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Validation and cross-cultural adaptation of the questionnaire ThyPRO in thyroid patients in Serbia

Primena upitnika ThyPRO kod bolesnika sa oboljenjem štitaste žlezde u Srbiji

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Abstract

Backgraund/Aim. The Thyroid Specific Patient Reported Outcome Measure (ThyPRO) questionnaire is self-administered and intended to measure quality of life of thyroid patients. The aim of this study was to investigate the validity and reliability of the translated new, ThyPRO questionnaire in Serbian patients with thyroid disease. **Methods.** The translation process followed an internationally accepted methodology. The questionnaire was validated in 100 consecutive thyroid patients hospitalized in a tertiary level hospital, between April and August 2012. Internal reliabilities of ThyPRO scales were assesessed using Cronbach's α coefficient. Association between age, gender, education, marital and employment status, place of living, diagnosis, current treatment, hormonal status and patient quality of life were determined using Pearson's (*r*) and Spearman's (*ϱ*) correlation coefficients. **Results.** Internal consistency and reliability for ThyPRO scales were satisfactory. Cronbach's α coefficients of 13 multi-item scales of the ThyPRO were > 0.83 (range 0.83–0.95). The scores, obtained by this questionnaire, correlated significantly with patients gender, employment status, diagnosis, current treatment and place of living. A highly significant inverse relationship was found between scores and hormonal status as well as between scores and disease duration. Patients' age, marital status and thyroid-stimulating hormone level did not influence any scale score. **Conclusion.** The ThyPRO may be useful in measuring health-related quality of life in patients with thyroid disease in Serbia.

Key words:
quality of life; questionnaires; thyroid diseases; hypothyroidism; hyperthyroidism.

Apstrakt

Uvod/Cilj. Upitnik za kvalitet života osoba sa oboljenjem štitaste žlezde *The Thyroid Specific Patient Reported Outcome Measure* (ThyPRO) je upitnik za samostalno popunjavanje i meri kvaliteta života tih bolesnika. Cilj ovog rada bio je da se ispita validnost i pouzdanost novog prevedenog specifičnog upitnika, ThyPRO kod bolesnika sa bolešću štitaste žlezde u Srbiji. **Metode.** Proces prevođenja je obavljen uz poštovanje internacionalno prihvaćene metode prevođenja upitnika. Upitnik je validiran na 100 uzastopnih bolesnika sa bolešću štitaste žlezde, koji su bili hospitalizovani od aprila do avgusta 2012. godine u instituciji tercijarnog nivoa zdravstvene zaštite. Interna pouzdanost skala ThyPRO upitnika je ispitana pomoću Cronbach-ovog α koeficijenta. Povezanost godina, pola, nivoa obrazovanja, bračnog statusa, zaposlenosti, mesta življenja, dijagnoze, trenutne terapije, hormonskog statusa i kvaliteta života bolesnika ispitana je korišćenjem Pearson-ovog (*r*) i Spearman-ovog (*ϱ*) koeficijenta korelacije. **Rezultati.** Interna konzistencija i pouzdanost skala ThyPRO upitnika je bila zadovoljavajuća. Cronbach-ov α koeficijent je bio veći od 0.83 (0.83–0.95) za 13 skala ThyPRO upitnika. Skorovi su statistički značajno korelirali sa polom bolesnika, zaposlenošću, dijagnozom, sadašnjom terapijom i mestom življenja. Visoko statistički zanačajan inverzni odnos je otkriven između skorova i hormonskog statusa i skorova i dužine trajanja bolesti. Godine starosti, bračni status i nivo tireostimulišućeg hormona nisu uticali na skorove ni jedne skale ovog upitnika. **Zaključak.** Upitnik ThyPRO se može koristiti u ispitivanju kvaliteta života povezanog sa zdravljem kod bolesnika sa bolešću štitaste žlezde u Srbiji.

Ključne reči:
kvalitet života; upitnici; tireoidna žlezda, bolesti; hipotireoidizam; hipertireoidizam.

