Quality of Life in Oncology

Anna Stickel and Ute Goerling

> Sittin' on the front porch
> ice cream in my hand
> meltin' in the sun
> all that chocolate on my tongue
> and that's
> good enough reason to live
> good enough reason to live…
> And if I die young, at least I got some chocolate on my tongue… (The Wood Brothers 2006)

Abstract

Continuous improvements in the diagnosis and treatment of cancer lead to improved cure rates and longer survival. However, in many patients, the disease becomes chronic. In this context, the patients' quality of life (QOL) becomes a crucial issue. After an introduction about QOL, results from different areas of cancer treatment are presented considering their impact on QOL. Finally, implications are discussed for researchers, clinicians, and patients.

Keywords

Psycho-oncology · Quality of life · Cancer treatment

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1 Introduction

Quality of life (QOL)—everyone knows what it is, but it probably means something different to each individual. For some, being able to travel to foreign countries is important for their appraisal of good QOL, for others, it is having time for their hobbies or enjoying little things like the pleasure of chocolate melting on one's tongue.

In the face of a chronic disease, QOL is an issue of special value. Cancer and its treatment are debilitating and thus have an impact on QOL, depending on the individual's perception of the situation. Cancer care has become more successful, yet also more complicated. Therefore, understanding what cancer survival means to patients is an important intention in current research (see also Chapter "Cancer Survivorship in adults"). Not only the efficacy of treatments but also their toxicity and associated problems for patients are receiving increasing attention.

Many parameters elucidating the effects of cancer are not quantifiable with laboratory tests or imaging procedures. Therefore, variables such as social functioning, sense of well-being, fatigue, or global QOL are ascertained by self-reports. These self-reports add to the picture of biomedical outcomes and are important for gaining a better understanding of the consequences of cancer and its treatments (Osoba 2011).

Thus, apart from objective criteria like survival time, time to recurrence, side effects, etc., the interest in patients' experiences has grown and their subjective perceptions of living with cancer are valued more.

2 What Exactly Is Quality of Life?

2.1 Terms and Definitions

Different terms and definitions revolve around the rather elusive multidimensional construct: Patient function, health status, life satisfaction, quality of life, health related quality of life, or patient-reported outcomes. Yet there is no universal definition (Leplège and Hunt 1997).

QOL is always highly individual. It depends on the present lifestyle, past experiences, future hopes, dreams, and ambitions. QOL should include all aspects of life and experiences in life and take account of disease and treatment. An individual has a good QOL, when experiences are in accordance to hopes. The opposite is true when the experiences the individual makes do not match the hopes that he/she cherishes. QOL is time-dependent and gives information about the difference between hopes or expectations of the individual and his/her experiences at a given moment (Calmann 1984).

Already Aristotle (384–322 BC) refers to the fundamental problem of QOL-research: "and often the same person changes his mind: when he becomes ill, it is health, and as long as he is healthy it is money." Patients may change their personal scale about what is important in the course of their disease and the question is how?

In 1993, the World Health Organization published following definition:

"Quality of life is defined as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, and their relationship to salient features of their environment." (WHOQOLGroup 1993, p. 153).

To distinguish QOL of the general population from the QOL of patients the term "health related quality of life (HRQOL)" was introduced. A more inclusive term, however, is "patient reported outcomes" (PRO) which comprises any feedback given directly by the patient, e.g., satisfaction with care (Osoba 2011).

2.2 Measures in Quality of Life

A proper estimation of QOL is challenging. Already 100 years ago, there were efforts to include aspects of QOL in the use and evaluation of medical treatment. "Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (WHO 1946).

Early evaluation instruments of QOL focused on physical aspects of disease (Fayers and Bottomley 2002). In 1948, the American oncologist David A. Karnofsky developed an index that allows the doctor to give an estimation of the patient's physical condition on a scale (Karnofsky index, Karnofsky and Burchenal 1949). Another observer-rated assessment of QOL in oncology was developed by Spitzer. The doctor can value the activity, daily life, health, social support, and future perspective of the patient and create a total score. However, this time economic method has a significant drawback: it is open to different interpretations (Spitzer et al. 1981). Later the patients' expectations, perceptions as well as values received increasing attention and emotional and social aspects were added in assessments (Schumacher et al. 1991).

