>
</tr>
<tr>
<td></td>
<td>Gut and/or liver: ++ to +++</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Extreme decrease in clinical performance</td>
<td></td>
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</tbody>
</table>

*+ – ++++: The stage of GvHD in the different organs
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Acute GvHD  Chronic GvHD

(Images from the Department of Hematology)

Health-Related Quality of Life (HRQL)
In the care and treatment of patients with cancer, it is important to take into consideration the patients’ QoL and not just the response to treatment and survival. QoL may be difficult to define and closely related concepts such as health and HRQL are often used synonymously (42). However, negatively perceived health does not automatically mean that the person’s QoL is affected negatively. Our approach to QoL and the components of the concept are guided by our basic view of life and the fields in which we operate (43, 44).

The concept of HRQL is based on the concept of health and QoL (45). It can be defined as the subjective assessment of the impact of disease and treatment across the physical, psychological, social, and somatic domains of functioning and well-being. There is agreement that the concept HRQL should at least include physical, psychological, and social function. Physical function is the ability to perform daily activities despite disease and/or treatment. Psychological function ranges from severe psychological distress to a positive sense of well-being. Social function includes quantitative and qualitative aspects of social relations and interactions, and social integration (46).

To understand the significance of the concept of HRQL, it is important to have knowledge of the concepts of health and QoL. There are different approaches to the concept of health, and some authors argue that there cannot be a complete definition of health because people’s definition of health depends on their own socio-demographic factors. The World Health Organization proposed that health should be defined as “a dynamic state of complete physical, mental, spiritual and social well-being and not merely the absence of disease or infirmity” (47). In summary, despite the different definitions and approaches to health, it can be stated that health is a holistic concept including psychological, physical, social, and spiritual parts. QoL is a multidimensional concept, no standard definition exists. Instead, there are several
different of definitions and models (44, 48, 49). The WHO’s QoL Group has defined QoL as “individuals’ perceptions 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 concern.” It is a subjective evaluation which is influenced by the cultural, social, and environmental context (50).

Measurement of HRQL
QoL measurements can be relevant for establishing whether a new treatment is preferable to a standard treatment or if two treatments are equal in terms of survival, but differ in side effects or results. Measurements of the QoL can provide information on the need for increased support during and after treatment. Measuring the QoL can be a prognostic indicator, which means that the patients’ assessment of their QoL before treatment can predict survival. QoL questionnaires can be used in clinical practice to facilitate communication between the patients and healthcare professionals and to identify problems (23).

The most reliable source to obtain an impression of an individual’s HRQL is from the individual him/herself (17). A variety of instruments have been developed to evaluate HRQL, including generic-, disease- and domain-specific instruments (45, 46). A combination of a generic- and disease-specific instrument is an advantage, but this depends on the objective of the study (42). A generic instrument is developed to be used in a general population to assess a wide range of domains and gives a general, broad knowledge of the individual’s HRQL. This kind of instrument makes it possible to make comparisons between different patient populations (45, 46). Some examples of generic instruments are the Nottingham Health Profile, which provides a description of a patient’s perceived emotional, social and physical health problems, and the Sickness Impact Profile, which provides a descriptive profile of changes in a person’s behavior due to sickness (46, 51). In a disease-specific instrument the focus of the questionnaire is based on the area related to the disease and effects of the treatment given (45). Cancer-specific instruments are, for example, the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ C-30), and the Functional Assessment of Cancer Therapy - General (52). Both questionnaires can be supplemented with specific modules to reach a deeper understanding of a specific disease, symptom, or treatment. Domain-specific instruments are designed to measure a specific aspect of HRQL, for example, the Multidimensional Fatigue Inventory, which measures fatigue, and the Hospital Anxiety and Depression Scale, which detects anxiety and depression (46, 53).
HRQL in Patients undergoing HSCT

When the study in this thesis on patients undergoing allogeneic HSCT started in 2001, most QoL studies on patients undergoing HSCT had a retrospective and/or cross-sectional design. Nine studies with a longitudinal and prospective design had follow-ups during the inpatient period to varying degrees (16-18, 54). McQuellon et al. (55, 56) and Larsen et al. (57) made assessments at baseline and discharge. Some of the studies had no baseline assessment with the disadvantage that there is no baseline value to compare the results with, which makes it difficult to evaluate how the transplantation affected the patients (58, 59). Finally, there were three studies that had several follow-ups at baseline and during the inpatient period (19, 20, 54). Hann et al. (19) studied fatigue and QoL in patients with breast cancer undergoing autologous HSCT and compared them with women without cancer. Patients gave their assessments at baseline, on the day of reinfusion, and towards the end of treatment. The patients in the study reported significantly more frequent and severe fatigue than women without cancer, and fatigue had a significantly greater impact on daily functioning and QoL. Fatigue was related to both medical factors (i.e., time since transplant) and psychosocial factors. Gaston-Johansson et al. (20) did a study with 24 patients undergoing autologous HSCT to investigate the psychological response and QoL. The assessments were made two weeks before HSCT, two days prior to the transfusion of stem cells, and 5, 10, and 20 days afterwards. The results showed that poor health and functioning had the most negative impact on QoL, whereas the family had the most positive impact. There was a significant negative correlation between depression and QoL. Patients were affected by different symptoms, fatigue, anxiety and depression during the inpatient period which tended to improve by the end of the hospitalization. QoL was correlated with fatigue and emotional function. A study by Courneya et al. (54) on physical exercise and QoL in patients undergoing autologous HSCT at baseline, and on weekly basis until discharge; they found that physical exercise correlate with QoL.

The patients’ experiences of their HRQL after discharge depends on several factors, such as HRQL at HSCT, age at HSCT, type of transplantation (i.e. autologous or allogeneic), complications after HSCT, especially chronic GvHD (60, 61). Chao et al. (62) investigated QoL in 58 patients undergoing autologous HSCT at baseline, 90 days after HSCT, and then every 3 months up to one year after HSCT. At discharge, the main problem was fatigue, and the patients’ QoL was the lowest at the 90-day follow-up and then improved by one year. At the one-year follow-up they reported an above-average to excellent QoL on a linear analog scale. In another study, Lee et al. (63) found that 53% of the patients undergoing autologous HSCT (n = 93) felt that their life had returned to normal and 37% felt that their health was very good or excellent 6 months after HSCT. Thirty-one percent of the patients undergoing allogeneic HSCT (n = 112) felt that their life had returned to normal and 33% felt that their health was very good or excellent.
Studies have shown that it takes approximately one year for patients undergoing autologous or allogeneic HSCT to improve their HRQL to the baseline value (64, 65), and that their HRQL improves significantly over time (66). For patients with, for example, chronic GvHD, it takes more time to improve HRQL (65). At the two-year follow-up, 63% of the patients undergoing autologous HSCT and 68% of those undergoing allogeneic HSCT experienced that their life had returned to normal, but fatigue and sexual difficulties were still a problem for over 30% of the patients (63).

