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Advanced age does not increase morbidity after total thyroidectomy. Result of a prospective study

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ABSTRACT

Background: It is well known that total thyroidectomy is feasible on elderly patients but is linked to complications because of their underlying comorbidities. In this study we analyzed the specific risks linked to surgery, hypoparathyroidism and recurrent nerve palsy.

Methods: materials-methods:Prospective, multicentre trial conducted at 13 hospital sites. The primary endpoint was the percentage of patients with postoperative hypocalcaemia (albumin-corrected serum calcium level <2 mmol/L at day 2). Secondary endpoints included recurrent nerve palsy rate at day 2, the percentage of patients with hypocalcaemia (serum calcium level <2 mmol/L) and recurrent nerve palsy at month 6, operating durations and postoperative pain. Patients were separated in two groups: <70 years and ≥70 years old.

Results: In total, 1329 patients who underwent total thyroidectomy were included (median age 51.17 years [18.10; 80.90], 80% women, and hyperthyroidism in 20%, 101 ≥70 years old). Rates of hypocalcaemia at day 2 and month 6 were 20.02% and 1.98% respectively. Nasofibroscopy showed postoperative abnormal vocal cord motility in 9.92% cases (hypo-motility 5.76% - immobility 4.16%) and 0.95% at month 6 (hypo-motility 0.48%, immobility 0.48%). Patients ≥70 years had a lower (but non-significant) postoperative and definitive hypocalcaemia rate than patients < 70 years: 14.85% vs 20.44% at day 2 ($p = 0.1773$) and 0% vs 2.15% at month 6 respectively ($p = 0.2557$). Abnormal vocal cord motility rate was 12.00% in patients ≥70 years vs 9.75% in patients <70 years at day 2 ($p = 0.4702$), and 2.06% in patients ≥70 years vs 0.86% at month 6 ($p = 0.2340$).

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Conclusions: Total thyroidectomy in patients ≥70 years is feasible and safe. Age does not increase the morbidity.
The study is registered with ClinicalTrials.gov number NCT01551914.
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Introduction

According to the World Health Organization (WHO), the proportion of people aged 60 and over in the world population will almost double between 2015 and 2050, from 12% to 22%. Thyroid disorders and presence of thyroid nodules increase with age. According to Gervasi et al.[1] in 2012, 90% of women over 60 years and 80% of men over 80 years presented with thyroid nodules. The prospective cohort of Gervasi and the prospective comparative study of Tartaglia in 2014 showed the feasibility of total thyroidectomy in elderly people.[1,2] Indeed, they highlighted similar early (bleeding, seroma, transient hypocalcaemia, postoperative recurrent laryngeal nerve palsy (RLNP)) and permanent (hypoparathyroidism, permanent RLNP) postoperative complications in young and elderly patients. However, some studies[3] revealed complications linked to the vulnerability of elderly people because of underlying comorbidities. Postoperative specific morbidity has rarely been studied. Therefore, this raises the question of optimal perioperative management in the elderly to obtain an overall benefit from surgery without decompensation of underlying fragility.

An exact definition of the geriatric patient does not exist in medical literature. There are many age definitions: 60 years, 65 years and 75 years.

The WHO defines a person as elderly from the age of 60 years. In French regulations, the age of 60 has been adopted for certain benefits or provisions relating to the elderly.

However, geriatric problems (comorbidities, loss of autonomy, fragility) concern relatively few individuals aged 60–70 years.

Therefore, our study targeted a population ≥70 years likely to have comorbidities. The objective was to focus on the surgical risk, in other words, to analyse if RLNP and hypoparathyroidism rates following total thyroidectomy were increased in patients aged ≥70 years.

Methods

Study design and participants

The FOThyr study was a prospective, multicentre, single blind trial, with patients enrolled at 13 sites in France.[4] All patients, aged 18–80 years, scheduled to undergo total thyroidectomy (TT) were eligible for enrolment into the trial if they had Graves' disease, toxic or non-toxic thyroid goitre, or any thyroid nodule requiring TT under cervicotomy. The exclusion criteria were: thyroid cancer, known or suspected preoperatively based on ultrasound or cytological assessment (to avoid lymph node dissections associated to thyroidectomy); a calcitonin level >30 pg/mL; planned partial thyroidectomy; abnormal motility of vocal cords; sub sternal goiter (>3 cm below the sternal notch); surgery using videoscopy; and prior history of cervical surgery. Preoperative calcium, phosphorus, calcitonin, TSH and albumin serum measurements were obtained for all patients. Preoperative vocal cord examination was only performed in cases with voice abnormality.

