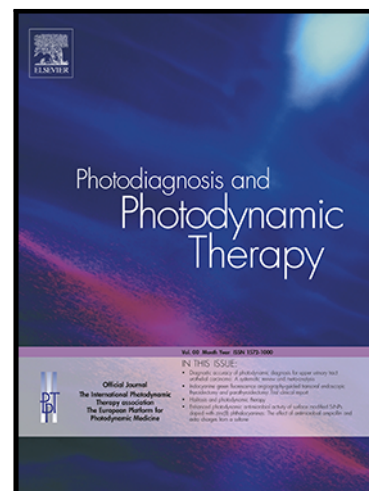


Journal Pre-proof

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Highlights

- No questionnaire has been developed which focuses on QoL after mTHPC-PDT treatment of head and neck pathologies.
- The majority of patients reported improved QoL following mTHPC-PDT.
- mTHPC-PDT confers improvement in QoL score with figures comparable to other treatment modalities.

Journal Pre-proof

Quality of life following photodynamic therapy for head and neck pathologies: an exploratory study

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Quality of life following photodynamic therapy for head and neck pathologies: an exploratory study

Abstract

Introduction

Healthcare related quality of life (QoL) is defined as the impact one's level of health and wellbeing has on a number of domains, including physical, mental, spiritual and social functions. Photodynamic therapy (PDT), a cancer treatment modality, is increasingly used to treat or palliate head and neck pathologies. Due to the complex nature of this area of the body, both the pathology and the treatment of it can severely affect the quality of life. Thus far, no questionnaire has been developed which focuses on quality-of-life post-PDT of head and neck pathologies.

Patients and methods

We have developed the University College London Quality of Life Questionnaire for Patients undergoing PDT in the Head and Neck, using meta-tetra(hydroxyphenyl)chlorin (mTHPC) as the photosensitiser. This was modified from the University of Washington quality of life (UW-QOL) questionnaire. Thirty-eight patients who received mTHPC-PDT for various head and neck pathologies completed the questionnaire, with a mean follow-up of 56 days.

Results

All patients reported improved QoL following mTHPC-PDT. The main problem that was reported was post-PDT pain, which is a common side effect. Visual symptoms, breathing, speaking and swallowing problems improved significantly in the 4th week following treatment and significant improvement in activities of daily living, social life, mood and anxiety were reported in the subsequent weeks.

Conclusions

mTHPC-PDT confers improvement in QoL score in selected head and neck cancer patients with figures comparable to other treatment modalities. This exploratory study demonstrated patterns of QoL outcome. Further work needs to be done for survey validation and inclusion of a larger cohort which will allow optimal sub-group analysis and help guide further interventions.

Keywords: mTHPC-PDT; QoL; cancer; head and neck

Introduction

Healthcare related quality of life (QoL) is defined as the impact one's level of health and wellbeing has on a number of domains, including physical, mental, spiritual and social functions. QoL is usually discussed in terms of how negatively it has been affected by a certain illness (such as malignancy, acute or chronic disease) or its management. The World Health Organization (WHO) defines QoL in relation to "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". Such perceptions are influenced by the aforementioned domains.¹⁻³

Due to the small and complex anatomy of the head and neck, any pathology of the oral cavity, oropharynx, laryngopharynx or larynx can adversely affect the breathing and swallowing mechanisms as well as speech production. Tumours of the nasopharynx can cause problems like pain, trismus, nasal obstruction and bleeding as well as breathing and speech problems. The effects of these problems aren't limited to physical dysfunction: many cause issues with one's social life (for example speech problems may make social interactions more difficult) which impacts on emotional and mental state. Severe mal odour has also been attributed to head and neck cancer, which can cause social isolation. Large tumours and vascular anomalies can cause disfigurement, erode through skin and small blood vessels and lead to ongoing problems like sinus formation, recurrent bleeding and infections.⁽²⁻³⁾

Treatment interventions themselves can negatively affect form and function, for example surgery can involve large surgical resections and reconstruction while radiotherapy can involve large radiation fields. In cancer therapy, maintaining the balance between a good QoL and cancer elimination is a challenge that is sometimes hard to achieve.²⁻³

QoL assessments are an ever more essential part of clinical care, as a more patient centered approach is taken, with treatments aimed at not only improving disease free survival, but overall function of the patient and their perception of function within their community. As such the importance of having a validated questionnaire specific to the treatment delivered is increasing. QoL questionnaires further help healthcare professionals (HCP) identify treatment related issues of concern: it has been shown that HCPs are often insufficiently aware of their patients QoL.⁴ Cancer patients are uniquely vulnerable even post treatment with a large population study conducted in Australia demonstrating the discrepancy in QoL between cancer survivors and the general population.⁵ Having a reliable metric to continually assess QoL in cancer patients may allow clinicians to close this gap in QoL.