In summary, there were no earlier prospective and longitudinal studies covering patients’ HRQL from baseline and the whole inpatient period. This means that there is not sufficient information about patients’ HRQL during the most acute phase of the transplantation and the time when their HRQL actually returned to the baseline value. In addition many of the studies had both autologous and allogeneic patients in their study population. This encouraged us to design a study from baseline and the whole inpatient period and to study patients undergoing autologous and allogeneic HSCT separately.

The overall purpose of this thesis was to evaluate HRQL in patients undergoing autologous HSCT and allogeneic HSCT. The studies covered the whole inpatient period and the following three years in order to arrive at a comprehensive assessment of the patients’ HRQL over time. The purpose was also to identify symptoms that the patients experienced during treatment, how they developed over time, and how long they persisted after HSCT.
AIMS

Study I
The aim of this study was to make a comprehensive assessment of the frequency and severity of different symptoms and HRQL for patients undergoing auto-SCT before, during, and up to 3 years after transplantation.

Study II
The overall purpose was to evaluate HRQL in patients undergoing allogeneic HSCT and to identify symptoms that they experienced during treatment, how they developed over time, and how long they persisted after HSCT.

METHODS

Design
The studies in this thesis are descriptive, prospective, and longitudinal.

Table 3. Presentation of the method for data collection and data analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>Title</th>
<th>Data collection</th>
<th>Data analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>A prospective evaluation of patients’ health-related quality of life during auto-SCT: a 3-year follow-up.</td>
<td>Questionnaire: EORTC QLQ C-30</td>
<td>Descriptive Multivariate regression Chi-2</td>
</tr>
<tr>
<td>II</td>
<td>Early and long-term follow-up of health-related quality of life following allogeneic hematopoietic stem-cell transplantation</td>
<td>Questionnaire: EORTC QLQ C-30</td>
<td>Descriptive Multivariate regression Wilcoxon signed-rank test</td>
</tr>
</tbody>
</table>

Setting
The two studies in this thesis were conducted at the Department of Hematology, University Hospital, in Linköping.

The Department treats patients from the south-east region in Sweden with medical diseases within the blood-forming system, such as a lack of different types of blood cells (erythrocytes, granulocytes, platelets) and tumors based on blood-forming cells, such as leukemia, lymphoma, and myeloma. The population in the south-east region comprises more than 1 million inhabitants. The first autologous HSCT in Linköping was performed in 1991 and the first allogeneic HSCT was performed in 1996. In recent years, about 66 transplantations have been performed every year and one third of them have been allogeneic HSCTs.
Inclusion Criteria
The inclusion criteria for participation in the studies were at least 18 years of age, ability to speak and read the Swedish language, ability to give informed consent, participation in the data collection procedure, having one’s first autologous HSCT (Study I) or first allogeneic HSCT (Study II).

Study Population
During the inclusion period from September 2001 to January 2008, 111 patients were accepted for autologous HSCT and 110 for allogeneic HSCT, a total of 217 patients.

Regarding patients treated with autologous HSCT, 15 were not included: 5 due to a second HSCT, 1 was < 18 years old, 2 had language problems, 1 for logistical reasons, 5 declined participation, and 1 patient died, thus providing a study population of 96 patients in Study I.

In the allogeneic group, 3 patients were not included due to language problems, 7 due to a second HSCT, 2 due to syngeneic HSCT, 1 was too ill, and 3 declined participation, which gives a study population of 94 patients in Study II.

Treatment Regimens
The conditioning treatments given to the patients in the studies are based on recommendations by the EBMT, national guidelines, and local treatment strategies (35, 36, 67).

The treatment regimens for patients in Study I were chemotherapy with myeloablative conditioning (MAC). Patients diagnosed with MM received melphalan, patients with lymphoma (including Hodgkin’s disease) and multiple sclerosis received BEAM (becenun, etoposide, cytarabine, melphalan). Patients diagnosed with testicular cancer received CEC (cyclophosphamide, eto.poside, carboplatin), patients diagnosed with acute myeloid leukemia received ZAM (idarubicin, cytarabine, melphalan), and patients with sarcoma received BuM (busulphan, melphalan).

Depending on the type of disease, patients in Study II with high-risk disease (19%) received one of the following MAC regimens: TBI + FAM (fludarabine, cytarabine, melphalan), or BEA,M, or BuCy (busulphan, cyclophosphamide), or FluBu (fludarabine, busulphan), or FLAMSA-Cy (fludarabine, cytarabine, amsacrine, cyclophosphamide)-TBI. Patients with no high-risk disease (81%) underwent one of the following RIC regimens: FCM (fludarabine, cyclophosphamide, and melphalan) or FC +ATG (fludarabine, cyclophosphamide and antithymoglobulin) or FAM, some patients with an addition of mitoxantrone and idarubicin.
Data Collections and Procedure

Questionnaire in Studies I–II
In the two studies included in this thesis, HRQL was measured using EORTC QLQ C-30. It is a multidimensional, cancer-specific, self-administered instrument, tested cross-culturally for reliability and validity (68-70). The instrument has been translated and validated in 81 languages and used in more than 3000 studies worldwide (71). It consists of 30 items divided into three major domains: functional status, symptom status, and global health/QoL. Functional scales consist of physical function (5 items) and apply to the ability to manage daily life: for example, if the patient has trouble executing strenuous activities, such as taking long/short walks, if the patient must sit/lie down during the daytime and if they can manage their own personal hygiene. Role function (2 items) involves areas related to work, daily activities, and leisure activities. Emotional function (4 items) covers areas of tension, anxiety, irritability, and depression. Social function (2 items) concerns whether the patients’ physical function or medical treatment has interfered with their family life or social activities. Cognitive function (2 items) is about problems concentrating and remembering. There are three symptom scales that measure fatigue (3 items), which addresses whether the patient needed rest, felt weak, and has been tired, or experienced nausea and vomiting (2 items), and pain (2 items), where the patient is asked to answer whether he/she has had pain and whether his/her daily activities were affected by pain. There are five single items measuring dyspnea, insomnia, appetite loss, constipation, and diarrhea, and one item measuring financial impact. Global health/QoL consists of two items, the first question concerns overall health and the second question concerns the overall QoL. The functional and symptom scales/items comprise four levels (response alternatives: not at all, a little, quite a bit, very much). Overall QoL is measured on a 7-point scale, ranging from 1 (very poor) to 7 (excellent). For all items in the instrument, the patient makes an assessment of the past week. All scales and items are transformed according to the EORTC scoring manual into a 0–100-point scale. Higher scores for functional scales and QoL status indicate a high level of function and higher scores on the symptom scales and single items indicate more severe symptoms or impairments (72). Clinical data were extracted from the patients’ medical records.

Procedure
At admission for HSCT, the patients received oral and written information about the study from one of the authors (UF). The patients gave their verbal consent to participate in the study. Questionnaires were filled in at baseline, before the start of conditioning, then once a week for four weeks, at months 2, 3, and 6 and then every six months up to three years after HSCT (Figure 2). After discharge from inpatient hematological care, questionnaires were sent to the patients together with a prepaid return envelope. The questionnaires were distributed and collected by one of the authors (UF). Late
responders received new questionnaires as a reminder after 2–4 weeks. Questionnaires answered later than a month after the expected date was not included in the analysis.

