Quality of life aspects in the management of thyroid cancer

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**SUMMARY**

While there is agreement that quality of life (QoL) is a central aim of medical treatment, the methods of its evaluation as well as its role in the patient’s overall treatment experience are under continuous scrutiny. Different perspectives on patients’ QoL have emerged; from the treating physician, from the psychologist, and naturally from the patient himself/herself. This article provides insights into each of these views within the context of thyroid cancer where, as a consequence of increasing incidence and decreasing mortality rates, QoL aspects deserve close attention. Physicians often find themselves in situations where they perform a balancing act between what they know is best from a somatic point of view and learning about what is best for the individual patient. For psychologists in the field of oncology, a main area of interest is the incorporation of the patient’s perspective into research by using patient-reported outcomes (PROs) which include QoL assessment. PROs can also be used in clinical practice as a way to start a conversation about symptoms and QoL aspects that perhaps patients might not volunteer, and this allows physicians to address QoL issues more directly. Patients usually appreciate being asked about all aspects of QoL, and need sound information about how their QoL might be affected by the disease and its treatment. By examining and understanding the different perspectives on QoL, and how QoL differs in patients with thyroid cancer compared with other cancers, it is hoped that the QoL can be enhanced in this particular patient group.

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**Introduction**

This paper summarises presentations and discussions from the Quality of Life and Follow Up session of a physician-only meeting held in Vienna, November 23, 2013 entitled Thyroid cancer: from nodule to cure – the controversies. The meeting was organised by the Austrian Society of Nuclear Medicine and Molecular Imaging and the Medical University of Vienna. The session presented three different perspectives on the QoL of thyroid cancer patients; those of the treating physician, the psychologist, and the patient. QoL is becoming an increasingly important issue but is difficult to define and address. Particularly in the case of thyroid cancer, the symptoms may have a broad range (from emotional to physical discomfort, depending on the thyroid hormone status), which can affect the patient severely. The patient does not know what kind of symptoms they may be facing and is often left alone with their diagnosis and fears. Time pressure and the reluctance to ‘burden’ the physician with ‘emotional’ symptoms may silence the patient, and the physician often only sees the favourable prognosis of thyroid cancer compared with other cancer types and neglects to address QoL issues. A specific questionnaire may help to bridge these two perspectives and allow both sides to understand what and where the patient’s discomforts are and what the physician can do to relieve them. Some symptoms may last for a specific time (e.g. hormonal withdrawal prior to ablative radioiodine treatment), and explaining this would help the patient to understand and accept the symptoms; or the situation could be avoided by using a different form of treatment (e.g. by using recombinant TSH stimulation). However, in Austria only a minority of patients receive this kind of preparation for radioiodine treatment and this is usually for thyroid remnant ablation. Therefore, the problems with symptoms caused by hormone withdrawal are less significant. In the majority of patients, if it is considered that subsequent therapeutic administration of radioiodine will not be required, exogenous stimulation by recombinant human thyrotropin (rhTSH) is used for diagnostic purposes. In cases where radioiodine treatment may be required, some centres still prefer endogenous stimulation for all patients. Additionally, some treatments e.g. TSH-suppressive therapy after radioiodine treatment, can lead to several symptoms such as palpitation, restlessness, and nervousness, which may last for the rest of the patient’s life. Since thyroid...
hormone disorders may lead to emotional ‘rollercoaster rides’, a psychologist may be invaluable to help the patient cope with their symptoms. However, until the physician knows where the patient’s discomforts are, they cannot be treated or managed.

The physician’s view – Dr. Alexander Becherer

The physician’s view of QoL in thyroid cancer patients can be explained and explored by examining case studies.

The first case presented was a 36 year-old female patient, with a slightly painful nodule in the anterior neck, and who had been showing symptoms for 1 month. Apart from a heart rate of 96 bpm, she was clinically euthyroid. On palpation, the nodule was moveable, rather dense, and likely situated in the isthmus on the left side. The physician’s first assumption based on anamnesis and clinical findings was that this was most likely a cyst, and the patient was told that most of the nodules with this history are benign. The patient was relieved and very happy.

However, ultrasound showed that it was not a cyst, but a 17 mm hypoechoic nodule with irregular boundaries. As no TSH level was known, scintigraphy with Tc-99 m pertechnetate demonstrated that the lesion was cold. Thus, fine needle aspiration cytology (FNAC) was indicated. The patient was given the updated news and was understandably very distressed.

The case illustrated that although it is better for patients (and improves the quality of their experience) to be given a firm diagnosis as soon as possible, particularly if the diagnosis is a benign one, this is often not possible based on statistical probabilities. The physician should wait for the results of the whole bundle of diagnostic tests because speculative diagnoses (even if statistically probable) can lead to great distress once a different diagnosis is made. However, in thyroid nodules scintigraphy can be done immediately and gives a result very quickly, which is much better for the patient than waiting for the thyrotropin result to determine whether a nodule is hyper- or hypofunctioning.