Several valuable quality of life questionnaires have been developed and successfully used when assessing the level of function and dysfunction in cancer patients; this includes patients diagnosed and treated for head and neck cancer. These questionnaires have been used to assess outcome following the conventional treatment modalities (surgery, radiotherapy and chemotherapy). Of these

questionnaires, the most used include the: European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ) Head and Neck-35 (QLQ-H&N35), EORTC Treatment of Cancer QLQ Core-30 (EORTC QLQ C30), M. D. Anderson Dysphagia Inventory (which is dysphagia specific) and University of Washington quality of life questionnaire (UW-QOL).⁶⁻⁷ No questionnaire was used to assess the quality of life following photodynamic therapy, and in particular in the management of head and neck pathologies.

The 'University of Washington quality of life (UW-QOL) questionnaire' is one of the most practical and commonly used questionnaires in head and neck units. Hassan and Weymuller stated that 'the advantages of the UW-QOL head and neck questionnaire are that: 1) it is brief and self-administered 2) it is multi-factorial, allowing sufficient detail to identify subtle change 3) it provides questions specific to head and neck cancer and 4) it allows no input from the health provider, thus reflecting the QOL as indicated by the patient'. The currently used version (IV) of the UW-QOL questionnaire includes 12 single question domains. These include pain, appearance, activity, recreation, swallowing, chewing, speech, vision, taste, saliva, mood and anxiety.²

PDT is known to cause no cumulative toxicity and is advantageous in that previous treatments, such as chemoradiotherapy and surgery, are not contraindications. PDT relies on the administration of a photosensitiser (in this case tetra(hydroxyphenyl)chlorin [mTHPC]) followed by application of light of specific wavelengths which excite the photosensitiser, resulting in cell death. The ability of the photosensitiser to accumulate in cancerous lesions, and the delivery of light only to the area of the lesion render PDT a selective modality, limiting damage to surrounding tissues.^{8,9}

mTHPC-PDT-related adverse events in the head and neck include pain and local tissue oedema, which may compromise breathing, swallowing, speech production or vision, depending on the pathology location. Additionally, an important aspect of post-treatment recovery is avoidance of intense light due to residual photosensitisation and patients are advised to avoid direct sunlight for a period of up to 4 weeks. This can affect social interactions and impact mental health in a way the other conventional therapies may not. There are stark differences in both treatment toxicity and post-treatment function when comparing mTHPC-PDT to conventional therapies which have widely accepted QoL questionnaires as outlined above. As of yet there has not been a method of assessing PDT related QoL. This highlights the need for a head and neck, mTHPC-PDT specific questionnaire for this subset of patients.⁹⁻¹⁰

This study evaluates the quality of life of a cohort of patients treated with mTHPC-PDT for various pathologies of the head and neck. This has been based on the creation of a QoL questionnaire modified from University of Washington quality of life questionnaire (UW-QOL)

Patients and methods

- Treatment protocol

Identical 'intent to treat' protocols were used to treat 38 consecutive patients who presented with various pathologies of the head and neck, including oral dysplasia, oral and oropharyngeal cancer, salivary gland and vascular tumours and skin cancer. The patient quality of life was assessed as the main endpoint of this study. These patients were followed up as part of this study for a mean of 56 days (Table 1).

mTHPC is approved for the treatment of advanced/recurrent head and neck cancers. The application of photodynamic therapy at the Head and Neck Unit, University College London Hospitals (UCLH) is commonly practiced. Every treated patient was provided with "patient information sheet" and signed a "consent form" prior to the intervention and was regularly updated on the treatment progress and outcome. Each patient was also provided with a Quality-of-Life questionnaire and advised to complete it as accurate as possible.

Photodynamic therapy was usually offered under local or general anaesthesia. Each patient underwent examination under anaesthesia (EUA) of the pathological area. 0.05-0.15mg/kg meta-tetrahydroxyphenylchlorin (mTHPC) was administered topically or systemically with drug-light interval (DLI) of 48-96hrs depending on the size, location and type of pathology. Post-treatment pain control was applied according to the UCLH post-PDT pain protocols.

The patients' data were entered into proformas, which were validated and checked by interval sampling. The fields included a range of clinical, operative and histopathological variables.