Figure 2. Distribution of questionnaires during the study

Data Analysis
In accordance with the scoring manual for EORTC QLQ C30, missing data were classified as missing items (one or more missing answers to questions in a questionnaire) or missing forms (when the whole questionnaire is missing for a patient) (72). This means that if a single item is missing, it is not included, whereas e.g. physical function, which consists of 5 items, is included if 3 items are answered. In this study, a questionnaire was not included if patients had failed to answer half of the questionnaire.

The procedure for correcting the values for missed items is described in the scoring manual (72). It is recommended by EORTC that the mean value is used instead of the median to create an opportunity to compare the results with other studies using EORTC QLQ C-30 (http://groups.eortc.be/qol/faq).

In the two studies, multiple regression analyses adjusted for gender and age were applied separately each time when differences between and within groups were examined. The analysis between patients with MM and lymphoma in Study I was performed at baseline, week 2, month 2, and year 3. The baseline value was used in order to have an output value, week 2, the time when the patients’ HRQL was most affected; month 2, the time when the patients HRQL had returned to the baseline value, and year 3, because that was the time of the final assessment. The analysis between MAC and RIC in Study II was performed from baseline to 3 months after HSCT, thereafter it was considered to be too small cohort in the MAC group for comparison. The analysis between the acute GvHD group and the no GvHD group was performed from baseline to 3 months after HSCT as acute GvHD often occurs within 3 months after HSCT. Chronic GvHD occurs from 3 months after HSCT and therefore the analysis took place from 3 months following HSCT until the 3-year follow-ups. Regardless of acute or chronic GvHD, the overall health/QoL scale was analyzed from baseline to the 3-year follow-up. When comparing groups a p-value of < 0.01 was regarded as significant and the low significance level was set to avoid false-positive
results. To test if characteristics differed between patients at baseline and the respondents at the 3-year follow-up in Study I, a Chi-2 test was conducted on the categorical data. In both studies Wilcoxon signed-rank test was performed to test for the difference in every item between baseline and the follow-ups in weeks 2 and 3 and, in year 3 (analysis was performed in study I after the article was submitted). This non-parametric test was chosen because the data were not normally distributed. In both the Chi-2 test and the Wilcoxon signed-rank test a p-value of 0.05 was considered significant. The analyses in the two studies were performed using SPSS 17.0, PASW Statistics 18 and STATISTICA.

Ethical Considerations
Patients in both studies were informed both verbally and in writing that participation in the study was completely voluntary and could be discontinued at any time without affecting the patient's continued treatment. The patients were asked to fill out the questionnaire, even at times when clinical experience indicated that they could feel most negatively affected. This could be regarded as troublesome for the patient, but is probably outweighed by the patients' interest in reporting their symptoms. Since the researcher (UF) has taken an active part in the distribution and collection of the questionnaires, there is a risk that the patients had an emotional relationship with the researcher. This may lead to the patients feeling that they could not refuse to participate in the study and that they filled out the questionnaire not for their own sake, but for the sake of the researcher. The advantage of the researcher distributing the questionnaires is that the response rate is probably higher since the researcher desires as high a response rate as possible, while another person, for example, a member of the medical staff, who hands out the questionnaires, perhaps does not prioritize that task as highly as a researcher. The researcher has not had an active part in the daily care of the patients in the study. Since the study started, no patients have discontinued participation due to the questions being too offensive or too difficult to answer. Approval was given by the Regional Ethical Review Board, 2003 (Dnr 03-366).
RESULTS

Study Group
The majority of the patients in Study I were diagnosed with MM (58%) or lymphoma (33%) and in Study II leukemia. The mean age of the patients in Study I was 54 years and the majority was men; in Study II the mean age were 48 years, with an equal distribution of men and women. Disease status at transplantation in Study I was complete remission in 11%, no complete remission (i.e., partial remission or minimal response) in 71% of the patients. In Study II the disease status was complete remission (CR) in 61% and no complete remission in 15% of the patients. The patients in Study I were hospitalized for about 20 days and on 10 of these days with neutrophil counts < 0.5 x 10⁹/L, which means in clinical practice isolation, compared to 32 days in Study II and 16 days with neutrophil counts < 0.5 x 10⁹/L. During the study period the number of patients remaining in the both studies was reduced over time, leaving 53 patients (55%) in Study I and 38 patients (40%) in Study II at the 3-year follow-up (Figure 3). The majority of the patients who remained in the studies at the 3-year follow-up were in CR (43% in Study I and 92% in Study II) (Table 1). The main reason for drop-outs in the studies was death (31% in Study I and 47% in Study II). In study I, 3 patients declined further participation in the study and 2 patients were too ill to complete the questionnaire, but died shortly thereafter and are therefore included in the group of patients who died during the study period. The main causes of death were relapse (87% in Study I and 30% in Study II), infection (30% in Study II), and GvHD (26% in Study II) (Figure 3). In Study II acute GvH was reported in 57% of the patients, with a majority of grades 1 and 2. Chronic GvHD was seen in 53% of the patients, most of them with extensive chronic GvHD (Table 4).

Figure 3. Study sample size and patient drop-outs from baseline up to 3 years post HSCT.
Table 4. Patient characteristics in Studies I and II