Given the results of sonography and scintigraphy, the physician’s view was that the nodule had a significant chance of being a carcinoma. The patient was told that there was a 1 in 5 chance of the nodule being cancer (to make her aware of the possibility that she had a malignant disease, but without leaving her with a very pessimistic outlook). Finally, FNAC revealed papillary thyroid carcinoma. This highlighted the importance of not telling patients their results in detail if there is a possibility of changing the message. The patient underwent thyroidectomy a few days after receiving the FNAC result. She had a PTC ptT1Bn1a tumour, maximum diameter of 17 mm, BRAF V600E mutated, with 6 out of 39 metastatic lymph nodes. Her response to surgery and radioiodine ablation was excellent, with a stimulated thyroglobulin (Tg) of 0.5 ng/ml (IMMULITE® 2000 XPI, Siemens Healthcare, Erlangen, Germany, analytic sensitivity, 0.2 ng/ml) two months after radioiodine ablation.

In terms of QoL issues, the patient was concerned about her small son, whether she would be able to see him grow up, and whether he would lose his mother. She was also concerned about her ability to have more children, and if the treatment for her cancer would mean that she would lose her hair. A key learning point from this interaction was the importance of remembering that although physicians may tell patients ‘You have a carcinoma with an extremely favourable prognosis’, and try to make the most memorable words for the patient ‘an extremely favourable prognosis’, in fact the words that the patient mainly hears are only ‘you have a carcinoma’ [1].

The second case concerned a 74 year old female patient with a 14 year history of follicular thyroid carcinoma, pT4N0Mx. She had 6 diagnostic scans over 6 years and was in complete remission. Then her Tg level started to rise, and the patient was treated with radioiodine therapy. Following treatment the patient received 2 check-ups per year. No detectable lesions were found either by diagnostic scanning with 131Iodine, with 18F-FDG, or with ultrasound. However, her Tg levels continued to rise without any discernible clinical symptoms.

The QoL issues in this case centred around helping the patient to accept that her Tg level was a laboratory finding which necessitated more frequent check-up visits, but did not influence her wellbeing. The patient had tooth problems with softening of adamantine, caused by xerostomia (an adverse effect of radioiodine). Initially the patient did not want to spend any money on her teeth because she believed ‘it’s not worth while investing money on my teeth because I’m going to die soon.’ However, the physician convinced her that the prognosis was good, and she had her teeth repaired and was very proud of them. The patient is currently in very good condition, is healthy, and enjoying life with her husband and grandchildren.

The third case report was of a 61 year-old male patient, with poorly differentiated follicular cancer pT4pT1Mx, that had relapsed locally twice already in the early course of the disease. Eventually he developed pulmonary metastases for which he underwent 3 operations on the right lung (first 9 years after his first diagnosis, then again 1 year later, and finally a further year later). The patient also underwent external radiotherapy for metastases in the left lung. He had been treated for the last 2 years with a tyrosine kinase inhibitor, which had slowed the progression of the cancer. The patient had no symptoms from the lesions, but treatment with sorafenib affected his QoL due to the development of severe hand-foot-syndrome, and subsequent mild diarrhoea when he switched his medication from sorafenib to pazopanib. However, the hand-foot-syndrome resolved and the patient controlled his diarrhoea during the day with other medication, and was able to continue to work as a travelling salesman. The patient was very, and would have not even attended his monthly check-ups if he had not needed a new prescription for pazopanib and on the insistence of his wife. She said that the main reason for her husband missing the check-ups was his fear of receiving bad news. His main complaints were diarrhoea, his hair becoming white, and a lack of compliance with his antihypertension medicine.

In summary, although this patient had a severe, progressive disease, he had an acceptable QoL. This is because he had different coping strategies than those of the patient in case study 2 – illustrated by the fact that he had bought a new sports car, showing that he saw his prognosis in a different way.

In general, it is important to remember that thyroid cancer is a disease with rising incidence but decreasing mortality in Austria and throughout the whole world [2,3], and this gap often leads us to believe that a patient should not be ‘worried’ by their thyroid cancer [1]. However, this is not very helpful, and physicians should avoid telling patients ‘it could have been worse’ because the patient is occupied with their own fate, asking why this happened specifically to them, even when they appear to be trying to make the best out of their situation.

Hypocalcaemia is an issue in QoL (even more than laryngeal nerve palsy, when it occurs unilaterally), and the side effects of radioiodine should be considered, although there is no risk of infertility or genetic changes [4,5]. Most patients live long enough to experience side effects and they can adversely affect QoL. For example, xerostomia occurs in 10–20% of patients [6,7]. There is a low risk of induction of a second malignant tumour by radioiodine, however, discussions centreing around this are controversial. Data on this issue are heterogeneous but there is a probable hazard ratio of 1.2 and females are more at risk than men.