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Introduction

The new thyroid-specific quality of life patient-reported outcome measure (ThyPRO) for benign thyroid disorders, is a specific quality of life questionnaire newly developed in Denmark, by Watt et al. [1–5]. It is the first specific questionnaire for patients with different thyroid diseases which was validated and standardized. The questionnaire includes 13 domains that cover physical and mental symptoms, well-being, function, and the impact of thyroid diseases on social and daily life and the overall health-related quality of life (HRQoL) of patients with thyroid diseases. The suffix PRO, in the name of the questionnaire, means 'patient report outcome', a term that is increasingly used instead of HRQoL. The questionnaire went through the four phases of the development: issue generation in which HRQoL issues of possible relevance for thyroid diseases were identified; operationalization in which relevant issues were selected and converted into items in a draft questionnaire; pre-testing in which a draft questionnaire was tested and revised based on problems observed within cognitive interviews; and quantitative scale validation to test internal consistency, reliability and validity of the constructed scale on a large sample of patients.

The questionnaire was validated and found to be useful in clinical studies. ThyPRO has been translated in 7 languages and culturally adapted [1–5].

The aim of this study was to investigate validity and reliability of the translated and culturally adapted ThyPRO questionnaire in a group of 100 patients with thyroid disease in Serbia.

Methods

The Serbian version of ThyPRO (ThyPROsr) questionnaire was conducted in 100 consecutive patients with thyroid diseases hospitalized in a tertiary level hospital for thyroid surgeries from April to August 2012. Inclusion criteria were: age over 16 years, benign thyroid disease and obtained written informed consent. Ethical approval for the study was received from the Ethics Committee of the Medical Faculty, University of Belgrade, Serbia. Exclusion criteria were major psychiatric disorders, proven malignancy and severe, chronic disease. All of the 102 patients admitted in this period fulfilled the inclusion criteria, but 2 of them had major psychiatric disorder and were excluded from this study. Since thyroid surgery is elective surgery, no patient had severe chronic disease that might influence HRQoL.

In this study HRQoL was assessed by ThyPROsr questionnaire. ThyPRO consists of 84 items, covering physical and mental symptoms, well-being and everyday life functioning and the impact of thyroid disease on participation, social and daily life. Items are grouped in 13 scales, goitre symptoms, hyperthyroid symptoms, hypothyroid symptoms, eye symptoms, tiredness, cognitive impairment, anxiety, depressivity, emotional susceptibility, impaired social life, impaired daily life, impaired sex life, cosmetic complaints, and 1 single item which measures general HRQoL. Each of the 13 ThyPRO scales is scored as a summary score and linearly transformed to the range 0–100 with increasing scores indicating decreasing HRQoL, meaning more symptoms or greater impact of disease. In addition, ThyPRO contains one item not included in any multi-item scale [5].

According to the internationally accepted methodology for translation and cultural adaptation of a HRQoL questionnaire, we followed the guidelines set up by the European Organisation for Research and Treatment of Cancer (EORTC) group [6] for the production of Serbian version of ThyPRO. This translation process involved 5 steps. Firstly, two independent translations of English version of ThyPRO questionnaire into Serbian were performed by two independent professional translators whose native language is Serbian with excellent knowledge of English language. Then, better of these two translations, was chosen as a "forward translation" by the coordinator. Then, "forward translation" was re-translated into English by professional whose native language is English with excellent knowledge of Serbian language. The developer of ThyPRO, Serbian coordinator, two qualified translators, clinicians and epidemiologist discussed controversial items to generate a version of the ThyPROsr which would be the most appropriate for the cultural environment of Serbia and acceptable for testing on thyroid patients. Then, in order to check the Serbian population's understanding and interpretation of the translated items, cognitive interviews were conducted within five thyroid patients, by the appropriate consultant recruited from the Health Research Associates (HRA). Finally, the results of these tests were discussed in the same group of experts. That stage led to the final Serbian version of ThyPRO. In order to assess patient's acceptability of ThyPROsr, the mean time required for completing the questionnaire was measured. The patients answered the questionnaire in the presence of a physician, who dealt with HRQoL assessment, so there was no missing data, nor reading and/or writing problems. Sociodemographic data and information about comorbidity were collected using demographic questionnaire. Other necessary data, laboratory results, previous and current treatment, exact diagnosis and duration of disease were collected from medical records.