Today, self-reports are considered more appropriate than observer ratings of QOL. The questionnaires need to be short but nevertheless sensitive. They should allow cross-disease comparisons but also assess the specific nature of a certain disease. Finally, they must be reliable and valid.

Since 1964 certain projects in the United States assessing the needs and QOL of healthy individuals aim at resolving long-term deficits. The National Cancer Institute confirms that all clinical trials should include QOL as an outcome measure since 1991.

In the endeavor to improve QOL-research, several institutions created groups to give advice on the design, implementation, and analysis of QOL studies. For example, the Quality of Life Group (QLG) of the European Organisation for Research and Treatment of Cancer (EORTC) was established in 1980 (Fayers and

Bottomley 2002). One of the group's main achievements is the development and continual improvement of the Quality of Life Questionnaire. Its 30-item core measure (QLQ-C 30) includes a global health status/QOL scale, functional scales, symptom scales, and several single questions on frequently reported symptoms and financial concerns (see Table 1). In order to identify clinically relevant symptom burden or impairment, thresholds have recently been estimated for the key domains: physical functioning, emotional functioning, fatigue and pain using anchor items assessing burden, limitation and need for help (Giesinger et al. 2016b). Further, a single summary score has been suggested in order to reduce the risk of type I errors due to multiple testing (Giesinger et al. 2016a). Especially for palliative care, the QLG developed the 15-item EORTC QLQ-C15-PAL (Groenvold et al. 2006).

The QLQ-C 30 should be supplemented by modules specific to a tumor site, treatment modality, or additional QOL dimensions. The modules which have already been validated are presented in Table 2. The QLQ-C30 and QLQ modules are applicable cross-culturally as they are available in many different languages and are the most extensively used questionnaires in clinical trials in Europe (Fayers and Bottomley 2002).

In North America, the predominantly used tool is the Functional Assessment of Cancer Therapy Scale. Its general version (FACT-G, Version 3) has 27 items from which the subscales physical, social, emotional, and functional well-being can be derived (Cella et al. 2002, 1993) and which can be summed to a total score. Additionally, a broad range of tumor-, treatment-, or symptom-specific modules can be used (Luckett et al. 2011).

Table 1 The EORTC core questionnaire

		Number of items
QLQ-C30	Global health status	2
	Functional scales	
	Physical functioning	5
	Role functioning	2
	Emotional functioning	4
	Social functioning	2
	Cognitive functioning	2
	Symptom scales	
	Fatigue	3
	Nausea and vomiting	2
	Pain	2
	Dyspnoea	1
	Insomnia	1
	Appetite loss	1
	Constipation	1
	Diarrhea	1
	Financial impact	1

Table 2 The EORTC modules

Modules (validated)	Name[a]
Bone metastases	QLQ-BM 22
Brain cancer	QLQ-BN 20
Breast cancer	QLQ-BR 23
Cervical cancer	QLQ-CX 24
Colorectal cancer	QLQ-CR 29
Colorectal Liver metastases	QLQ-LMC 21
Elderly Cancer patients	QLQ-ELD 14
Endometrial	QLQ-EN 24
Gastric cancer	QLQ-STO 22
Head and neck	QLQ-H&N 35
Hepatocellular carcinoma	QLQ-HCC 18
Information	QLQ-INFO 25
Lung	QLQ-LC 13
Multiple myeloma	QLQ-MY 20
Neuroendocrine carcinoid	QLQ-GINET 21
Oesophageal cancer	QLQ-OES 18
Oesophago-gastric cancer	QLQ-OG 25
Oral health	QLQ-OH 15
Ovarian	QLQ-OV 28
Prostate	QLQ-PR 25

[a] The number after the abbreviation indicates the number of items

These two most widely used tools (EORTC QLQ-C30 and FACT-G) differ in scale structure, social domains, and tone. Their psychometric properties are comparable and thus cannot be used as a criterion in selecting one of these questionnaires (Luckett and King 2010). However, a direct comparison of similar scales from both questionnaires showed differences in their responsiveness, statistical efficiency, and power (King et al. 2014).