- Quality of life (QoL) questionnaire

We have developed a quality-of-life questionnaire for patients undergoing mTHPC-PDT (Appendix I). The questionnaire was based on the structure of the "University of Washington Quality of Life Questionnaire for Head and Neck Cancer Patients" to allow future comparisons. Our new 'University College London Quality of Life Questionnaire for Patients Undergoing Photodynamic Therapy in the Head and Neck (UCL-QoL-PDT-H&N ver. 1)' involved the following sections:

Quality of life (QoL) parameters (Appendix 1) pre-PDT:

- Pain: patients report on their pain levels related to their pathology.
- Visual problems: this was a presentation specific to patients presenting with vascular anomalies of the face.
- Breathing, swallowing and speech problems: these were presentations specific to patients with oral and oropharyngeal carcinomas. No laryngeal tumours were part of the study cohort. Furthermore, taste impairment and reduction in saliva production (dry mouth) were also presentations specific to these patients, which were directly related to chemo radiation.

The questionnaire combined questions about nasal airway and tracheotomy,

however it is well recognized that tracheotomy can have significant negative effect on QOL which will be addressed in the follow-up study. None of the patients had SaO₂ below 92%. Oxygen therapy has been administered when indicated. All the patients who had feeding tube before PDT was related to disease progression and previous interventions and not PDT.

- Facial disfigurement: this was questioned as a likely presentation by patients with advanced cancers, salivary gland and vascular tumours of the head and neck.
- Activity of daily living, impact on social life, mood, anxiety and quality of life: patients also commented on these parameters being directly affected by their pathology. This was to ensure a baseline is achieved to allow comparisons post- mTHPC-PDT.

Patients were also asked to comment on some parameters specific to mTHPC-PDT (e.g. related to photosensitiser administration/reaction, photosensitivity reactions) as well as previously offered treatments and whether their current pathology was life threatening or not.

Patients were asked to report on their physical, mental health and quality of life parameters at specific intervals post- mTHPC-PDT: Day 1 to 3, Day 4 to 7, Day 8 to 14, Day 15 to 21, Day 22 to 28, Day 29 to 35, Day 36 to 42, Day 43 to 49 and Day 50 to 56. These specific intervals were selected based on the authors' experience that it is likely to correspond with various stages of tissue reaction/changes and subsequent healing post- mTHPC-PDT.

Furthermore, patients were asked to comment if they perceive their physical, mental health or quality of life changes to be a "minor" or "major" concern at the following durations: pre- mTHPC-PDT treatment and post- mTHPC-PDT treatment (Day 15 to 21, Day 29 to 35 and Day 50 to 56).

General questions with regard to mTHPC-PDT were included at the end of the questionnaire. These 4 questions were addressed to the patient:

- Could you please state the pros and cons of the treatment?
 - Was the clinical information provided with regard to the treatment and light precautions adequate? If not, how would you suggest improving it?
 - Was the treatment up to your expectations? If not, please state your reasons.
- Would you have photodynamic therapy again? If not, please state your reasons.

All patients completed the entire UCL-QoL-PDT-H&N ver. 1 questionnaire (Appendix I).

Statistical analysis

The results from this 36-page questionnaire were statistically analysed and significant results were highlighted. This was performed using the SPSS 17 (statistical package for social scientists) by an independent statistician. The results were cross-tabulated and the Chi-squared statistic was used to test for differences in the

incidence of outcome. Fisher's exact test was used for the analysis of contingency tables and therefore to measure the *p*-value.

Results

The patient population comprised 20 males and 18 females. The mean age of the patient population was 58.0 years. The most common race amongst the population group was Caucasian (79%). The most common primary sites were the oral cavity, mid face and oropharyngeal region. Six patients had oral dysplasia, five had oral squamous cell carcinoma [SCC] (3 patients T4N1M1, 2 patients T4N2M1 – all previously had surgery, radiotherapy and chemotherapy) and eight had oropharyngeal SCC (all patients T4N1M1 – all had previously surgery, radiotherapy and chemotherapy); other pathologies were benign salivary gland tumours (n=4), vascular anomalies (n=10) and five skin SCC patients (3 patients T1N0M0, 2 patients T2N0M0). mTHPC-PDT was offered in 3 modes: surface illumination, interstitial application and US-guided interstitial application based on the location of the pathology (Table 1).

All patients received one round of mTHPC-PDT as part of this QoL assessment study. Twenty-one patients in this study reported that they believed that their disease is life threatening. This cohort of patients had oral or oropharyngeal SCC and severe vascular anomalies of the head and neck. The majority of those patients have received surgery and chemo radiation as a curative (with little success) or palliative option (Appendix IIa).

