Hyperparathyroidism in octogenarians: A plea for ambulatory minimally invasive surgery under local anesthesia

Hyperparathyroïdie primaire de l’octogénaire : aspect clinique et intérêt de la chirurgie mini-invasive sous anesthésie locale en ambulatoire

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Abstract

Background. – With the current aging of the world’s population, diagnosis of primary hyperparathyroidism is being reported in increasingly older patients, with the associated functional symptomatology exacerbating the vicissitudes of age. This retrospective study was designed to establish functional improvements in older patients following parathyroid adenomectomy under local anesthesia as outpatient surgery. Materials and methods. – Data were collected from 53 patients aged 80 years or older who underwent a minimally invasive parathyroid adenomectomy. All patients underwent a preoperative ultrasound, scintigraphy, and were monitored for the effectiveness of the procedure according to intra- and postdosage of parathyroid hormone (PTH) at 5 min, 2 h and 4 h. Results. – Mean preoperative serum calcium level was 2.8 mmol/L (112 mg/L) and mean PTH was 180 pg/ml. Thirty-eight patients were operated under local anesthesia using minimally invasive surgery and 18 patients were operated under general anesthesia. In 26 cases, the procedure was planned on an outpatient basis but could only be carried out in 21 patients. Fifty-one patients had normal serum calcium and PTH levels during the immediate postoperative period. Two patients were reoperated under general anesthesia, since immediate postoperative PTH did not return to normal. Four patients died due to reasons unrelated to hyperparathyroidism. Five patients were lost to follow-up six months to two years postsurgery. Of the 44 patients (83%) with long-term monitoring for PTH, none had recurrence of biological hyperparathyroidism. Excluding the three asymptomatic patients, 38 of the 41 symptomatic patients (93%) with long-term follow-up were considering themselves as “improved” or “strongly improved” after the intervention, notably with respect to fatigue, muscle and bone pain. Two patients (4.9%) reported no difference and one patient (2.4%) said her condition had worsened and regretted having undergone surgery. Conclusion. – In patients 80 years or older, minimally invasive surgery as an outpatient under local anesthesia offered an excellent risk/benefit ratio given its many advantages: simplicity, speed, absence of general anesthesia, ease of monitoring, direct voice control intraoperatively, very low morbidity, effectiveness in treating primary hyperparathyroidism in more than 95% of first intention patients, and the possibility of immediate or delayed recovery in the event of multiglandular disease going unnoticed.

Keywords: Parathyroids; Primary hyperparathyroidism; Non invasive surgery; Outpatient surgery; Parathyroidectomy under local anesthesia

Résumé

Introduction. – Le vieillissement actuel de la population amène à poser le diagnostic d’hyperparathyroïdie primaire chez des patients de plus en plus âgés dont la symptomatologie fonctionnelle aggrave les vicissitudes de l’âge. Notre étude a pour but est de présenter les améliorations fonctionnelles apportées par l’adénomectomie parathyroïdienne sous anesthésie locale et en chirurgie ambulatoire. Matériel et méthode. – Cinquante-trois sujets de plus de 79 ans ont été opérés par chirurgie mini-invasive. Tous les patients ont subi une échographie, une scintigraphie, et un contrôle de l’efficacité de l’intervention par des dosages per- et postopératoires de la PTH à 5 min, 2 h et 4 h. Résultats. – La calcémie moyenne était de 2,8 mmol/L (112 mg/L), la PTH de 180 pg/ml. Trente-huit patients ont été opérés sous anesthésie locale en chirurgie ambulatoire. Les patients âgés de plus de 80 ans ont été considérés comme “améliorés” ou “très améliorés” par rapport à l’intervention, notamment à propos de la fatigue, de la douleur musculaire et osseuse. Deux patients (4,9%) n’ont pas ressenti de différence et un patient (2,4%) a déclaré que son état avait empiré et regreté d’avoir été opéré. Conclusion. – Chez les patients de plus de 80 ans, la chirurgie mini-invasive en ambulatoire offre un excellent rapport bénéfice-risque, propice à l’optimalité de la prise en charge des patients atteints de maladie multiglandulaire, avec une faible morbidité et une réduction de la durée d’hospitalisation.

