

## RELATIONSHIP BETWEEN QUALITY OF LIFE AND HEALTH-RELATED MEASURES INCLUDING SYMPTOMS, BIOCHEMICAL MARKERS AND TUMOR BURDEN

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### ABSTRACT

**Objective:** Examine the relationship of quality of life measures in neuroendocrine tumor patients using the Norfolk QOL-NET by correlating the total questionnaire score with each of the Norfolk QOL-NET domains, with tumor burden, biochemical status and the Norfolk Carcinoid Symptom Score tool.

**Methods:** During their visits to the Neuroendocrine Unit at Eastern Virginia Medical School, 29 adult patients diagnosed with neuroendocrine tumor (s) signed the consent form and completed the Norfolk QOL-NET. Data related to current tumor burden, biochemical status and the validated Carcinoid Symptom Score was obtained from their files matching the date they completed the questionnaires.

**Results:** The Norfolk QOL-NET total score correlated positively with all of its domains - physical functioning (r=0.96, p<0.0001), Depression (r=0.73, p<0.001), gastrointestinal (r=0.78, p<0.001), Flushing (r=0.62, p<0.0003), respiratory (r=0.65, p<0.0002), positive attitude (r=0.52, p<0.004), and cardiovascular (r=0.46, p<0.012); with the Norfolk Carcinoid Symptom Score (r=0.6, p<0.0001); with tumor burden (r=0.52, p=0.004), and serotonin (r=0.62, p=0.013). Serotonin was the only biochemical marker that correlated positively with a poor quality of life in patients with neuroendocrine tumors.

**Conclusions:** We demonstrated a strong correlation between Norfolk QOL-NET and symptoms, biochemical markers and tumor burden. Norfolk QOL-NET seems sensitive to symptom change, physical functioning, respiratory and cardiovascular disease progression or remission. Norfolk QOL-NET should be an important tool for measuring patients' perception of the burden of their disease, relating to the tumor burden and the biochemical abnormality as well as the impact of treatment modalities. The Norfolk quality of life tool may also be a useful guide in deciding changes in therapy to alter apparent health status as well as an endpoint in clinical studies.

### OBJECTIVES

The purpose of this study was to examine the relationship of QOL measures in NET patients using Norfolk QOL-NET and its 7 domains with tumor burden, biochemistry and the Norfolk Carcinoid Symptom Score.

Permission: The Institutional Review Board at Eastern Virginia Medical School approved the administration of the Norfolk QOL-NET for development and validation purposes. All subjects gave informed consent to participate in the study and for the reporting of the information as de-identified data.

### BACKGROUND

To fulfill the need for a disease-specific tool to measure quality of life in patients with neuroendocrine tumors, the Norfolk QOL-NET was developed in 2004 at the Neuroendocrine Unit at Eastern Virginia Medical School. We aimed to capture the spectrum of symptoms and the impact of physical and psychological functioning related to NETs by eliciting patients' own perceptions of their illness. The questionnaire was developed using a rigorous design method that included an item pool from patient input and a panel of health-care professionals using the Delphi method to reach consensus on the questions for content validity. After approval by four national thought leaders who ensured that the items embraced all aspects of the disease, the QOL-NET was presented to a focus group of 20 patients and pilot tested for readability and content. All suggestions were discussed until the group reached meaningful and acceptable changes. We then explored the questionnaire's structure through interpretation of psychometric factor analysis; determined its discriminatory capability; analyzed its reliability and reproducibility and correlated the scores of the QOL-NET with tumor burden, biochemical markers, and symptom score.

Vinik EJ, Carlson, C.A., Silva, M.P., Vinik, A.I.  
Development of the Norfolk Quality of Life Tool for Assessing Patients with Neuroendocrine Tumors, *Pancreas*, 38: 3, 497-508, 2009.

