



Original research

Outcomes of parathyroidectomy in renal hyperparathyroidism in patients with No access to renal transplantation in Singapore



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HIGHLIGHTS

- Retrospective cohort study of 81 dialysis patients undergoing subtotal (SPTX) and total parathyroidectomy (TPTX).
- Parathyroid hormone (PTH) and phosphate levels were significantly lowered in TPTX compared to SPTX ($p = 0.004, 0.003$).
- Calcium levels significantly decreased in both groups but both groups had patients with symptomatic hypocalcaemia.
- 11 patients developed biochemical recurrence at a median follow up of 4 years with median PTH of 67.1 pmol/L at recurrence.
- Rate of recurrence was higher in patients who underwent SPTX (20.8% vs 10.5%).

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ABSTRACT

Background: Total parathyroidectomy with autotransplantation (TPTX + AT) and subtotal parathyroidectomy (SPTX) are considered standard surgical treatments for refractory renal hyperparathyroidism. However, there is little data available comparing their outcomes in an area with poor access to renal transplant and calcimimetics.

Methods: Patients with renal hyperparathyroidism who underwent TPTX + AT and SPTX in a tertiary institution from 2006 to 2013 were studied. Patient characteristics, pre- and post-operative biochemical marker levels, and outcomes including recurrence rates, post-operative morbidity and mortality were analysed.

Results: 87 patients underwent parathyroidectomy for renal hyperthyroidism. Transplant patients were excluded in this study. 81 patients were on long-term dialysis, with a median time of 7 years from initiation of haemodialysis to parathyroidectomy. 57 patients (70.4%) underwent TPTX + AT while 24 (29.6%) underwent SPTX.

Post-operatively, there was significant decrease in parathyroid hormone (PTH), calcium and phosphate levels in both groups. PTH and phosphate levels were significantly lowered with TPTX compared to SPTX ($p = 0.004, 0.003$). Symptomatic hypocalcaemia was seen in both groups.

In a median follow-up of 4 years, 11 patients developed biochemical recurrence, with a median time of 29 months to recurrence. Median PTH at recurrence was 67.1 pmol/L. Rate of recurrence was higher in patients who underwent SPTX (20.8% vs 10.5%), with a shorter median time to recurrence (median 62.1 vs 81.3 months). 2 patients required resection of the autograft.

Cohort mortality was 11 patients (13.4%), with 3 deaths secondary to cardiovascular events.

Conclusion: Total parathyroidectomy with autoimplantation is superior to subtotal parathyroidectomy in the short to intermediate term.

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1. Introduction

1.1. Background

Renal hyperparathyroidism is a significant complication of

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patients with end stage renal failure (ESRF) and contributes substantially to the morbidity experienced by this group of patients [1,2]. Results from the Dialysis Outcomes and Practice Patterns Study (DOPPS) have shown that a very high serum PTH (more than 600 pg/ml) was associated with a 21% increase in all-cause mortality risk [3]. The best treatment for renal failure is kidney transplantation but is limited by availability of organs for transplantation. Singapore has the 2nd highest incidence of kidney failure due to diabetes mellitus [4] and a low kidney transplant rate in comparison to other developed countries like France, Sweden and USA [5].

In 2004 the drug cinacalcet hydrochloride (Sensipar®) was approved in the United States for clinical use in patients to maintain parathyroid hormone levels. Since then the drug has been commonly prescribed in the US and UK, with up to 30 percent increase in prescription [6], but the efficacy of the drug remains uncertain. The UK National Institute for Health and Clinical Excellence in 2011 issued recommendations that cinacalcet use should be limited to people with elevated PTH concentrations refractory to standard therapy, with a normal or high serum calcium concentration, and in whom surgical parathyroidectomy is contraindicated because the risks of surgery outweigh the benefits [7].

In the absence of an increasing supply of donor kidneys and the lack of affordable access to calcimimetics due to cost (S\$6000 per annum) in Singapore, most patients with ESRF would develop THPT. Hence, surgery is the only viable option to treat renal parathyroid disease which cannot be managed with medical treatment and persists longer than 6 months According to Kidney Disease: Improving Global Outcomes (KDIGO) guidelines [8]. Currently there are three surgical options for renal hyperparathyroidism, namely, subtotal parathyroidectomy, total parathyroidectomy without autotransplantation and total parathyroidectomy with autotransplantation.

