

Surgical Management of Medically Refractory Secondary Hyperparathyroidism: Operative Choices and Prevention of Persistent or Recurrent Disease

Junming Shi, Chuanchang Yin*

Department of Hernia Surgery, The First People's Hospital of Jingzhou Affiliated to Yangtze University, Jingzhou, China
Email: 804426440@qq.com, *yinchuanchang@yangtzeu.edu.cn

How to cite this paper: Shi, J.M. and Yin, C.C. (2026) Surgical Management of Medically Refractory Secondary Hyperparathyroidism: Operative Choices and Prevention of Persistent or Recurrent Disease. *Journal of Biosciences and Medicines*, 14, 134-149. <https://doi.org/10.4236/jbm.2026.1410009>

Received: September 5, 2026

Accepted: October 16, 2026

Published: October 19, 2026

Copyright © 2026 by author(s) and Scientific Research Publishing Inc.
This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).
<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Parathyroidectomy is considered when secondary hyperparathyroidism (SHPT) remains poorly controlled despite tolerable medical treatment. In patients receiving long-term dialysis, the decision often follows progressive gland enlargement, persistent disturbances of mineral metabolism, or symptoms that no longer respond adequately to medication. This narrative review examines surgical referral, the choice of operation, and the management of disease that persists or recurs after surgery. Subtotal parathyroidectomy preserves a cervical remnant; total parathyroidectomy may be performed with or without autotransplantation. Each approach leaves a different risk of recurrent hyperparathyroidism and sustained loss of parathyroid function. The available evidence does not establish one procedure as preferable for every patient. Operative planning therefore requires consideration of transplantation prospects, bone disease, the feasibility of long-term supplementation, and access to follow-up. Particular attention is given to ectopic and supernumerary glands, interpretation of intraoperative parathyroid hormone, and postoperative hungry bone syndrome. Sampling and calcium-management pathways are described alongside proposed definitions of biochemical control, persistence, recurrence, and clinically meaningful chronic hypoparathyroidism. These definitions and pathways require local adaptation and prospective validation. The benefit of adjunctive cervical thymectomy or selective exploration of central-compartment fat also remains to be established in comparative studies that measure both durable control and operative morbidity.

Keywords

Secondary Hyperparathyroidism, Parathyroidectomy, Chronic Kidney Disease, Dialysis, Hungry Bone Syndrome, Recurrent Hyperparathyroidism

*Corresponding author.

1. Introduction

Secondary hyperparathyroidism develops within the broader disturbances of chronic kidney disease-mineral and bone disorder (CKD-MBD). Declining kidney function alters phosphate excretion, calcium balance, and vitamin D activation, with consequences for parathyroid hormone (PTH) secretion, bone turnover, and soft-tissue or vascular calcification. After years of dialysis, enlarged nodular glands may respond poorly to the measures that previously controlled PTH [1]-[7].

Initially, increased PTH secretion is an adaptive response to phosphate retention, reduced calcitriol production, and lower ionized calcium. Continued uremic stimulation can lead from diffuse parathyroid hyperplasia to nodular growth. Reduced expression of calcium-sensing and vitamin D receptors in nodular tissue provides a biological explanation for declining treatment responsiveness. Thus, satisfactory control with phosphate binders, vitamin D receptor activators, or calcimimetics earlier in the course of kidney disease may not persist indefinitely [4]-[7].

The consequences of SHPT extend beyond the laboratory result. Bone pain, fractures, proximal weakness, pruritus, and fatigue may accompany poorly controlled mineral metabolism. Severe disease can also contribute to vascular and valvular calcification and make dialysis care more difficult. In selected dialysis cohorts, parathyroidectomy has been associated with improved biochemical control and survival; the observational design of these studies limits causal interpretation [1] [3] [8] [9]. Perioperative complications and early rehospitalization must be considered when discussing any possible longer-term benefit [10].

Once surgery is being considered, several decisions remain: the amount of tissue to retain, the location of any remnant or graft, the extent of exploration for additional glands, and the arrangements for postoperative calcium replacement. This review addresses those decisions and their implications for persistent or recurrent SHPT [11] [12].

Calcimimetics have changed the circumstances in which patients reach surgical assessment. Some can continue medical treatment, whereas others have nodular gland enlargement and complications that remain inadequately controlled. For the latter group, reassessment should consider what further medication is likely to achieve and what may be lost through delay, particularly when skeletal disease, calcification, malnutrition, or other comorbidities are progressing [7] [13]-[22].

2. Literature Search Strategy

A targeted literature search was undertaken for this narrative review in PubMed, Web of Science, Scopus, and Google Scholar. The search concentrated on English-language publications from January 2000 to August 2026. Terms covered secondary or renal hyperparathyroidism, chronic kidney disease-mineral and bone disorder, and parathyroidectomy, including subtotal and total procedures and autotransplantation. Cervical thymectomy, ectopic and supernumerary parathyroid

glands, hungry bone syndrome, and persistent or recurrent hyperparathyroidism were also searched. Guidelines, consensus statements, systematic reviews, meta-analyses, large cohorts, and recent surgical reports received priority. Earlier papers were included where they described established operative principles or the pathophysiology underlying current treatment. The review was not designed as a systematic review or meta-analysis.