<table>
<thead>
<tr>
<th>Study population</th>
<th>Autologous HSCT (Study I)</th>
<th>Allogeneic HSCT (Study II)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (n)</td>
<td>96</td>
<td>94</td>
</tr>
<tr>
<td>Men/Women (n) (%)</td>
<td>62 (65%)/34 (35%)</td>
<td>47 (60%)/47 (50%)</td>
</tr>
<tr>
<td>Age, mean (range)</td>
<td>54 (18-70) years</td>
<td>48 (20-67) years</td>
</tr>
<tr>
<td>Marital status (n) (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/COhabiting/Partner</td>
<td>80 (83)</td>
<td>72 (77)</td>
</tr>
<tr>
<td>Single</td>
<td>16 (17)</td>
<td>22 (23)</td>
</tr>
<tr>
<td>Stem cell source (n) (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral blood hematopoietic cells</td>
<td>96 (100)</td>
<td>85 (90)</td>
</tr>
<tr>
<td>Bone marrow</td>
<td></td>
<td>7 (8)</td>
</tr>
<tr>
<td>Cord blood</td>
<td></td>
<td>2 (2)</td>
</tr>
<tr>
<td>Donor: Related donor/Unrelated donor (n) (%)</td>
<td></td>
<td>42 (45)/52 (55)</td>
</tr>
<tr>
<td>Conditioning regimens (n) (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAC/RIC</td>
<td>23 (14–34)</td>
<td>32 (18–162)</td>
</tr>
<tr>
<td>Days with neutrophil counts &lt; 0.5 MAC/RIC</td>
<td>10 (3–16)</td>
<td>16 (10–54)</td>
</tr>
<tr>
<td>Diagnosis (n)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute leukemia</td>
<td>Status at transplantation (n) Complete remission (CR) (2)</td>
<td>Status at transplantation (n) CR (47), PD* (2), Refr* (2)</td>
</tr>
<tr>
<td>Myelodysplastic syndrome</td>
<td>CR (1), noCR (45), Unknown (4)</td>
<td>CR (5), noCR (2), Refr (1)</td>
</tr>
<tr>
<td>Chronic myeloid leukemia</td>
<td>Relapse/Progression (5), Untreated (1)</td>
<td>CP* (6), Blast crisis (1)</td>
</tr>
<tr>
<td>Chronic lymphocytic leukemia</td>
<td>CR (8), noCR (20), Unknown (2)</td>
<td>noCR (2), PD (2)</td>
</tr>
<tr>
<td>Myeloproliferative disease</td>
<td>Relapse/Progression (2),</td>
<td>CR (1), CP (1), Refr (1), PD (1)</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td></td>
<td>CR (2), noCR (2), PD (1)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>noCR (1), Unknown (1)</td>
<td>noCR (1)</td>
</tr>
<tr>
<td>Prolymphocytic leukemia</td>
<td>noCR (2), Stable disease (1)</td>
<td>Sensitive disease (2), Aplasia (2)</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>Secondary progressive (1)</td>
<td></td>
</tr>
<tr>
<td>Testicular cancer</td>
<td>Other*</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute GvHD (n) (%)</td>
<td>Not applicable</td>
<td>37 (39)/17 (18)</td>
</tr>
<tr>
<td>Chronic GVHD (n/%)</td>
<td>Not applicable</td>
<td>19 (20)/31 (33)</td>
</tr>
<tr>
<td>Number of patients and diagnosis in the 3-year follow-up (n)</td>
<td>Status at the 3-year follow-up (n)</td>
<td>Status at the 3-year follow-up (n) 38</td>
</tr>
<tr>
<td>Acute leukemia</td>
<td>CR (1)</td>
<td>CR (22)</td>
</tr>
<tr>
<td>Myelodysplastic syndrome</td>
<td></td>
<td>CR (1)</td>
</tr>
<tr>
<td>Chronic myeloid leukemia</td>
<td></td>
<td>Relapse (1)</td>
</tr>
<tr>
<td>Myeloproliferative disease</td>
<td>CR (1)</td>
<td>CR (2)</td>
</tr>
<tr>
<td>Chronic lymphocytic leukemia</td>
<td></td>
<td>noCR (1)</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>CR (1), not in CR (16), Unknown (5), Relapse/Progression (6)</td>
<td>CR (1), Relapse (1)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>CR (20), not in CR (1), unknown (1)</td>
<td>CR (2)</td>
</tr>
<tr>
<td>Testicular cancer</td>
<td>CR (1)</td>
<td>CR (3)</td>
</tr>
<tr>
<td>Other</td>
<td>Not in CR (1)</td>
<td></td>
</tr>
</tbody>
</table>
| *MAC, Myeloablative conditioning; *RIC, Reduced intensity conditioning; * PD, Progressive disease; * Refr, Refractory; *noCR Partial remission or minor response; * CP, Chronic phase; * Other, 1 Multiple sclerosis, 2 aplastic anemia and 2 paroxysmal nocturnal hemoglobinuria; * GvHD, Graft versus Host Disease
Functional Scales
All functional scales significantly decreased in both studies during the first two to three weeks from baseline, showing a major impact on physical, role, and social function compared with baseline. Two months after HSCT nearly all function scales had returned to the same value as at baseline for patients in Study I and at one year for patients in Study II. Role, emotional, and social function had significantly improved in Study I at the 3-year follow-up compared to baseline, whereas role function was the only function that had improved in Study II (Table 5; Figure 4-5).

Symptom Scales and Single Items
Nearly all symptom scales and single scales in both studies significantly increased during the first two and three weeks from baseline. In Study II dyspnea reached the maximum value 2 months after baseline. The symptoms that patients assessed worst in both studies were nausea and vomiting, loss of appetite, fatigue, and diarrhea. Two months after HSCT all symptom scales and single scales had returned to the baseline value for the patients in Study I. One year after HSCT, fatigue, sleep disturbance, nausea, and vomiting had normalized to the baseline value in the patients in Study II. Appetite loss had returned to the baseline value at the 1½-year assessment, and about 2 years after HSCT, pain, dyspnea, and diarrhea had returned to the baseline value. Fatigue and dyspnea had significantly improved at the 3-year assessment in patients in Study I compared to baseline (Table 5; Figure 4-5).

Global Health status/QoL
The patients’ global health status/QoL in the two studies significantly decreased during the first two and three weeks. Thereafter, it gradually improved enough to return to the baseline value at about two months after HSCT in patients in Study I and one year after HSCT in patients in Study II. For patients in both studies, there was no further improvement in global health status/QoL after the one-year assessment (Table 5; Figure 4-5).
Table 5. Health-related quality of life in the two studies over a three-year period measured with the EORTC QLQ C-30 (0–100 points)\(^a\)

<table>
<thead>
<tr>
<th>Item</th>
<th>No. of respondents, mean (SD)</th>
<th>Study 1</th>
<th>Study II</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of respondents</strong></td>
<td></td>
<td>94(18)</td>
<td>93(16)</td>
</tr>
<tr>
<td><strong>Items, mean (SD)</strong></td>
<td></td>
<td>76(19)</td>
<td>71(16)</td>
</tr>
<tr>
<td><strong>Physical</strong></td>
<td></td>
<td>81(21)</td>
<td>75(19)</td>
</tr>
<tr>
<td>Role</td>
<td></td>
<td>86(21)</td>
<td>81(19)</td>
</tr>
<tr>
<td>Social</td>
<td></td>
<td>91(21)</td>
<td>86(20)</td>
</tr>
<tr>
<td>Emotional</td>
<td></td>
<td>96(21)</td>
<td>91(19)</td>
</tr>
<tr>
<td>Cognitive</td>
<td></td>
<td>101(21)</td>
<td>96(19)</td>
</tr>
<tr>
<td>Quality of life</td>
<td></td>
<td>106(21)</td>
<td>101(19)</td>
</tr>
<tr>
<td>Nausea &amp; Vomiting</td>
<td></td>
<td>111(21)</td>
<td>106(20)</td>
</tr>
<tr>
<td>Appetite loss</td>
<td></td>
<td>116(21)</td>
<td>111(19)</td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
<td>121(21)</td>
<td>116(19)</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td></td>
<td>126(21)</td>
<td>121(19)</td>
</tr>
<tr>
<td>Pain</td>
<td></td>
<td>131(21)</td>
<td>126(19)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td></td>
<td>136(21)</td>
<td>131(19)</td>
</tr>
<tr>
<td>Constipation</td>
<td></td>
<td>141(21)</td>
<td>136(19)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td></td>
<td>146(21)</td>
<td>141(19)</td>
</tr>
<tr>
<td>Financial</td>
<td></td>
<td>151(21)</td>
<td>146(19)</td>
</tr>
</tbody>
</table>

\(^a\) Pairwise comparison between baseline and week 2/3 and year 3 in Studies I and II. The analysis in study I was performed after the article was published.

