Impact of total thyroidectomy on quality of life at 6 months: the prospective ThyRQoL multicentre trial

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Abstract

Objective: This study is to determine the impact of complications after total thyroidectomy on health-related quality of life (HR-QoL) and to identify significant predictive factors of HR-QoL changes. HR-QoL is usually impaired in patients with thyroid diseases compared to the general population. Thyroidectomy is largely performed in the case of benign thyroid benign and can be associated with long-term complications (vocal cord palsy, hypoparathyroidism).

Design: The prospective ThyRQoL multicenter trial (NCT02167529) included 800 patients who underwent total thyroidectomy for benign or malignant non-extensive disease in seven French referral hospitals between 2014 and 2016.

Methods: HR-QoL was assessed using the MOS 36-item short form health survey (SF-36) self-questionnaire with a 6-month follow-up.

Results: We observed a significant improvement of HR-QoL 6 months after surgery ($P < 0.0001$). Postoperative complications were associated with a non-significant impairment of HR-QoL. In multivariable analysis, Graves' disease was associated with a significant improvement of HR-QoL (OR = 2.39 [1.49; 3.84]) and thyroid malignant disease with an impairment of HR-QoL (OR = 1.44 [0.99; 2.08]) after thyroidectomy.

Conclusion: We observed a significant improvement of HR-QoL 6 months after total thyroid surgery for benign thyroid disease.

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Introduction

Health-related quality of life (HR-QoL) is usually impaired in patients with thyroid diseases compared to the general population (1). Symptoms related to thyroid dysfunction,

compressive symptoms in the case of large goiter or orbitopathy in Graves' disease, or diagnosis of thyroid cancer may contribute to impair HR-QoL (1, 2). However,

even in the absence of symptoms, HR-QoL deterioration is still observed (1).

Thyroidectomy for benign disease is the most commonly performed endocrine surgery worldwide. Patients are particularly concerned about the potential consequences of thyroid surgery on their HR-QoL (3). Despite favorable outcomes, especially in the case of benign thyroid diseases, thyroidectomy can be associated with long-term, postoperative complications, the most frequent ones being vocal cord palsy (VCP) and hypoparathyroidism. Their incidence varies respectively from 0.5 to 20% and from 19 to 38% (4, 5, 6). Even in patients without complications, thyroidectomy may have a significant impact on daily life due to lifetime hormonal replacement (2, 7) or discomfort caused by persistent functional voice or swallowing symptoms (8, 9).

Hypoparathyroidism and voice disorders have been associated with HR-QoL impairment (9, 10, 11). Hormonal changes may also be involved in postoperative HR-QoL, especially because the adequate restoration of previous thyroid function is difficult to assess (7). The optimization of HR-QoL should be a main objective, especially in patients for whom the efficacy of the treatment is difficult to assess according to standard criteria.

The aims of this study were (1.) to determine the impact of complications after total thyroidectomy on HR-QoL in a large population and (2.) to identify significant predictive factors of HR-QoL changes.

Methods

Study design

From September 2014 to December 2016, patients with benign or non-extensive malignant thyroid pathologies, scheduled to undergo total thyroidectomy in seven French referral centers (Angers University Hospital, Limoges University Hospital, Nancy Regional University Hospital, Nantes University Hospital, Pitié-Salpêtrière Hospital, South Lyon Hospital Complex, and Vendée Hospital Centre), were prospectively included in this single-arm study. Exclusion criteria were age under 18 years, pregnancy or breastfeeding, suspected or confirmed medullary thyroid cancer, clinically and/or radiologically enlarged cervical lymph node(s), and preoperative voice disorders with confirmed VCP (Fig. 1).

The national committee 'Commission Nationale Informatique et Libertés' (CNIL) and the local ethics committees 'Comité Consultatif sur le Traitement

de l'Information en Matière de Recherche' (CCTIRS) and 'Groupe Nantais d'Ethique dans le Domaine de la Santé' (GNEDS) approved this study (CNIL #914165; CCTIRS #14.105; GNEDS #2012-06-07). All patients provided signed informed consent before surgery. The study is registered with ClinicalTrials.gov number NCT02167529, as the 'Quality of Life after Thyroidectomy (ThyrQoL)' study.