Evidence was assessed qualitatively, taking account of study design, relevance to renal SHPT, agreement across reports, and length of follow-up. Clinical recommendations were informed by guidelines and consensus documents, with evidence-graded recommendations distinguished from expert opinion. For treatment comparisons, randomized evidence and systematic reviews were considered before individual retrospective series. Pooling observational studies, however, does not eliminate the selection bias within them. Discrepant findings were examined in relation to the operation performed, dialysis or transplantation status, treatment era, outcome definitions, follow-up, and adjustment for confounding. Where these differences could not be resolved, the conclusions remain qualified. No formal risk-of-bias score or quantitative synthesis was undertaken. The targeted search may have omitted relevant publications.

3. From Medical Treatment Failure to Surgical Referral

Initial management generally combines dietary phosphate control and phosphate binders with vitamin D or vitamin D receptor activators and, when appropriate, a calcimimetic. The regimen has to accommodate calcium and phosphate concentrations, PTH trends, dialysis status, tolerability, and the patient's access to medication. Calcimimetics can postpone or avoid surgery in some patients. Parathyroidectomy nevertheless retains a role when an acceptable response cannot be maintained [1] [15]-[21].

A poor response to one prescription is insufficient to establish medical refractoriness. The relevant question is whether a feasible regimen can provide sustained biochemical and symptomatic control. Gastrointestinal intolerance, hypocalcemia, hypercalcemia, hyperphosphatemia, or an unmanageable medication burden may prevent adequate treatment even when additional drugs are available. Repeated escalation under those circumstances can delay surgical assessment without resolving the underlying problem [1] [13] [15]-[21].

KDIGO recommends parathyroidectomy for severe hyperparathyroidism unresponsive to medical or pharmacological treatment, but does not define a universal PTH cutoff [1]. The AAES guideline places the decision within multidisciplinary assessment and perioperative planning [13]. The frequently cited intact PTH concentration of 800 pg/mL has a more specific history: the 2003 KDOQI opinion-based recommendation referred to persistent concentrations above this level together with hypercalcemia and/or hyperphosphatemia refractory to treatment [23]. A later clinical review described concentrations above 800 pg/mL for more than 6 months despite exhaustive medical therapy as a practical context for

considering surgery [8]. The threshold can therefore prompt referral, but cannot by itself determine the operation or its timing. Nor does it justify waiting 6 months while complications progress. Calcium and phosphate control, skeletal symptoms, pruritus, calcification, and treatment intolerance remain part of the assessment [1] [13] [24].

Interpretation of serial PTH results requires attention to how the samples were obtained and analyzed. Whenever possible, comparisons should use the same assay and specimen type, with similar timing relative to dialysis and medication. A change in assay platform or sample handling may otherwise appear to be a change in disease activity. An unexpected increase should be confirmed and assessed with calcium, phosphate, and alkaline phosphatase before treatment is judged ineffective [1].

Referral becomes more difficult when severe bone disease is accompanied by malnutrition, cardiovascular instability, or repeated hospital admissions. Such patients may have greater operative risk by the time biochemical control is pursued. Earlier contact between nephrology, endocrine surgery, radiology, anesthesia, and the dialysis team allows time to address anemia, volume overload, electrolyte abnormalities, and anticoagulant exposure. Surgical assessment can begin while those problems are being corrected; referral need not imply immediate surgery.

The likelihood and timing of kidney transplantation also affect the choice of procedure. Hyperparathyroidism may improve after transplantation, although persistent or tertiary disease remains possible. A patient approaching transplantation and one likely to require dialysis for many more years may therefore have different reasons for retaining parathyroid tissue. These differences deserve explicit discussion before surgery [13] [14].

4. Preoperative Assessment and Localization

Preoperative assessment should establish the severity of SHPT and identify factors that may complicate recovery. Relevant measurements include intact PTH, calcium, phosphate, alkaline phosphatase, albumin, magnesium, and 25-hydroxyvitamin D. As a marker of bone turnover, alkaline phosphatase can help identify patients at risk of hungry bone syndrome (HBS). Ionized calcium is particularly useful when total calcium appears inconsistent with the patient's condition [1] [13] [25]–[28].

Nephrology and anesthesia review should cover anemia, coagulation, antiplatelet and anticoagulant exposure, cardiovascular disease, infection, and volume status. Dialysis scheduling needs to be considered alongside the anticoagulation used during the session. Recent heparin exposure, for example, may alter perioperative bleeding risk. These arrangements influence recovery even when the cervical dissection itself is uncomplicated.

Localization has a different purpose in renal SHPT from that in presumed single-gland primary hyperparathyroidism. Because several glands are usually involved, an image showing one dominant lesion does not justify limiting surgery

to that gland. Imaging is more useful for identifying ectopic, mediastinal, intrathyroidal, or supernumerary tissue and for planning a subsequent operation [13] [14] [24] [29]-[34].