*Higher scores for functional scales and QoL status indicate a high level of function and higher scores on the symptom scales and single items indicate more severe symptoms or impairments.*
Figure 4. Functional scales and symptom scales status in Study II for the total study population from baseline over a 3-year period, and global health status/QoL for the total study population and for patients on MAC or RIC regimens. Mean values are based on the patients answering the EORTC QLQ C-30 questionnaire. Higher scores for functional scales and QoL status indicate a high level of function, and higher scores on the symptom scales and single items indicate more severe symptoms or impairments.

Figure 5. Functional scales, global health status/QoL, and symptom scales status in Study I for the study population from baseline over a 3-year period. Mean values are based on patients answering the EORTC QLQ C 30 questionnaire. Higher scores for functional scales and QoL status indicate a high level of function, and higher scores on the symptom scales and single items indicate more severe symptoms or impairments.
Comparison between Patients with MM and Lymphoma in Study I
In week 2 patients with lymphoma experienced significantly worse physical function than patients with MM (27 vs. 53, p = 0.001), overall QoL (15 vs. 34, p < 0.001), fatigue (85 vs. 69, p = 0.009), pain (63 vs. 32, p = 0.003) and more appetite loss at month 2 (22 vs. 6, p = 0.005).

Comparison between Patients with MAC and RIC regimens in Study II
Patients treated with MAC had significantly worse scores than patients treated with RIC. At baseline regarding fatigue (15 points, p < 0.01), nausea and vomiting (19 points, p < 0.01), at week 3 regarding pain (23 points, p < 0.01) and sleep disturbance (29 points, p < 0.01), and at week 4 regarding appetite loss (33 points, p < 0.01) and diarrhea (29 points, p < 0.01). After month 3 the number of patients treated with MAC was 7 or less, and therefore no further testing between MAC and RIC was done.

GvHD and Its Impact on HRQL in Patients Undergoing Allogeneic HSCT, Study II
Patients with extensive chronic GvHD reported significantly more impaired physical and role function than patients with limited chronic GvHD and those with no chronic GvHD. With regard to physical function at 1½ years (69 points vs. 93 points and 88 points, p < 0.01), at 2 years (76 points vs. 92 points and 94 points, p < 0.01) and at 2½ years after HSCT (66 points vs. 91 points and 96 points, p < 0.01). They reported significantly impaired role function compared to patients with limited chronic GvHD at 1 year (36 points vs. 72 points, p < 0.01), at 1½ years (39 points vs. 77 points, p < 0.01) and at 2 years after HSCT (49 points vs. 83 points, p < 0.01) and those without chronic GvHD at 1 year (36 points vs. 74 points, p < 0.01) and at 2½ years after HSCT (44 points vs. 86 points, p < 0.01). Patients with chronic GvHD had a significantly worse global health status/QoL from month 6 after HSCT to the 1½-year follow-up as compared to those with no or limited chronic GvHD (p < 0.01), as shown in Figure 6.

Figure 6. Global health status/QoL from baseline over a 3-year period for patients affected by acute or chronic GvHD and patients without GvHD. Mean values are based on patients answering the questionnaire, separated according to the degree of GvHD. Higher scores for global health status/QoL indicate a high-level global health status/QoL.
DISCUSSION

HSCT is an established treatment for a variety of malignant diseases, as well as a small proportion of non-malignant disorders (1, 2). The number of HSCTs increases every year, and the main indication for allogeneic HSCT is patients with acute leukemia and, for autologous HSCT, patients with plasma cell disorders, followed by lymphoma (31). Irrespective of the treatment strategy, HSCT has a strong impact on the patients’ HRQL (10, 11). Measuring HRQL during and after HSCT is therefore important to highlight specific areas that affect the patients’ lives and to help healthcare professionals to improve their daily care (21, 22).

The two studies in this thesis provide unique data on the patients’ self-estimated HRQL and cover the whole transplantation period and the first three years thereafter. They give an overall picture of how patients experienced their HRQL before, during, and after the transplantation and how the symptoms fluctuate over time. The results provide a realistic picture of what the patients have to expect during and after the transplantation, which is important knowledge for both physicians and nurses who can more clearly inform patients before transplantation and gives patients a chance to mentally prepare for transplantation. Our results are consistent with those of other studies showing that it takes approximately one year after HSCT for patients to recover to the same level as before HSCT (73, 74). The assessments in these two groups of patients continued for 3 years after HSCT. The studies clearly show that recovery after HSCT differs between patients undergoing autologous HSCT and those undergoing allogeneic HSCT. In Study I nearly all values on the scales had returned to the baseline values at the second month, but in Study II it took approximately 1 to 1½ years after the HSCT. Our results are comparable with those of Hjermstad et al. (73), who found that role function, social function, and most of the symptom scales and single items had returned to the baseline value two months after autologous HSCT.

Already at baseline studies have shown that patients undergoing autologous and allogeneic HSCT have a more affected HRQL than the general population, probably due to the disease and earlier treatment (75, 76). This illustrates that most of the patients in the studies had a cancer diagnosis and had been pretreated with anti-tumor drugs before the transplantation which affected their HRQL both physically and psychologically. It is important to make the healthcare professionals aware of the fact that patients already have an affected HRQL before HSCT, and that the patients’ HRQL before HSCT can probably have an effect on the patients’ recovery after HSCT (77).

Patients’ HRQL decreased during hospitalization and weeks 2 and 3 were the times when the patients experienced that their HRQL was most severely affected. All functional scales significantly decreased in both studies. This is consistent with other studies showing that physical, cognitive, social (74, 78), role (16, 74, 79), and emotional function (79, 80) decreased during hospitalization. Some of the decreased physical function during the inpatient period is probably due to the limited ability to
perform physical activities during the isolation period, rather than an inability to perform these activities if the opportunity had existed. Studies have shown that physical activity during and after HSCT has beneficial effects on the patients’ HRQL (81-83). It is therefore important for healthcare professionals to find methods that encourage physical activity despite hospitalization and isolation, for example, virtual computer games (84).

In the two studies appetite loss, nausea, vomiting, and diarrhea, followed by fatigue, sleep disturbance, pain, and dyspnea, were the symptoms that affected patients most during hospitalization. These results are similar to the study by Grulke et al. (74) and the data reported by Larsen et al. (10). There are studies showing that patients experience fatigue as the symptom that affects them most (78, 85). Fatigue is a complex concept and is clearly different from the fatigue that occurs after normal physical or mental effort. There are several factors that can cause fatigue, for example, chemotherapy, anemia, malnutrition, depression, infection (86, 87), disease, nausea/vomiting, and loss of appetite (88). One of the reasons why fatigue is a major problem might be that many of the symptoms persist for a relatively short period and there may be ways to deal with certain symptoms, such as drugs for nausea, but fatigue simply occurs and it might be difficult to know how patients or healthcare professionals should managed or improved it. Physical activity is an intervention that could actually reduce fatigue. In a review by Cramp and Byron-Daniel (89), it is shown that there was no significant difference between patients with hematological diseases who exercise and the control group. On the contrary, a study by Wiskemann et al. (90) on the effects of a self-administered exercise program for patients undergoing allogeneic HSCT, found a significant reduction in cancer-related fatigue compared to a control group.