Procedures

Surgery was performed under general anesthesia with tracheal intubation. The surgical procedure consisted of extracapsular total thyroidectomy through a collar incision with a midline opening of the fascia. The strap muscles were not cut unless required. Accurate dissection close to thyroid capsule and single ligatures of superior lobe vessels were performed in order to preserve the external branch of superior laryngeal nerve. Recurrent laryngeal nerves (RLNs) were routinely identified and preserved, possibly with the help of intraoperative neuromonitoring (IONM, Medtronic®, Jacksonville, FL, USA), the use of which was left to the surgeon's choice. Lymph node dissection (central neck dissections only) was performed if malignant disease was suspected preoperatively or on frozen section. The decision of node dissection was made intraoperatively by the surgeon according to her/his habits. Drainage was left to the discretion of the surgeons. Replacement therapy with levothyroxine was introduced on the day after surgery, according to each center standard protocol. For RAI therapy dose, patients with T2N1a had 100 mCi; the rest of the cancer patients (T1N0, T1N1 and T2N0) had 30 mCi.

Outcome variables

Demographic, clinical, and biological (calcium, TSH) data were prospectively collected during the preoperative period and second and sixth months after surgery.

Plasma levels of calcium were measured on the day after surgery. Measurements were repeated if serum calcium was <2 mmol/L (80 mg/L) on postoperative day 2, along with the measurement of parathyroid hormone level (PTH). Hypoparathyroidism was defined by a postoperative serum calcium <2 mmol/L and requirement for calcium and/or vitamin D supplementation. It was defined as transient if solved within 6 months after surgery and permanent if persistent beyond 6 months after surgery.

Figure 1

Flowchart for the trial (ClinicalTrials.gov NCT02167529). A full color version of this figure is available at <https://doi.org/10.1530/EJE-19-0587>.

Pre- and postoperative laryngeal examinations were not systematic but performed only in the case of voice abnormality. VCP was defined as transient if solved within 6 months after surgery and permanent if persistent beyond 6 months after surgery.

Preoperative self-questionnaires were given to the patients during the preoperative consultation and collected at admission; postoperative self-questionnaires were sent to the patients and returned by mail 2 and 6 months after surgery.

HR-QoL assessment

The MOS 36-item short form health survey (SF-36) was used to assess pre- and postoperative HR-QoL. The SF-36 questionnaire is the most extensively used and validated generic instrument for measuring HR-QoL (12), including after thyroid surgery (13, 14, 15). It has been validated in its French translated version (16).

The SF-36 is a self-administrated questionnaire containing 36 items that describe eight dimensions of health: physical functioning (PF), social functioning (SF), role limitations due to physical problems (role physical – RP), bodily pain (BP), general mental health (MH), role limitations due to emotional problems (role emotional – RE), vitality (VT), and general health perception (GH) (17). Two summary scores can be computed: physical (PCS) and mental (MCS). All dimension and summary scores are scaled from 0 to 100, the higher the score the better the HR-QoL is. Variations of at least 5 and 2.5 points were considered as the minimally, clinically important differences for dimension and composite scores respectively (18).

Statistical analysis

The primary endpoint was defined as the variation of the mental health score of the SF-36 questionnaire between preoperative visit and postoperative month 6. MH score was chosen because we estimated that postoperative morbidity should have a greater impact on mental condition than on physical state.

Based on an expected incidence of complications between 3% and 4% at postoperative month 6 and an effect size on an anxiety scale between patients with and without complications estimated at 0.5 according to literature, calculations showed that 780 patients should be included to achieve a power of 80% and significance level of 0.05 (19).

We compared SF-36 scores between each endpoint using the ratio between patients' scores and the published reference scores of a sex- and age-matched French reference population (20). This ratio represents the percentage of the expected scores obtained by the patients, the expected scores being those of individuals of the same gender and age category, representative of the French general population. By definition, the general population has a mean ratio of 100%.