Ultrasonography is commonly obtained first and provides information about coexisting thyroid disease as well as the parathyroids. Technetium-99m sestamibi, particularly with SPECT/CT, can add localization information for ectopic or mediastinal glands. Discordant ultrasound and sestamibi findings, or suspected persistent or recurrent disease, may warrant contrast-enhanced CT, four-dimensional CT, or selected PET/CT protocols. Failure to localize a gland does not exclude clinically important SHPT and should not, by itself, reduce the intended extent of exploration [13] [14] [24] [29]-[34].

Thyroid nodules require assessment before the operation. If a lesion also needs treatment, that decision is better incorporated into the operative plan than made during an already difficult parathyroid dissection. An unplanned thyroid resection can prolong surgery and increase nerve exposure. This additional information is one reason to retain preoperative ultrasound even when its parathyroid localization is incomplete [13] [14] [24].

5. Operative Choices

Bilateral neck exploration is the usual basis of the initial operation for SHPT. The search includes expected gland locations, the posterior thyroid surfaces, tracheoesophageal grooves, thyrothymic ligaments, and accessible upper mediastinal sites. Removing a large gland does not account for the remaining hyperfunctioning tissue. The extent of exploration must also allow protection of the recurrent laryngeal nerves and avoidance of unnecessary injury [13] [14] [24] [29]-[32].

The operative record should specify the number and location of glands identified, tissue intentionally retained, remnant marking, and any autograft site. If PTH excess returns years later, these details help distinguish a known remnant or graft from tissue that may have been missed. An incomplete record can leave subsequent imaging difficult to interpret.

Subtotal parathyroidectomy leaves a small, vascularized cervical remnant after removal of most hyperplastic tissue. Retaining endogenous PTH secretion may reduce the risk of profound chronic hypocalcemia. The remnant, however, remains subject to uremic stimulation and may enlarge again. Preservation of native function can make this approach suitable for selected patients who can maintain reliable follow-up [13] [14] [24] [29]-[33] [35].

Remnant size and blood supply are consequential technical choices. Excess tissue can provide a source of recurrence, whereas a very small or poorly perfused remnant may provide little functional advantage over total removal. Published series differ in both remnant estimation and marking. Recurrence rates are consequently difficult to compare without a description of these methods and the duration of surveillance [13] [24] [33] [35].

For total parathyroidectomy with autotransplantation, all identified cervical

glands are removed and a small amount of confirmed parathyroid tissue is implanted, usually in the nondominant forearm. A forearm source of recurrent PTH excess can be easier to localize and approach than a lesion in a previously operated neck. PTH sampling from both arms may help establish graft involvement. Early hypocalcemia, failure of graft function, and later graft hyperplasia remain limitations of this procedure [13] [14] [24] [29]-[32] [35]-[37].

Autografts are placed in muscle pockets or subcutaneous tissue, with substantial variation in the amount implanted. Surgeons generally select the least nodular tissue available, although visual selection cannot reliably predict subsequent behavior. Graft function may be absent initially, recover later, or eventually become excessive as the tissue enlarges. Follow-up therefore needs to assess the graft as well as the cervical operative result [31] [35]-[37].

Total parathyroidectomy without autotransplantation avoids deliberately leaving a remnant or graft that could later become hyperplastic. It may be considered in selected patients with a high risk of recurrence, little prospect of transplantation, or substantial risk from future cervical reoperation. Occult ectopic or supernumerary tissue can still remain, so total removal cannot guarantee permanent absence of PTH secretion. Conversely, sustained low PTH may require prolonged calcium and active vitamin D supplementation. This burden must be weighed against the intended reduction in recurrent disease [13] [14] [24] [29]-[32] [36] [38] [39].

Comparative cohorts and systematic reviews report variable rates of recurrence, hypocalcemia, reoperation, and symptom improvement, partly because institutions use different definitions [35] [36] [38] [39]. They do not establish a preferred operation for all patients. **Table 1** sets out the principal advantages and limitations. In applying them, the discussion should address dialysis duration, transplantation prospects, bone turnover, access to follow-up, and local surgical experience, together with the patient's priorities concerning recurrence and chronic hypoparathyroidism.

Table 1. Practical comparison of operative strategies for SHPT.

1. Procedure	2. Main advantage	3. Main limitation	4. Practical note
5. Subtotal parathyroidectomy	6. Preserves native parathyroid tissue and may reduce the risk of chronic low PTH.	7. The cervical remnant can enlarge under continued uremic stimulation.	8. Record the remnant site, estimated size, and vascularity.
9. Total parathyroidectomy with autotransplantation	10. Removes cervical glands and may make graft-related recurrence easier to confirm and treat.	11. Early hypocalcemia, graft nonfunction, and later graft hyperplasia may occur.	12. Document the graft site and fragment number; consider bilateral forearm PTH sampling if recurrence is suspected.
13. Total parathyroidectomy without autotransplantation	14. Reduces recurrence from intentionally retained or grafted tissue.	15. May cause sustained low PTH and prolonged need for calcium and active vitamin D.	16. Reserve for selected patients after explicit discussion of long-term trade-offs.

Note: No operation is universally superior. Choice should reflect recurrence risk, transplant plans, bone turnover, follow-up reliability, and local expertise. See Section 7 for proposed outcome definitions. Sources: [13] [24] [35] [36] [38] [39].