Issues regarding physical function, role function, social function and pain are related to how these affect the patients’ daily life. The results in both studies clearly demonstrate that the patients’ daily life is affected by the treatment.

The improvement in HRQL after HSCT differs in both studies. In Study I the patients started to experience an improvement already at week 3, but for the patients in Study II, appetite loss, fatigue, dyspnea, and diarrhea were a problem up to 6 months after HSCT. These symptoms might be due to several factors, for example, gastrointestinal GvHD, infection, depression, and malnutrition (91, 92).

Three year after HSCT there was a significant improvement in role, social, and emotional function, fatigue, and dyspnea for patients in Study I. For patients in Study II, there was no further significant improvement in HRQL between one year and three years after HSCT, except for role function. Our results differ to the prospective study by Hjermstad et al. (73) on patients undergoing autologous and allogeneic HSCT, except in social function. They found that 3–5 years after stem cell transplantation, physical-, and social function and global QoL had improved in 40 patients undergoing autologous HSCT, whereas social function had improved in 35 patients undergoing
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Ulla Frödin

In their study, Grulke et al. (74) found an improvement in role and social function compared to baseline when more than one year had passed since HSCT. These results indicate that it takes longer for the patients’ HRQL to improve after an allogeneic HSCT than after an autologous HSCT. This is clearly reflected in HRQL among patients undergoing allogeneic HSCT due to a higher frequency of morbidity and mortality, caused particularly by life-treating infections (13, 38) and chronic GvHD (40, 93). Although the data collection started at the end of 2001, the treatment of these patients today is almost the same, which indicates that the results are still relevant.

In Study I comparisons were made between patients with MM and lymphoma. Patients with MM experienced more pain than patients with lymphoma at baseline, which is quite commonly seen by clinicians and probably associated with the disease (94). At week 2 there were significant differences between the two groups in physical function, quality of life, pain, and fatigue. The pain that patients with MM experienced during week 2 was probably not due to the disease itself. Gulbrandsen et al. (95) found in their study that after starting the high-dose treatment, there was an improvement regarding pain in patients with MM. A common side effect after high-dose treatment is mucositis, and Blijlevens et al. (96) have examined the incidence of oral mucositis in 109 patients with MM and 88 patients with lymphoma undergoing high-dose therapy with HSCT. They found that, regardless of the diagnosis, severe mucositis occurred in more than 40% of the patients. Therefore, the most probable cause of pain during week 2 for both patients with MM and lymphoma was mucositis (97, 98).

In Study II comparisons were made between patients treated with MAC and RIC. Patients treated with MAC were hospitalized longer than patients treated with RIC. They were also affected by more acute GvHD, but less chronic GvHD than patients treated with RIC. More patients died among those who were treated with MAC than among those treated with RIC. Patients treated with MAC had significantly more fatigue, nausea, and vomiting at baseline. In weeks 3 and 4 they reported significantly more pain, sleep disturbances, loss of appetite, and diarrhea than patients treated with RIC. Pain during the early phase is, as in Study I, probably due to mucositis, a common side effect after MAC, but it also affects some patients treated with RIC (99, 100). We need to become better at preventing and treating mucositis in patients undergoing both autologous and allogeneic HSCT by improved cooperation with the hospital dentistry department and by developing care plans. Our results differ compared to Bevans and colleagues (101). They measured HRQL using Short Form-36 Health Survey, the Functional Assessment of Cancer Therapy- general and BMT in patients treated with MAC and RIC regimens at baseline, days 0, 30, 100, 1 and 2 years after HSCT. They found no difference between groups during early recovery. Andersson et al. (102) used EORTC QLQ C-30 and the module High-Dose Chemotherapy (HDC 19) in patients treated with MAC and RIC regimens. They found that one month after HSCT, patients treated with MAC had significantly more sleep
disturbances, financial problems, and mouth and taste problems. A possible reason for the differences between the studies by Bevans and colleagues’ (101) and Andersson and colleagues’ (102) is that different HRQL instruments were used, probably because the instrument highlights different aspects of HRQL. These results clearly demonstrate the need for more comparative studies between patients treated with MAC and RIC during and after transplantation using the same HRQL instrument.

In Study II comparisons were also made between patients who were affected by any form of GvHD and patients who had not developed any GvHD. Patients with grades 3/4 acute GvHD had significantly more diarrhea than patients with GvHD grades 1/2, which is an obvious result because the amount of diarrhea indicates the severity of GvHD (40). Approximately half of the patients in our study were affected by acute or chronic GvHD. Patients who have or had extensive chronic GvHD had significantly impaired physical and role function and global QoL compared to those who had no or limited chronic GvHD. This result points out the effect that extensive chronic GvHD has on the patients’ HRQL (103-106) and stresses the importance of supporting patients affected by extensive chronic GvHD and implementing actions that increase HRQL. This could be information about the benefits of self-care to reduce the problems of chronic GvHD, such as increased physical activity to prevent stiffening joint, which can be common in chronic GvHD.

In Study I 30 patients died and 13 patients dropped out, leaving a study population of 53 patients at the three-year follow-up. In Study II there was a decrease in the study population by 60% from baseline through the three-year follow-up, leaving a study population of 38 patients at the end of the study. The main reason for dropping out of the two studies was death, which, in Study I, was caused by relapse, especially among patients with MM compared to patients with lymphoma (50% vs. 27%). The same result was found in a population-based study by the Nordic Myeloma Study Group: 56 out of 120 patients (47%) aged 60–64 years had died as a result of disease-related factors during a 4-year period. In patients who relapsed after transplantation the median survival was 16 months (107). The results in our study and the study by Lenhoff et al. (107) reflect the normal clinical picture that transplantation in patients with MM is not curative, but provides an opportunity for prolonged survival. In Study II 50% of the patients died and was caused by relapse (30%), infections (30%), and GvHD (26%), reflecting the fact that many patients had HSCT for advanced disease and the high risk of complications after HSCT. These data are comparable with a study by Bhatia et al. (108), who study late mortality after HSCT. They found that relapse, chronic GvHD and infection were the primary reasons for death. In a retrospective analyses with data from the EBMT data base show that of 56 505 patients transplanted between 1990 and 2005 with an allogeneic HSCT, 26 020 (46 %) had died, and of them 28 % from transplant-related causes (109). The high rate of drop-outs in both studies on patients experiencing relapse or complications leads to the finding that the majority of patients who filled in the 3-year follow-up questionnaire are patients who from a clinical point of view are doing well, with their
disease under control. In addition, the high death-rate indicates the importance of securing the best possible quality of life also for patients with poor prognosis. The HSCT has a severe impact on the lives of both patients and their families and if healthcare personnel identify symptoms and other problems early in the treatment phase they may ease the burden for the patient and the family.