Statistical analysis was performed following the intention to treat principle: statistical analyses are realized on all the included patients. Univariable analysis was performed using two-sample *t*-tests and χ^2 tests for continuous and categorical variables respectively. Multivariable analysis was performed using logistic regression. Statistical analyses were performed using the Stata software version 15 (StataCorp). Multivariable analysis was performed using logistic regression. All the significant variables at 25% were retained for this multivariate analysis, and then the variables not significant at 5% have been dropped one by one (Stepwise procedure). Graphics were made using Microsoft Excel version 14 (Microsoft Corporation).

Results

Patients' characteristics and perioperative status

Eight hundred patients were enrolled and included in this study. Their perioperative characteristics are summarized in Table 1. The most frequent surgical indication was benign nodular goiter (69%) (Fig. 1).

The classification of malignant tumor was T1NO for 116 patients, T1N1 for 36 patients, T2NO for 11 patients, and T2N1 for 27 patients. None were T3 or T4 or M1 in TNM classification. Seven hundred and ninety-one patients (99%) underwent total thyroidectomy, while nine (1%) had lobectomy, because of IONM signal loss after the resection of the first lobe (decision made intraoperatively by the surgeon).

HR-QoL evolution after surgery

Seven hundred and twenty-one patients (90%) completed the three SF-36 questionnaires. Forty-nine patients (6%) completed two SF-36 questionnaires including the preoperative questionnaire. Thirty patients (4%) completed only one questionnaire (Fig. 2 and Table 2).

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Table 1 Patients characteristics and perioperative outcomes, $n = 800$.

Characteristics	Values
Patients' characteristics	
Mean age at surgery, mean (years) $\pm$ s.d.	51.15 $\pm$ 13.48
Gender, n (%)	
Male	144 (18)
Female	656 (82)
Surgical indication, n (%)	
Benign nodular goiter	556 (69.5)
Graves' disease	112 (14)
Nodule with Bethesda IV cytology	54 (6.75)
Other [†]	78 (9.75)
Surgery, n (%)	
Total thyroidectomy	791 (98.9)
Unilateral lobectomy	9 (1.1)
Use of IONM	473 (59.1)
Unilateral IONM loss of signal	43 (9.1)
Associated lymph node dissection	88 (11)
Associated parathyroid procedure	93 (11.6)
Histological diagnosis, n (%)	
Benign thyroid disease	610 (76.25)
Malignant tumor*	190 (23.75)
Papillary thyroid cancer	161 (84.7)
Follicular thyroid cancer	27 (14.2)
Other ^Δ	9 (4.7)
Multiple malignant tumors	71 (37.4)
Tumor size [¶] , mm; median [Q ₁ ; Q ₃]	9 [3; 16]
N+	26 (13.7)
Associated thyroiditis	207 (25.9)
Thyroid weight, (g); median [Q ₁ ; Q ₃]	30.8 [20; 55]
Postoperative outcomes	
Immediate postoperative complications, n (%)	
Re-operation for hematoma ^c	11 (1.4)
Transient VCP [‡]	36 (4.5)
Transient hypoparathyroidism [‡]	87 (10.9)
Mean hospital length stay, (day)	1.88 $\pm$ 3.7
mean $\pm$ s.d.	
Median off-work duration, (day) median [Q ₁ ; Q ₃]	25 [18; 35]
Long-term postoperative complications, n (%)	
Permanent VCP [#]	6 (0.8)
Permanent hypoparathyroidism [§]	44 (5.5)

[†]Prophylactic thyroidectomy for familial history of medullary thyroid cancer, iatrogenic dysthyroidism, unspecified; *Seven patients had two different tumor types; ^ΔMedullary thyroid cancer ($n = 3$), Thyroid metastasis ($n = 2$), Solitary fibrous tumor ($n = 1$), Thyroid tumor of uncertain malignant potential ($n = 1$), Thyroid oncocyctic tumor ($n = 1$), Unspecified tumor ($n = 1$); [¶]Mean tumor size considering the largest tumor; ^cRe-operation for bleeding or compressive hematoma during the first 24 h postoperatively; [‡]Postoperative VCP solved within 6 months after the surgery; [#]Postoperative VCP persisting 6 months after the surgery; ^ΔHypocalcaemia <2 mmol/L at hospital discharge; [§]Need for calcium and/or vitamin D supplements on postoperative month 6. IONM, intraoperative neuromonitoring; TSH, thyroid Stimulating Hormone; VCP, vocal cord palsy.