Patients' report on the parameters assessed

Transient pain while administering the photosensitiser was reported by 84% of patients. It was noticed that a transient increase in pain levels were reported by the majority ($P<0.001$) of patients 1-7 days post- mTHPC-PDT. Soft tissue swelling as direct effect from PDT started on day 1 and started to settle down at day 15, with majority of patients ($P<0.001$) reporting mild swelling. Tissue sloughing as direct effect of mTHPC-PDT was reported on day 8 and continued until day 49 for the majority of patients but with various degrees of severity (Appendix IIa).

Moderate to severe levels of pains have been reported by patients diagnosed with oral dysplasia, oral and oropharyngeal malignancies, salivary glands and vascular tumours of the head and neck. Pain was either due to direct pressure of the tumour on nearby structures or due to tumour nerve invasion. Severe Pre- mTHPC-PDT pain (26% of patients) levels, that were either controlled by opiates or not controlled at all, has significantly reduced ($P<0.001$) starting from day 36 post-PDT with patient reporting mild pain not requiring pain killers (Appendix 2a-b).

Five patients, with symptoms including double vision, and other visual disturbances with eye pain, have reported complete resolution of symptoms from day 29 post-

mTHPC-PDT. The visual problems were directly related to increase in facial swelling leading on direct pressure on the eye (Appendix 2a-b).

Patients with oral and oropharyngeal carcinomas reporting moderate/severe breathing (92%), swallowing (54%) and speaking (31%) problems had significant improvement of their symptoms, varying from day 29 post-mTHPC-PDT for breathing difficulty patients ($P<0.001$), day 43 post- mTHPC-PDT for patients with swallowing problems ($P<0.001$) and day 15 post- mTHPC-PDT for patients with speech problems ($P<0.001$). Patients suffering from taste impairment and dry mouth as direct side effects of prior chemoradiation reported no worsening or improvement of symptoms post- mTHPC-PDT (Appendix 2a-b). Figure 1 illustrates the improvement in visual, speech, swallowing and breathing problems post- mTHPC-PDT.

When it comes to patient's perception to disfigurement caused by their pathology and effect on daily activity, only 17% of patients reported this parameter as severe pre- mTHPC-PDT and by day 36 post- mTHPC-PDT the severity of disfigurement has significantly reduced ($P<0.001$). Skin sensitivity post- mTHPC-PDT was highest on Day 29 with 3 patients reporting blistering and one patient reporting severe skin burn in one site. All patients recovered by day 50 post- mTHPC-PDT (Appendix 2a-c).

Significant improvements in activity of daily living (ADL) were reported on day 36 where all patients reported highest activity level (I am as active as I have ever been). When it comes to pathology impact on social life, 29% of patients reported various significant limitations to their social life. On day 36 post- mTHPC-PDT, only 2 patients continued to report this limitation ($P<0.001$). Anxiety symptoms were reported by 58% of the patients pre- mTHPC-PDT whilst depressive symptoms in 34% of patients. On day 43, 27% of patients continued to suffer from anxiety and 23% from depression (Appendix 2a and c). Figure 2 illustrates the improvement in pain levels, disfigurement perception, anxiety and depression levels, ADL and social life activities post- mTHPC-PDT.

Health-related QoL was poor-very poor in 45% of patients and this has significantly improved at day 43 post- mTHPC-PDT with only 18% of patients remained at these poor QoL categories ($P<0.001$). Similarly, overall QoL was poor-very poor in 45% of patients and this has significantly improved at day 50 post- mTHPC-PDT with only 18% of patients remained at these poor QoL categories ($P<0.001$), (Appendix 2a and c). Patients who perceived their physical, mental health or QoL changes to be a "major" concern pre- mTHPC-PDT have mostly perceived them to be of "minor" concern at day 29 post- mTHPC-PDT (Figure 3).

The four questions

- Pros and cons of mTHPC-PDT: 79% of patients reported it to be much more tolerated than any of the conventional modalities and lead to better QoL. While 32% reported severe pain as something they didn't expect following the treatment.
- Clinical information: 84% of patients believed that the clinical information provided with regard to the treatment and light precautions were adequate.
- Treatment expectations: 74% of patients reported that the mTHPC-PDT treatment

exceeded their expectations.

- Having another round of mTHPC-PDT: 95% of patients reported that they would consider further treatments, if needed.

Pathology type vs. patient's report of major concern QoL parameters

The QoL parameters which were highlighted as a "major concern" by patients (figure 3) has been reviewed per pathology (Table 2).

- Oral dysplasia: Anxiety was a significant factor in 50% of those patients, which stopped being a concern on day 15 post- mTHPC-PDT.