The protocol was reviewed and approved by our regional ethics committee (Comité de Protection des Personnes Ouest IV N° 58/2012) and by the CNIL (Commission Nationale de l'Informatique et des Libertés N°1170319). The study was performed in accordance with the Good Clinical Practice Guidelines and the Declaration of Helsinki. All patients provided written informed consent before randomization, without any stipend.

Procedures

All thyroidectomies were performed according to the same protocol, except for the utilization of intra-operative neuromonitoring (IONM, Medtronic, Jacksonville, FL, USA) which was left to surgeons' choice. After cervical Kocher incision, infra-hyoid muscles were opened along the midline and muscles were divided as necessary. Vessels of the upper pole were cut, preserving the external branch of the superior laryngeal nerve (whenever possible). Then, the parathyroid glands (whenever possible) and the recurrent laryngeal nerve (RLN) (mandatory) were visualized. Postoperative drainage was left at the surgeon's discretion. All surgeons were experienced in thyroid surgery (more than 30 a year) and used IONM for at least 1 year. For all patients operated on with IONM, RLN was systematically tested via a sterile single-use pulse-generated monopolar stimulator probe with a stimulation level at 1.0 mA, as previously described.[5] Thyroid hormone replacement was introduced on postoperative day 1.

Outcomes and evaluations

The primary endpoint was the percentage of patients with hypocalcaemia at day 2 (serum calcium level <2 mmol/L corrected for albumin level). Blood calcium and albumin tests were performed in the laboratories of the local hospitals. Secondary endpoints included the percentage of patients with hypocalcaemia (serum calcium level <2 mmol/L corrected for albumin level) at month 6, recurrent laryngeal nerve palsy (RLNP) at day 2 and at month 6, evaluation of postoperative pain, and duration of procedures. RLN function was evaluated by systematic vocal cord examination with nasofibroscopy, carried out before hospital discharge, and at 6 months after surgery in case of postoperative abnormal motility. Clinical examination was performed by the surgeon during hospitalization to detect haematomas. Pain was evaluated at 4 h, 18–24 h and 2 days after surgery, using a numeric pain rating scale and use of analgesic drugs; this information was collected by a ward nurse.

Statistical analysis

Hypocalcaemia at day 2 and at month 6 and transient RLNP rate and definitive RLNP were compared between age groups (<70 years old versus ≥ 70 years old) with Chi-square test and Fisher test. Postoperative pain was compared between the two groups with linear mixed models taking into account repeated measures. Operative times were compared between groups with Student *t*-test. A p-value less than 0.05 was considered statistically significant. Statistical analyses performed with the software SAS® version 9.3. The study is registered with ClinicalTrials.gov number NCT01551914.

Results

Patients

From March 2012 to June 2014, 1329 patients were enrolled in the study at our 13 sites, 267 men and 1062 women. Median age was 51.17 years [18.10; 80.90]. Median BMI (kg/m^2) was 25.58 [16.36; 56.39] and median TSH level (μunits/mL) was 0.80 [0.00; 82.30]. In this cohort, 995 patients were in euthyroidism (79.6%). Total thyroidectomy was performed in 1297 patients (97.8%). The histopathological examination revealed 21.91% of incidental thyroid cancers, mostly of the papillary type (median size of cancers was 6 mm). These patients were included since thyroid cancer had not been known or suspected preoperatively. Lymph node dissection (LND) (central in all cases) was performed in 14.14% of cases (41 patients), with a median number of 5 (1–11) nodes harvested. One hundred and one patients were ≥70 years old (7.60%) and 1228 were under 70 years (92.40%).

Postoperative data (hypocalcaemia and RLNP rates) are presented in Tables 1 and 2.

Twenty percent of the patients had postoperative hypocalcaemia with a median age of 48.34 years [18.20; 80.42]. There was no statistically significant difference between the 2 groups ($p = 0.1773$) but a trend of a lower hypocalcaemia rate for people ≥70 years old; 14.85% versus 20.44%. There was no difference of RLNP rate between the 2 groups ($p = 0.4702$). Nine patients had no postoperative vocal cords examination.

People older than 70 years were in less pain ($p = 0.0245$) (Table 3a). No global difference of operating time was found between the two groups. Results are detailed in Table 3b.

