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Abstract

In general, quality of life (QOL) in the broad sense refers to the well-being of individuals and societies. This concept covers not only physical/financial affluence, quantity of service, and individual self-care but also the spiritual aspect and self-actualization. In the medical care field, QOL influences not only the evaluation of treatment but also the treatment method. At present, concepts of values in life are diverse, and medical care considering both survival and QOL has become necessary. Therefore, QOL instruments using scales corresponding to the purpose in various areas have been developed. They have sometimes been revised because the concept of QOL varies across ages. Furthermore, QOL in oncology has characteristics different from that in other diseases. Cancer is a life-threatening disease, and many cancer patients have a mental shock when they are first notified to have cancer. QOL markedly varies before, during, and after treatment. For malignant tumors, it is significantly different depending on the stage of progression, onset site, extent of adverse events caused by treatment, and degree of residual disability. Even if a cancer survivor had a good course, QOL is often different from that before they develop cancer. Therefore, QOL evaluation in cancer patients is very difficult.

Keywords

Head and neck cancer • Oral cancer • QOL

18.1 QOL Definition

In general, quality of life (QOL) in the broad sense refers to the well-being of individuals and societies. This concept covers not only physical/financial affluence, quantity of service, and individual self-care but also the spiritual aspect and self-actualization. The 36th president of the United States, Lyndon Baines Johnson, declared national QOL improvement as part of his Great Society policy (1964) [1]. Since then, the term QOL has been generally used. In the medical care field, attention has

been focused on improvement in QOL in the areas of terminal care of cancer and independent living of disabled persons since the 1970s. For elderly welfare, attention has been focused on seeking the reason for living or sensation of happiness for improvement in QOL. Thus, eventually, the concept of QOL became popular. At present, the World Health Organization (WHO) defines QOL as “an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns” [2].

18.1.1 QOL in Health Care

QOL is considered a multidimensional concept that is divided into health-related QOL (HRQOL) and non-health-related QOL (NHRQOL). The true impact of health and disease on

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QOL is known as HRQOL [3, 4]. It is conceptualized as those aspects of QOL that are influenced directly by the health of a person. Development of tools to measure HRQOL in individuals over time has produced important benefits. On the other hand, NHRQOL indirectly affects health and disease. Most QOL studies in the medical care field, including cancer treatment, focus on HRQOL [3, 4].

It is generally accepted that HRQOL includes numerous domains. There is a wide range of potential domains, but not all of them are relevant to all studies. However, wherever possible, relevant domains should be considered. For example, the following domains have been proposed: (1) physical status and functional abilities; (2) psychological status and well-being; (3) social interactions; (4) economic and/or vocational status and factors; and (5) religious and/or spiritual status. Among these, religious and/or spiritual status may be not so familiar to Japanese people [3–6].

Religion is a collection of cultural systems, belief systems, and worldviews that establishes symbols that relate humanity to spirituality and moral values. They tend to derive morality, ethics, religious laws, or a preferred lifestyle from their ideas about the cosmos and human nature. Spirituality has been defined in numerous ways, including a belief in a power operating in the universe that is greater than oneself, a sense of interconnectedness with all living creatures, and an awareness of the purpose and meaning of life and the development of absolute personal values. One can find meaning, hope, comfort, and inner peace in life through spirituality. Although spirituality is often associated with religious life, many believe that personal spirituality can be developed outside of religion. Acts of compassion and selflessness, altruism, and the experience of inner peace are all characteristics of spirituality. It is unclear how spirituality and religion are related to health. Some studies show that spiritual or religious beliefs and practices create a positive mental attitude that may help a patient feel better and improve the well-being of family caregivers [5, 6].

NHRQOL indirectly involves health and is classified into the following four domains: (1) personal–internal (including concepts of value/faith, hope/target, personality, and capabilities to cope); (2) personal–social (including social network, family structure, social group, economic conditions, and employment status); (3) external–natural environment (including air, water, land, climate, and geography); and (4) external–social environment [including cultural facilities, exposure to the culture, religious facilities, schools, commercial establishments, medical facilities and services, public policy, safety, traffic, communication, social amusement, characteristics (disposition), demographic composition, and commercial establishments]. NHRQOL is considered important in the public health field for health promotion rather than the medical care field [4].