When the studies in the thesis were initiated, a decision was made to have a study population of 100 patients in each study in order to have two equal groups. One of the reasons for the number of patients in the studies was to have an acceptable inclusion period since it takes at least five years to include 100 patients in the allogeneic group. A limitation in the studies was the large number of drop-outs. In order to have an acceptable study population at the end of a study in the future, it is important to have multi-center studies so as to have the opportunity to include more patients in the studies.

METHODOLOGICAL CONSIDERATIONS

For the purpose of the study, a quantitative approach using a self-administered questionnaire was chosen since the aim was to conduct a population-based study on HRQL in patients undergoing HSCT at one treatment center. It was important to design a study that covers the entire inpatient period in order to investigate how the patients’ HRQL changes during this time so as to have the opportunity to compare different diagnoses (i.e., MM vs. lymphoma in Study I) and treatment effects (i.e., RIC vs. MAC in Study II). Since the questionnaire was designed to capture HRQL during the preceding week and a 4 week-hospitalization, five forms, including baseline, were used. The strengths of the two studies were the frequent and regular follow-ups covering the whole inpatient period, as well as a long follow-up period. This clearly gives an indication of how the patients’ HRQL was affected, especially in the acute phase of the transplantation. The studies demonstrated quite well what symptoms the patients experienced to be most severe and at what time in the acute phase of the transplantation they occurred, which correlates quite well with the effect of the treatment given. The studies have also demonstrated the time at which HRQL begins to improve and return to the baseline value. These results have mainly added to the general knowledge of HRQL in patients undergoing HSCT, especially when it comes to informing the patients about what he/she can expect during the transplantation and how long it will take to recover. Based on the results, another important insight is that, the healthcare professional knows when the patients need more support and what patient group is affected more than others. A weakness in our methodological approach is that the EORTC QLQ C-30 provides a general knowledge of the patients’ HRQL, but not a deeper understanding. It would have been an advantage to have more instruments during the study period. If the module High-Dose Chemotherapy (HDC 19) had been translated into Swedish when the studies were initiated, we
would have used it together with the EORTC QLQ C-30. This module is directed to patients undergoing HSCT (110).

**Questionnaires**
The EORTC QLQ C-30 was selected to measure HRQL. According to the EORTC the translation into Swedish was done by a translation agency. It is a good overview tool and has been well used in other studies. We assumed it would make it possible to compare our results with those of other studies within the same study population. As a rule, the patients did not find it difficult to complete the questionnaire, although some of them indicated that it was difficult to answer the questions about physical function during the inpatient period because they had limited opportunities to, for example, carry heavy bags or suitcases, or take walks outside. In a comparison between EORTC QLQ C-30 and FACT-BMT, Kopp et al. (111) measured HRQL in patients undergoing HSCT and concluded that both instruments cover different aspects of HRQL, but that EORTC QLQ C-30 is more relevant during and immediately after transplantation since its main focus is on measuring physical and functional aspects of QoL and also symptoms. The instrument does not measure frequency or distress, only severity. For instance, patients are asked to answer whether they have diarrhea. The response alternatives are not at all, a little, quite a bit, and very much. This is a subjective evaluation about the patients’ symptoms/HRQL and can be interpreted in several ways; either the number (many diarrheas, but not so much every time) or the amount of diarrhea (not as many diarrheas but large amount) or many diarrheas and large amount. The questionnaire had some disadvantages with regard to the question about pain. It asks only if you have pain, but not where the pain comes from, which is a very relevant question because the support given by the health professional differs if the pain is caused by mucositis or, for example, headache. With regard to the term global health status/QoL, the patients are asked to rate their overall health during the past week and to rate their overall quality of life during the past week. In some articles the term is specified as global QoL (76, 104, 112) or global health (74, 75, 113). In Study I, the term was not used consistently as global health/QoL and QoL, as well as overall QoL were used. To avoid this in Study II, global health status/QoL has been used consistently. Both previous versions and the current version of the questionnaire have been tested for validity and reliability in patients with various types of cancer but, unfortunately, not specifically in patients with hematological diseases (68, 70, 114). Bjordal et al (114) tested the validity and reliability of the current questionnaire (EORTC QLQ C-30) in 622 patients from 12 countries with head and neck cancer. They found that the questionnaire has good validity, and they found better reliability in the physical function in this version than in the former questionnaire. Michelson et al. (69) did a study to obtain reference values for EORTC QLQ C-30 from a random sample of the Swedish population. They performed a reliability analysis and Cronbach’s alpha was over 0.80 for functional scales (except cognitive function) and global QoL.
An important aspect of the clinical validity of a questionnaire is its ability to detect change over time. The results in studies I and II provide valid data since they confirm the clinical experience concerning how these patients feel during and after HSCT. The results follow the expected fluctuations in the patients’ HRQL and give a good overall clinical picture of how the patients felt during and after HSCT. Our results also conform to the results of other studies, indicating good validity. When healthcare professionals evaluate results from HRQL studies, it is important that patients can experience changes in HRQL as significant, although there is no statistical significance in some parts of the HRQL questionnaire. On the other hand, some parts of the questionnaire can be statistically significant, but not be of any importance at certain times, which is the case in for instance, social and role functions during the inpatient period. It has been recommended that a change in mean value of 10 points or more on a 0 ± 100 scale should be defined as being clinically significant (115). In these studies there were no clinically significant variables in the HRQL questionnaire at the assessments at week 2, 3 and 3 years.

Statistics
Studies have demonstrated differences in age and sex within some variables (60, 116, 117). For example, in a review by Braamse et al. (60), strong evidence was found indicating that female were more likely to suffer from depression after HSCT than men and that older age predicted better social function after HSCT. Heinonen et al (116) found in their study that females reported worse fatigue, emotional well-being compared to men, but men in turn were more dissatisfied with social support regardless of marital status. Since sex and age are parameters that may affect HRQL. Therefore, data were adjusted for sex and age when comparisons were made on the group level in both studies (118). One advantage of adjusting for age and sex is that it makes possible comparable groups, with equal distributions of males and females, and no extremes in ages. In cases of a gender imbalance in the group, another advantage is that, for instance, the value for nausea and vomiting may become lower for men because they actually experience this less. It is the same thing with age; younger people experience more nausea than older people. To find out the differences between men and women, it would have been an advantage to make a comparison between these two groups, but the disadvantage is that there would be two relatively small groups. This could be compensated for by analyzing all of the material in both studies, and then adjusting for age and gender. Mean values were used in the analysis to enable comparison of the results with other studies instead of median, which should have been a natural choice since the study material is not normally distributed. Standard deviations for the different scales and individual items are often large, indicating wide distribution of the material. In the thesis both parametric and non-parametric tests are used, since the tests have different objectives.
CONCLUSION

The conclusions drawn from both studies are that week 2 and 3 is the period in which patients undergoing HSCT need the most supportive care. Patients with lymphoma in Study I indicated a lower HRQL during this period compared with patients with MM and may therefore need extra support during this period. The patients recovered quickly after autologous HSCT, suggesting that transplantation was well tolerated by the majority of them. Three years after HSCT, there was a significant improvement in role, social, and emotional function, fatigue and dyspnea for patients in Study I. Patients on MAC regimens in Study II experienced a worse HRQL at baseline than patients with RIC regimens, and subsequently more pain, sleep disturbance, and appetite loss in weeks 3 and 4. Patients with extensive chronic GvH experienced reduced HRQL compared to patients with limited or no chronic GvHD. In Study II, it took at least one year for the patients’ HRQL to return to the baseline level. The only function that had improved significantly three years after HSCT was role function. The result clearly demonstrates the negative impact allogeneic HSCT has on patients’ HRQL. The results provide an opportunity to individualize the information before the transplantation, depending on whether the patient should undergo autologous or allogeneic HSCT.