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mini-invasive et 18 patients ont été opérés sous anesthésie générale. Dans 26 cas, l’intervention a été réalisée en ambulatoire mais celle-ci n’a pu être effective que 21 fois. Cinquante et un patients présentaient, en postopératoire immédiat, des valeurs normales de calcémie et de PTH. La courbe postopératoire immédiate de PTH n’était pas revenue dans les valeurs normales chez deux patients qui ont été ré-opérés, sous anesthésie générale. Dans un délai de 6 mois à 2 ans, 4 patients sont décédés sans rapport avec l’hyperparathyroïdie, 5 patients ont été perdus de vue. En revanche, nous avons pu contrôler 44 patients (83 %). Aucun ne présentait de récidive de l’hyperparathyroïdie biologique. Sur le plan subjectif, hors les trois patients asymptomatiques qui le restaient, 38 patients se sont dits « amélioré » ou « très amélioré » à la suite de l’intervention (93 %) en particulier sur le plan de l’asthénie, des douleurs musculaires et osseuses, 2 patients n’ont ressenti aucune différence (4,9 %), une patiente s’est dite « aggravée » regrettant l’acte opératoire (2,4 %). Conclusion. – Chez le sujet âgé de plus de 79 ans, la technique mini-invasive par chirurgie ambulatoire et sous anesthésie locale nous semble avec un excellent rapport bénéfice/risque car elle présente de nombreux avantages : simplicité, rapidité, absence d’anesthésie générale, contrôle direct de la voie en peropératoire, morbidité très faible, efficacité sur le traitement de l’hyperparathyroïdie primaire dans plus de 95 % en première intention, possibilité de reprise immédiate ou différée en cas de lésions multiples passées inaperçues.

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Mots clés : Parathyroïdes ; Hyperparathyroïdie primaire ; Chirurgie mini-invasive ; Chirurgie ambulatoire ; Parathyroïdectomie anesthésie locale

1. Introduction

While primary hyperparathyroidism (HPT) can affect all age groups, it is principally seen in older individuals. In a Swiss study performed in 2004, disease prevalence per 100,000 inhabitants increased from 11.1 individuals in the 30 to 34 years age group to 34 individuals in the age group older than 80 years [1]. Given the current aging of the world’s population, HPT is likely to be diagnosed in increasingly older patients. Specialists in rheumatology, endocrinology, internal medicine and gerontology are increasing solicited to treat this pathology in older patients. Despite the large number of studies describing the value of parathyroid adenectomy, notably when performed under local anesthetic, many physicians are reluctant for their patients to undergo surgery in light of potential surgical risks. This was unequivocally reported in a study performed by the Swiss Federal Ministry in 2004, which determined the annual rate of hospitalization for HPT according to age, and compared it to the rate of parathyroidectomies performed during the same period [1]. While hospitalizations increased constantly from 30 years of age, reaching 97.4 per 100,000 inhabitants at the age of 80 years, the number of parathyroidectomies increased up to 74 years of age (with a peak of 45 procedures per 100,000 inhabitants), and decreased consistently thereafter reaching only 25 procedures per 100,000 inhabitants over the age of 80 years.

However it is widely recognized that the majority of patients suffering from HPT present with functional symptomatology which worsens the difficulties associated with aging, notably due to the associated asthenia and pain [2–7]. As a consequence, this illness not only affects the patient’s quality of life but also increases the workload of individuals caring for them. The current aging of the population is accompanied by improved physiologic condition in many patients, allowing them to maintain intellectual, physical and in some cases professional activities well beyond the legal age of retirement. We thus performed a study evaluating patients aged 80 years and older, with this population expected to account for 350 million individuals in 2050 [8]. The study was designed to demonstrate functional improvements following adenomectomy under local anesthesia and as outpatient surgery.