Patients need an account of the likely consequences of each procedure, including the meaning of biochemical control and the possibility of further treatment. Some may accept long-term supplementation to reduce the chance of recurrent hyperparathyroidism; others may place greater value on retaining endogenous function. Limited access to follow-up can make either recurrence or supplementation difficult to manage. The chosen procedure should reflect which demands the patient can realistically sustain.

6. Ectopic and Supernumerary Glands

A missed gland can account for persistent SHPT despite apparently adequate cervical resection. The shared embryological migration of the inferior parathyroids and thymus explains the occurrence of parathyroid tissue in the cervical thymus, thyrothymic ligament, perithymic fat, and mediastinum. Additional sites include the retroesophageal space, carotid sheath, and thyroid parenchyma. Supernumerary glands may be embedded in perithymic or central-compartment fat and overlooked during the initial search [13] [14] [24] [29]-[32] [34].

Cervical thymectomy is used by many surgeons, particularly when an inferior gland cannot be found or imaging points to the thymus. It gives access to a recognized site of occult parathyroid tissue. Its rationale should be distinguished from that of routinely clearing central-compartment adipose tissue. Broader fat dissection can increase exposure of the recurrent laryngeal nerves, lymphatic channels, and small vessels [13] [24] [33] [34].

Exploration of central-compartment fat is most readily justified by a missing gland or an anatomically defined ectopic target. An inadequate intraoperative PTH decline may add to that concern, but first requires the sampling and interpretation checks described in Section 6. Further dissection should depend on the combined biochemical and anatomical findings; an isolated PTH result is insufficient. Whether routine removal of a wider area of fat improves recurrence rates enough to justify the additional dissection remains unresolved.

Evaluation of an extended operation should document what the additional dissection actually yields. The number and location of confirmed additional glands are more informative than the volume of fat removed. Any improvement in durable biochemical control also needs to be assessed alongside voice changes, bleeding, chyle leak, hypocalcemia, and length of stay. Those outcomes determine whether the extension offers a clinical advantage.

7. Intraoperative Adjuncts and Postoperative Care

Intraoperative PTH can help assess the result of resection, but its interpretation in SHPT is affected by renal function, the assay, and the involvement of several glands. A decline may occur despite remaining occult tissue; a slower decline may occur without surgical failure. Criteria derived from single-gland primary hyperparathyroidism therefore require caution when applied to renal disease [13] [14] [24] [29]-[32] [37].

One proposed approach for a center to define and audit is peripheral sampling after induction of anesthesia, before substantial gland manipulation, followed by samples 10 and 20 minutes after the last intended resection. The record should include the assay, sampling site, resection time, and any delay in collection or processing. A 20-minute result can provide the main assessment point, provided that both the proportional fall and absolute PTH concentration are interpreted in relation to the planned procedure [40] [41].

The cutoff should be chosen before surgery and checked against local outcomes. Ohe et al. studied 86 patients with secondary or tertiary renal hyperparathyroidism prospectively: after total parathyroidectomy with autotransplantation, a fall of at least 80% at 20 minutes was associated with their definition of cure [40]. In a retrospective cohort of 501 patients with SHPT, Zhang et al. identified a 20-minute cutoff of 88.9% [41]. Differences in population, assays, and endpoints limit transfer of either threshold to another setting, particularly to subtotal resection. When the local criterion is not met, the team should check timing and sample handling and, where appropriate, obtain a later sample, such as at 30 minutes. Interpretation then requires review of the glands identified, confirmation of the specimens, and imaging. Additional exploration should pursue a plausible source of residual tissue rather than follow an abnormal result alone.

Frozen section can resolve uncertainty when a small specimen resembles parathyroid, lymph node, fat, or a thyroid nodule. Confirmation of tissue identity does not establish completeness of resection. Autofluorescence and other optical techniques may assist identification in selected cases, but the extent and safety of exploration still depend on the anatomical findings.

Direct identification and careful dissection of the recurrent laryngeal nerve are especially important for posterior or ectopic glands and in a scarred operative field. Nerve monitoring may provide additional information in selected high-risk cases, but does not substitute for atraumatic dissection. Voice change after surgery, or concern arising from a difficult operation, should prompt consideration of laryngoscopy.

Hypocalcemia commonly determines the intensity of early postoperative care. In HBS, rapid skeletal uptake of minerals after the fall in PTH can create a prolonged need for calcium replacement. Higher alkaline phosphatase, severe skeletal disease, younger age, and lower preoperative calcium have been associated with this risk. Findings for preoperative PTH and dialysis duration are less consistent [25]-[27]. A recent systematic review found considerable heterogeneity and incomplete evidence for preoperative measures intended to prevent post-parathyroidectomy hypocalcemia [28]. Perioperative planning should therefore identify patients likely to need intensive monitoring and ensure access to oral calcium, calcitriol, and a monitored intravenous calcium protocol.