SF-36 score ratios were higher 2 months after surgery for GH (94% vs 91%; $P=0.0112$) and MH (92% vs 87%; $P<0.0001$), showing improved QoL in these

domains (Table 2). At the 6-month evaluation, all the ratios were significantly higher than those obtained at the preoperative visit, reflecting improved QoL in all SF-36 QoL domains (Fig. 2 and Table 2). In absolute terms, differences between preoperative and 6-month score were clinically relevant (>5 points) for emotional domains (SF, RE) but not for physical domains.

HR-QoL evolution compared to the general French population

Compared to the sex- and age-matched French reference population, SF-36 scores were significantly lower in our population in almost all domains, both before and after surgery (Table 3).

Factors associated with HR-QoL significant changes

No statistically significant differences in SF-36 dimension or composite scores were observed, neither between patients with or without permanent hypoparathyroidism (Fig. 3) nor between patients with or without permanent VCP 6 months after surgery.

In bivariate analysis, thyroidectomy for Graves' disease ($P<0.0001$), thyroid weight ($P=0.0281$), and diagnosis of thyroid malignant tumor ($P=0.017$) were associated with significant changes of the SF-36 MH score at the 6-month evaluation, defined by a variation of 5 points or more (Table 4). In multivariable analysis, age, sex, BMI, thyroidectomy for Graves' disease, thyroid weight, and diagnosis of malignant tumor were tested. In multivariable analysis, thyroidectomy for Graves' disease remained significantly associated with an improvement of the MH score 6 months after surgery (OR=2.39 [1.49; 3.84]). There was a trend toward the impairment of the MH score in patients diagnosed with thyroid malignant tumor (OR=1.44 [0.99; 2.08]). Interestingly, complications were significantly more frequent in patients with lymph node dissection: 15% vs 6% at month 2 ($P=0.002$) and 15% vs 5% at month 6 ($P<0.001$).

Impact of total thyroidectomy on professional activity

Median off-work duration after total thyroidectomy was 25 days [18; 35].

It significantly increased in the case of postoperative complications (42 days [30; 73] vs 24 days [18; 34]; $P=0.0003$). Permanent VCP (112 days [44; 180]; $P=0.0468$)

Figure 2

Evolution of SF-36 ratios on postoperative month 6 (ratio between the score of the population of the study and a French reference population matched on age and sex).

and permanent hypoparathyroidism (46 days [30; 76]; $P=0.0014$) both specifically increased off-work period significantly compared to patients without permanent complications.

Discussion

This prospective multicenter observational study (without intervention – patients received standard care, i.e. thyroidectomy for thyroid disease) reports statistically significant improvement in HR-QoL after total thyroidectomy for benign thyroid diseases, using the validated questionnaire SF-36 at 6 months. This improvement, observed in all the eight measured domains of HR-QoL, was more important for mental health scores.

These results are similar to those found in the literature (21, 22, 23, 24, 25, 26, 27, 28).

At the second postoperative month evaluation, a statistically significant improvement was already observed for GH and MH scores, whereas the RP score was significantly decreased, before increasing above baseline values at month 6. Sorensen *et al.* showed similar evolution patterns in HR-QoL evolution after surgery, but with an initial improvement more marked and persistent up to postoperative month (28). Generally, the worse the preoperative HR-QoL, the more important the HR-QoL improvement was (23, 24, 25, 26, 27, 28).

Preoperative HR-QoL was significantly impaired in our population compared to a French referral population. Despite significant improvements after surgery, postoperative HR-QoL remained impaired compared to the general population. The improvement seemed to be more important in mental domains as measured by SF-36, compared to physical domains. We have no formal explanation for the difference of HR-QoL between the general population and 6-month post thyroidectomy patients. We may hypothesize that our follow-up is too short to observe a 'normal' HR-QoL after thyroidectomy. Most of the studies also find a persistent impairment compared to general population. Some studies described an improvement in HR-QoL after surgery up to general population levels; the longer the follow-up, the more the HR-QoL tends to be close to that of general population (29, 30, 31).