1.2. Objective

The purpose of this study is to investigate the outcomes of parathyroidectomy, including control of biochemical marker levels, recurrence, morbidity and mortality, in renal hyperparathyroidism in Singapore in patients with no access to renal transplant or calcimimetic therapy. We compare these outcomes between total parathyroidectomy with autotransplantation and subtotal parathyroidectomy in the surgical management of renal hyperparathyroidism refractory to medical therapy.

2. Methods

2.1. Study design, setting, participants

This is a retrospective study from a prospectively collected database of patients undergoing parathyroid surgery for refractory renal hyperparathyroidism in a tertiary hospital unit over a period of 8 years. From January 2006 to December 2013, 87 patients with refractory renal hyperparathyroidism were referred to the endocrine surgical unit in National University Hospital of Singapore for parathyroidectomy. All patients were undergoing long-term renal replacement therapy with either haemodialysis or peritoneal dialysis. Patients (n = 6) who received renal transplant prior to surgery were excluded from this study as they have a lower likelihood of recurrent disease than those with ongoing dialysis.

2.2. Indications for surgery

Referral for surgery were based on KDOQI guidelines [9], which include symptoms as well as biochemical levels. Patients with

intact PTH levels above 800 pg/ml (88 pmol/L), hypercalcaemia and or hyperphosphataemia that were not controlled with medical therapy were indicated for surgical management. Patients with symptomatic hyperparathyroidism including pathological fractures or bone pain were also treated surgically regardless of PTH levels.

2.3. Surgical procedures

Patients were treated with either a total parathyroidectomy with autotransplantation (TPTX + ATx) or subtotal parathyroidectomy (SPTX) with bilateral cervical thymectomy (see Fig. 1). For autotransplantation, the most normal-appearing parathyroid gland, as determined by the absence of nodular enlargement on inspection, was transplanted into the brachioradialis after mincing into small cubes of 1 mm or finely minced parathyroid tissue (total volume equivalent to that for implantation) in saline injected into the deltoid [10]. Patients who underwent a subtotal PTX (SPTX) had all four glands identified and the smallest, preferably non-nodular, parathyroid gland was partially excised, leaving behind a small fragment with its intact blood supply. This procedure was routinely accompanied by bilateral cervical thymectomy.

Pre-operatively, serum PTH, calcium, phosphate and ALP levels were taken at the time of decision for surgery. Post operatively the patients received routine oral supplementation of 0.5 mcg calcitriol and 1 g oral calcium. When the serum calcium dropped to less than 2 mmol/L or if the patient was profoundly symptomatic, intravenous calcium was replaced until the calcium was in normal range.

2.4. Follow-up

2.4.1. Variables and data sources

Post-operative biochemical levels of PTH, calcium, and phosphate were taken at the first reading within 48 h of surgery. Post-operative ALP levels were taken 3 months after surgery. Post-operatively, patients underwent long-term follow-up with nephrologists for recurrence of renal hyperparathyroidism. Serum PTH and calcium levels were measured at regular intervals. Biochemical recurrence is assumed when PTH levels increases more than 3 times above the normal upper limit more than 6 months after parathyroidectomy. The first line management of recurrent hyperparathyroidism is with medical therapy, followed by resection of the autograft or parathyroid gland in refractory

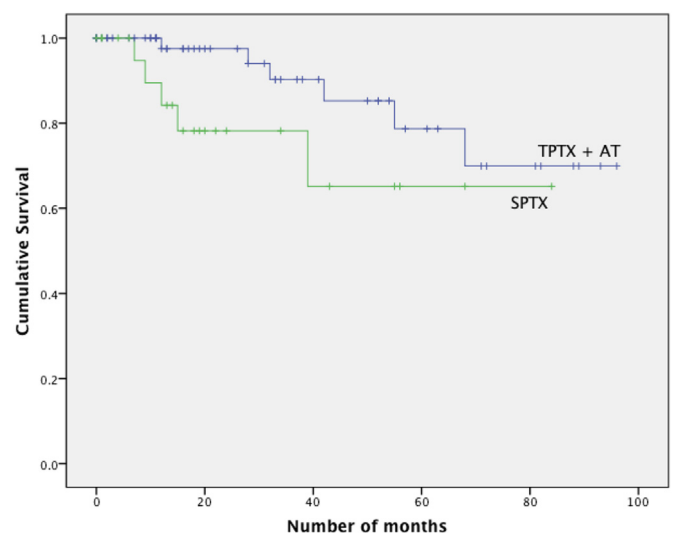


Fig. 1. Kaplan Meier estimates of survival without recurrence in TPTX + AT vs SPTX.

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