HRQOL and NHRQOL are mutually influential and, as understood from above, there are common items between

them. Depending on health status, the weight-to-volume ratio of HRQOL and NHRQOL varies. The healthier the person is the more important NHRQOL is compared with HRQOL. In the presence of disease or disability, HRQOL is more important than NHRQOL [4].

18.1.2 QOL in Oncology

Previously, outcome indices of cancer treatment included prolonged survival and reduced tumor load, based on the standpoint of medical providers. However, paternalism of cancer treatment has become unacceptable because of a shift in the health paradigm, which includes increased respect for the autonomy of patients, legal necessity for disclosure and informed consent, culture maturity, and health economics. Thus, the outcome of cancer treatment has changed. Specifically, QOL and cost performance of treatment have become new indices. From cancer treatment, patients tend to seek care rather than cure.

On the other hand, emphasis on the right of the patient to choose a medical treatment has often led to anxiety-provoking situations for patients. In modern society, extensive medical information can be obtained from the Internet or other sources. However, improper or incorrect information is also abundant. Therefore, cancer treatment according to evidence-based medicine (EBM) has been followed widely, leading to the creation of treatment guidelines by public institutions. In the future, although cancer treatment is performed according to EBM, it may become necessary to adapt with each patient's wishes and may become more complicated. In respecting the autonomy of patients, it is necessary to clarify EBM of QOL.

QOL in oncology has characteristics different from that in other diseases. Cancer is a life-threatening disease, and many cancer patients have a mental shock when they are first notified to have cancer. QOL markedly varies before, during, and after treatment. For malignant tumors, it is significantly different depending on the stage of progression, onset site, extent of adverse events caused by treatment, and degree of residual disability. Even in the same category of oral cancer, QOL is different between lingual cancer and gingival carcinoma. Furthermore, even if a cancer survivor had a benign course, QOL is often different from that before they develop cancer. Therefore, QOL evaluation in cancer patients is very difficult.

18.2 Quantitative Measurement

18.2.1 Purpose of Evaluation

QOL is basically a subjective concept consisting of multiple factors. Although qualitative research cannot be disregarded as a means to comprehend QOL, it is difficult to perform

qualitative evaluation. In general, a study of QOL is conducted quantitatively, in principle, and the composing domains and items differ depending on the purpose.

As mentioned above, the concept of QOL was developed partly in a political aspect. In seeking for what is the most desirable life for people, it was necessary to develop useful instruments. In this context, the objective of QOL measurement to evaluate the life status of the citizens is necessary for public administration to plan a policy. As a concrete example, it is utilized for the planning of health promotion in the public health field [3, 4].

On the other hand, in the medical care field, QOL influences not only the evaluation of treatment but also the treatment method. At present, concepts of values in life are diverse, and medical care considering both survival and QOL has become necessary. Therefore, QOL instruments using scales corresponding to the purpose in various areas have been developed. Furthermore, they have sometimes been revised because the concept of QOL varies across ages.

18.2.2 Criteria for the Evaluation of QOL Questionnaires

At present, some excellent QOL measurement instruments have been authorized. However, QOL is subjective and heavily dependent on individual patients. Therefore, there are no questionnaires that can be used for all people. It is also difficult to evaluate whether an individual QOL measurement instrument is more valid. Several authors have suggested standards for the development and evaluation of instruments to measure health status. One of the most elaborate lists was proposed by the scientific advisory committee (SAC) of the Medical Outcomes Trust in 1994 [7, 8]. SAC defined a set of eight key attributes of instruments to measure health status and HRQOL: (1) conceptual and measurement model; (2) reliability; (3) validity; (4) responsiveness; (5) interpretability; (6) respondent and administrative burden; (7) alternate forms; and (8) cultural and language adaptations.

1. Conceptual and measurement model

The concept to be measured needs to be defined properly and should match its intended use. There are two types of QOL measurement instruments: one evaluates using both subjective and objective indices and the other evaluates using only a subjective index.