2. Patients and methods

Between 2 May 2010 and 30 June 2014, 517 patients with HPT were operated in our institution. Among them, 53 (10.2%) [1], were aged 80 years or older and were included in this retrospective study. The average age was 83 years (range, 80 to 94 years) with a male:female ratio of 1:3. All patients underwent a preoperative echoscintigraphy. When possible (i.e., when the echoscintigraphy confirmed the adenoma was unique and in the absence of a serious thyroid pathology and associated behavioral disorders), excision under local anesthetic with minimally invasive surgery was proposed. When social circumstances permitted (patient was accompanied, possibility for night monitoring, hospital/domicile distance less than 50 km) as well as medical status (no serious comorbidities), surgery was performed as an outpatient. In other cases, the patient was hospitalized for 24 to 72 h. When the above conditions were not fulfilled (unconfirmed adenoma, suspicion of multiglandular disease, goiter requiring surgery, conditions preventing local anesthesia), the patient underwent a general anesthetic. From February 2013, when social and/or medical circumstances allowed, all surgery without thyroidectomy was performed as an outpatient.

2.1. General anesthetic

For general anesthetic, techniques varied according to the physician performing the procedure, but was performed according to regulations from the French Society of Anesthesia and Resuscitation.

2.2. Local anesthetic

For local anesthetic, anesthetic was administered by the anesthetist according to the patient’s level of anxiety, and the surgery was performed as previously described [9,10]. In brief, a 1%
Xylocaine® infiltration was administered to the cutaneous and subcutaneous tissues; the thyroid was approached externally by without cutting the subhyoid muscles; the adenoma was located using the morphologic exams; excision of the adenoma with constraint of the vascular pedicle using a titanium clip; closure of the skin by intradermic suture; during the surgical procedure, the patient maintained consciousness in order to preserve vocal control.

2.3. Blood sampling, evaluations and follow-up

All patients underwent blood sample collection from the peripheral or jugular vein to establish the intra and postoperative profile of parathyroid hormone (PTH). The patient was then transferred to the postoperative surveillance ward prior to being released to the outpatient or regular ward. Three blood collections were made to establish the profile: prior to the surgical incision, prior to surgical closure, and at the time the patient was released from the postoperative ward, typically one to two hours postsurgery. Results of the PTH evaluations were obtained two to four hours after blood collection. If the PTH value was within normal ranges (Fig. 1a), patients registered as an outpatient were released from the hospital with instructions for further monitoring. Hospitalized patients were released 24 or 48 h later. Initially, patients were released with a prescription for calcium (4 g/day) combined with vitamin D (Unalpha®) for 10 days, however vitamin D supplementation was stopped from September 2011 and calcium intake was reduced to 1 g/day. Calcium monitoring was prescribed once a week for four weeks. The patient returned for a visit one month postsurgery and PTH, calcium and vitamin levels were evaluated. If these parameters had not returned to normal (Fig. 1b), the patient underwent a classic cervicotomy with evaluation of all parathyroid sites.

Asymptomatic patients could be released and their case discussed subsequently during a multidiscipline meeting. A patient was considered cured if at one month postsurgery, the PTH profile intra- and immediately postsurgery remained within normal ranges and if the four calcium parameters and PTH were within normal ranges (excepting hypocalcemia and hypovitaminosis D). All patients were contacted between six months and three years postsurgery and were evaluated for PTH, calcium and vitamin D.

Two patients undergoing thyroid surgery in whom parathyroid adenomas were identified fortuitously were not retained.

3. Results

3.1. Immediate postsurgery outcome

Clinical events causing or reported during the surgery are presented in Table 1. Most were symptomatic, notably almost permanent hypertension (72%), as well as severe asthenia (53%), and bone pain (47%). Asymptomatic events were infrequent (6%), as were acute events when calcium levels exceeded 3.7 mmol/L (8%). This was reported in an 88-year-old woman suffering from long-term hypercalcemia and who underwent emergency hospitalization for worsening hypertension. Mean preoperative calcium levels were 2.8 mmol/L (112 mg/L), and PTH was 180 pg/ml. From an anatomopathologic perspective, the lesion(s) identified were adenomas in all but two cases where there was pre-existing hyperplasia. However, multiglandular disease were identified in three patients (5.7), one of whom had previously undergone surgery in another center. Adenomas were located cervically in 50 cases and mediastinally in three. All patients underwent a cervicotomy with the exception of one patient with a mediastinal adenoma who had undergone an unsuccessful cervicotomy several years earlier; the patient suffered from severe osteoporosis, justifying a sternotomy. Six patients had undergone a thyroidectomy prior to the parathyroid surgery.