At month 6, there was no difference of hypocalcaemia rate between the 2 groups ($p = 0.2557$). Data were missing for 16 patients. At month 6, there was no difference of RLNP rate between the 2 groups ($p = 0.2340$). However, data was missing for 67 patients.

Discussion

With continued growth of life expectancy, aging of population leads to a growth in detection of thyroid problems in elderly patients and, as a consequence, in the number of potential thyroidectomy in elderly patients.

Our study is the largest prospective study evaluating surgical specific complications of total thyroidectomy. Little postoperative data was missing. This work is in line with literature[6,7]; there are no more complications related to surgery in elderly people. In other words, total thyroidectomy is feasible for people over 70 years old without increasing recurrent and parathyroid morbidity.

Review of literature concerning the results and safety of thyroid surgery in elderly shows various conclusions. Firstly, the cross-sectional study of Sosa et al.[8] showed differences of complication rates between the 2 groups (elderly and young patients). These differences were both surgical and non-surgical. Morbidity rate was lower in young patients. More precisely, these results concerned perioperative complications rates, endocrine specific complications rates (hoarseness and hypocalcaemia), hospital mortality, mean total costs, and length of stay at hospital. But it should be emphasized that surgery was conducted by non-expert surgeons.

Grogan et al.,[9] in a prospective cohort, included patients between 16 and 89 years old. They reported more complications in elderly; 5%, versus 1%. These complications were all not linked to surgery but linked to underlying comorbidities: cardiac, respiratory, infectious … In the unicentre study of Mekel et al.,[3] non-surgically related complications were significantly more frequent in the elderly (18.9%) compared to young patients (5.2%).

On the other hand, the review of Ng et al., in 2012,[10] the retrospective studies of Bliss et al., Passler et al., Lang et al., Syebt et al.,[11–14] comparing surgical and non-surgical complications of total thyroidectomy in elderly versus young people, observed that total thyroidectomy was feasible in elderly people given the low percentage of complications: 3% for surgical complications and 4.5% for non-surgically related complications. Authors reported no difference of morbidity according to age. Moreover, there was no difference concerning surgical complications between elderly and young people regardless of study. All these results show that age does not increase surgical complications. These studies are based on large populations. Most of them are however based on single institutions and retrospective, without specialized high-volume units. A recent study compared the rate of postoperative complications in patients aged over 65 years (elderly) and over 80 years (super-elderly) to patients aged 21 through 40 years after thyroid surgery in ambulatory conditions.[15] Outpatient thyroid surgery was as safe in appropriately selected elderly and super-elderly patients as it was in a control group of youthful patients. Therefore, at time of ambulatory surgery, age alone cannot contra-indicate it.

Moreover, little data concerning postoperative pain is available in literature. In our study, postoperative pain was not different according to age. Duration of the procedure was also similar in both groups.

Despite this study is large and prospective, it has some limitations.

Firstly, thyroid cancers preoperatively diagnosed and substernal goitres were not included; it is known that they increase with age and that it is a real surgical indication in the elderly person even with comorbidities. Another limitation was that the participating centres were specialized in endocrine surgery, but we did not take into account the real experience of each surgeon concerning total thyroidectomy.

Finally, this study was not designed to compare morbidity of

Table 1
Age and hypocalcaemia at day 2: univariate analysis.

		<70 years N = 1228	≥70 years N = 101	Total N = 1329	p-value
Hypocalcaemia day 2	No	977 (79.56%)	86 (85.15%)	1063 (79.98%)	0.1773
	Yes	251 (20.44%)	15 (14.85%)	266 (20.02%)	

Table 2
Recurrent laryngeal nerve palsy at day 2: univariate analysis.

RLNP	<70 years N = 1300	≥70 years N = 29	Total N = 1320	p-value
Missing Data	8	1	9	0.4702
Yes	119 (9.75%)	12 (12.00%)	131 (9.92%)	
No	1101 (90.25%)	88 (88.00%)	1189 (90.08%)	

Table 3a
Age and pain Gobal effect of age on the three times of measure: p = 0.0245.

		<70 years old N = 1228	≥70 years old N = 101	Total N = 1329	p-value
Operating duration	N	1189	94	1283	0.0832
	Min-Max	[30.00; 328.00]	[41.00; 262.00]	[30.00; 328.00]	
	Average	101.42	94.59	100.92	
	Standard deviation	42.73	35.99	42.30	
	Median	93.00	90.00	92.00	

Table 3b
Operating duration and age.