2. Reliability

Reliability is the degree to which the instrument is free of random error, which means free from errors in measurement caused by chance factors that influence measurement. The question of reliability arises as the function of scales is stretched to encompass the realm of prediction. One of the most popular reliability statistics in current use is Cronbach's alpha. Cronbach's alpha is a coefficient of internal consistency or average correlation of items in a

survey instrument to gauge its reliability. In general, survey instruments are required to have a minimum Cronbach's alpha value of 0.7 and a correlation coefficient with another instrument of 0.75 [7, 8]. The reproducibility of these instruments should be determined using variance analysis. In Japan, WHO quality of life (WHOQOL) instrument is reported to have a Cronbach's alpha value between 0.87 and 0.97 and a correlation coefficient with general health questionnaire (GHQ) between -0.45 and -0.47 [9].

3. Validity

Validity is the degree to which the instrument measures what it purports to measure. Validity of a measurement instrument does not refer to the instrument itself but to whether particular interpretations of its scores are well justified. It is inappropriate to speak of a measurement instrument as inherently valid or invalid. It is only meaningful to consider the validity of a specified purpose or interpretation of the resulting scores. Because multiple types of inferences may be entertained for scores from a given instrument, depending upon the situation in which it is to be used, the validity of each inference must be established. Several QOL measurement instruments in Japan are translated or somewhat revised from those developed in Europe and the United States [9, 10]. These partially include questionnaire entries not reflecting Japanese culture and way of life. Therefore, the responsive rate of these entries may be low; thus it is difficult to apply corresponding ones in foreign countries, without any modifications.

4. Responsiveness

Responsiveness has been defined as the ability of a questionnaire to detect clinically important changes over time, even if these changes are small. An intervention study on the same specimen (sample, population) must describe changes in score over time. Where measurement instruments are used, the sample number for the study must enable statistical analysis. In clinically comparative studies, random sampling is expected, and the same treatment method is required including absence or presence of the control group.

5. Interpretability

Interpretability is the degree to which one can assign easily understood meaning to an instrument's score. Investigators should provide information about what (change in) score would be clinically meaningful [7-10].

6. Respondent and administrative burden

Burden refers to the time, effort, and other demands placed on those to whom the instrument is administered (respondent burden) or on those who administer the instrument (administrative burden) [7, 8].

7. Alternate forms

Alternative means of administration include self-report, interviewer administered, computer assisted, etc. It is often important to know whether these modes of administration are comparable [7, 8].

8. Cultural and language adaptations or translations

QOL measurement instruments repeatedly evaluate the expression of language/manner of speaking and understandability of questionnaire contents in each country to obtain equivalency in evaluation in different culture or language. Extremely complicated processes are required to develop a measurement instrument enabling comparison of QOL between different countries [7–10].

18.2.3 QOL in Oral Cancer

It is beyond controversy that the target of oral cancer treatment is permanent cure of the tumor, if there is a possibility of a permanent cure and the patient desires it. However, the evaluation of treatment for oral cancer must consider not only the survival rate of the patients but also their QOL. In addition, QOL should be evaluated taking survival into consideration [11].

QOL questionnaires used for oral cancer patients are divided into four groups: (1) general QOL questionnaire, (2) QOL questionnaire for general cancer, (3) specific QOL questionnaire for head and neck (oral) cancer, and (4) oral HRQOL (OHRQOL) (Table 18.1).

18.2.3.1 General QOL Questionnaire

1. WHOQOL instruments [2, 9, 11, 12]

Several instruments have been developed to investigate QOL; however, most of them are developed by researchers in Europe and the United States. In these, the definition of QOL is different depending on the researcher,

leading to different composition of each QOL instrument. Therefore, the WHO started to develop new QOL instruments in 1992, taking into consideration the international comparison in each country including developing countries. After meetings over a 2-year period by QOL experts and professionals in each medical institute in each country, QOL was 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.” The concept of QOL is composed of the following six domains:

- (a) Physical health
Energy and fatigue; pain and discomfort; sleep and rest
- (b) Psychological
Body image and appearance; negative feelings; positive feelings; self-esteem; thinking, learning, memory, and concentration
- (c) Level of independence
Mobility; activities of daily living (ADL); dependence on medicinal substances and medical aids; work capacity
- (d) Social relationships
Personal relationships; social support; sexual activity
- (e) Environment
Financial resources; freedom; physical safety and security; health and social care: accessibility and quality; home environment; opportunities for acquiring new information and skills; participation in and opportunities for recreation/leisure; physical environment (pollution/noise/traffic/climate); transport
- (f) Spirituality/religion/personal beliefs

