Role of surgery in the treatment of renal secondary hyperparathyroidism

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It is generally considered that nearly all patients with chronic renal disease develop secondary hyperparathyroidism (sHPT). However, data on the exact prevalence are lacking. In the past 20 years, therapy for sHPT has been influenced profoundly by the introduction of new options for medical treatment. Medication with oral calcitriol and vitamin D analogues as well as calcimimetics led to a decrease in parathyroidectomies (PTXs) between 1994 and 1998, and again between 2002 and 2005, with increasing numbers since 2006. An association between the duration of dialysis and PTX has been demonstrated in studies before and after the introduction of vitamin D analogues and calcimimetics. The rate of PTX in patients treated with dialysis for more than 10 years was ten times higher than that in patients treated for less than 5 years.

The target ranges for calcium, phosphorus, parathyroid hormone (PTH) and alkaline phosphatase are achieved in only a minority of patients. Up to 32 per cent of patients require PTX after months or years of expensive medical treatment. The cost of calcimimetic therapy, such as cinacalcet, is €240–1300 per month depending on the dose used. In contrast, the cost of PTX is approximately €4000 and surgery is potentially a definitive treatment for many patients. It is therefore not surprising that the cost of medical treatment has already exceeded that of surgical therapy after 9 months of cinacalcet treatment.

The optimal treatment of sHPT in patients on haemodialysis is successful kidney transplantation. Nevertheless, sHPT persists after transplantation in about 40 per cent of patients, even those with good kidney function. Some 3–5 per cent of patients require PTX after transplantation. PTX may be associated with a decrease in renal function or even transplant failure, and so the indication for PTX in patients after renal transplantation has to be considered carefully.

PTX is recommended in patients with chronic kidney disease stage 3–5 D (moderate to severely reduced renal function; glomerular filtration rate less than 60 ml per min per 1.73 m² or need for dialysis) and for patients with ‘severe sHPT’ that cannot be controlled by medical treatment. Owing to the lack of prospective randomized trials, this recommendation is based on the experience of endocrine referral centres and disease severity is not clearly defined. However, patients with hypercalcaemia, severe radiologically or histologically proven osteopathy, severe hyperphosphataemia and PTH levels exceeding 800 pg/ml are generally considered to have severe sHPT. The presence of vascular or soft tissue calcifications, so-called ciphyaxis, as well as muscle or bone pain or pruritus, are also regarded as indications for surgery. Some authors even consider enlarged parathyroid glands visualized by ultrasonography, with a diameter of more than 10 mm, and a nodular–hyperplastic transformation, as an indication for PTX.

The aim of the preoperative evaluation is to establish the diagnosis of sHPT. Apart from a complete medical history, physical examination and biochemistry, the evaluation should include radiography of the hand to verify renal osteopathy. An ultrasound examination of the neck should be performed to detect surgically relevant thyroid pathologies, but not to localize the parathyroid glands; a bilateral neck exploration is mandatory for sHPT. There are three options for the surgical treatment of sHPT: subtotal PTX (3–5-gland resection), total PTX with autotransplantation, and total PTX without autotransplantation. Subtotal PTX and total PTX + autotransplantation should be complemented by a bilateral cervical thymectomy as the thymus represents the most common site of ectopic or supernumerary parathyroid glands and also frequently contains nests of parathyroid cells. If total PTX without autotransplantation is performed, thymectomy should not be carried out to avoid permanent postoperative hypoparathyroidism. Although the level of evidence is poor regarding the most effective procedure, the guideline produced by the Kidney Disease Outcome Quality Initiative recommends subtotal PTX and total PTX + autotransplantation as standard procedures. Resection of fewer than 3–5 glands in patients with asymmetrical parathyroid hyperplasia is not an option owing to a high risk of recurrence.
The optimal surgical procedure should have a low rate of persistent and recurrent disease as well as a low rate of complications, including postoperative hypocalcaemia. These objectives cannot be guaranteed with any of the procedures at hand. Total PTX + autotransplantation and subtotal PTX carry a non-negligible risk of recurrence, and, although difficult to estimate, total PTX a risk of adynamic bone disease. After total PTX, the duration of operation and recurrence rate for sHPT seem to be lower. A prospective randomized trial that compared total PTX + autotransplantation with subtotal PTX showed better results for total PTX + autotransplantation in terms of postoperative levels of calcium, phosphate and alkaline phosphatase, as well as improvement in clinical symptoms and osteopathy. Reoperations after total PTX + autotransplantation were less common, and those performed had a lower complication rate. Recurrence after total PTX + autotransplantation developed in 5–4 per cent of patients by 5 years after surgery, but only 1 per cent required a cervical reoperation, a procedure that carries an increased risk of recurrent laryngeal nerve palsy. The authors therefore tend to favour total PTX + autotransplantation as the standard procedure for sHPT. The results of a prospective randomized multicentre trial (TOPAR-PILOT) performed between 2007 and 2013 to compare total PTX and total PTX + autotransplantation are anticipated with interest. Hopefully, these results will provide better evidence as a base for future recommendations.

In patients with persistent or recurrent sHPT, a detailed report of the previous operation is mandatory. Positive imaging enables a focused surgical approach, which has the lowest complication rate. In contrast to primary surgery, imaging studies to localize the enlarged parathyroid gland(s) are indicated. These investigations should at least include ultrasound examination of the neck and sestamibi single-photon emission CT scintigraphy. MRI of the neck and mediastinum or methionine PET–CT, depending on results of previous localization studies, could be considered.

The decision for medical or surgical treatment of sHPT requires an interdisciplinary discussion between nephrologists and surgeons. Information important to this decision includes: the underlying kidney disease, clinical symptoms, PTH and calcium values, and estimated duration of dialysis before kidney transplantation. Patients with severe sHPT, including PTH levels exceeding 800 pg/ml and hypercalcemia or hyperphosphatemia despite medical treatment, will benefit from surgical treatment. In patients with a high perioperative risk or patients with persistent or recurrent disease, and in patients without localized parathyroid glands on imaging, medical treatment should be preferred.

Disclosure
The authors declare no conflict of interest.

References