- Oral and oropharyngeal SCC patients: these 2 cohorts of 13 patients with advanced recurrent carcinoma reported problems related to breathing, swallowing, speech and disfigurement which all have resolved by day 50 post- mTHPC-PDT, or even before in some cases. Mood and anxiety were prominent and significant problems for these 2 cohorts, with many improved but not fully resolved by day 50 post-mTHPC-PDT. It is worth highlighting the fact that swallowing has significantly worsened in these two cohorts on day 15 before it fully improves on day 50. This was expected as direct effect from tissue swelling post- mTHPC-PDT.

- Salivary gland tumours: disfigurement, impact on social life and anxiety were significant factors in 50% of those patients, which stopped being a concern on day 50 post- mTHPC-PDT.

- Vascular tumours: visual problems, disfigurement, impact on social life and anxiety was a major concern for a third of this cohort. Most of these symptoms has improved on day 50 post- mTHPC-PDT.

- SCC skin cancer: apart from one patient reporting skin photosensitivity pre- mTHPC-PDT, no major concerns were raised by any patient in this cohort.

Discussion

The routine application of QoL questionnaires in head and neck patients improves information regarding how and to what extent patients feel that treatment is improving their quality of life making it possible to support patient needs.

Due to the complex nature of the head and neck region, pathology and its treatments can cause symptoms which severely disrupt social function and quality of life. Therefore, it is important to develop a QoL questionnaire specific to the constellation of symptoms seen in these patient groups. Such a questionnaire allows comparisons to be drawn between mTHPC-PDT and the conventional treatment modalities: surgery, chemotherapy and radiotherapy. Since the head and neck is such a compact region, these modalities often lead to side effects and post-intervention symptoms.

In our study, the University of Washington questionnaire had to be modified to accommodate for tissue changes resulting from the mTHPC-PDT intervention and also to review the effect of the common mTHPC-PDT side effects on the QoL. This was the first study that looked at QoL in head and neck patients undergoing mTHPC-

PDT. Further work needs to be done for survey validation and inclusion of a larger cohort which will allow optimal sub-group analysis and help guide further interventions.

mTHPC-PDT has been identified as an acceptable treatment by the patients in this study when compared to other conventional modalities, as it was associated with good quality of life and less morbidity.

The response to mTHPC-PDT treatment was not assessed as part of this study. The primary aim of this study was to investigate quality of life as an outcome of mTHPC-PDT treatment. Therefore, it is important to consider that any conclusions drawn do not necessarily reflect the efficacy of the treatment modality.

Nevertheless, the patients seem to agree that the intervention is better tolerated than other conventional modalities and has the advantage of being repeatable. Disadvantages associated with mTHPC-PDT include the pain or discomfort associated with the photosensitiser administration, post-PDT pain and the light precautions that have to be taken to avoid systemic photosensitisation reactions. Perfusion discomfort is also known as a common side effect in chemotherapy treatments.⁵

Pain was the main problem, which peaked in the first 48-72 hours, while the local tissue oedema lasted for about 8 days. Patients experienced the greatest changes (i.e. improvement) in functional scale during the fourth week following mTHPC-PDT. There was significant improvement in swallowing, speech and breathing in the majority of patients suffering from oral and oropharyngeal carcinomas. Day 43 post-PDT was mainly associated with significant improvement of mental health, social life, health-related and overall QoL. The timing of tissue sloughing and subsequent regeneration seems to be related to these improvement in QoL parameters.

There are over a dozen different QoL questionnaires validated for head and neck cancer patients. In the UK the most commonly used include the University of Washington, European Organisation for Research and Treatment of Cancer and Functional Assessment of Chronic Illness Therapy. Advantages of QoL questionnaires are that they provide information for the patient and a multidisciplinary team, thus promoting more effective multidisciplinary team working, identification of poor outcome groups and areas of dysfunction. This facilitates targeted interventions to improve specific aspects of quality of life in patients with head and neck cancer).¹¹⁻¹³

Summary

In our study all patients reported improved QoL following treatment with mTHPC-PDT and when patients were asked to compare mTHPC-PDT to previous treatments they had, a better overall quality of life was reported. The main problem that was reported was post- mTHPC-PDT pain. Visual symptoms, breathing, speaking and swallowing problems improved significantly in the 4th week following treatment and significant improvement in activities of daily living, social life, mood and anxiety were reported in the subsequent weeks. mTHPC-PDT confers improvement in QoL score in selected head and neck cancer patients with figures comparable to other treatment

modalities. The development of a more specific QoL questionnaire, and scoring system, will further highlight areas of further innovation in the delivery of photodynamic therapy.