The calcium plan should be agreed before the operation. An initial schedule is ionized calcium measurement every 4 - 6 hours for 48 - 72 hours, followed by at least twice-daily measurement until stable. Symptoms or active changes to an in-

fusion require more frequent assessment [23]. Phosphate and magnesium need surveillance during the same period [25]-[27]. If calcium is falling modestly without symptoms and oral intake is possible, divided oral calcium and calcitriol can be started or increased. The response should be reviewed at the next planned measurement, with correction of magnesium deficiency where present [25]-[27].

Tetany, seizures, hypocalcemia-associated QT prolongation or arrhythmia, a rapid continuing fall in calcium, or inadequate control with oral treatment warrants urgent assessment for intravenous replacement under an institutional monitoring protocol [26] [27]. KDOQI gives an opinion-based biochemical trigger of ionized calcium below 0.9 mmol/L or albumin-corrected total calcium below 1.80 mmol/L. Clinical deterioration may require intervention before those concentrations are reached [23]. Ionized calcium is preferable when corrected total calcium conflicts with the clinical picture. Intravenous replacement requires ECG and repeated biochemical assessment, while oral calcium and calcitriol are adjusted. The infusion can be reduced when calcium remains stable on sufficient oral treatment [23] [26] [27].

Dialysis management and calcium replacement need to be coordinated from the outset. Continued hypocalcemia, a requirement for intravenous replacement, or concurrent magnesium, phosphate, or volume disturbances should trigger review of the dialysis prescription. This may involve the timing of dialysis, temporary adjustment of dialysate calcium, and reassessment of calcimimetics and phosphate binders [25]-[27]. Discharge does not end surveillance: the calcium nadir may occur about 2 weeks after surgery. A stable replacement regimen, early laboratory review linked to dialysis visits, and instructions about recurrent symptoms are needed before the patient leaves hospital [25].

Mineral replacement should also account for hypophosphatemia associated with HBS and hypomagnesemia that impedes calcium correction. Phosphate depletion may contribute to weakness, but excessive replacement can promote calcium-phosphate precipitation. Decisions about replacement should therefore be individualized with the dialysis team [25]-[27]. The sequence described here combines published guidance with cohort experience; it has not been prospectively validated as a renal-SHPT treatment algorithm.

8. Persistent and Recurrent SHPT

Reports of postoperative SHPT use different PTH cutoffs and follow-up periods. The definitions below are proposed for consistent discussion within this review; they are not a validated consensus standard for renal SHPT [13] [24] [37] [41]. Outcome reporting should identify the operation, assay reference range, kidney or transplantation status, and concurrent PTH-lowering treatment.

Biochemical control is defined here as sustained control of excessive parathyroid activity within a prespecified target appropriate to renal status, together with acceptable calcium and phosphate concentrations and no progressive SHPT symptoms requiring treatment escalation. KDIGO's suggested iPTH range for pa-

tients receiving dialysis is approximately 2 - 9 times the assay's upper normal limit, considered with serial calcium and phosphate results [1]. That range guides chronic CKD-MBD treatment; it has not been validated as a surgical cure end-point or as a target to apply automatically after transplantation. An early postoperative PTH below the range alone does not establish failure. Reports of control should state the medication needed to maintain it.

Persistence denotes excessive PTH secretion within the first 6 postoperative months when biochemical control has not been documented. For reporting, PTH above the prespecified upper target should be confirmed on at least two measurements, preferably separated by at least 4 weeks, after assessment of assay comparability and reversible metabolic or treatment-related causes. Associated symptoms and calcium-phosphate abnormalities should be recorded. The proposed interval is for classification and must not delay urgent treatment. An isolated early PTH result is insufficient to diagnose persistence.

Recurrence denotes renewed PTH excess after 6 months, following documented biochemical control throughout the initial 6-month period. Confirmation uses the repeat measurements and clinical assessment described for persistence. Where the early postoperative record cannot establish control, the outcome is indeterminate. Six months of observation can characterize initial control or persistence, but is too short to demonstrate freedom from later recurrence.

For this review, clinically meaningful chronic hypoparathyroidism requires hypocalcemia with low or inappropriately normal PTH beyond 12 months after surgery and a continuing need for calcium plus active vitamin D to prevent recurrent hypocalcemia or symptoms. Repeated biochemistry and treatment requirements should support the diagnosis; necessary supplementation should not be withdrawn unsafely to demonstrate it. The 12-month boundary is adapted from international guidance on postsurgical hypoparathyroidism and has not been specifically validated for renal SHPT [42]. Prolonged HBS, magnesium deficiency, and other causes of low calcium must also be assessed. Isolated low PTH or calcium use solely for phosphate binding does not meet this definition, nor does either finding establish adynamic bone disease.

The distinction matters when looking for a source of ongoing PTH secretion. Persistence can reflect incomplete exploration, a missed ectopic or supernumerary gland, or removal of tissue mistaken for parathyroid. Recurrent disease may originate in a cervical remnant, forearm graft, residual cervical tissue, parathyromatosis, or an occult gland that enlarges later. Before ordering further localization studies, the original operative and pathology reports should be reviewed with the gland count, graft site, and earlier images. These records provide the context needed to interpret a new scan [13] [14] [24] [29]-[32] [34] [37].