The most relevant factor influencing HR-QoL improvement was Graves' disease. Other studies report the improvement of HR-QoL after surgery for Graves' disease, but the superiority of surgery compared to medical treatment or iodine therapy has not been

Table 2 Evolution of SF-36 scores: ratios between the scores of our study population and those of the French reference population matched on age and sex.

SF-36 scores	Before surgery (%)	2 months after surgery (%)	P	6 months after surgery (%)	P
PF	99	100	0.49	102	0.0003
RP	90	81	<0.0001	96	0.0039
BP	97	100	0.054	101	0.0132
GH	91	94	0.0112	95	0.0002
VT	81	79	0.14	88	<0.0001
SF	87	89	0.32	95	<0.0001
RE	85	84	0.48	94	<0.0001
MH	87	92	<0.0001	94	<0.0001
PCS	99	99	0.0190	101	0.20
MCS	88	89	0.087	94	<0.0001

A ratio of 100% reflects a similarity in our population and in the reference population.

BP, bodily pain; GH, general health perception; MCS, mental composite score; MH, general mental health; PCS, physical composite score; PF, physical functioning; RE, role-emotional; RP, role-physical; SF, social functioning; VT, vitality.

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Table 3 Comparison of SF-36 scores between the study population and the French reference population matched on age and sex, before surgery, at month 2 and at month 6.

SF-36 scores	ThyrQoL population (mean $\pm$ S.D.)	Ratio of the scores to the sex- and age-matched French reference population (mean $\pm$ S.D.)	P
Preoperative			
PF	81.8 $\pm$ 20.35	99% $\pm$ 26%	0.0145
RP	72.32 $\pm$ 36.79	90% $\pm$ 48%	<0.0001
BP	69.19 $\pm$ 26.16	97% $\pm$ 37%	0.0063
GH	61.95 $\pm$ 19.77	91% $\pm$ 30%	<0.0001
VT	47.65 $\pm$ 21.51	81% $\pm$ 37%	<0.0001
SF	70.17 $\pm$ 25.27	87% $\pm$ 32%	<0.0001
RE	68.32 $\pm$ 38.03	85% $\pm$ 48%	<0.0001
MH	58.4 $\pm$ 20.74	87% $\pm$ 31%	<0.0001
PCS	49.51 $\pm$ 8.62	99% $\pm$ 18%	0.1960
MCS	41.79 $\pm$ 11.5	88% $\pm$ 24%	<0.0001
Postoperative month 2			
PF	82.57 $\pm$ 19.59	100% $\pm$ 25%	0.2377
RP	64.36 $\pm$ 40.43	81% $\pm$ 53%	<0.0001
BP	71.09 $\pm$ 24.41	100% $\pm$ 36%	0.6327
GH	63.77 $\pm$ 20.16	94% $\pm$ 31%	<0.0001
VT	46.69 $\pm$ 21.28	79% $\pm$ 37%	<0.0001
SF	71.47 $\pm$ 24.98	89% $\pm$ 32%	<0.0001
RE	67.31 $\pm$ 40.1	84% $\pm$ 51%	<0.0001
MH	61.64 $\pm$ 19.87	92% $\pm$ 30%	<0.0001
PCS	48.96 $\pm$ 8.24	99% $\pm$ 18%	0.0046
MCS	42.55 $\pm$ 11.75	89% $\pm$ 25%	<0.0001
Postoperative month 6			
PF	84.13 $\pm$ 20.34	102% $\pm$ 26%	0.2687
RP	76.65 $\pm$ 35.23	96% $\pm$ 46%	0.0007
BP	71.94 $\pm$ 25.76	101% $\pm$ 36%	0.5912
GH	64.55 $\pm$ 20.57	95% $\pm$ 31%	<0.0001
VT	51.88 $\pm$ 20.51	88% $\pm$ 35%	<0.0001
SF	76.05 $\pm$ 23.3	95% $\pm$ 29%	<0.0001
RE	75.45 $\pm$ 37.02	94% $\pm$ 47%	<0.0001
		94% $\pm$ 29%	
MH	63.1 $\pm$ 19.46	94% $\pm$ 29%	<0.0001
PCS	50.01 $\pm$ 8.66	101% $\pm$ 18%	0.4308
MCS	44.61 $\pm$ 10.94	94% $\pm$ 23%	<0.0001

BP, bodily pain; GH, general health perception; MCS, mental composite score; MH, general mental health; PCS, physical composite score; PF, physical functioning; RE, role-emotional; RP, role-physical; SF, social Functioning; VT, Vitality.

proven (32, 33). Graves' disease has been shown to be associated with particularly impaired HR-QoL, which could explain these good results (1, 23).