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of Life Questionnaire. Arch Otolaryngol Head Neck Surg. 2010
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Tables

Table 1: Demographics of 38 patients treated with photodynamic therapy.

	No. (%)		No. (%)
Age		Diagnosis (cont.)	
Minimum	38	Vascular anomalies	10 (26.3)
Maximum	88	Skin cancer (SCC)	5 (13.1)
Mean	58.0±6.4		
		Previous treatment	
Gender		Surgery	25 (65.8)
Male	20 (52.6)	Radiotherapy	12 (31.6)
Female	18 (47.4)	Chemotherapy	12 (31.6)
		Photodynamic therapy	20 (52.6)
Race		Current treatment plan (PDT)	
Caucasian	30 (78.9)	Surface illumination	13 (34.2)
Indian	5 (13.2)	Interstitial application	4 (10.5)
Middle-Eastern	2 (5.3)	US-guided interstitial	21 (55.3)
Afro-Caribbean	1 (2.6)		
		Photosensitizer	
Location		mTHPC (0.15mg/kg,96hrs,20J/cm ²)	27 (71.1)
Oral cavity	13 (34.2)	mTHPC (0.1mg/kg,96hrs,20J/cm ²)	6 (15.8)
Oropharyngeal region	9 (23.7)	mTHPC (0.05mg/kg,48hrs,40J/cm ²)	5 (13.1)
Upper face	2 (5.3)		
Midface	10 (26.3)	Anesthetic mode	
Lower face	4 (10.5)	No anaesthesia	3 (7.9)
		Regional/local anaesthesia	6 (15.8)
Diagnosis		General anaesthesia	29 (76.3)
Oral dysplasia	6 (15.8)		
Oral SCC	5 (13.2)	Rounds of PDT	
Oropharyngeal SCC	8 (21.1)	1 round (at the end of the study)	38 (100)
Salivary gland tumours	4 (10.5)		

Table 2: Quality of life following PDT: disease vs. major concern on QoL and response

Site/pathology		Pre-PDT	15 to 21	Day 29 to 35	Day 50 to 56
Oral dysplasia 6 patients	Pain	1	0	0	0
	Anxiety	3	0	0	0
Oral SCC 5 patients 3 patients T4N1M1, 2 patients T4N2M1 – all previously had surgery, radiotherapy and chemotherapy	Pain	2	1	0	0
	Swallowing problems	1	6	1	0
	Disfigurement	1	1	0	0
	Activity of daily living	1	1	0	0
	Impact on social life	2	1	0	0
	Mood	4	5	3	1
Oropharyngeal SCC 8 patients all patients T4N1M1 – all had previously surgery, radiotherapy and chemotherapy	Anxiety	6	6	3	1
	Pain	4	2	0	0
	Breathing problems	8	8	1	0
	Swallowing problems	1	8	3	0
	Speaking problems	1	0	0	0
	Activity of daily living	3	3	0	0
	Impact on social life	1	1	0	0
Salivary gland tumours 4 patients	Mood	8	8	5	1
	Anxiety	8	8	6	3
	Pain	1	0	0	0
	Disfigurement	2	4	1	0
Vascular anomalies 10 patients	Impact on social life	2	2	2	0
	Anxiety	2	2	1	0
	Pain	2	2	1	0
	Visual problems	3	2	0	0
	Disfigurement	3	8	1	0
	Impact on social life	3	2	4	1
Skin cancer (SCC) 5 patients 3 patients T1N0M0, 2 patients T2N0M0	Mood	1	4	3	0
	Anxiety	3	6	2	2
	Skin photosensitivity	1	0	1	0

Figures

Figure 1: Patient report on change in visual, breathing, speaking, swallowing, taste and saliva caused by their pathology pre- mTHPC-PDT and subsequent follow-ups post- mTHPC-PDT.

Figure 2: Patient report on change in pain levels, impression on their disfigurement, activities of daily living and psychosocial aspects pre- mTHPC-PDT and subsequent follow-ups post- mTHPC-PDT.

Figure 3: Patient report on health-related quality of life and overall quality of life pre- and post- mTHPC-PDT. Also, patient report on their concerns where related to physical or mental health symptoms and whether they perceive them as minor or major and the change in their perception at various intervals pre- mTHPC-PDT and subsequent follow-up post- mTHPC-PDT.

Appendices

Appendix 1: University College London Quality of Life Questionnaire for Patients Undergoing mTHPC-PDT in the Head and Neck (UCL-QoL-PDT-H&N ver. 1)

Appendix 2a: QoL parameters pre- mTHPC-PDT.