ThyPROsr scale scores were calculated as a row summary scores, and then were linearly transformed to the range of 0–100. Lower values indicate better HRQoL, while higher values indicate worse HRQoL.

Internal reliabilities of ThyPROsr scales were assessed for multiple item scales using Cronbach's α coefficient. Cronbach's α coefficient ranges from 0–1, where 1 means perfect reliability.

Clinical validity was assessed comparing means of the summary scores with patient's age, gender, education, marital and employment status, place of living, clinical diagnosis, disease duration, current treatment and hormonal status. Pearson's (r) and Spearman's (q) correlation coefficients were used to investigate the relationship between the scores and the main clinical and demographic variables, as

suitable. A $p < 0.05$ was regarded significant. All the tests were formulated 2-tailed.

Results

The average age of the 100 consecutive patients included in the study was 48.77 years, and 88% of them were female, 12% male. All of them completed ThyPROsr questionnaire in the presence of the physician who dealt with HRQoL assessment and endocrine surgery. All the patients comprehend the questionnaire. There were no missing data. The average time to complete the questionnaire was 16 minutes.

Demographic and clinical characteristics of the patients with thyroid disease are shown in Table 1.

Table 1
Demographic and clinical characteristics of patients with thyroid disease

Characteristics	Values
Gender, n (%)	
female	88 (88)
male	12 (12)
Age (years), $\bar{x} \pm SD$	48.77 ± 13.13
Education (years), n (%)	
0–10	17 (17)
11–13	49 (49)
14–16	13 (13)
> 16	21 (21)
Marital status, n (%)	
single	12 (12)
married/unmarried couple	74 (74)
divorced	9 (9)
widow	5 (5)
Current employement status, n (%)	
unemployed	27 (27)
employed	45 (45)
retired	24 (24)
student	4 (4)
Diagnosis, n (%)	
non toxic goitre	51 (51)
toxic goitre	20 (20)
Graves' disease withTAO	19 (19)
Graves' disease without TAO	3 (3)
Hashimoto disease	7 (7)
Disease duration (years), $\bar{x} \pm SD$	7.23 ± 7.98
Current treatment, n (%)	
L-thyroxine	8 (8)
antithyroid drugs	30 (30)
other	0 (0)
none	62 (62)
Hormonal status, n (%)	
euthyroid	72 (72)
subclinical hypothyroid	3 (3)
subclinical hyperthyroid	25 (25)
hypothyroid	0 (0)
hyperthyroid	0 (0)

TAO – thyroid associated ophthalmopathy; $\bar{x}$ – mean value; SD – standard deviation.

Most of the patients accepted the questionnaire well, found it clear enough and easily understandable, while none of the items found to be unpleasant and embarrassing. Just one male patient, age of 68, found items concerning sexual function and satisfaction irrelevant, and one female patient, age 18, answered the questions concerning sexual function and satisfaction although she had no sexual experience yet.

The mean scale scores, internal consistencies (Cronbach's α) and reliabilities for these 13 scales ranged from 0.832 on hypothyroid symptom scale to 0.951 on cognitive problems scale (Table 2).