In contrast, we found that the diagnosis of malignant tumor was associated with postoperative HR-QoL impairment. The knowledge of having thyroid cancer can impair HR-QoL, although these tumors usually have favorable long-term prognosis (34, 35). Adjuvant iodine therapy could be implicated in this impairment, even though we did not report iodine therapy as a significant factor of HR-QoL modification. The 6-month duration of follow-up in our study could also explain this result, as studies with longer follow-up periods report the improvement of HR-QoL after thyroid surgery for malignant disease (29, 31).

But several other studies showed that even years after initial therapy, thyroid cancer survivors still have a decreased QoL (36, 37, 38, 39). We may hypothesize that the higher rate of complications in patients who underwent lymph node dissection (15% vs 5% at month 6) could explain this impairment.

We did not find a statistically significant impact of postoperative complications on HR-QoL. Postoperative complications had a negative impact on HR-QoL, although decrease of SF-36 scores after complication did not reach significance. Professional activity was significantly impaired by complications, leading to a doubled off-work period in our study. Work ability and HR-QoL have been proved to be closely related, suggesting a relevant impact of complications after total

Figure 3

Comparison of SF-36 scores on postoperative month 6 between patients without complication and patients with hypoparathyroidism (differences were not statistically significant).

thyroidectomy (40). Off-work period was 10 days longer than that recommended in France; meanwhile, standard off-work period at hospital discharge was 3 weeks. It suggests that more than half of our patients felt the need for extended work stoppage.

We report a non-significant decrease of all the SF-36 scores at 6 months in the case of permanent hypoparathyroidism. All the studies that investigated the relationships between HR-QoL and hypoparathyroidism reported a significant impairment of HR-QoL, irrespective of the cause of hypoparathyroidism (41, 42, 43). Standard treatment of hypoparathyroidism, consisting of calcium and vitamin D supplementation, does not allow the substitution of the missing hormone or the restoration of normal phospho-calcic metabolism. Moreover, PTH receptor located in the CNS could be implied (44). Supplementation with 1-84 PTH has shown good results in HR-QoL improvement (45).

VCP was not associated with HR-QoL modification in our study although vocal impairment is traditionally associated with diminished HR-QoL (46, 47). Spector *et al.* reported HR-QoL impairment in the case of VCP (10). However, the impact of voice alteration on HR-QoL is highly variable across patients (48, 49). The use of IONM, leading to lobectomy rather than thyroidectomy in case of loss of signal, could have avoided bilateral VCP, which could have severely impaired HR-QoL.

We did not find a significant effect of hormonal balance on HR-QoL. These results are similar to those of literature, in which no significant impact of hormonal

substitution has been shown on HR-QoL (49, 50, 51, 52, 53). However, the serum TSH levels defining hormonal balance are debated and no protocol of hormonal substitution has shown superiority (54, 55).

The main limitation of our study could be the choice of a generic rather than a disease-specific questionnaire of HR-QoL (33). Thyroid-specific patient reported outcome (ThyPRO), the most commonly used specific questionnaire to assess HR-QoL in thyroid diseases, has been described as more sensitive than SF-36 for therapeutic evaluation (56). HR-QoL modifications, more pronounced with ThyPRO than with SF-36, might have shown more meaningful results (26, 27). However, we believe that SF-36 score allows a general QoL evaluation, regardless of the underlying thyroid disease or specific thyroidectomy-related morbidity. It has also the advantage to be the most extensively used and validated generic instrument for measuring HR-QoL (12). Moreover, SF-36 has been validated in French, which is not the case of the ThyPRO questionnaire.

Another limitation is the heterogeneity of the included patients with benign goiters, small cancers, and Graves' diseases. The management of thyroid cancer, including lymph node dissection and iodine therapy, significantly differs from the management of benign disease. Anymore, the clinical impact of Graves' disease and benign goiter is different. The underlying disease may override postoperative complications.