Therefore, in summary, physicians should not give positive diagnoses too readily, even if the statistics are in favour of good news. It is easier to turn indifferent news into good news than vice
versa. Patients fear every check-up visit. Therefore, it is wise to schedule them as infrequently as possible. New drugs for treating iodine-refractory tumours open new fields of possibilities and also bring new side effects and new issues in medical training (if management is not done by oncologists). Physicians should be made aware of all side effects; it is crucial to realise that an informed patient tolerates much more than an uninformed patient.

The psychologist's view – Dr. Eva Gamper

QoL encompasses a range of different concepts that are very difficult to put into practice. In health care, for many years the solution to this was to restrict the measurement of QoL to some of the symptoms, side-effects, and functioning, and to have these items rated by physicians. However, it was realised that these proxy ratings had limitations, such as a low inter-rater reliability [8,9], a moderate agreement between proxy and patient reports [10,11], and loss of information through interpretation and translation into medical terms [12]. Therefore, the use of patient reported outcomes (PROs) as an additional source of information is increasing in importance. According to the FDA, the definition of a PRO is the report of a patient's health condition coming directly from the patient without any interpretation of the patient's response by a clinician or anyone else [13].

The core concept of PRO research is health-related QoL (HRQoL), which comprises QoL domains that are influenced by the disease and its treatment, i.e. HRQoL provides a measure that assesses a patient's psychological, social and somatic status [14] and is expected to predict the effect of therapy. In thyroid cancer research HRQoL measurement is still uncommon. This could be because incident rates are small and it is very hard to collect sufficient data. However, it could also be due to a general opinion that QoL assessment is less important in this patient group because, compared with other cancer patients, they feel quite ‘well’. In addition, the prognosis is good, so there is no ‘trade-off’ to be made between survival and QoL when developing the treatment plan. However, does a good prognosis coupled with favourable treatment options (which might be the predominant features of thyroid cancer from a patient’s point of view) really directly correlate with a good patient-reported HRQoL? The information found in the literature shows that patients that have to go through thyroid withdrawal (i.e. endogenous TSH stimulation) clearly have an impaired HRQoL in physical as well as in psychosocial domains [15–17]. Furthermore, this patient group reports worse HRQoL than patients with exogenous TSH stimulation [18–20]. There are conflicting results concerning the influence of age and gender, and on if and when patients in recurrence reach general population levels of QoL [17,21–23]. Usually patients’ HRQoL decreases with age, except for anxiety and depression which might be more pronounced in younger patients. Furthermore, women report more impairments than men, especially in the emotional dimensions. The question of whether these age and gender patterns are thyroid cancer specific or if they only reflect general response patterns (which can also be found in the general population) has been investigated by Singer et al. [24]. They found that after controlling for the effects of age and gender, thyroid cancer patients still reported significantly more impairment than the German general population in all but two domains (constipation and diarrhoea) of the Quality of Life Questionnaire Core-30 (QLQ-C30: functioning: physical, role, emotional, social, cognitive; symptoms: fatigue, nausea/vomiting, pain, dyspnea, sleep, appetite, constipation, diarrhoea, financial impact, and global QoL). In line with previous findings, patients reported not only physical but severe psychosocial problems, especially in role functioning. The QoL impairments reported by thyroid cancer patients therefore cannot be attributed to the fact that the majority of the patients are female and that females generally tend to self-report more problems in questionnaires.

In summary, there are two very different perspectives on thyroid cancer to be kept in mind. There is the medical expert, who compares thyroid cancer with other cancers and might focus on its good prognosis and favourable treatment options (with few side effects and little social stigma). The expert may not even realise if the patient is under-reporting symptoms, as a low level of impairment would fit the picture of the disease. Then there is the patient who, although they need to know about the favourable prognosis and treatment options, still has to deal with a cancer diagnosis for the rest of their life. Additionally, the patient may also have physical impairments never experienced before, and which may erode their QoL. In the case of radioiodine treatment, s/he has to deal with an unusual treatment including isolation for radioprotection, which might augment the feeling of being socially marginalized as well. A range of emotional, social, and cognitive issues can become very burdensome and sometimes patients even worry about the appropriateness of these problems and may feel guilty for taking psychological counselling help as they are expected to be ‘alright’.

HRQoL assessment can contribute a great deal to bridging the gap between these two perspectives. It adds value by incorporating the patient perspective into both thyroid cancer research and clinical practice. Patients are very willing to provide information on many aspects of their QoL and this can help the physician to understand patients’ concerns. Patients can be told what other patients have perceived, and this can improve patient-centred care and patient–physician communication. HRQoL assessment should be encouraged; it is easy to perform and provides a lot of valuable information.

