



Psychological Morbidity and Support

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30.1 Introduction

Allo-HSCT is associated with significant physical and psychological morbidity that may have a negative impact on patients' and on their relatives' health-related quality of life (HRQoL) (Majhail and Rizzo 2013). Patients suffer a broad range of acute and chronic impairments of health-related quality of life (HRQoL), concerning physical, emotional, cognitive and social constraints. Psychosocial difficulties have been identified throughout the HSCT process, from pre-transplant to recovery phase and even for long-term survivors. Insofar, psychological support of HSCT recipients and caregivers is based on a—where ever possible—preventive, concrete and sustainable approach, comprising a broad range of aspects of HRQoL. Psychooncological interventions are planned and conducted regularly in

an interdisciplinary approach, taking into consideration medical, social and nursing issues.

30.2 The Period Preceding HSCT

Since HSCT often appears to be the only therapeutic cure, this can cause high expectations in patients and their families, who may overestimate HSCT's benefits and underestimate the procedure's morbidity and mortality risks. Several authors are adamant about the importance of pragmatic information, specifically regarding prognosis, post transplant effects and the impact of HSCT on QOL. This information not only could guide patients in their decision to undergo the treatment (or not) but could also help them and their close relatives to face the persistent side effects post-HSCT (Jim et al. 2014). Studies show that specific pre-transplant distress predicts psychosocial problems during and after HSCT (Schulz-Kindermann et al. 2002). This suggests a thorough medical as well as psychosocial preparation about risks and challenges with concomitant illustration of possible coping resources. Understanding of the information about the prognosis can be associated with depression and a worsening QOL over time (Applebaum et al. 2016).

Frequently described are anxious-depressive symptoms and sleep disruption pre-HSCT, linked to the burden of uncertainty about treatment outcomes. Baseline anxiety and depression predict

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worsening HRQoL during hospitalisation and post-treatment adjustment, even identifying these symptoms as risk factors for survival (Artherholt et al. 2014). This suggests a thorough survey of the psychosocial anamnesis and a brief screening in the course of treatment and survivorship. To avoid evitable strain, short instruments to measure distress, anxiety, depression and HRQoL—like the Distress Thermometer, Patient Health Questionnaire, Cancer Treatment-Related Distress Scale and EORTC QLQ-C30—should be implemented. Attention should always involve caregivers as well as minor children of patients. Finally, HSCT teams should screen patients' and families' met and unmet needs, including psychosocial support. Regarding preparation for HSCT, patients who are in a fairly stable physical state should take advantage of psychological support before admission to inpatient treatment. Psychological interventions cover different approaches like psychodynamic interviews, introduction in relaxation techniques, communication skills (regarding problem-focused communication with staff and with caregivers) and coping with side effects (pain, nausea, fatigue, restlessness, sleep disorder; see Syrjala et al. 2012).

30.3 Hospitalisation for HSCT

During hospitalisation, patients grapple with considerable changes, including a loss of physical abilities and autonomy. HSCT hospitalisation constraints, combined with poor physical condition, may increase patients' feelings of isolation and dependence, negatively affecting psychological well-being (Tecchio et al. 2013). Symptoms of depression, anxiety, sleep disruption and adjustment disorders are frequently reported (El Jawahri 2015). Unlike anxiety, which does not change over time, depression levels increase more than twofold after 2 weeks of isolation (Tecchio et al. 2013).

These symptoms can go unrecognised and have been known to interfere with HSCT medical treatment. Depression during hospitalisation is associated with longer hospital stay, increased

risk of mortality (Prieto et al. 2005), post transplant anxio-depressive symptoms and post traumatic stress syndrome (PTSS) (El-Jawahri et al. 2016).

Depressive symptoms are risk factors for a poorer outcome after HSCT. It is noteworthy to follow a precise diagnostic process, differentiating depression and demoralisation. The latter focuses on an attitude of senselessness and hopelessness, while depression has a pronounced somatic level, overlapping with fatigue. Recent research has explored psychoneuroendocrinology and psychoneuroimmunology to identify pathways that may mediate between psychosocial factors and disease outcomes (Costanzo et al. 2013). These authors have recommended the treatment of sleep and circadian disturbances, as well as the option of psychotropic medications and cognitive-behavioural interventions in the HSCT setting.

A significantly positive correlation between the presence of a family caregiver (FC) during hospitalisation and HSCT survival has been established (Foster et al. 2013). The support provided by the HSCT team can also help patients to better cope with hospitalisation and facilitate psychological adjustment after discharge, reducing difficulties in the transition towards outpatient care.

Psychooncological interventions concerning depressive and anxious symptomatology rely on psychoeducational, psychodynamic and biobehavioural approaches, incorporating adequate coping potential. Specific techniques to ameliorate anxiety but also side effects like pain, sleeplessness, nausea or restlessness comprise relaxation, imagery and hypnotherapeutic approaches. Particularly in cases of fear and panic, pharmacological approaches with benzodiazepines and certain antidepressants should be taken into account.