The relatively high rate of permanent hypoparathyroidism, defined by the need of calcium and/or vitamin D supplementation, can be questioned. Some physicians may maintain patients with treatments, regardless of it formally required.

Another limitation is due to the absence of systematic postoperative vocal cords examination. This may underestimate our permanent VCP rate. Finally, because of too many missing data, the impact of RAI therapy on QoL could not be evaluated in our series.

Moreover, we did not study the impact of quality of wound healing or swallowing disorders after surgery, which could be a confounding factor (8). Our results are supported by a large population and mostly by an excellent follow-up on postoperative month 6.

Most patients with thyroid disease experience significantly impaired HR-QoL. Our results, issued from a large multicenter prospective study, show a significant improvement of HR-QoL after total thyroid surgery for benign thyroid disease. However, postoperative HR-QoL scores did not reach those of a reference sex- and age-matched population. Postoperative complications did not impair significantly the HR-QoL changes. Thyroidectomy

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Table 4 Factors associated with a significant modification of postoperative MH score at postoperative month 6 (bivariate analysis).

Characteristics	MH score decrease ≥ 5 (n = 205) (28%)	Stable MH score (Δ MH ≤ 5) (n = 189) (26%)	MH score increase ≥ 5 (n = 340) (46%)	P
Age, mean $\pm$ s.d. (year)	52.7 $\pm$ 13.2	52.8 $\pm$ 12.9	50.4 $\pm$ 13.4	0.052
Sex				0.065
Male	22%	21%	15%	
Female	78%	79%	85%	
BMI				0.15
BMI < 18 kg/m ²	3%	1%	3%	
BMI 18-25 kg/m ²	42%	51%	49%	
BMI 25-30 kg/m ²	30%	30%	26%	
BMI ≥ 30 kg/m ²	25%	18%	22%	
Professional activity				0.89
Active worker	65%	67%	66%	
Unemployed	35%	33%	34%	
Preoperative THS level				0.26
Serum TSH < 0.2 μ UI/L	14%	15%	17%	
Serum TSH 0.2-4 μ UI/L	82%	81%	76%	
Serum TSH > 4 μ UI/L	4%	4%	7%	
Surgical indication				< 0.0001
Benign nodular goiter	81%	73%	66%	
Graves' disease	4%	12%	19%	
Nodule Bethesda IV	7%	7%	6%	
Other*	8%	8%	9%	
Associated lymph node dissection	12%	13%	9%	0.37
Associated parathyroid procedure [†]	14%	10%	10%	0.53
Re-operation for hematoma [‡]	2%	2%	1%	0.44
Permanent hypoparathyroidism [§]	6%	4%	6%	0.58
Permanent VCP [‡]	$< 1\%$	1%	1%	0.88
Malignant tumor	32%	26%	21%	0.017
Associated thyroiditis	26%	27%	28%	0.86
Thyroid weight, mean $\pm$ s.d. (g)	75.3 $\pm$ 19.2	72.6 $\pm$ 18.5	71.6 $\pm$ 18.8	0.0281
Postoperative radioactive iodine therapy	17%	12%	13%	0.29
Euthyroidism at 6-month postoperative (Serum TSH 0.2-4 μ UI/L)	73%	72%	75%	0.76

*Medullary thyroid cancer (n = 3), thyroid metastasis (n = 2), solitary fibrous tumor (n = 1), thyroid tumor of uncertain malignant potential (n = 1), thyroid oncocytic tumor (n = 1), unspecified tumor (n = 1); [†]Re-operation for bleeding or compressive hematoma during the first 24 hours postoperatively;

[‡]Associated parathyroidectomy and/or reimplantation; [§]Need for calcium and/or vitamin D supplements on postoperative month 6; [‡]Postoperative VCP persisting 6 months after the surgery.

MH, General mental health.

for malignant disease was associated with an impairment of HR-QoL.

Our study may provide information to physicians and surgeons, to help them in choosing the most appropriate treatment; it may also help in providing the patients with better information on what to expect after total thyroidectomy in terms of HR-QoL, depending on their disease, especially in the case of Graves' disease.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this study.

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