Furthermore, item banks and computerized adaptive testing (CAT) have been developed to gain a more comprehensive coverage of QOL issues (Cella et al. 2007). The Patient-Reported Outcomes Measurement Information System (PROMIS) was funded by the National Institutes of Health (NIH) and aims to enable an efficient, flexible, and precise measurement of PROs (http://www.nihpromis.org/). A computerized adaptive testing (CAT) version of the EORTC QLQ-C30 is also currently being developed (http://groups.eortc.be/qol/eortc-cat).

3 Quality of Life During Oncological Treatment

Treatments differ in their impact on QOL. In the case of various treatment options with curative objective, relapse free survival was previously considered as the only target criterion. Again, QOL must be seen as an important parameter and should be discussed with the patient. Efforts in early diagnosis, state of the art diagnostics, and multimodal therapy concepts prolong survival time, but what is the price the patient has to pay? Which of the therapies offering an improved life expectancy is superior considering their impact on QOL? Is a treatment which is less effective but also less detrimental to QOL more preferable than an aggressive therapy? The same thoughts apply to palliative treatment options. How much QOL does a person need to endure survival eight weeks longer?

Thus, the selection of tools for assessing QOL should also be determined by the treatment choice. For example, one questionnaire was developed specifically for patients after high-dose chemotherapy or palliative care (Sprangers et al. 1998) or a module was created to detect cancer-related fatigue, which can occur as a side effect but also as a long-term consequence of the antitumor therapy (Weis et al. 2013).

Below we will briefly discuss QOL-research in selected areas of oncologic therapy. This—by no means exhaustive—overview aims to demonstrate the complexity, diversity, and problems of QOL issues.

3.1 Surgery

The influence of surgical approaches on QOL has been examined in the context of different tumor entities. Interventions changing the body image are of particular interest. A number of studies, for example, examine the impact the creation of an anus praeter has on QOL (Grumann et al. 2001; Mrak et al. 2011). For almost 100 years, the abdominoperineal extirpation represented the standard therapy in surgery of rectal cancer (Pachler and Wille-Jorgensen 2012). In the context of the development and improvement of surgical techniques, and depending on the location of the tumor, an anterior sphincter-preserving resection then became the preferred treatment. This decision was not least due to the assumption that QOL is significantly better for patients whose sphincter function is preserved. In a systematic review on this topic, Pachler and Wille-Jorgensen (2012) evaluated 35 studies, matching their inclusion criteria, involving 5127 patients. None of the selected studies were randomized, 20 were retrospective and 15 prospective. Disease-specific instruments (e.g., EORTC-C30 and QLQ-C38, FACTC) were used in 23 studies. Seven studies used general questionnaires and five combined general with disease-specific questionnaires. Contrary to general expectations, a total of 14 studies showed that patients after abdominoperineal extirpation do not have poorer QOL compared to patients after an anterior resection. A small influence due to a stoma could be found in three trials. In 12 studies, patients who experienced an abdominoperineal extirpation showed a significantly poorer QOL on one or more subscales. However, in five studies, a significantly better QOL was found in some subscales after anterior resection. One study describes an improved QOL in patients after abdominoperineal extirpation. A recent systematic review focused on ostomy-related problems and their impact on QOL of colorectal cancer ostomates. Sexual problems, a depressed mood, gas, constipation, dissatisfaction with appearance, change in clothing, travel difficulties, feeling exhausted, and worried about noises were issues associated with impaired QOL (Vonk-Klaassen et al. 2016).

Comparisons of open versus laparoscopic surgery and robot-assisted surgery are further topics in literature (Bertani et al. 2011). King et al. (2006) compared the laparoscopic resection with the open resection of colorectal cancer in a randomized trial and came to the conclusion that patients have a shorter residence time in the hospital after laparoscopic resection. However, the groups did not differ concerning QOL.

A review on the outcome of oncoplastic breast-conserving surgery evaluated 88 studies (Haloua et al. 2013). Only one trial used QOL as an outcome measure (Veiga et al. 2010). This study compared the results of oncoplastic breast-conserving surgery with breast-conserving surgery, and concluded that oncoplastic surgery has a positive impact on QOL of women with breast cancer.

Little to no attention seems to be given to studies on the impact of palliative surgery on QOL. In a review, De Mestier et al. pointed out that QOL has not been evaluated in studies examining the impact of tumor resection in patients with colorectal cancer and unresectable synchronous liver metastases (de Mestier et al. 2014).