Ultrasound and sestamibi SPECT/CT are common initial investigations before reoperation. If they do not establish an adequate target, contrast CT, four-dimensional CT, PET/CT, or selective venous sampling may be considered. Further investigation is useful when it clarifies the likely source of PTH and the route by

which it can be approached [13] [14] [24] [29]-[32] [37].

In patients with a forearm graft, PTH sampling from both arms can help separate graft-related from cervical or mediastinal disease. A marked increase on the grafted side supports graft involvement. Absence of such a gradient leaves other sites under consideration and should lead to reassessment before forearm exploration [13] [31] [37].

Repeat cervical surgery involves scarred planes and altered anatomy, with additional risk to the recurrent laryngeal nerves. It should generally be undertaken by surgeons experienced in renal hyperparathyroidism and directed at an identified target. Where a forearm graft accounts for recurrent disease, graft re-exploration may entail less morbidity than another neck operation. **Table 2** relates common postoperative patterns to the assessment and management priorities.

Table 2. Approach to persistent or recurrent SHPT after parathyroidectomy.

1. Clinical pattern	2. Common explanation	3. Assessment priority	4. Management principle
5. Persistent excess PTH within 6 months without documented control	6. Missed ectopic or supernumerary gland, incomplete exploration, or non-parathyroid tissue removed.	7. Confirm serial biochemistry and assay comparability; review operative and pathology records, then targeted imaging.	8. Do not reoperate until a plausible anatomical target is defined.
9. Recurrence after subtotal parathyroidectomy following documented initial control	10. Regrowth of the <i>in-situ</i> remnant or enlargement of an occult additional gland.	11. Assess remnant location, serial PTH, calcium, phosphate, and imaging.	12. Consider selective reoperation in an experienced center when symptoms and biochemistry justify it.
13. Recurrence after autotransplantation following documented initial control	14. Forearm graft hyperplasia or residual cervical/mediastinal tissue.	15. Use bilateral forearm PTH sampling and targeted imaging.	16. Treat graft-dependent disease through forearm re-exploration when appropriate.
17. Mild biochemical abnormality without clear target	18. Medical under-treatment, nonadherence, assay variation, or nonsurgical metabolic driver.	19. Reassess medication, dialysis adequacy, phosphate control, and serial trends.	20. Avoid reoperation based on PTH alone without clinical and anatomical support.

Note: These patterns use the proposed working definitions in Section 7. Recurrence requires documented initial control through 6 months; an isolated high PTH value does not establish persistence or recurrence. Sources: [13] [24] [34] [37] [41].

9. Current Gaps and Future Work

Most comparative evidence comes from retrospective studies. Differences in definitions and follow-up complicate comparison of cure, persistence, recurrence, chronic hypoparathyroidism, and HBS. Quality of life, transplantation status, and reoperation are also reported inconsistently. These limitations reduce confidence that differences between series represent an effect of the procedure itself [13] [14] [24] [29]-[32] [35] [36] [38] [39].

Multicenter work would be more informative if the same biochemical and patient-reported outcomes were collected across centers. Analyses should account for dialysis duration, bone turnover, transplantation plans, gland size, imaging

findings, and previous calcimimetic treatment. Variation in these characteristics may explain some apparent differences between operations. The proposed definitions in this review offer a basis for explicit reporting, but their thresholds and time windows still need prospective validation.

Two uncertainties have direct implications for operative practice. The first concerns the yield and morbidity of a more extensive search for ectopic or supernumerary tissue. The second concerns prediction and prevention of postoperative hypocalcemia. Studies addressing either question need to relate their findings to patient outcomes, including nerve injury, bleeding, and lymphatic complications, rather than relying on gland counts alone.

Comparisons also require a sufficiently detailed description of care. Reports should specify surgical indications, preoperative medication, the glands identified, whether thymectomy was performed, use of intraoperative PTH, and the calcium-management regimen. Recurrence definitions and the duration of surveillance are indispensable. Without this information, an apparent advantage may reflect differences in patient selection or observation time.

10. Conclusion

Surgery offers a treatment option when severe SHPT remains uncontrolled despite a feasible medical regimen. Referral should take account of the clinical course and treatment burden as well as serial biochemical results. The choice among subtotal resection and total resection with or without autotransplantation requires discussion of recurrent disease, retained parathyroid function, and the likely need for supplementation. Systematic exploration and planned postoperative calcium care are essential components of treatment. If PTH excess persists or returns, review of the operative history and targeted localization should precede consideration of reoperation. Current comparative evidence supports decisions adapted to the patient's renal course and capacity for follow-up, while better standardized studies are needed to establish the relative long-term outcomes of the available procedures.

Financial Disclosure or Funding

No specific funding was received for this work.

Ethics Approval and Consent to Participate

Not applicable because this is a narrative review and no human participant data were collected.

Data Availability

No new datasets were generated or analyzed for this article.

Use of Artificial Intelligence Tools

ChatGPT (OpenAI) was used to assist with language editing and organization

during manuscript preparation. The authors reviewed the text and checked the references and scientific content. The authors take responsibility for the accuracy and integrity of the final manuscript.