Appendix 2b: QoL parameters post- mTHPC-PDT 1.

Appendix 2c: QoL parameters post- mTHPC-PDT 2.

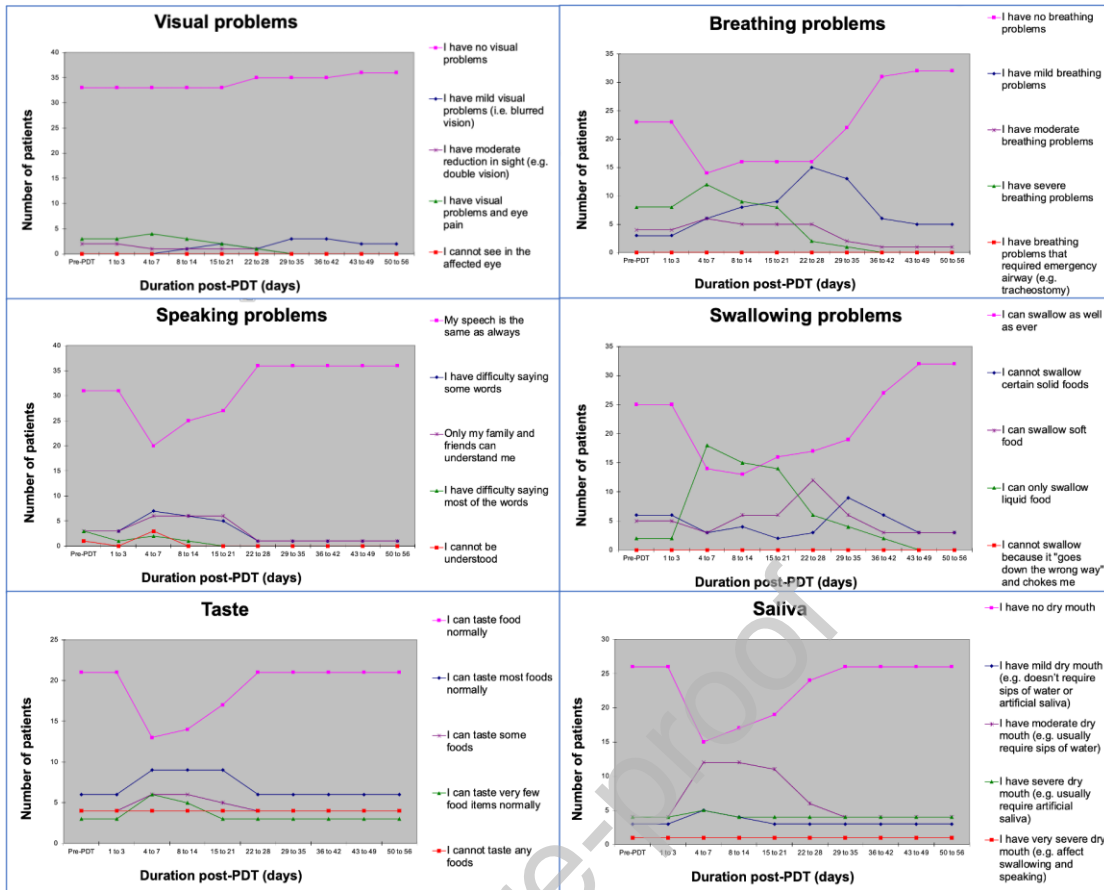