3.2 Chemotherapy

Studies on QOL during chemotherapy with curative objective address nausea, vomiting, and fatigue, among other aspects. The negative impact of chemotherapy-induced nausea and vomiting despite antiemetic therapy could be shown in a multicenter study in various tumor entities (Fernández-Ortega et al. 2012). Chemotherapy in women with breast cancer was found to have a negative impact on cognition and fatigue (de Ruiter et al. 2011). The latter showed a poorer QOL compared to the patients with no indication for adjuvant chemotherapy. A further study comparing younger versus older adults with acute myeloid leukemia receiving an intensive chemotherapy showed a diminished QOL and physical function. However, the patients' age had no influence on QOL (Mohamedali et al. 2012). A recent trial including patients with different tumors undergoing cancer chemotherapy showed that especially difficulties managing everyday tasks have a negative impact on QOL (Wagland et al. 2016).

Several studies can be found in the literature on the effect of therapy on QOL in systemic cancers in childhood, enabling an extended follow-up period (Kanellopoulos et al. 2013).

Drug trials often explore QOL in various treatment arms. Thus given the same overall survival rate in different arms, treatment decisions can be made according to the results of QOL assessments. The question of using chemotherapy in palliative situations is especially challenging. Studies have demonstrated the willingness of patients to accept side effects while gaining relief from disease associated symptoms (Archer et al. 1999).

3.3 Radiotherapy

Radiotherapy is a further essential element in cancer treatment in curative, as well as palliative care, however, once again not without consequences for the patients' QOL. Fatigue is one of the most common side effects and late sequelae of radiotherapy. Research indicates that up to 80% of the patients suffer from fatigue during and after radiotherapy (Jereczek-Fossa et al. 2002).

Due to the fact, that radiotherapy often is organ-preserving, the maintenance of a good QOL is expected. However, prospective studies on this subject are still rare. A review on the use of intensity-modulated radiotherapy in patients with head and neck cancer was able to detect only 10 studies in which QOL data was collected, out of 65 studies matching the search criteria (Scott-Brown et al. 2010). Only one study was randomized. According to its results, the expected positive impact of intensity-modulated radiotherapy versus conventional radiotherapy could not be detected. The authors assume that there is no relationship between loss of function and global QOL.

A further study with over 500 patients with head and neck cancer demonstrated that a quarter of patients treated with radiotherapy had more than 10% weight loss, which was associated with a diminished QOL (Langius et al. 2013).

In a secondary analysis comparing different radiation doses (74 Gy vs. 60 Gy), patients (n = 360) with unresectable stage III non-small cell lung cancer receiving concurrent chemotherapy showed significantly worse QOL in the high-dose arm at 3 months. Interestingly, the provider-reported toxicities were similar in both treatment arms (Movsas et al. 2016).

4 Relevance of Quality of Life

4.1 Relevance for Researchers

> … oncology has generated some of the most productive research in medicine for the development and utilisation of QoL measures. (Fallowfield 2009, p. 2)

Although QOL issues have gained increasing attention in recent years, QOL outcomes are still often not presented. A recent study analyzed protocols of 173 cancer trials and corresponding publications (Schandelmaier et al. 2015). About half of the protocols included specified QOL outcomes, and for only 20% of the trails data on QOL was reported in associated publications. The most frequent reasons for this the lack of reporting were non-specification of QOL outcomes in the protocol, non-publication of the whole study, and non-publication of the results considering QOL.

However, the methodology in HRQOL research has improved and the compliance with its measurement has grown (Bottomley et al. 2005; Efficace et al. 2003). Several reviews about QOL studies examine their reporting standard, presentation, and interpretation for QOL (Bottomley et al. 2005; Brundage et al. 2011; Cocks et al. 2008). Different researchers have proposed guidelines for developing and evaluating study protocols (Cocks et al. 2011; Efficace et al. 2003) and are working on international standards for the analysis of QOL outcomes (Bottomley et al. 2016). Also statistical challenges have been addressed (Bonnetain et al. 2016).