Author Contributions

Conceptualization, J.S. and C.Y.; methodology, J.S. and C.Y.; investigation, J.S.; data curation, J.S.; writing—original draft preparation, J.S.; writing—review and editing, J.S. and C.Y.; visualization, J.S.; supervision, C.Y.; project administration, C.Y. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare that they have no conflict of interest.

References

- [1] Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group (2017) KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). *Kidney International Supplements*, **7**, 1-59.
- [2] Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group (2009) KDIGO Clinical Practice Guideline for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). *Kidney International Supplements*, **113**, S1-S130.
- [3] Ketteler, M., Block, G.A., Evenepoel, P., Fukagawa, M., Herzog, C.A., McCann, L., *et al.* (2018) Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder: Synopsis of the Kidney Disease: Improving Global Outcomes 2017 Clinical Practice Guideline Update. *Annals of Internal Medicine*, **168**, 422-430. <https://doi.org/10.7326/m17-2640>
- [4] Cunningham, J., Locatelli, F. and Rodriguez, M. (2011) Secondary Hyperparathyroidism: Patho-Genesis, Disease Progression, and Therapeutic Options. *Clinical Journal of the American Society of Nephrology*, **6**, 913-921. <https://doi.org/10.2215/cjn.06040710>
- [5] Rodriguez, M., Nemeth, E. and Martin, D. (2005) The Calcium-Sensing Receptor: A Key Factor in the Pathogenesis of Secondary Hyperparathyroidism. *American Journal of Physiology-Renal Physiology*, **288**, F253-F264. <https://doi.org/10.1152/ajprenal.00302.2004>
- [6] Slatopolsky, E., Brown, A. and Dusso, A. (1999) Pathogenesis of Secondary Hyperparathyroidism. *Kidney International*, **56**, S14-S19. <https://doi.org/10.1046/j.1523-1755.1999.07304.x>
- [7] Tsai, S., Kan, W., Jhen, R., Chang, Y., Kao, J., Lai, H., *et al.* (2024) Secondary Hyperparathyroidism in Chronic Kidney Disease: A Narrative Review Focus on Therapeutic Strategy. *Clinical Medicine*, **24**, Article 100238. <https://doi.org/10.1016/j.clinme.2024.100238>
- [8] Lau, W.L., Obi, Y. and Kalantar-Zadeh, K. (2018) Parathyroidectomy in the Management of Secondary Hyperparathyroidism. *Clinical Journal of the American Society of Nephrology*, **13**, 952-961. <https://doi.org/10.2215/cjn.10390917>
- [9] Komaba, H., Taniguchi, M., Wada, A., Iseki, K., Tsubakihara, Y. and Fukagawa, M. (2015) Parathyroidectomy and Survival among Japanese Hemodialysis Patients with

- Secondary Hyperparathyroidism. *Kidney International*, **88**, 350-359.
<https://doi.org/10.1038/ki.2015.72>
- [10] Ishani, A., Liu, J., Wetmore, J.B., Lowe, K.A., Do, T., Bradbury, B.D., *et al.* (2015) Clinical Outcomes after Parathyroidectomy in a Nationwide Cohort of Patients on Hemodialysis. *Clinical Journal of the American Society of Nephrology*, **10**, 90-97.
<https://doi.org/10.2215/cjn.03520414>
 - [11] Yuen, N.K., Ananthakrishnan, S. and Campbell, M.J. (2016) Hyperparathyroidism of Renal Disease. *The Permanente Journal*, **20**, 15-127.
<https://doi.org/10.7812/tpp/15-127>
 - [12] van der Plas, W.Y., Noltjes, M.E., van Ginhoven, T.M. and Kruijff, S. (2020) Secondary and Tertiary Hyperparathyroidism: A Narrative Review. *Scandinavian Journal of Surgery*, **109**, 271-278. <https://doi.org/10.1177/1457496919866015>
 - [13] Dream, S., Kuo, L.E., Kuo, J.H., Sprague, S.M., Nwariaku, F.E., Wolf, M., *et al.* (2022) The American Association of Endocrine Surgeons Guidelines for the Definitive Surgical Management of Secondary and Tertiary Renal Hyperparathyroidism. *Annals of Surgery*, **276**, e141-e176. <https://doi.org/10.1097/sla.0000000000005522>
 - [14] Bartz-Kurycki, M. and Dream, S. (2024) Surgical Management of Secondary and Tertiary Hyperparathyroidism. *Surgical Clinics of North America*, **104**, 825-835.
<https://doi.org/10.1016/j.suc.2024.02.011>
 - [15] Block, G.A., Martin, K.J., de Francisco, A.L.M., Turner, S.A., Avram, M.M., Suranyi, M.G., *et al.* (2004) Cinacalcet for Secondary Hyperparathyroidism in Patients Receiving Hemodialysis. *New England Journal of Medicine*, **350**, 1516-1525.
<https://doi.org/10.1056/nejmoa031633>
 - [16] Chertow, G.M., Block, G.A., Correa-Rotter, R., *et al.* (2012) Effect of Cinacalcet on Cardiovascular Disease in Patients Undergoing Dialysis. *New England Journal of Medicine*, **367**, 2482-2494. <https://doi.org/10.1056/nejmoa1205624>
 - [17] Palmer, S.C., Nistor, I., Craig, J.C., Pellegrini, F., Messa, P., Tonelli, M., *et al.* (2013) Cinacalcet in Patients with Chronic Kidney Disease: A Cumulative Meta-Analysis of Randomized Controlled Trials. *PLOS Medicine*, **10**, e1001436.
<https://doi.org/10.1371/journal.pmed.1001436>
 - [18] Block, G.A., Bushinsky, D.A., Cunningham, J., Drueke, T.B., Ketteler, M., Kewalramani, R., *et al.* (2017) Effect of Etelcalcetide vs Placebo on Serum Parathyroid Hormone in Patients Receiving Hemodialysis with Secondary Hyperparathyroidism: Two Randomized Clinical Trials. *JAMA*, **317**, 146-155.
<https://doi.org/10.1001/jama.2016.19456>
 - [19] Block, G.A., Bushinsky, D.A., Cheng, S., Cunningham, J., Dehmel, B., Drueke, T.B., *et al.* (2017) Effect of Etelcalcetide vs Cinacalcet on Serum Parathyroid Hormone in Patients Receiving Hemodialysis with Secondary Hyperparathyroidism: A Randomized Clinical Trial. *JAMA*, **317**, 156-164. <https://doi.org/10.1001/jama.2016.19468>
 - [20] Ballinger, A.E., Palmer, S.C., Nistor, I., Craig, J.C. and Strippoli, G.F. (2014) Calcimimetics for Secondary Hyperparathyroidism in Chronic Kidney Disease Patients. *Cochrane Database of Systematic Reviews*, No. 12, CD006254.
<https://doi.org/10.1002/14651858.cd006254.pub2>
 - [21] Alvarado, L., Sharma, N., Lerma, R., Dwivedi, A., Ahmad, A., Hechanova, A., *et al.* (2022) Parathyroidectomy versus Cinacalcet for the Treatment of Secondary Hyperparathyroidism in Hemodialysis Patients. *World Journal of Surgery*, **46**, 813-819.
<https://doi.org/10.1007/s00268-022-06439-7>
 - [22] Fligor, S.C., Li, C., Hamaguchi, R., William, J. and James, B.C. (2021) Decreasing Surgical Management of Secondary Hyperparathyroidism in the United States. *Jour-*