Fig. 1

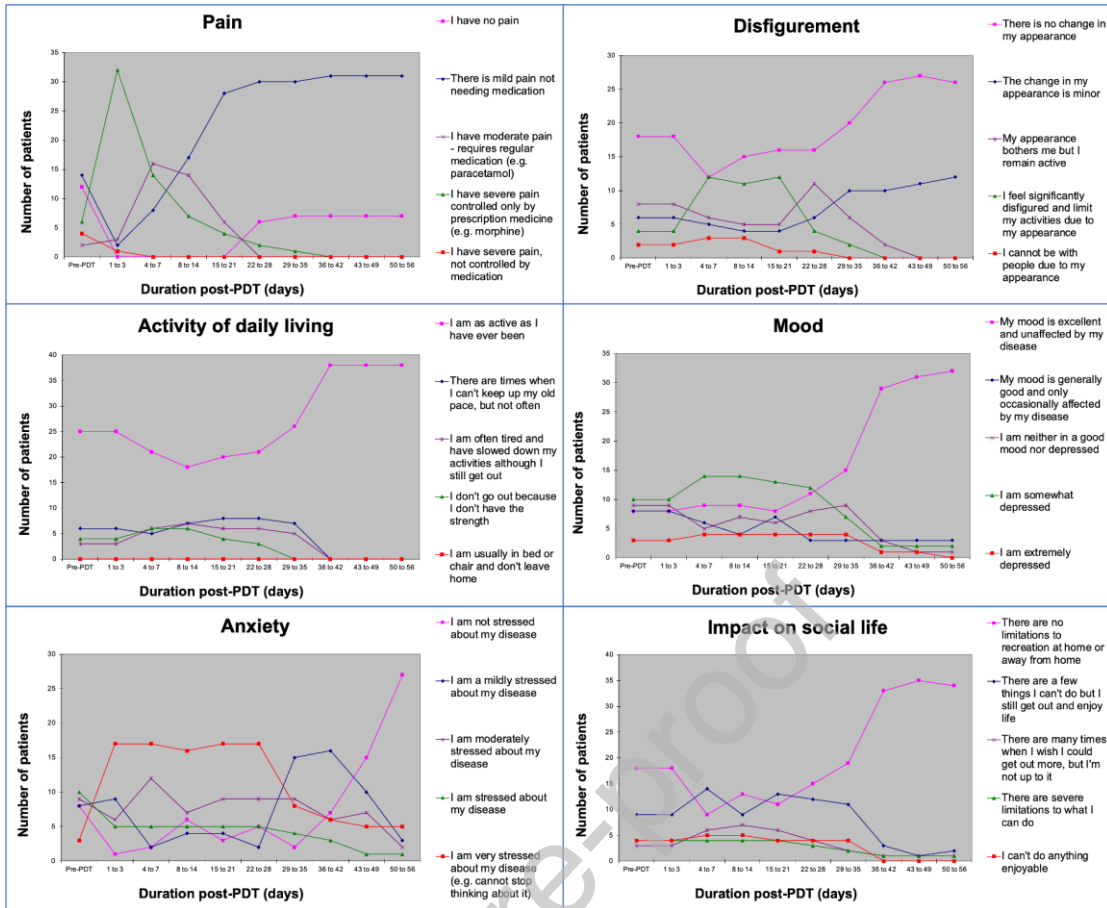


Fig. 2

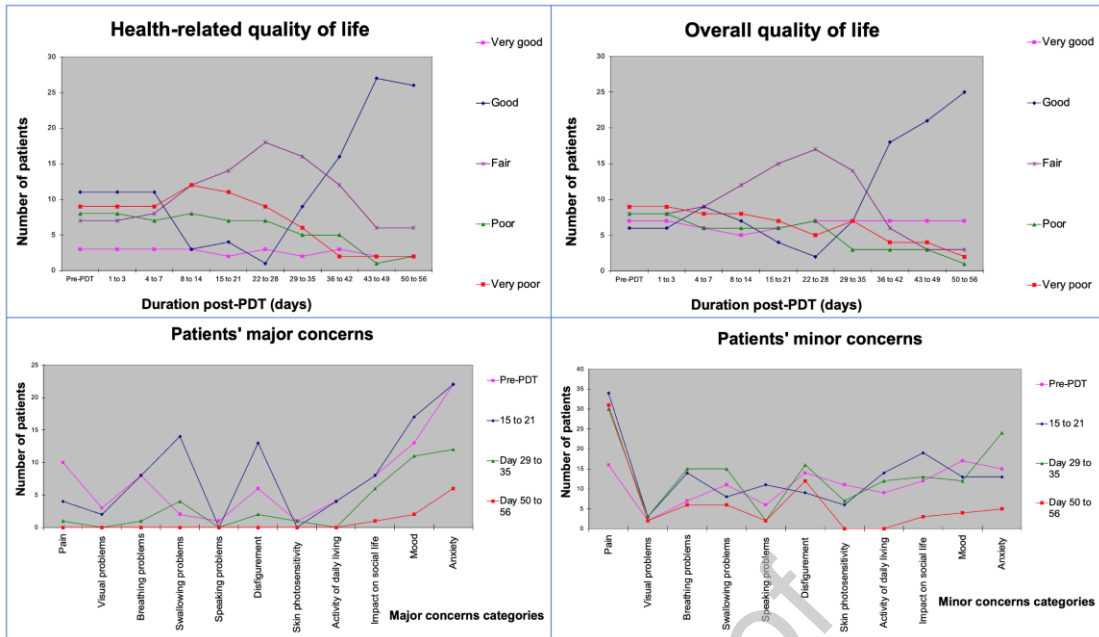


Fig. 3