The presentation of results in QOL-research has increasingly become a matter of debate as the meaningfulness of statistical significance has been questioned in the clinical context. Statistical significance cannot be equated with clinical significance, especially if the later was not defined a priori and used to determine the sample size for a trail (Cocks et al. 2008). Different guidelines have been published on how to rate the importance of change (Cocks et al. 2012; King 1996, 2001; Osoba et al. 1998). It has been proposed that a change of 10 points on a scale from 0 to 100 (Osoba et al. 2005) or the 0.5 standard deviation (Norman et al. 2003) is clinically meaningful. However, the clinical interpretation of QOL differences is lacking as clinical significance is mostly not addressed in papers (Cocks et al. 2008). A recent review described signs of improvement over time in the publication of data on clinical significance (Rees et al. 2015).

A further problem is that QOL results are often published in separate papers. However, self-reports should complement standard biological endpoints (like tumor regression, time to progression, survival) and be described in a single publication (Osoba 2011).

Conflicting findings in comparative analyses of research results make unequivocal treatment decisions difficult for clinicians. Divergent results may occur through the use of different questionnaires. Hence, a generic questionnaire may not be sensitive to differences, for example, in certain surgical procedures. Many studies lack the pre-therapeutic assessment of QOL. Furthermore, the influence of important factors such as social status, and gender differences remain unconsidered. In order to give careful consideration to these aspects, prospective, methodologically well planned, and comprehensive studies are needed.

But how can we interpret results of QOL-research? Why does a patient with a colostomy rate his QOL as good as or better as a patient, whose natural anus could be preserved? Why does a woman after mastectomy evaluate her QOL as comparably good as a woman after breast-conserving surgery? These issues are known as the paradox of QOL-research in literature (Herschbach 2002).

As described above various dimensions are assessed in QOL-research. However, the patient's preference is often ignored, i.e., which dimensions are given more weight by which patient. Their ratings can vary considerably (Osoba 1994). Furthermore, the weighting of the dimensions may change over time. Ultimately, the patient's expectations to the outcome of cancer therapy play a significant role, which arise from the comparison of the actual state and the desired state.

4.2 Implications for Clinicians

It has been criticized that study results are not receiving enough attention from clinicians and the routine assessment of QOL has not been implemented into clinical practice. There are fears that this might be too expensive or time-consuming. However, research has shown that the regular use of QOL measurements increases the practitioner's awareness, facilitates the conversation about QOL issues, and thus has been shown to be of value for doctor–patient communication (Detmar et al. 2002; Velikova et al. 2004, 2010). Communication between doctor and patient is an essential aspect in the treatment of oncological patients. The majority of patients want support from their doctor. Thus, talking about QOL helps the doctor give the right kind of support. Patients receiving adequate information and who are content with the practitioner interaction show a better QOL (Velikova et al. 2004).

In addition, evidence for a positive relationship between QOL data and duration of survival in cancer patients has been reported in different reviews (Gotay et al. 2008; Montazeri 2009; Quinten et al. 2009, 2011). A recent review of PROs in radiation oncology presented evidence for the prognostic value of QOL instruments for outcome (e.g., local control and survival) (Siddiqui et al. 2014). In patients with non-small cell lung cancer, certain domains on QOL, measured at diagnosis (Fiteni et al. 2016) and after the initial treatment (Lemonnier et al. 2014), have been shown to be related to survival.

Different parameters such as pain, physical functioning and appetite loss can provide prognostic information beyond clinical measures. This was described across different disease sites and therefore taking into account QOL parameters can improve survival prediction of cancer patients (Quinten et al. 2009). Fiteni et al. discussed that data on QOL possibly may also be useful in determining subgroups of patients who will benefit from doublet chemotherapy (Fiteni et al. 2016).

Thus, clinicians may benefit from the possible predictive value of QOL assessments in the treatment of cancer patients, as they may be used as early warning systems. Although patient and clinician ratings of clinical symptoms have been shown to differ, both are described as valuable in the estimation of overall survival (Quinten et al. 2011). Future research should examine whether and to what extent improvements in QOL have the potential to increase survival.

In palliative situations, healthcare providers have the opportunity to effectively improve the QOL of their patients, especially in early stages of palliative care. Early support through specialized palliative interventions has been shown to lead to a greater improvement in QOL compared to usual care in patients newly diagnosed with non-small-lung cancer. Patients in the intervention group reported less depression and additionally showed a longer median survival (Temel et al. 2010).