In 1994, a pilot questionnaire was developed in English. It consisted of 300 standardized items, which were extracted from these six domains. This was verified by the administration of the WHOQOL Pilot Form in 15 field centers to 250 patients and 50 “healthy” respondents. These data were statistically analyzed, and the WHOQOL-100, composed of standardized and cross-nationality equivalent response scales of 100 common items, was completed. Furthermore, the WHOQOL-BREF (WHOQOL-26), an abbreviated 26-item version of the WHOQOL-100, was developed using data from the field trial version of the WHOQOL-100. The WHOQOL instruments can be used in particular cultural settings, but at the same time, results are comparable across cultures. The WHOQOL is now available in over 20 different languages, and its development in further languages is progressing. Their sensitivity to change is currently being assessed. Domain scores of the WHOQOL-BREF have been shown to correlate at approximately 0.9 with those of the WHOQOL-100. The WHOQOL-BREF has also been used in several studies in Japan [9].

Table 18.1 QOL questionnaires using for oral cancer patients

1. General QOL questionnaire
(a) WHOQOL instruments
(b) Medical outcomes study 36-item short form (SF-36)
(c) Karnofsky performance status (KPS)
2. QOL questionnaire for general cancer
(a) The European organization for research and treatment of cancer quality of life questionnaire (EORTC QLQ)-C30
(b) Functional assessment of cancer therapy scale general version (FACT-G)
(c) Quality of life questionnaire for cancer patients treated with anticancer drugs (QOL-ACD)
(d) Functional living index for cancer (FLIC)
3. Specific QOL questionnaire for head and neck cancer
(a) EORTC QLQ-H&N35
(b) The University of Washington quality of life questionnaire (UW-QOL)
(c) FACT H&N
4. Oral HRQOL (OHRQOL)
(a) The general oral health assessment index (GOHAI)
(b) Subjective oral health status indicators (SOHSI)
(c) Oral health impact profile (OHIP)

2. Medical outcomes study 36-item short form (SF-36) [11, 13, 14]

SF-36 is a questionnaire used to measure health status in general and was developed by Ware et al. In SF-36, one item is designed to assess perceived change in health status, and each of the remaining 35 items contributes to a score on one of the eight scales: physical functioning, role-physical, bodily pain, general health perception, vitality, social functioning, role-emotional, and mental health. Scores on these eight scales can be used to compute a summary index of physical health and a summary index of mental health. The Japanese version of SF-36 was developed, and Fukuhara et al. have verified its translation, adaptation, and validation.

3. Karnofsky performance status (KPS) [11, 15]

KPS is one of the earliest and most commonly used indices of patients' performance status. Recent papers still refer to the Karnofsky scale for validating a new measure. Administered by an observer, this 11-point rating system assesses symptoms, physical activities, self-care, and ability to work, with scores from 0 (dead) to 100 (normal). Although KPS is based on physical performance and dependency, it has been shown to be a valid, if crude, predictor of survival. The WHO has recommended an alternative five-point scale that is simple and easy to use. At present, KPS is used to confirm the validity of a new QOL instrument.

18.2.3.2 QOL Questionnaire for General Cancer

1. The European organization for research and treatment of cancer QOL questionnaire (EORTC QLQ)-C30 [11, 16–20]

The EORTC QOL Study Group has developed a measurement strategy for the assessment of QOL in clinical trials. A core QOL questionnaire—the EORTC QLQ-C30—is used together with diagnosis-specific modules to increase the coverage, sensitivity, and specificity of the assessments in various patient and treatment groups.