		<70 years old N = 1228	≥70 years old N = 101	Total N = 1329
Pain H04	Average	2.81	2.68	2.80
	Standard deviation	2.07	2.00	2.06
Pain H18-H24	Average	2.03	1.47	1.99
	Standard deviation	1.85	1.45	1.83
Pain Day 2	Average	1.24	0.93	1.22
	Standard deviation	1.61	1.31	1.59

patients between <70 years and ≥70 years. This limits its power. Nevertheless, the results are those of a large series and are reflect of the real-life practice in thyroid surgery.

Conclusion

Despite these limitations, we conclude that age is not a risk factor of morbidity after total thyroidectomy: Age does not significantly increase the morbidity of total thyroidectomy in patients older than 70 years of age.

Conflicts of interest

Author Eric Mirallié has received a speaker honorarium from Company Medtronic

Niki Christou declares that she has no conflict of interest.
Claire Blanchard declares that she has no conflict of interest.
François Pattou declares that he has no conflict of interest.
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Fréderic Sebag declares that he has no conflict of interest.
Franck Jegoux declares that he has no conflict of interest.
Emmanuel Babin declares that he has no conflict of interest.
Alain Bizon declares that he has no conflict of interest.
Cécile Caillard declares that she has no conflict of interest.
Muriel Mathonnet declares that she has no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.amjsurg.2018.07.029.

References

1. Gervasi R, Orlando G, Lerose MA, et al. Thyroid surgery in geriatric patients: a literature review. *BMC Surg*. 2012 Nov 15;12(1):S16.
2. Tartaglia F, Russo G, Sgueglia M, et al. Total thyroidectomy in geriatric patients: a retrospective study. *Int J Surg*. 2014 Oct 1;12:S33–S36.
3. Mekel M, Stephen AE, Gaz RD, et al. Thyroid surgery in octogenarians is associated with higher complication rates. *Surgery*. 2009 Nov;146(5):913–921.
4. Blanchard C, Pattou F, Brunaud L, et al. Randomized clinical trial of ultrasonic scissors versus conventional haemostasis to compare complications and economics after total thyroidectomy (FOThyr). *BJS Open*. 2017;1(1):2–10.
5. Mirallié E, Caillard C, Pattou F, et al. Does intraoperative neuromonitoring of recurrent nerves have an impact on the postoperative palsy rate? Results of a prospective multicenter study. *Surgery*. 2017 Nov 8;2018(163):124–129. https://doi.org/10.1016/j.surg.2017.03.029. Epub.
6. Canonico S, Pellino G, Pameggiani D, et al. Thyroid surgery in the elderly: a comparative experience of 400 patients from an Italian University hospital. *Int Surg*. 2014 Sep 1;99(5):523–527.
7. Guarino S, Di Cosimo C, Chiesa C, et al. Perioperative care in elderly patients undergoing thyroid surgery. *Int J Surg*. 2014 Oct 1;12:S78–S81.
8. Sosa JA, Mehta PJ, Wang TS, et al. A population-based study of outcomes from thyroidectomy in aging Americans: at what cost? *J Am Coll Surg*. 2008 Jun 1;206(6), 1097–105.
9. Grogan RH, Mitmaker EJ, Hwang J, et al. A population-based prospective cohort study of complications after thyroidectomy in the elderly. *J Clin Endocrinol Metab*. 2012 May 1;97(5):1645–1653.
10. Ng SH, Wong KP, Lang BHH. Thyroid surgery for elderly patients: are they at increased operative risks? *J Thyroid Res*. 2012.
11. Bliss R, Patel N, Guinea A, et al. Age is no contraindication to thyroid surgery. *Age Ageing*. 1999 Jul 1;28(4):363–366.
12. Passler C, Avanessian R, Kaczirek K, et al. Thyroid surgery in the geriatric patient. *Arch Surg*. 2002 Nov 1;137(11):1243–1248.
13. Lang BH-H, Lo CY. Total thyroidectomy for multinodular goiter in the elderly. *Am J Surg*. 2005 Sep 1;190(3):418–423.
14. Seybt MW, Khichi S, Terris DJ. Geriatric thyroidectomy: safety of thyroid surgery in an aging population. *Arch Otolaryngol Neck Surg*. 2009 Oct 1;135(10):1041–1044.
15. Grubey JS, Raji BS, Duke WS, et al. Outpatient thyroidectomy is safe in the elderly and super-elderly. *Laryngoscope*. 2017 Jun 2;128(1):290–294. https://doi.org/10.1002/lary.26707, 22018 Jan Epub.