Precise and repeated pain diagnostics are paramount, deriving multidisciplinary pain management, including medication, ongoing information about pain management and psychological interventions. There is some evidence for effectiveness of relaxation, imagery, hypnosis and cognitive-behavioral therapy (Syrjala 2014).

30.4 Post-HSCT

Data show that patients in remission for 2–5 years post-HSCT have a high probability of long-term survival. Nevertheless, HSCT-related morbidity is substantial, negatively affecting psychological functioning and social integration. HSCT's late effects on physical and psychic well-being have been well described, notably for chronic graft versus host disease, the severity of which is significantly related to impaired psychosocial functioning and diminished QOL (Majhail and Rizzo 2013).

Regarding psychopathology post-HSCT, several studies reported high rates of anxiety and depression, even several years after transplantation. Notwithstanding, research on psychological issues after HSCT has shown inconsistent results due to varying outcome measures, participation biases and cohort size and composition (Sun et al. 2011).

Although some studies have shown that depression and anxiety rates do not differ significantly from those of siblings or population norms, others reveal rates of psychological distress of 14% to 90% in survivors of HSCT (Sun et al. 2011). Even though some results demonstrate that physical morbidity tends to decrease by 1-year post-HSCT and psychosocial condition improves gradually over 1–5 years (Sun et al. 2013), other research reports depressive symptoms as long as 5 or even 10 years after HSCT (Jim et al. 2016). An unsettling fact is that depression post-HSCT has been associated with higher mortality and increased risk of suicide (Tichelli et al. 2013).

Depressive symptoms and sleep disorders are related to cognitive dysfunctions. Sleep disruption remains an issue for 43% of HSCT patients after transplant (Jim et al. 2016). These rates of disruption are substantially higher than those of the general population. Incidence of cognitive dysfunction in the first 5 years after HSCT is up to 60% (Scherwath et al. 2013). Poor neurocognitive functioning and psychosocial outcomes lead to lax medication management and adherence to recommended monitoring guidelines, which in turn may increase post-treatment morbi-mortality risks (Mayo et al. 2016).

Psychological interventions for depressive symptoms focus on dysfunctional, exaggerated cognitions and on an increase of activities. Psychopharmacological treatment is often recommended additionally, offering a broad range of substances, which can and should be adapted to respective indications and to the broad range of further medication. In the case of severe demoralisation, existential and meaning-centred approaches are advisable and show some evidence.

Concerning lasting traumatic experiences, in cross-sectional studies between 5 and 19% fulfilled a diagnosis of post-traumatic stress disorder (PTSD). In one of the rare prospective studies, PTSD symptomatology was observable at all time points (Esser et al. 2017a). Therefore, psychological support should not only be offered in the acute phase but already before HSCT and in the long term. Impairment by pain and pain intensity were risk factors for elevated levels of PTSD symptomatology. This highlights the importance of informing patients early enough that pain might occur and to introduce techniques for dealing with it. Since medical complications predicted severity of PTSD symptomatology 1 year after HSCT, medical professionals should be aware of psychological strain among patients suffering from long-term medical complications.

Psychosocial issues have also been explored in QOL research. Some studies in this domain stated that even if medical problems remain, the patients' emotional well-being seems to improve throughout the rehabilitation period. Nonetheless, fatigue, sleep disorders, neurocognitive impairment, neurobehavioural problems and sexual dysfunction persist. Esser et al. (2017b) identified in a prospective study three stable symptom complexes: exhausted (incl. fatigue), affective (incl. irritability and depressive symptoms) and gastrointestinal (incl. nausea). Fatigue was most persistent and also most severe and predictive for HRQoL. Fear of relapse, feelings of disability and barriers to social rehabilitation are frequent concerns, even several years after the procedure, with only a minority of disease-free transplant survivors consider themselves having 'returned to normal' (Syrjala et al. 2012).

These psychosocial difficulties are not systematically approached in current HSCT follow-up: despite their incidence, anxious-depressive symptoms are not often reported which should be treated by HSCT physicians. Barriers to approaching psychosocial issues are, on one hand, patients' fear of being stigmatised and, on the other hand, doctors who tend to prioritise strictly medical aspects. Health professionals often poorly evaluate psychological symptoms: anxiety is overrated, depression is underestimated, and consistency between the patients and the medical team's evaluations seems insufficient. Most patients receive prescriptions for these lingering symptoms, even over long periods, yet half of them benefit of follow-up by specialised professionals due to organisational and emotional obstacles (Mosher et al. 2010).

Anxieties after HSCT may be treated in a cognitive-behavioural approach, relying on working directly with fear-related contents and applying this to the broad range of oversimplified anxieties. For progression anxiety, manualised psychooncological therapies are well-tried, combining psychoeducational elements with group-format psychological therapy. Cognitive-behavioural therapy has demonstrated effectiveness in the treatment of PTSD with cancer patients in a significant number of studies, including patients with HSCT (DuHamel et al. 2010). Concerning fatigue, there are several promising approaches combining psychosocial counselling with physical training.