It was designed to be cancer-specific, multidimensional in structure, appropriate for self-administration, applicable across a range of cultural settings, and suitable for use with additional site- or treatment-specific modules. The EORTC QLQ-C30 (version 3.0) consists of 30 questions. Of these, 24 questions form nine multi-item scales presenting various aspects of HRQOL, five functional scales (physical functioning, social functioning, emotional functioning, role functioning, and cognitive functioning), three symptom scales (fatigue, pain, nausea, and vomiting), and a global condition (health and QOL). The remaining six questions form single-item scales describing different cancer relevant symptoms. During the scoring procedure, raw EORTC QLQ-C30 scores are linearly transformed into 0–100 scales. For global health status and the five functioning

scales, a score of 100 corresponds to a high HRQOL. For financial difficulties and the eight symptoms, a score of 100 implies maximum difficulty or symptom burden [16–18]. Subsequent versions were built on the same basic principles, culminating in the core 30-item EORTC QLQ-C30 (version 3.0) questionnaire, representing over 20 years of continuous development, refinement, and validation. It is a copyrighted instrument, which has been translated and validated into 81 languages and has been used in more than 3000 studies worldwide. At present, the QLQ-C30 (version 3.0) is the most recent version and should be used for all new studies [19].

While the EORTC QLQ-C30 is an important tool for assessing the generic aspects of QOL, it has limitations. Therefore, a modular approach was adopted for disease-specific treatment measurements. An essential aspect of the “modular” approach to QOL assessment adopted by the EORTC QLG (QOL Group) is the development of modules specific to tumor site, treatment modality, or a QOL dimension, to be administered in addition to the EORTC QLQ-C30. The modules, like the core questionnaire, are designed for use in cancer clinical trials. These modules include head and neck (QLQ-H&N35), bone metastases (QLQ-BM22), hepatocellular carcinoma (QLQ-HCC18), brain (QLQ-BN20), information (QLQ-INFO25), breast (QLQ-BR23), lung (QLQ-LC13), cervical cancer (QLQ-CX24), multiple myeloma (QLQ-MY20), colorectal (QLQ-CR29), neuroendocrine carcinoid (QLQ-GINET21), colorectal liver metastases (QLQ-LMC21), oesophageal (QLQ-OES18), endometrial (QLQ-EN24), oesophago-gastric (QLQ-OG25), gastric (QLQ-STO22), ovarian (QLQ-OV28), prostate (QLQ-PR25), and elderly cancer patients (QLQ-ELD14) [20].

The Japanese Version of the EORTC QLQ-C30 [17, 21]

The EORTC QLQ-C30 was developed in European countries. A Japanese version of the EORTC QLQ-C30 was also drawn up by EORTC itself. However, in Japan, where language and culture are different from European countries, is it possible to use the Japanese EORTC QLQ-C30 as a universally applicable instrument? To date, some cross-cultural validations have conducted. In evaluating psychometric testing, internal consistency by Cronbach's alpha, item discrimination by multitrait scaling analysis, and validity analysis with the ECOG performance score (PS) and the KPS scale were performed. These results show that the Japanese EORTC QLQ-C30 is potentially useful as an instrument and is universally applicable across cultures.

2. Functional assessment of cancer therapy scale general version (FACT-G) [11, 22–24]

The FACT-G is one of the most widely used cancer-specific QOL instruments that was developed by Cella et al [22, 23]. It has been validated across a wide range of

cancer patients, cultures, and languages and can be used to assess the impacts of cancer and its treatment on the physical and psychosocial well-being of patients. The fourth version of FACT-G consists of 27 Likert-type questions covering four domains: physical well-being (seven items), social/family well-being (seven items), emotional well-being (six items), and functional well-being (seven items). Scoring is on a 0–4 Likert-type scale, with higher scores representing better outcome. Summary scores can be calculated for each of these four domains, alongside a single overall score for the instrument. FACT-G meets all conditions such as ease of use (simplicity), credibility, validity, and responsiveness in clinical oncological studies.

The Japanese Version of the FACT-G [25]

FACT-G was translated and its usefulness was verified by Fukumoto et al. [25]. To determine if the FACT-G could be used in Japan, a cross-cultural validation was performed. The Japanese version was created through an iterative forward–backward translation sequence used throughout the FACT multilingual translation project. While evaluating psychometric testing, its construct validity was investigated by factor analysis and multitrait scaling analysis, and its clinical validity was estimated by known-groups comparison using stage, PS, and patient location and validated longitudinally by PS. The FACT-G (version 3.0) was administered to 180 patients with lung cancer. Analyses showed that the scales of physical well-being, functional well-being, emotional well-being, and relationship with doctors were constructively valid in Japan. Japanese patients felt that familial relationships were different than relationships with friends and neighbors, indicating that the social/family well-being scale needed cultural adaptation. Two items concerning coping with illness and acceptance of illness did not load predictably onto their respective scales and were considered cross-culturally problematic. However, clinical validity demonstrated its sensitivity. Japanese FACT-G (version 4.0) has been improved to address the weakness in an attempt to become an instrument that is applicable across cultures.

