

# Intramuscular and subcutaneous forearm parathyroid autograft hyperplasia in renal dialysis patients: A retrospective cohort study

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**Background.** Intramuscular and subcutaneous forearm parathyroid autograft are proved to have compatible short-term outcome. However, long-term clinical courses have not been studied.

**Methods.** A single-surgeon retrospective cohort study of parathyroid autograft hyperplasia from August 1998 to January 2013 was performed. According to the location of their parathyroid autograft, patients were divided into an Intramuscular group and a Subcutaneous group. Clinical parameters were analyzed to assess the risk factors and clinical course of autograft hyperplasia.

**Results.** There were 888 consecutive patients who underwent total parathyroidectomy with forearm autotransplantation for renal hyperparathyroidism during the period. The median age at the time of total parathyroidectomy with forearm autotransplantation was 54.2 years (range, 12–86) and the median follow-up time was 4.0 years (range 0.1–16). Autograftectomy was performed on 29 of 888 patients. The incidence of autograftectomy was 15 of 65 in the Intramuscular group and 14 of 823 in the Subcutaneous group; the incidence of repeated autograftectomy was 4 of 65 in the Intramuscular group and 1 of 823 in the Subcutaneous group. The cumulative frequency of autograftectomy was greater in the Intramuscular group than that in the Subcutaneous group (11.6 vs 3.1% at 6 years,  $P < .001$ ). The location of the autograft was the only significant factor affecting the autograftectomy frequency ( $P = .002$ ). The Intramuscular group reoperation patients experienced a longer period between their first operation and the autograftectomy (6.6 vs 3.3 years,  $P = .003$ ), longer operating times (79 vs 37 minutes,  $P = .002$ ), and a greater level of pre-autograftectomy systemic intact parathyroid hormone (1,044 vs 559 ng/L,  $P = .014$ ) than the Subcutaneous group.

**Conclusion.** Intramuscular parathyroid autotransplantation results in a high incidence of autograftectomy, repeated autograftectomy, and a high cumulative frequency of autograftectomy. (Surgery 2015;158:1331-8.)

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TOTAL PARATHYROIDECTOMY WITH AUTOTRANSPLANTATION, rather than subtotal parathyroidectomy, is most often chosen by surgeons in Asia for renal hyperparathyroidism patients.<sup>1</sup> After total parathyroidectomy, the parathyroid autograft can be weighed, measured, and selected precisely to prevent nodular hyperplastic parathyroid tissue transplanting.<sup>1-3</sup>

When graft-related recurrent hyperparathyroidism occurs, it is definitely easier and safer to manage the autograft than to perform cervical reoperation for the remnant parathyroid gland.<sup>4</sup>

Autotransplantation over different sites has been reported with comparable results. Forearm autotransplantation, however, allows the measurement of differential parathyroid hormone levels at the antecubital veins of the arm<sup>5,6</sup> that cannot be applied in presternal or abdominal autotransplantation.<sup>7-9</sup> Therefore, the nonshunt-bearing forearm is recommended as the best parathyroid autotransplantation site in the case of renal hyperparathyroidism.

Parathyroid autotransplantation into the muscular or subcutaneous tissue has been practiced

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for many years.<sup>7,10</sup> Studies evaluating forearm parathyroid autografts either in the muscular or subcutaneous tissue have shown comparable results regarding short-term graft function<sup>11,12</sup>; however, no study comparing the long-term clinical course of intramuscular and subcutaneous autografts has yet been reported. This study is conducted to identify not only a better location for forearm parathyroid autotransplantation between the muscular and subcutaneous tissue but also the risk factors of autograft hyperplasia.

## METHODS

Patients who underwent total parathyroidectomy with forearm autotransplantation for renal hyperparathyroidism between August 1998 and January 2013 at National Cheng Kung University Hospital (NCKUH) were enrolled into the study. Histories of the operations, including first and reoperative findings and procedures, pathologic findings, and postoperative courses were reviewed retrospectively. The cutoff date for analysis was April 6, 2014. According to the location of their parathyroid autograft, the patients were divided into an Intramuscular group and a Subcutaneous group.

After total parathyroidectomy, all parathyroid glands were measured and weighed after trimming off all surrounding tissues. An intraoperative frozen section was used routinely for confirmation. Relatively smaller parathyroid glands were selected for transplantation. In some cases, more than one parathyroid donor gland maybe required. In the Intramuscular group, about 70 mg of parathyroid autograft was divided into 30 pieces and implanted individually into the brachioradial muscle after making a 2.5-cm skin incision over the nonshunt-bearing forearm. In the Subcutaneous group, about 90 mg of parathyroid autograft was minced with scissors and divided into 4 equal parts. Each part was implanted into a separate subcutaneous pocket over the ventroradial side of the proximal nonshunt-bearing forearm. Persistent renal hyperparathyroidism was defined as an intact parathyroid hormone (iPTH) level >70 ng/L within 1 month postoperatively. Long-term hypoparathyroidism was defined as an iPTH level <10 ng/L persistently for more than 6 months.

The operative indications for autograft hyperplasia included an iPTH level >400 ng/L, detection of hypertrophic autograft by imaging studies, and refractory to medical treatment. Operations for forearm autograft hyperplasia were performed under local anesthesia, unless the neck or mediastinum missed parathyroid

coexisted. Enlarged autografts were marked under sono-guiding preoperatively and were removed accordingly. In the Intramuscular group patients, complete autograftectomy of all palpable and sono-identifiable autografts without graft reimplantation was performed. In the Subcutaneous group patients, the pockets of small autograft were preserved if the size was less than 3 mm.<sup>3</sup> If autograft hyperplasia occurred in all 4 pockets, graft reimplantation was performed after complete autograftectomy.

These patients would have received long-term follow-up, either in the outpatient department of NCKUH or in local referral clinics. The last follow-up date was obtained from the latest medical records in NCKUH or from the telephone survey data, whichever was later. Those considered as "lost to follow-up" refers to those patients with inactive medical files in NCKUH for more than 2 years or where there was no response to the telephone survey.

**Statistical analysis.** Continuous variables were expressed as median and range, unless stated otherwise. Categorical and ordinal variables were expressed as numbers and percentages. Statistical significance was assessed by the Mann-Whitney *U* test for continuous and ordinal variables, and by the  $\chi^2$  test and Fisher exact test for categorical variables. The simple and multiple Cox regression model was used to assess the effect of the variables on the frequency of autograftectomy. All candidate predictor variables were included. A backward stepwise elimination procedure was used. The model routine ceased removing variables when no variable had a significance level greater than 0.05. The Cox analysis was stratified by the date, May 2008, when half of the patients were operated. The missing data were treated with the listwise deletion method. The cumulative frequency of autograftectomy was estimated with Kaplan-Meier curves and differences were tested with a Mantel-Cox (log rank) test. Statistical analysis was conducted using the SPSS version 17.0 (SPSS Inc, Chicago, IL) software package.

## RESULTS

There were 888 consecutive patients who underwent total parathyroidectomy with forearm autotransplantation for renal hyperparathyroidism during the period of the study. A total of 65 of 888 (7.3%) patients were in the Intramuscular group and 823 of 888 (92.7%) patients were in the Subcutaneous group. All intramuscular autotransplantations were performed in the first 5 years of the study. In the initial operation,

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