### METHODS

Norfolk QOL-NET developed at the Neuroendocrine Unit at EVMS in 2004 72 Questions  
7 Domains  
Depression.....10  
Respiratory.....8  
Flushing.....8  
Gastrointestinal.....7  
Cardiovascular.....6  
Physical functioning.....26  
Positive Attitude.....3  
Treatment Questions.....4  
(included in the total score)

### SUBJECTS

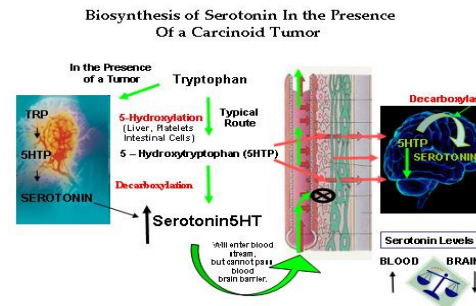
Patients (n)	Men	Women	Age Mean ± SD	Race
29*	17 (58.62%)	12 (41.38%)	59 ± 11 years	89.66% White

### Relationship between Total Norfolk QOL-NET, it's Domains, Tumor Burden, Biochemistry and Symptoms,

	Total Norfolk QOL		Domain 1 Depression		Domain 2 Flushing		Domain 3 Respiratory		Domain 4 Gastrointestinal		Domain 5 Disposition		Domain 6 Cardiovascular		Domain 7 Physical Functioning		Positive Attitude	
	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p
Total Norfolk QOL			0.73	<0.001	0.62	0.0003	0.65	0.0002	0.78	<0.001	0.46	0.012	0.96	<0.001	0.52	0.004		
Tumor Burden	0.52	0.0004	0.42	0.023	0.24	0.216	0.02	0.935	0.58	0.001	0.38	0.343	0.56	0.002	0.38	0.146		
Serotonin	0.62	0.013	0.76	0.03	0.98	0.78	0.32	0.25	0.62	0.033	0.29	0.3	0.62	0.013	0.32	0.07		
CgA	0.06	0.764	-0.11	0.433	-0.26	0.176	0.08	0.663	0.03	0.891	0.34	0.07	0.07	0.739	0.32	0.39		
Carcinoid Symptom Score	0.67	<0.0001	0.37	0.001	0.58	0.001	0.51	0.003	0.6	0.006	0.35	0.018	0.7	<0.001	0.59	0.009		

NORFOLK QOL-DN correlated with tumor burden (r=0.52, p=0.004), with Serotonin (r=0.62, p=0.013) and with the Norfolk Carcinoid Symptom Score (r=0.6, p<0.0001); Serotonin was the only biochemical marker that correlated positively with a poor QOL particularly depression in patients with neuroendocrine tumors. There was no correlation with Chromogranin A (CgA) or 5-HIAA (not shown).

### PROPOSED PATHOGENESIS OF DEPRESSION



### CONCLUSIONS

We showed a strong correlation between the total Norfolk QOL-NET score and each of its 7 domains with symptoms, tumor burden, and biochemical markers

The strongest correlation between the total Norfolk QOL-NET score and its domains, was with Physical Functioning

All the domains of the Norfolk QOL-NET - except for Depression - correlate positively with the Carcinoid Symptom Score

Tumor burden correlates with the Physical Functioning, Gastrointestinal and depression domains

Serotonin was the only biochemical marker that correlated with the total Norfolk QOL-NET score as well as with three domains: Physical Functioning, Gastrointestinal and Depression

The relationship between high levels of circulating Serotonin in patients with neuroendocrine tumors and poor quality of life, - particularly depression - led to the premise that SHTP, the precursor of serotonin is deviated into tumor production of serotonin, which does not cross the blood brain barrier leading to a deficiency in brain serotonin

Norfolk QOL-NET is sensitive to symptom change, physical functioning, respiratory and cardiovascular progression or remission

Norfolk QOL-NET may be a useful guide for changes in therapy to alter apparent health status as well as an end-point in clinical studies