3. QOL questionnaire for cancer patients treated with anti-cancer drugs (QOL-ACD) [26–28]
The EORTC QLQ-C30 and FACT-G are questionnaires developed in Europe and the United States, and the Japanese versions have been developed. However, there is a possibility that different QOL items are considered important in different nations or cultures. Therefore, development of a QOL scale fitting with the lifestyle of patients was sought in Japan. Thus, QOL-ACD was developed by the Japanese QOL Research Group as a generic questionnaire according to a multidimensional construct that could be used to assess QOL of Japanese patients undergoing chemotherapy for different types of

cancer. The QOL-ACD is a 22-item, self-administered questionnaire, which consists of four domains evaluating functional well-being (items 1–6), physical well-being (items 7–11), mental well-being (items 12–16), and psychosocial well-being (items 17–21), as well as a face scale (item 22). The entire questionnaire is shown in Appendix A. The four domains were originally designated as daily activity, physical condition, psychological condition, and social attitude, respectively [26, 27]. For all items and domains, a higher score represents better QOL. QOL-ACD is also reported to be useful in patients with head and neck cancer [28].

4. Functional living index for cancer (FLIC) [11, 29, 30]

The FLIC was developed at the Manitoba Cancer Treatment and Research Foundation Centre in Winnipeg. The questions were selected from a first-generation questionnaire consisting of approximately 250 questions. The FLIC contains 22 items to which the patient must respond by placing a slash mark on a linear analog scale that is divided into seven equal intervals. The score from each item is condensed to a composite score, and the higher the composite score, the better the QOL. Domains studied include physical well-being, emotional state, social ability, and family/situation factors. The FLIC has been translated into Japanese and used in several clinical studies; however, validity and reliability have not been confirmed.

18.2.3.3 Specific QOL Questionnaire for Head and Neck Cancer

1. EORTC QLQ-H&N35 [11, 20, 21, 31–39]

The EORTC Quality of Life Group develops tumor site-specific modules to be used with a core questionnaire, the EORTC QLQ-C30. One of the first was the module for head and neck cancer patients, the EORTC QLQ-H&N37 [31], later revised and shortened to its final version with 35 items, the H&N35 [32]. This module consists of 7 multi-item scales measuring pain in the mouth, problems with swallowing, senses, speech, social eating, and social contact and 11 single-item scales assessing problems with teeth, mouth opening, dry mouth, sticky saliva, coughing, feeling ill, as well as use of analgesics, nutritional supplements, feeding tube, and finally weight gain and weight loss. The period of the QLQ-H&N35 module is “During the past week.” Items from 1 to 30 are scored on a four-point Likert scale as follows: “not at all” (1), “a little” (2), “quite a bit” (3), and “very much” (4); items from 31 to 35 use a “no” (1) and “yes” (2) format as choices to answer [32]. The module has been translated into 53 languages [20] and is used worldwide as one of the standard instruments for measuring QOL in head and neck cancer patients [33–35]. Some issues have been raised that may hamper the use of the H&N35. One criticism is that patients may feel annoyed by some of the items, for

example, those enquiring about problems with sexual functioning [36, 37]. A matter of debate is whether this presents difficulty for the researcher who feels uncomfortable in asking such questions or for the patient who feels embarrassed or irritated in answering. Another criticism concerns items that may not be applicable to some of the patients. For example, questions about swallowing solid food administered to patients who are tube fed or about hoarseness when the larynx has been removed [38, 39]. Little is known about the use of the H&N35 in research, the manner in which psychometric issues are reflected in different languages, and how well the multi-item scales are accepted by patients and investigators.