The patient’s view – Dr. Heying Duan

Dr. Duan is a nuclear medicine expert, and has also been a thyroid cancer patient, and therefore offered a unique perspective on the disease. In October 2002, Dr. Duan found a lump in her neck. She presented to her physician in January 2003 and was referred to the nuclear medicine department. Two nodules in her thyroid were discovered, which were classified as cold nodules by scintigraphy and surgery was performed 2 weeks later. Histology revealed a papillary thyroid carcinoma (pT2 without lymph node metastases). The diagnosis and treatment influenced Dr. Duan to become a nuclear medicine physician, and although she uses her personal experience to reassure patients, she tries hard to maintain her objective perspective.

In terms of QoL, when Dr. Duan had her first appointment her TSH was slightly above 4.0 μU/L, which would not normally be treated, but she had severe fatigue. After surgery, the symptoms were even worse: constant tiredness and feeling cold, even anxiety attacks, and a range of other symptoms from total apathy to restlessness. When diagnosed, one of the first questions she had was ‘will I die soon?’ but Dr. Duan then rationalised the diagnosis and tried not to blame herself or anyone else for the situation. She was also afraid for her fertility, especially after radioiodine therapy. Currenty, Dr. Duan has no symptoms and her QoL is not affected at all by her thyroid cancer.

In retrospect, Dr. Duan would have liked more information about hypothyroidism and its related symptoms; at the time, she did not understand if the symptoms were because of her diagnosis, if they were permanent, or if they would change her personality. Thankfully, the symptoms vanished following T4 substitution.

Dr. Duan felt that if the physicians had asked her more in depth questions about her QoL when she was experiencing the symptoms, she would have understood more clearly that her experiences were related to the hypothyroidism as a result of her
thyroid carcinoma. In addition these symptoms would eventually disappear.

Dr. Gamper added that even carrying out a QoL assessment has the potential to improve patients’ QoL. Computer-assisted assessments allow real-time feedback of the patient’s QoL profile and enable the physician to very quickly get an overall picture of the patient’s health status and to structure the consultation accordingly. QoL assessment can also help to overcome ‘white coat silence’ – patients are often reluctant to discuss all of their symptoms with their physician because of time pressures and a desire to not ‘burden’ the physician with emotional, social, or ‘minor’ health problems. Thus, the questionnaire can be an effective and time-saving communication tool, allowing the physician to quickly appraise if a patient needs symptom management, more medical information, or referral to psycho-oncologists or social workers.

It is very difficult for patients to differentiate in HRQoL between disease-related QoL issues and other general stresses. Dr. Duan believes that the patient’s attitude to their diagnosis is paramount. If the patient deals with the diagnosis in a positive way, they can cope with the stresses and strains caused both by their disease and by their everyday life much more easily.

Still, every person has a different way of coping and counterintuitively, thyroid cancer patients often have more severe psychological problems than patients with a poor prognosis, who are occupied by juggling their treatment and side effects and are confronted with trying to survive every day. Singer et al. [24] reported that thyroid cancer patients asked for psychological counselling support, but there are no published outcome data. Psychologists with training in psychooncology do not need extra training to counsel thyroid cancer patients because many of the issues that arise are common to all cancer patients. They certainly need background knowledge of thyroid cancer including treatment options and sequelae. In particular, the symptoms of hypo/hyperthyroidism as these might easily be misinterpreted as psychiatric symptoms.

Whatever perspective is examined, it is key to understand that QoL and emotional burden is not directly related to the severity of the disease and that more research is needed to learn about thyroid cancer patients’ needs. However, the three cases presented highlight some fundamental points to be considered regarding the treatment of thyroid cancer patients and their QoL:

- A firm diagnosis improves the quality of patients’ experiences because speculative diagnosis can cause distress.
- Despite the physician giving a favourable prognosis at diagnosis, the patient is likely to focus on the negative elements of the cancer diagnosis.
- QoL can be improved by explaining that the frequency of laboratory tests and check-ups do not necessarily relate to progression.
- Patients have very different coping strategies which have an impact on their QoL.
- Even though there is decreasing mortality associated with thyroid cancer, telling patients ‘it could have been worse’ should be avoided.
- Hypocalcaemia and the side effects of radiiodine can adversely affect QoL.
- It is easier to turn indifferent news into good news than vice versa.
- A patient, who is informed, and aware of all of the side effects of treatment, is likely to be more tolerant of treatment than an uninformed patient.
- The use of PROs as an additional source of information is of increasing importance.

HRQoL measurement in thyroid cancer maybe uncommon because of the misconception that QoL is less important in this group of patients than in other cancer patients.

Conflict of interest
None declared.

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