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# Original research

# Long-term function of parathyroid subcutaneous autoimplantation after presumed total parathyroidectomy in the treatment of secondary hyperparathyroidism. A clinical retrospective study



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#### ABSTRACT

Introduction: Parathyroidectomy (PTx) is recommended in patients affected by secondary hyperparathyroidism (2HPT) of chronic kidney disease-mineral bone disorders (CKD-MBD), resistant to medical treatment. Analyzing total parathyroidectomy with muscular or subcutaneous autoimplantation (TPai) outcomes in hemodialysis (HD) 2HPT patients, and monitoring intact parathyroid hormone (iPTH) levels, we evaluated long-term functional results of subcutaneous parathyroid glandular tissue autoimplantation.

Methods: 40 HD 2HPT patients, resistant to medical treatment, and awaiting for renal transplantation, underwent total parathyroidectomy with subcutaneous autoimplantation of 9-12 fragments of not nodular hyperplasia parathyroid tissue in not dominant forearm. iPTH were analyzed 24 h, and 3-6-12-24 months after surgery. The 1.08-6.99 pmol/L range was taken as reference of normal iPTH level based on which eu- (1.08-6.99), hypo- (<1.08), aparathyroidism (0) and persistence or relapse (>6.99) of disease were determined.

Results: In every case PTai determined an extraordinary improvement of quality of life, associated with a notable reduction of iPTH serum level. Immediate normalization of iPTH was achieved in 50% of cases; hypoparathyroidism in 25% of cases and persistence of disease in 25% were observed. Long term follow-up showed a reduction of hypoparathyroidism and an increase of relapse rate up to 20%. Grafting resection was never performed.

*Discussion:* Subcutaneous autotrasplantation is a very simple and fast surgical technique. Nevertheless, similar success and recurrence rates were reported following muscular or subcutaneous grafting, as confirmed in our experience.

*Conclusions:* Subcutaneous grafting was effective as muscular implantation, with comparable functional results, but avoiding its potential complications.

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# 1. Summary

Analyzing total parathyroidectomy with muscular or subcutaneous autoimplantation (TPai) outcomes in hemodialysis (HD) 2HPT patients, and monitoring intact parathyroid hormone (iPTH) levels, we evaluated long-term functional results of subcutaneous parathyroid glandular tissue autoimplantation. 40 HD 2HPT patients, resistant to medical treatment, and awaiting for renal transplantation, underwent total parathyroidectomy with

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subcutaneous autoimplantation of 9–12 fragments of not nodular hyperplasia parathyroid tissue in not dominant forearm. In every case PTai determined an extraordinary improvement of quality of life, associated with a notable reduction of iPTH serum level. Long term follow-up showed a reduction of hypoparathyroidism and an increase of relapse rate up to 20%. Subcutaneous grafting was effective as muscular implantation, with comparable functional results, but avoiding its potential complications.

## 2. Introduction

Incidence of secondary hyperparathyroidism (2HPT) of chronic Kidney disease-mineral bone disorders (CKD-MBD) increases with dialysis vintage, and, prior the calcimimetic era, parathyroidectomy (PTx) became necessary in 15% of cases after 10 years, which raised to 38% after 20 years [1]. It induces a higher mortality rate particularly due to irreversible cardiovascular complications and also anemia, becomes a risk factor for unfavourable cardiovascular outcomes [2,3]. Therefore, in 2HPT patients, resistant to medical treatment, early surgery could offer an improved quality of life and possibly a higher long-term survival rate. Successful surgical treatment often results in a dramatic reduction of iPTH levels relieving the patient from clinical symptoms [4-7], and different papers showed that PTx can also improve mortality and cardiovascular morbidity [8-13]. In the surgical management of 2HPT several techniques have been proposed. Total PTx (TP) without implantation was in the past reserved to patients not candidates to renal transplantation, while subtotal PTx (sTP) and total PTx with muscular or subcutaneous autoimplantation, preserving a small amount of abnormal parathyroid tissue, are the most common procedures. Implantation was proposed in different sites: neck, forearm, abdomen, pre-sternum [14–17]. In the preoperative evaluation of the most efficacious technique, grafting failure, recurrence and technical difficulties associated with reintervention, must be considered. In case of 2HPT recurrence, to avoid the complications associated with resection of muscular hypertrophied grafts, subcutaneous implantation was introduced. Different papers demonstrated that subcutaneous technique could be effective as muscular grafting, but with less morbidity [18,19]. We evaluated long-term functional results of subcutaneous parathyroid glandular tissue autoimplantations, and, reviewing TPai literature, we compared subcutaneous and muscular autoimplantation published data.