Operative and anesthetic characteristics are summarized in Table 2. A total of 38 patients (72%) underwent local anesthesia with minimally invasive surgery, with a conversion to general anesthesia when required by technical difficulties for two patients (3.7%) in whom thyroid cancers were discovered fortuitously during the HPT surgery. One 82 years old patient had a medullary carcinoma identified by chance during the operation, while a papillary cancer was also identified by chance during an adenectomy performed under local anesthetic in a second patient. In addition, 18 patients were operated under general anesthetic, 15 of which were planned. General anesthetic was planned due to an unconfirmed or too deep localization of the adenoma (eight cases), the presence of a goiter (five cases), and
patient refusal/hypersensitivity (two cases). Three patients were reoperated under general anesthetic; one patient was switched from a local to a general anesthetic during the surgery, and two patients were reoperated due to persisting elevated immediate postsurgery PTH levels (one local and one general).

Outpatient surgery was planned in 26 cases (49%), however this could only be performed in 21 of these patients (40%). Five patients were unable to undergo outpatient surgery: surgery was longer than expected (two cases); conversion from local to general anesthetic (one case); surgery initiated too late (one case); and PTH profile that did not return to within normal ranges (one case).

Outpatient surgery was not proposed for a range of reasons, principally due to a distance of more than 50 km between the patient’s home and the hospital (ten cases), absence of an accompanying person or of the possibility of monitoring (Table 3). Fifty-one patients had normal calcium and PTH levels immediately postsurgery and were still normal one month later (other than hypovitaminosis D). For two patients who underwent minimally invasive surgery for a parathyroid adenoma (one outpatient and one hospitalization), immediate postsurgery values did not return to normal. Both patients were reoperated under general anesthetic within 48 h in order to ablate the contralateral parathyroid adenoma. Ultimately, PTH values returned to within normal ranges for all patients.

No postsurgery bruising or recurrent paralysis was seen. One patient who underwent general anesthetic for a sternotomy experienced postsurgery pneumonia. No cases of hypocalcemia were recorded. Two patients operated under local anesthetic experienced postsurgical hypercalcemia, both of whom had been receiving vitamin D and high oral calcium doses in the context of the initial protocol for several years. During high temperatures, there is an elevated risk of postsurgical hypercalcemia in older patients who drink small amounts of fluid. Since the protocol was modified, operated patients experienced less serious vitamin D deficits. Patients are now released from hospital with a prescription for 1 g oral calcium per day for 10 days and no further cases of hypercalcemia have been reported.

### 3.2. Long-term postsurgery outcome

Four patients (7.5%) died due to reasons unrelated to their HPT. Despite repeated efforts, five patients (9.4%) were lost to follow-up. We were thus able to monitor 44 patients (83%), none of whom presented a relapse of biological HPT. From a subjective perspective, other than the three asymptomatic patients, 38 patients (93%) considered their symptoms to have “improved” or “strongly improved” following surgery, notably in terms of fatigue, as well as muscle and bone pain, two patients (4.9%) reported no difference, and one patient (2.4%) considered symptoms to be “worse” and regretted having undergone surgery.

### 4. Discussion

Since 1994, several studies have been performed to evaluate HPT surgery in older patients [6,11–13], notably in patients in their eighties [2,5,14–16]. These studies, like the study described here, all plead in favor of a surgical approach which must nonetheless be weighed up against the risks associated with increasing age, comorbidities, and patient or family reluctance to undergo surgery considered more serious in older patients. Five studies have included patients aged 80 years and older [2,5,14–16]; the patient and surgical characteristics described in the current French study are coherent with those presented previously for populations in the USA and Canada. The number of patients aged 80 years and older increases steadily and varies between 4 and 7% in the series of published studies. In
daily practice, these patients represent 10 to 12% of all patients operated for HPT. Primary HPT complicates (or is the cause of) several discomforts: fatigue, hypertension, reduction of bone mass, pain (general, muscle, joint or bone), anxiety, depression, vertigo, nephrolithiasis, and digestive disorders. It also increases the risk of death from cardiovascular causes [17]. Unlike asymptomatic cases, which account for between 20 and 50% of younger patients, these consequences justify systematic surgical intervention. Studies performed in patients in their eighties have shown that truly asymptomatic cases are rare. Coherent with this, our study found a 6% rate of asymptomatic patients. Symptoms are dominated by asthenia, present in 60 to 80% of patients [5,14]. Symptoms are often revealing [15], incapacitating or may only identified spontaneously during discussion with the patient, as was seen in our study. Patients know how to describe and evaluate them.