The Japanese Version of the EORTC QLQ-H&N35 [10, 21]

The Japanese version of the EORTC QLQ-H&N35 was developed by translating the original EU-English version, performing cultural adaptation, and further performing initial psychometric tests for use in Japanese head and neck cancer patients [10, 21]. Phase 1: The first intermediate Japanese version was produced according to the EORTC QOL Unit translation project guideline. The second intermediate version was the result of the backward translation project and two peer-to-peer discussion settings by health-care professionals related to the project. Phase 2: Focus group discussions with team members and semi-structured interviews with 108 participants were conducted to produce the final Japanese version. Cultural adaptation and validation yielded scores of the Japanese version of the QLQ-H&N35 module that are reliable by internal consistency (Cronbach's alpha) and the validation results showed acceptable correlation results by Pearson's product moment correlation coefficient (r). The questionnaire was well accepted, and the response rate was high (93.9 %). Convergent validity was moderate to high (from $r=0.55-0.97$, $P<0.01$), and discriminant validity was low; Cronbach's alpha coefficients of most scales had good reliability ($\alpha \geq 0.70$), except that of the pain scale. In Japan, however, some correlation patterns between scales differed from that in the original European countries and cultures. The use of both qualitative and quantitative methods was important in developing the Japanese version of the QLQ-H&N35 module [10, 21].

2. The University of Washington quality of life questionnaire (UW-QOL) [11, 40–46]

The UW-QOL (version 4.0) is a patient self-completed questionnaire and currently tests 12 specific domains relating to the head and neck cancer patient. These are pain, appearance, activity, recreation, swallowing, chewing, speech, shoulder function, taste, saliva, mood, and anxiety. The brevity and simplicity of scoring in UW-QOL make it an easy measure in a busy clinical setting. A UW-QOL composite score from 0 to 100 was obtained by

averaging the scores of the domains. When two or more domains were not answered, no composite score was calculated. Scoring is scaled, so that a score of 0 represents the worst QOL and a score of 100 represents the best QOL. The composite 12 (the average of the 12 domain scores) has been used by some investigators when describing HRQOL outcomes, although its psychometric properties have not been reported [11, 40–44].

Factor analysis is a useful method for understanding how items in a questionnaire relate to each other. It can be used to determine whether these data fit to a single construct (and, hence, a single composite-derived score) or whether multiple constructs are suggested. The derivation of multiple subscales, if appropriate, should improve sensitivity and responsiveness because more items of a similar construct are brought together. The UW-QOL has face, content, and construct validity [11, 40–44]. Although factor analysis has been reported for other head and neck cancer-specific questionnaires, to our knowledge, it has never been reported for the UW-QOL (version 4.0). The issue of interpreting clinically significant changes in patient-reported outcomes is important, especially when designing randomized trials. Such variables have been published for the Functional Assessment of Cancer Therapy–Head and Neck instrument [41, 45].

The UW-QOL domains and global scales have, at most, six discrete options and a skewed response, and these are difficult to handle in this context. Any composite or subscale score will have a wider numerical range and greater potential for being able to assess clinical effect in treatment evaluation studies and for calculating sample sizes.

The Japanese Version of the UW-QOL [46]

The UW-QOL was translated into Japanese with the consent of Professor Ernest Weymuller at the University of Washington. Then, after performing cultural adaptation, it was tested and has been used in Japanese head and neck cancer patients. However, the reliability and validity of the Japanese version have not been reviewed in detail [45].

3. FACT H&N [11, 47–52]

The FACT-G (version 4.0) consists of 27 items that yield scores in four domains (physical well-being, seven items; social/family well-being, seven items; emotional well-being, six items; and functional well-being, seven items). The FACT H&N contains 12 items (eating, swallowing, speaking, and aesthetics) that are specific to head and neck cancer patients. Each question consists of a declarative statement rated on a 0–4 Likert-type scale. Higher scores represent better QOL [11, 47–52].

The Japanese Version of the FACT H&N [51, 52]

Japanese patients felt that familial relationships were different than relationships with friends and neighbors,

indicating that the social/family well-being scale needed cultural adaptation. Therefore, the social/family well-being scale in the Japanese version of FACT-G is composed of nine items: seven items of the FACT-G original and additional two items. Therefore, the Japanese version of FACT H&N is composed of 41 items: 29 items of the Japanese version of FACT-G and 12 added head and neck cancer-specific items. However, at present, the reliability and validity of the Japanese version have not been reviewed in detail.