## 3. Study design

A retrospective analytical cohort study, in a group of 40 HD patients with severe 2 HPT, unresponsive to medical treatment, awaiting for renal transplantation, addressed to our Institution from regional HD centres, and selected for PTai, was performed. iPTH levels >53-84 pmol/L, serum P level >6.5 mg/100 mL, US enlarged parathyroid glands (>1 cm or >500 mm<sup>3</sup>) and persisting clinical symptoms, six months after medical therapy, were considered the main criteria for PTai. Cardiovascular disease was defined as presence of hypertension, peripheral artery disease, ECG signs of cardiac hypertrophy, US cardiac valves calcification, ventricular hypertrophy, arrhythmia, coronary or cerebrovascular disease. Anemia was evaluated according to the Royal College of Physicians (UK) National Clinical Guideline Centre [20]. Ptx was considered successful when postoperative iPTH level was <26.52 pmol/L. The 1.08–6.99 pmol/L range was taken as reference of normal iPTH level based on which eu- (1.08–6.99), hypo- (<1.08), aparathyroidism (0) and persistence or relapse (>6.99) of disease were determined. Hypocalcemia was considered to be present < 1.99 when serum calcium was mmol/L (normal value = 2.10-2.55 mmol/L). During 24 months follow-up, surgical outcomes, survival and functional results of the autoimplantations were evaluated.

## 4. Methods

Data were retrospectively collected from 40 consecutive patients (14 $\sigma$  and 26  $\circ$ ), affected by 2HPT of CKD-MBD, on standard three-weekly HD, and submitted to PTai between January 2006 and January 2008. All patients gave informed consent to participate in the study. Preoperative medical treatment consisted in phosphate chelators (Ca carbonate, sevelamer, lanthanum carbonate), dialysis baths with various Ca concentrations, vitamin D and its analogues. The ESA treatment regimen consisted in three-weekly recombinant human ESA (alfa-erythropoietin) injections – 5.200  $\pm$  3824.48 IU, in 38/40 patients. 2/40 patients was treated with alfa darbepoetin 30 (30 µg/every 15 days).

High-resolution neck ultrasonography, ENT examination, technetium- 99m-sestamibi scintigraphy of the neck and mediastinum, were the main preoperative diagnostic procedures. 12-lead ECG and epiaortic 2-dimensional and color doppler transthoracic echocardiogram, by experienced in center cardiologists, and peripheral artery color doppler ultrasonography examination were pre and postoperatively performed. iPTH, Ca, P, alkaline phosphatase (ALP) and FT<sub>3</sub>, FT<sub>4</sub>, TSH, thyroglobulin were measured along with fine needle biopsy of the thyroid nodules; to minimize the dilution effect on laboratory assays, all blood samples were obtained before dialysis. The Liaison®NTact®PTH Assay (DiaSorin Inc-Stillwater, MN, USA), based on chemiluminescence immunoassay (CLIA), was used for the quantitative determination of iPTH (Coefficient of variation: CV% intra assay 1.7-3.7; CV% inter assay 2.6-5.9; limit of detection 0.07 pmol/L). Indications to surgical procedure were set according to both K/DOQI 2003 guidelines and Y Tominaga et al. [10,15] Regarding the surgical procedures, paunderwent total parathyroidectomy transplantation (TPai) of 9-15 fragments of non-nodular glandular tissue, in 3 subcutaneous pockets of the non-dominant forearm. In 22 out of 40 patients (55%) with thyroid gland disease, 16 total thyroidectomy and 6 hemithyroidectomy procedures were performed. In all cases, 4 parathyroid glands at least were removed (the nature of the tissue was confirmed via intraoperative histological examination). Only in a few cases, a HD treatment was required immediately after surgery, due to an electrolyte imbalance. The majority of patients required intravenous administration of calcium, due to postoperative hypocalcemia. Patients completed long-term follow-up monitoring of iPTH from the implantation site and from the contralateral arm, in order to evaluate the gradients.

#### 5. Results

#### 5.1. Demographics

Patient mean age was 52 years (range 25–72), and mean dialysis vintage was 96 months (1–28 years). Mean preoperative iPTH was 165.79 pmol/l (range 82.66–495.16), and mean serum calcium level was 2.37 mmol/l (range 2.18–2.91) (Table 1). All patients reported diffuse pruritus, arthromyalgia and mood alterations, while the incidence of baseline cardiovascular pathologies is reported in Table 2. No case of calciphylaxis was reported. 22 patients (55%) suffered from coexisting thyroid pathology. None of them had iron deficiency or external blood loss and a mild or moderate anemia (Hb level 7 - <12 gr/dl) was observed. Preoperative instrumental tests (both cervical ultrasound and sestamibi scintigraphy) were not useful in identifying supernumerary glands, that is the exact number of glands or their precise location [21].

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