A significant relationship emerged between gender and cosmetic complaints scale ($\rho = -0.232$; $p < 0.05$), with higher scores in females indicating lower HRQoL in this domain. Also, we found a significant inverse relationship between education and goitre symptom scale ($\rho = -0.249$; $p < 0.05$) and education and eye symptom scale ($\rho = -0.222$; $p < 0.05$), with better HRQoL in the higher educated patients. Employment status significantly correlated with hyperthyroid symptom scale ($r = 0.203$; $p < 0.05$) and anxiety scale ($r = 0.198$; $p < 0.05$) with the employed patients scoring lower, indicating better HRQoL. Disease duration significantly correlates with goitre symptoms scale ($\rho = 0.221$; $p < 0.05$), cognitive problems scale ($\rho = 0.220$; $p < 0.05$) and impaired sex life scale ($\rho = 0.206$; $p < 0.05$), with shorter disease duration scoring lower, indicating better HRQoL. Significant inverse relationships emerged between hormonal level and some ThyPRO health items. Thyroxine (T4) level significantly correlated with impaired social life scale ($r = -0.276$; $p < 0.05$), hypothyroid symptoms scale ($r = -0.256$; $p < 0.05$) and eye symptoms scale ($r = -0.230$; $p < 0.05$). Triiodothyronine (T3) level significantly correlated with impaired social life scale ($r = -0.277$; $p < 0.05$). Higher T4 and T3 level scored lower scores on these ThyPRO health rating scales. Other factors significantly affecting symptom scale scores were: place of living, current treatment and diagnosis. We also found a significant correlation between current treatment and impaired daily life scale ($\rho = -0.272$; $p < 0.01$) and current treatment and cosmetic complaints scale ($\rho = -0.301$; $p < 0.01$), with lower scoring and better HRQoL in patients without current treatment. Domicile significantly correlated with impaired social life scale ($\rho = 0.198$; $p < 0.05$), showing that patients who lived in the capital, Belgrade, had better social life than patients who live in a country town or in a village. The diagnosis correlated with cosmetic complaints scale ($\rho = 0.323$; $p < 0.01$). The patients with non toxic and toxic goitre had less cosmetic complaints than those with Grave's disease-associated ophthalmopathy, thyreoid-associated ophthalmopathy (TAO), Grave's without TAO and Hashimoto disease. Patient's age, marital status and thyrotropine (TSH) level did not influence any scale score.

Discussion

ThyPROsr was found understandable and it was well accepted in Serbian patients with thyroid disease. The patients had physicians help and supervision during completion of the questionnaire, as it was the case in similar studies previously conducted in Serbian patients [7]. There was no

missing data. None of the items were found embarrassing by the patients. Just 2 patients commented items concerning sexual function and satisfaction as irrelevant.

In Serbian thyroid patients, internal consistency reliability for ThyPROsr scales ranged from 0.832 on hypothyroid symptom scale to 0.951 on cognitive problems scale. These reliability coefficients in Serbian patients with thyroid diseases indicate that the scales assessed by the ThyPROsr were appropriately measured.

Table 2

Descriptive statistics and reliability for the Serbian version of Thyroid Specific Patient Reported Outcome Measure (ThyPROsr)

Scales of measurement	Non toxic goitre (n = 51)	Toxic goitre (n = 20)	Graves' disease with TAO (n = 19)	Graves' disease without TAO (n = 3)	Hashimoto disease (n = 7)
	$\bar{x} \pm SD$	$\bar{x} \pm SD$	$\bar{x} \pm SD$	$\bar{x} \pm SD$	$\bar{x} \pm SD$
Goitre symptoms scale	25.22 ± 18.05	24.09 ± 18.54	22.37 ± 18.59	8.33 ± 8.60	33.44 ± 31.65
Hyperthyroid symptoms	28.49 ± 20.43	30.78 ± 19.59	39.97 ± 25.72	15.62 ± 14.32	31.25 ± 17.30
Hypothyroid symptoms scale	30.15 ± 25.08	26.62 ± 19.96	41.45 ± 28.35	37.50 ± 37.50	36.61 ± 37.05
Eye symptoms scale	16.73 ± 15.73	14.37 ± 15.62	37.01 ± 29.80	4.17 ± 7.22	11.61 ± 7.15
Tiredness scale	47.97 ± 24.64	53.04 ± 20.93	52.82 ± 28.71	51.19 ± 32.21	49.49 ± 22.34
Cognitive problems scale	22.79 ± 22.54	22.71 ± 23.28	18.42 ± 20.19	25.00 ± 43.30	8.93 ± 11.39
Anxiety scale	37.34 ± 26.80	30.00 ± 18.56	42.10 ± 28.53	34.72 ± 28.36	37.50 ± 20.41
Depressivity scale	38.30 ± 23.09	35.36 ± 16.95	41.16 ± 29.22	40.48 ± 48.49	38.26 ± 17.46
Emotional susceptibility	32.84 ± 23.91	29.17 ± 16.03	35.96 ± 25.18	42.59 ± 33.14	30.95 ± 24.08
Impaired social life scale	15.32 ± 18.51	14.37 ± 17.10	20.72 ± 30.12	27.08 ± 46.91	18.75 ± 35.90
Impaired daily life scale	21.32 ± 24.22	18.96 ± 24.72	30.92 ± 28.98	31.94 ± 35.92	31.55 ± 25.78
Impaired sex life scale	28.19 ± 34.26	27.50 ± 37.30	40.79 ± 32.50	33.33 ± 28.87	39.29 ± 42.35
Cosmetic complaints scale	14.79 ± 18.01	23.33 ± 21.52	29.60 ± 27.07	30.56 ± 31.27	36.31 ± 24.38