18.2.3.4 OHRQOL

Oral state has significant influence on daily life including mastication, swallowing, articulation, and aesthetics. Thus, QOL questionnaires concerning not only oral cancer patients but also patients with oral diseases in general have been developed. OHRQOL is composed of items such as functioning, psychological aspects, pain/discomfort, and social aspect. Functioning includes mastication, swallowing, and articulation. Most OHRQOL instruments have no authoritative Japanese versions, and the validity and reliability of the Japanese version have been barely verified [53].

1. The general oral health assessment index (GOHAI) [53–55]

GOHAI was developed for elderly people. However, it was demonstrated to be applicable for other age groups and has been used extensively. The GOHAI is a 12-item measure that assesses oral health-related problems affecting people in three hypothesized dimensions: physical function, psychosocial function, and pain or discomfort. The characteristic of GOHAI is that the number of questions is as small as 12 items, and thus, the burden on respondents is reduced. However, psychosocial aspects are reflected more heavily on evaluation than functioning compared with other OHRQOL instruments [53–55].

2. Subjective oral health status indicators (SOHSI) [53, 56, 57]

SOHSI is a descriptive oral health survey of general populations developed by Locker et al. This instrument comprises the following scales: ability to chew, ability to speak, oral and facial pain symptoms, other oral symptoms, eating impact scale, communication/social relations impact scale, ADL scale, and worry/concern scale. The response format varies with each scale. The scales ability to chew, ability to speak, oral and facial pain symptoms, and other oral symptoms have a yes/no dichotomous response. The eating impact scale, ADL scale, and worry/concern scale have five-point rating scales of the frequency of occurrence of each item of the categories: all the time (scored 5), very often (scored 4), fairly often (scored 3), sometimes (scored 2), and never (scored 1). These indicators are useful for descriptive oral health surveys of general populations. All questions were administered as a self-completed questionnaire [53, 56, 57].

3. Oral health impact profile (OHIP) [53, 58, 59]

The OHIP, developed by Slade et al., is one of the most commonly used measures of OHRQOL. This instrument contains 49 questions for seven dimensions, which has its foundation in the classification of impairments, disabilities, and handicaps developed by the WHO. These dimensions are hierarchically ordered so that the impacts described by the dimensions are considered gradually more disruptive to one's life. The dimensions are functional limitations, physical pain, psychological discomfort, physical disability, psychological disability, social disability, and handicap [53, 58, 59].

18.3 QOL in Cancer Clinical Trials [60]

Oncological research has a direct influence on the prognosis of patients. Therefore, QOL in cancer clinical trials should not be a primary endpoint but should be included as an exploratory secondary endpoint. QOL investigation is often conducted in Phase III trials. However, where the purpose is to investigate feasibility in QOL investigation, a trial with only a single arm is conducted in some cases. With regard to reconstructive therapy for head and neck cancer, QOL can be a primary endpoint.

18.4 QOL and Health Economics [53, 60]

Societal aging has advanced because of the change in social structure and the progression of medicine, and the rate of chronic diseases has become higher than that of acute diseases. Accordingly, medical care-related annual expenditure in the national budget has been ever increasing. Therefore, scientific evaluation of cost–benefit performance for treatment, diagnosis, and prevention of diseases has become critical. In medical checkups, contribution to survival tends to be regarded as more important than early discovery. Furthermore, the health paradigm has shifted from overcoming diseases to alleviation of symptoms, coexistence with diseases, and maintenance/promotion of health, and thus, QOL evaluation has been considered important.

Even in medical policy, it is necessary to analyze decreases in medical expenses from not only a macroeconomic viewpoint but also from a microeconomic viewpoint based on QOL evaluation of patients and to conduct efficient distribution of medical expenses. One of the analysis methods of health economics includes cost–utility analysis (CUA). This evaluates health from both aspects of quantity of life and QOL and indicates the satisfaction level of life. Utility expresses the severity of disease or symptom as a product of time and the QOL index during the time. Utility is indicated quantitatively using a scale from 0 (=death) to 1 (=health).

Representative time indices using QOL indices include quality adjusted life-year (QALY) and disability adjusted life-year (DALY). QALYs and DALYs are reciprocal, and CUA evaluation compares expense per 1 QALY unit (expense/QALY). At present, CUA is one of the most useful evaluation methods in health economics.

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