CLINICAL IMPLICATIONS

Based on the results of the studies, there are several clinical implications. First of all, healthcare professionals are recommended to perform regular monitoring of HRQL and symptoms for early identification of patients who need extra care. Implementation of different measurement tools in clinical routine is recommended to facilitate the care for patients with severity symptoms, for example a scale measuring oral toxicity. Exercise programs or virtual computer games could be valuable to increase patients’ physical function during and after transplantation. The results will help the healthcare personnel to inform patients and help the patients to understand what they have to expect during and after the transplantation, and that the recovery after the transplantation takes time for patients undergoing allogeneic HSCT.

FUTURE RESEARCH

It is desirable to conduct a comparative study between Studies I and II during the inpatient period and up to five years after HSCT to see if there are any differences between autologous and allogeneic transplantations. Since the EORTC QLQ-C30 does not cover aspects of QoL which may be important in the long term, such as chronic GvHD, sexuality, work, etc., an interview study with patients from Study II would be important, with the addition of the EORTC QLQ-C30 and the module High-Dose Chemotherapy (HDC 19), in order to compare how HRQL has evolved over time. To
increase physical activity in patients undergoing transplantation, research on the use of virtual computer games would be interesting.

Andra vanliga biverkningar är illamående och kräkningar, aptitförlust, muntorrhet, smakförändringar, slemhinneskador (mucosit), diarré, trötthet, håravfall, sömnproblem och feber. Patienter som genomgår allogen HSCT kan drabbas av ytterligare komplikationer beroende på att deras nya immunförsvar inte är fullt utvecklat.

Sjukdom och behandling har en stor inverkan på livet och livskvalitén för majoriteten av patienter med cancerdiagnos och studier visar att patienternas hälsorelaterade livskvalité (HRQL) påverkas av att genomgå HSCT. Mätningar av HRQL under och efter HSCT är därför viktigt för att lyfta fram de specifika områden som påverkar patienternas dagliga liv och därmed hjälpa vårdpersonal att förbättra den dagliga omvårdnaden.

andningssvårigheter, sömnpåverkan, aptitlöshet, förstoppning, diarré och ekonomiska svårigheter.

Patienternas funktionsstatus, symtomstatus och globala hälsostatus/QoL påverkades signifikant i båda studierna under de första två till tre veckorna jämfört med värdet innan start av behandling. Patienternas skattningsavstånd av andfåddhet i studie II avvek något från detta mönster, där nåddes det maximala värdet först två månader efter utgångsvärdet. De symtom som påverkade patienterna mest i båda studierna var illamående, kräkning, aptitlöshet, fatigeförsämring och diarré. I delstudie I förbättrades värdena för patienternas funktionsstatus, symtomstatus och globala hälsostatus/QoL till samma värde som innan behandling redan två månader efter HSCT medan det för patienterna i delstudie II tog ett till två år att återgå till utgångsvärdet. Tre år efter HSCT förbättrades ytterligare flera av HRQL-variablerna signifikant för patienterna i delstudie I jämfört med innan behandling medan för patienterna i delstudie II var rollfunktion den enda variabel som förbättrades signifikant. I delstudie I uppgav patienter med lymfom signifikant sämre värden än patienter med multipel myelom under vecka 2 avseende fysisk funktion, global hälsostatus/QoL, fatigeförsämring, smärta och vid 2 månaders uppföljningen signifikant sämre värd avseende aptitlöshet. Patienter som erhållit MAC i studie II uppgav redan innan start av behandling signifikant sämre värden än patienter som behandlades med RIC avseende fatigeförsämring, smärta, illamående och kräkning. Patienter som behandlats med MAC hade även under veckorna 3 och 4 signifikant sämre värden avseende sömnsvårigheter, aptitlöshet och diarré. Patienter med svår kronisk Graft versus host disease (GvHD) i studie II uppgav en signifikant försämrad fysisk funktion, rollfunktion och globalt hälsostatus/QoL än patienter med lindrig eller ingen kronisk GvHD. Resultaten i båda studierna ger en god överblick över patienternas symtom och HRQL under och efter HSCT och visar på den ökade vikten av tätsamma förbättringar och uppföljningar. Resultaten visar också när patienterna behöver ökat stöd till exempelsymtomkontroll. Resultaten ger en realistisk bild av vad patienterna har att förvänta sig under och efter transplantationen, vilket är viktigt kunskap för både läkare och sjuksköterskor som tydligare kan informera patienterna före transplantation om ett troligt scenario avseende områden som kan påverka deras HRQL, vilket ger patienterna en möjlighet att mentalt förbereda sig för transplantationen. Resultaten visar också när patienterna behöver ökat stöd till exempel med förbättrad hantering av mucositis, vilket skulle kunna reducera en del av smärtsymptomatiken. Vidare kan vårdpersonalen stödja patienterna med att ge verktyg för att öka deras fysiska aktivitet under och efter vårdtillfället. Ökad fysisk aktivitethar visat sig har positiv inverkan på exempelvis fatigeförsämring.

Slutsatserna från båda studierna är att vecka 2 och 3 är den period då patienterna behöver mest stöd framförallt patienter med lymfom som genomgår autolog HSCT och de patienter som behandlas med MAC och som genomgår allogen HSCT. För dessa patienter skulle ett systematiskt arbete kring förebyggande av vissa symtom och att tidigt i förloppet inducera behandling vara lämpligt. Resultaten visar också på att patienter med omfattande kronisk GvHD behöver ökat stöd genom att exempelvis...
informera om nyttan av egenvård för att minska problemen med kronisk GvHD. Det skulle till exempel kunna vara att öka den fysiska aktiviteten i syfte att mjuka upp patientens leder som kan stelna till vid kronisk GvHD. Den snabba återhämtningen av patienterna i studie I tyder på att behandlingen trots allt tolereras relativt väl. För patienterna i studie II tog det minst ett år för deras HRQL att återgå till samma värde som innan behandlingen och den enda funktion som förbättrades signifikant vid 3-årsuppföljningen var rollfunktionen. Resultaten visar tydligt den negativa påverkan som allogen HSCT har på patienternas HRQL.

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