30.5 Close Relatives

Family caregivers (FC) can contribute to patients' recovery and to better survival following HSCT (Ehrlich et al. 2016). That said, the HSCT impact on FC has not been sufficiently explored, with most studies suffering from limitations due to small and heterogeneous samples.

Current research shows that FC experience a significant burden across the treatment trajectory. At the time of transplant, FC report high levels of fatigue, sleep disorders, depression and anxiety

(El Jawahri 2015). FC may have more emotional difficulties than patients, and their well-being can be impaired well past post transplant. FC face negative effects in their own family and professional and social lives and express marital dissatisfaction after HSCT (Langer et al. 2017).

Qualitative data indicate that the main FC difficulties are related to long-term HSCT consequences and the unpredictable, uncertain character of their evolution. Assuming not only daily tasks but also the patients' psychological support, FC may feel overwhelmed by the complex demands of the caregiving role and the social impact of a lengthy rehabilitation (Applebaum et al. 2016).

In spite of the obstacles met during this post transplant period, FC rarely benefit from regular psychosocial support. Attention should also involve patients' minor children. The current trend has been to outsource part of the patient care. Research should better explore FC's real-life experience in order to propose targeted interventions during HSCT's various stages.

30.6 Related Donors

Related donors (RDs) deserve particular attention. Although positive effects of related donation have been demonstrated—such as deep personal satisfaction and a higher degree of self-esteem—there is also a negative impact. The incidence of pain and depressive symptoms is higher in RDs than in unrelated donors. Unexplained chronic pain could be associated with psychological distress related to the recipient's medical condition and HSCT outcomes. Data suggest that psychological support and follow-up should also be offered to RD (Garcia et al. 2013).

Like for patients, sufficient information, preparation and guidance should be available for FC and RD. That is, not only the tremendous task should be emphasised but also probable problems and risks, as well as available resources of

care. Several interventions were developed to support FC, like problem-solving skills, cognitive-behavioural interventions and expressive talking (Applebaum et al. 2016).

30.7 Adolescents and Young Adults (AYA)

The adolescent and young adult group (AYA) represents a particular group that significantly varies from non-AYA patients, especially in psychosocial aspects (Pulewka et al. 2017). Research reveals that a quarter of AYA patients who experienced HSCT reported depression and anxiety symptoms, with nearly half meeting the criteria for post-traumatic stress (Syrjala et al. 2012).

HSCT appears to be a risk factor for poor health-related quality of life (HRQoL) and social functioning in AYA cancer survivors (Tremolada et al. 2016). Qualitative studies show that this population encounters difficulties in physical (sexuality and fatigue), psychological (depression, adherence and dependency issues, fear of the future, uncertainty) and social domains (changes in roles and relationships, educations and financial issues, family problems). Evidence-based psychosocial interventions in this population are sparse and should include specific problems, such as family relationships and social integration (school and work). Recent approaches use group formats enhancing self-help resources of peers, activity coaching and motivational interviewing.

30.8 Paediatric Patients

In their review of the literature, Packman et al. (2010) shows that HSCT paediatric patients experience acute psychological symptoms such as anxiety and depression before and during hospitalisation, as well as significant peer isolation, behavioural problems and post-traumatic stress symptoms after HSCT. Declines in cognitive abilities, social functioning and self-esteem have also been observed.

It is noteworthy that the accord between parent and child is better regarding physical conditions than it is with psychological issues. This discrepancy between the child's and the parents' evaluations also holds true regarding HRQoL post-HSCT (Chang et al. 2012).

HSCT may lead to disruptions in family life: parents and siblings (notably, donors) also report high levels of anxiety, depression and post-traumatic stress symptoms (Packman et al. 2010).

Paediatric HSCT survivors report psychosocial difficulties and decreased QOL with a high risk for anxiety, depression and behavioural problems. Childhood survivors' specific issues are related to sexual dysfunction, impoverished self-image and social adjustment. As follow-up of childhood HSCT patients is fundamental, special attention should be paid to the risk of withdrawal as they journey towards adulthood (Cupit et al. 2016).

Key Points

- The previously discussed rates of psychological morbidity in HSCT patients emphasise the need for clinical assessment throughout the procedure and at regular intervals.
- Given their vital role in the patients' recovery process, HSCT teams should also assess FC for psychological adjustment and family functioning.
- Particular attention should be given to RDs, who do not benefit systematically from a medical and psychological follow-up.
- Regardless of the overwhelming evidence of psychological morbidity in HSCT patients and in FC, barriers still exist in discussing psychosocial issues in routine care.
- Systematic screening may contribute to stimulate discussion of psychological symptoms, but quality psychosocial

care requires team training and an effective multidisciplinary approach.

- Psychological support should be installed low threshold and as far as possible attached to the transplant centre.
- Effectiveness of psychooncological interventions is proven widely and should be adapted to patients and FCs all along the course of HSCT.

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