A further issue of discussion is the facilitation of using QOL information for clinical doctors. Bezjak et al. (2001) recommend increasing the knowledge of oncologists on QOL literature by presenting findings in a comprehensible manner and emphasizing their clinical relevance. Furthermore, doctors should address QOL issues and explore the patients' perceptions of QOL. Finally, the application and interpretation of QOL questionnaires should be facilitated, e.g., by using modern technology displaying clear and simple graphics with current and previous as well as normative QOL data.

4.3 Significance for People Affected by Cancer

In a European population based survey (n = 9344), random households were asked what they would prioritize in the face of a serious illness like cancer: improving their QOL, prolonging survival or both. Across different countries 57–81% chose improving QOL, 2–6% preferred extending life and 15–40% described both as being equally important (Higginson et al. 2013). Thus, QOL issues seem to be of great value to the population.

Patients need to be informed about their disease, possible treatments, and the outcome of medical care. Information on the impact of a disease or treatment on their QOL is essential to patients especially while participating in decision-making about the cancer care they undergo (Bottomley et al. 2005; Cella et al. 2002; de Haes and Stiggelbout 1996). Both the psychosocial impairments (see Chapter "Psychosocial Impact of Cancer") and the worry and fear of recurrence or progression of the disease (see Chapter "Fear of Progression in Cancer Patients and Survivors") have a negative impact on QOL.

But also moving beyond active treatment, QOL remains an important topic for cancer survivors. Research has reported different results on the QOL of cancer survivors. Although cancer survivors have generally not been described as more vulnerable to the effects of day-to-day hassles, Costanzo et al. proposed a higher sensitivity to interpersonal tensions (Costanzo et al. 2012).

Cancer survivors may also be preoccupied with fears of recurrence, existential and spiritual problems, and experience difficulties in making new decisions considering their future life (Hewitt et al. 2005). Further challenges may be the adjustment to long-term and late effects like infertility and fatigue or changes in their social network, for example, the loss of friendship due to the lack of support during treatment (Cella 1988). Each of these issues can have a major influence on QOL in the individual. A recent study in patients suffering from thyroid cancer pointed out that fatigue-related issues are highly relevant across different cultures (Singer et al. 2016).

In a study with cervical cancer survivors (n = 173) 5, 10 and 15 years after diagnosis Le Borgne et al. (2013) showed a similarly good global QOL in cancer survivors compared to healthy controls. However, survivors 15 years after diagnosis reported more psychological burdens and—in case of prior radiotherapy—also more physical sequelae like sexual dysfunctions. Low income and comorbidities were further factors impairing QOL. A comparison of patients in a cancer rehabilitation program (n = 1879) with healthy controls (n = 2081) showed an impaired QOL in cancer patients. The differences between cancer patients and control were most striking in younger patients (Peters et al. 2016). Knowing different risk factors helps patients and healthcare professionals arrange appropriate interventions.

On the other hand, it has been reported that cancer survivors often benefit from the cancer experience. A new appreciation of life, deeper spirituality, personal improvement, improved relationships, help orientation, and increased attention to their own health have been described as advantages of cancer survivorship in literature (Documet et al. 2012). Positive psychological change in the face of challenging life events, so-called posttraumatic growth, has been shown to develop relatively quickly after the diagnosis of breast cancer (Danhauer et al. 2013). An exploratory study with 39 breast cancer survivors 4.5–5 years after diagnosis showed that 2/3 described their lives as good or even better than before the diagnosis (Salander et al. 2011). Thus, cancer survival also seems to bring many opportunities to improve QOL (Hewitt et al. 2005). The development of a healthy lifestyle can give survivors a sense of control and more self-awareness as well as setting new priorities can help increase life satisfaction.

5 Challenges in Quality of Life-Measurements

A review of 794 randomized trials showed that in 25.4% (200/794) HRQOL was a primary outcome (Brundage et al. 2011). 14% of the trials published their findings on QOL in a further publication. In general, the question remains, which and how many papers on QOL where actually accepted for publication (publication bias). Planning and conducting clinical trials is associated with strict ethical requirements. How is the QOL of seriously ill people? Are patients with extremely impaired QOL even able to provide a realistic assessment of their situation? How do researchers deal with missing data? Missing data lead to less power, i.e., the fewer study participants, the lower the probability to detect differences.