TAO – thyroid associated ophthalmopathy; $\bar{x}$ – mean value; SD – standard deviation.

Over the last few years there has been increasing focus on the HRQoL of the patients with thyroid cancer and patients with overt thyroid dysfunction. Limited reports are available on the HRQoL of patients with euthyroid or subclinical hyperthyroid or hypothyroid benign thyroid diseases [8–11]. We have identified several studies which evaluate the influence of different types of thyroid surgeries on HRQoL of the patients with benign thyroid diseases and low-risk, well-differentiated, thyroid carcinoma [12–14]. Studies which investigate factors that might influence HRQoL of patients with different benign thyroid disease, are lacking. To the best of our knowledge just two studies have investigated HRQoL in patients with different benign thyroid diseases, using ThyPRO. In those studies, none of the objective factors, including age, gender and type of thyroid dysfunction had a significant effect on patients' HRQoL [15,16].

We found highly significant inverse relationship between T4 and T3 level in euthyroid patients and some of HRQoL items, such as hypothyroid and eye symptoms and impaired social life. TSH did not influence any component of HRQoL. However, previous studies revealed somewhat different results. Most of the studies investigated HRQoL in thyroid cancers survivors. HRQoL is significantly better in patients under TSH-supressive doses of levothyroxine than in short-term hypothyroid patients, after 4 weeks of levothyroxine withdrawal [17]. It was also been shown that the HRQoL is worse in overt and subclinical hyperthyroid and hypothyroid patients than in healthy control group [18], but it normalizes upon achicving euthyroid state [19]. Some studies have shown that patients with lower TSH level have worse HRQoL [20–22], while other showed, similarly as our study, that TSH level does not influence HRQoL [22–24]. Patients with shorter lasting disease had significantly less goitre symptoms, cognitive problems and impaired sex life, indicating better HRQoL, than patients with longer lasting disease. Hoftijzer et al, [22] in their study reported the same findings. We have found less cosmetic complaints in male than in female patients. Significantly better HRQoL in males has been previously shown in several studies [25,26]. Higher educated patients had significantly better quality of life in some domains, goitre symptoms and eye symptom, than patients with lower education, quite similarly as demonstrated by Tan et al. [27] in their study. Being employed had a positive influence on some aspects of HRQoL, as it was presented by Tan et al. [27]. Patients with non toxic and toxic goitre had less cosmetic complaints and better quality of life than patients with autoimmune thyroid diseases, TAO, Graves without TAO and Hashimoto thyroiditis. Although, Miccoli et al. [28] had shown in their study that type of thyroid disease had no influence on HRQoL, recent studies have supported the hypothesis that thyroid autoimmunity *per se* affects the HRQoL regardless of hormonal status [16,29,30]. In our study, patient's age and marital status did not influence the HRQoL. Quite different results have been previously published. Miccoli et al. [28] also did not find significant difference in HRQoL depending on patient's age, but some other studies showed that HRQoL is better in younger patients as could be expected [25,27,31,32].

Conclusion

Serbian version of ThyPRO is a well accepted questionnaire. When administered with the help and supervision of the physician, it is easily filled-in, with no missing data. Reliability and validity of Serbian version of ThyPRO were good. Serbian version of ThyPRO questionnaire can be used for assessing health-related quality of life in Serbian patients with various benign thyroid disease.

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