Table 1 summarizes other symptoms, showing that approximately 8% of patients are hospitalized for acute HPT. The frequency of comorbidities and their severity are clearly the second element highlighted by these studies, with treated hypertension in more than two thirds of cases, along with a history of cardiovascular disease, dyspnea and diabetes [13,15,16].

For over 20 years, routine practice of parathyroid ultrasound and scintigraphy, identifying a single lesion in more than 80% of cases [18–20], has allowed the emergence of a minimally invasive surgery notably under local anesthetic [8,19]. This has strongly contributed to reducing anxiety associated with the risks underlying a general anesthetic, and to the difficulties of exploratory surgical procedures over all parathyroid sites, which can be long and laborious. Since then, several minimally invasive surgical techniques have been developed (video-surgery, excision of single adenomas or unilateral exploration under local or general anesthetic), however, we used the initial technique developed in 1991. According to Green et al., more than two thirds of surgeons currently perform minimal surgery in the USA, compared with 10% ten years earlier [21]. This technique has increased value in patients in their eighties in whom the number of hyperplasias decreases, giving single lesions in more than nine out of ten cases. The monitoring protocol implemented in this study to evaluate the efficacy of the adenectomy using intra- and postsurgery PTH levels is unusual compared to those typically used, which evaluate over a shorter postsurgery period requiring a decrease in PTH levels of at least 50% relative to the initial value [22]. Since the routine use of this monitoring starting in 1996, we have consistently required a return to normal ranges of PTH to be sure that the operation had been successful. Empirically, this requires longer durations of observation, which logistically does not present any difficulties since patients remained hospitalized for a minimum of four to five hours in the surgical outpatient ward.

In our patient cohort, surgery was performed under local anesthetic in 72% of case. Two patients required repeat operations the following day due to nonnormalized PTH values, in order to remove the contralateral adenoma. Overall, all patients had normalized values when released from hospital and the criteria for cure were all fulfilled one month postsurgery and remained so with long-term follow-up. Several studies performed in patients under the age of 80 years relating to quality of life have been important for understanding the benefits of surgical treatment. In summary, a meta-analysis performed in 2010 by Morris and Zelada showing a favorable effect of surgery on the general signs associated with the disease (susceptibility to fatigue, fatigue, bone pain, depression) and confirm a favorable impact on quality of life [23]. The only study performed specifically in patients 80 years and older, by Egan et al. in 2007, also presented positive conclusions. Six of the eight domains analyzed by the SF-36 were significantly improved [15].

An anterior cervicotomy does not necessarily contraindicate performing an adenectomy under local anesthetic. Among the six patients who had previously undergone a cervicotomy, four could be operated with minimally invasive surgery. This is coherent with Dimas et al. who also performed this procedure [24]. The potential seriousness of the surgery is reduced by the nature of a local anesthetic which has the added advantage of allowing vocal control throughout the procedure; the financial, social and human costs are reduced due to the fact that it is an outpatient hospitalization. Complications are also less common with minimally invasive surgery [25].

From January 2013, when social and medical conditions permitted, we extended our outpatient surgical program to patients – including those aged 80 years and over – who were operated under general anesthetic. Recently a number of authors [26,27] appear to have reopened the long-standing debate between systematic exploration of the four parathyroid sites versus surgery limited to the identified lesions. We consider this approach to be outdated. It is potentially inappropriate to only propose a single technique to treat all patients when there are at least ten available. We consider it more judicious to select the technique according to the group being treated. Thus in older patients, particularly those aged 80 years and older, use of a minimally invasive technique as outpatient surgery and with local anesthetic is, in our opinion, the optimal choice with its excellent benefit/risk ratio, presenting numerous advantages: simplicity, rapidity, absence of a general anesthetic, direct vocal control, very low morbidity, efficacy treating HPT in more than 95% of primary intention interventions, the possibility of immediate or delayed reoperation in the event that multiple lesions are not identified, without counting the economic argument already highlighted in several studies [28,29].

Disclosure of interest

The authors declare that they have no competing interest.

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References