Another possibility of bias in longitudinal assessments is the so-called response shift effect. In the context of QOL measurement and cancer patients, response shift implies changes in patients' internal standards, values, and understanding or perception of QOL while adapting to their disease and its treatment (Dabakuyo et al. 2013). Part of the psychological adaption in the process of disease, for example, may be a change in the patient's concept of "worst pain imaginable." Furthermore, patients may set new priorities and develop a new concept of QOL (Luckett and King 2010). Thus, the correct interpretation of results in QOL measurement may require the assessment and adjustment for response shift effects.

More specific measurements assessing particular symptoms may be more responsive to change than a global measure of QOL. Further disadvantages of a global measure are its greater vulnerability to response shift effects and its inability to show changes in single dimensions of QOL. Nevertheless, if the relative burden of one disease is to be compared with others, the assessment of overall QOL may be more appropriate and also more convenient (Luckett and King 2010).

Furthermore, other sources of error in studies cannot be excluded: social desirability is a phenomenon which occurs repeatedly. There is a possibility that patients answer in ways not to offend their doctor. On the other hand, patients may perceive QOL assessments as time-consuming and sometimes as an additional burden.

In literature, one repeatedly encounters studies in which the QOL of cancer patients after treatment is compared with the QOL of healthy subjects due to missing control groups. It appears questionable if such comparisons are appropriate.

6 Quality of Life of Health Care Providers

The impact cancer has especially on the family of patients is described in Chapter "Family Caregivers to Adults with Cancer: The Consequences of Caring *Psychosocial burden of family caregivers to adults with cancer*. But what would oncology be without the professional health care providers? "Cancer is often seen as precipitating an existential crisis; a crisis of spirit and an opportunity for meaning. This is true not only for the patient with cancer and his or her family and loved ones, but also, interestingly enough, for oncologists and cancer care providers." (Breitbart 2006).

We have performed extensive literature searches on QOL. Alone, the keyword search in PubMed "quality of life and cancer" reveals over 61,200 entries. Healthcare providers appear only in the context of QOL-research, when it comes to observer-rated assessments of QOL of patients.

In a very impressive paper, Laurie Lyckholm (2001) reports on handling stress, burnout, and grief in the practice of oncology. Causes of stress are seen in insufficient personal or vacation time, a sense of failure, unrealistic expectations, anger, frustration, as well as feelings of inadequacy or self-preservations, reimbursement and other issues related to managed care and third-party payers, and last but not least grieving. Burnout can manifest itself in substance abuse, marital conflict, overeating and substantial weight gain, higher frequency of mistakes in clinical care, inappropriate emotional outbursts, interaction problems, depression and anxiety disorders, and even suicide. Lack of or inadequate training of communication and management skills are also considered causes of burnout (Ramirez et al. 1996). In a survey of 7288 physicians in the United States, 45.8% reported at least one of the following symptoms of burnout: loss of enthusiasm for work, feelings of cynicism (depersonalization), and low sense of personal accomplishment (Shanafelt et al. 2012). A recent review reports alarmingly higher rates (> 50%) of burnout among surgeons (Dimou et al. 2016). High prevalence of burnout has also been shown for oncologists (Cass et al. 2016; Deng et al. 2016).

Thus few but meaningful results on QOL of healthcare providers make further research in this area necessary, in order to provide effective interventions and strategies for these individuals. Ultimately, this would, in turn, be advantageous for the patients.

7 Summary

Cancer itself has a negative impact on the QOL of patients. However, individual conditions, values and resources influence this impact. Generally and in various definitions HRQOL is considered as a multifactorial concept. In the assessment of QOL, observer-rated assessments were increasingly replaced by self-reports of patients. Meanwhile, validated assessment tools for different research questions and treatment settings exist in different languages. Many improvements have been made in QOL-research. However, there are still many trials with study designs of low quality (not randomized or prospective, etc.) and where QOL is missing as an outcome measure. Furthermore, the variety of research results is often inconsistent, making it difficult to draw clear conclusions.

Nevertheless, information on possible changes in QOL is not only relevant for researchers, as described above, but also has implications for clinicians and for people affected by cancer. Ideally, it forms a basis for shared decision-making.

Last but not least more attention must be paid to the QOL of healthcare providers, which in turn would be beneficial to the patients and their families.

"…and that's good enough reason to live…" (The Wood Brothers 2006)

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