- nal of Surgical Research*, **264**, 444-453. <https://doi.org/10.1016/j.jss.2021.03.013>
- [23] National Kidney Foundation (2003) K/DOQI Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease. *American Journal of Kidney Diseases*, **42**, S1-S201.
 - [24] Lorenz, K., Bartsch, D.K., Sancho, J.J., Guigard, S. and Triponez, F. (2015) Surgical Management of Secondary Hyperparathyroidism in Chronic Kidney Disease—A Consensus Report of the European Society of Endocrine Surgeons. *Langenbeck's Archives of Surgery*, **400**, 907-927. <https://doi.org/10.1007/s00423-015-1344-5>
 - [25] Ho, L., Wong, P., Sin, H., Wong, Y., Lo, K., Chan, S., *et al.* (2017) Risk Factors and Clinical Course of Hungry Bone Syndrome after Total Parathyroidectomy in Dialysis Patients with Secondary Hyperparathyroidism. *BMC Nephrology*, **18**, Article No. 12. <https://doi.org/10.1186/s12882-016-0421-5>
 - [26] Jain, N. and Reilly, R.F. (2017) Hungry Bone Syndrome. *Current Opinion in Nephrology and Hypertension*, **26**, 250-255. <https://doi.org/10.1097/mnh.0000000000000327>
 - [27] Tai, Y., Shen, H., Nai, W., Fu, J., Wang, I., Huang, C., *et al.* (2023) Hungry Bone Syndrome after Parathyroid Surgery. *Hemodialysis International*, **27**, 134-145. <https://doi.org/10.1111/hdi.13067>
 - [28] Landsberg, A., Brockman, N.K., Sevinc, E., McClurg, C., Elliott, M.J., Girard, L., *et al.* (2025) Interventions to Reduce the Risk of Hypocalcemia after Parathyroidectomy for People with Advanced Chronic Kidney Disease: A Systematic Review. *Canadian Journal of Kidney Health and Disease*, **12**.
 - [29] Pitt, S.C., Sippel, R.S. and Chen, H. (2009) Secondary and Tertiary Hyperparathyroidism, State of the Art Surgical Management. *Surgical Clinics of North America*, **89**, 1227-1239. <https://doi.org/10.1016/j.suc.2009.06.011>
 - [30] Tominaga, Y., Matsuoka, S. and Uno, N. (2009) Surgical and Medical Treatment of Secondary Hyperparathyroidism in Patients on Continuous Dialysis. *World Journal of Surgery*, **33**, 2335-2342. <https://doi.org/10.1007/s00268-009-9943-3>
 - [31] Tominaga, Y., Uchida, K., Haba, T., Katayama, A., Sato, T., Hibi, Y., *et al.* (2001) More than 1,000 Cases of Total Parathyroidectomy with Forearm Autograft for Renal Hyperparathyroidism. *American Journal of Kidney Diseases*, **38**, S168-S171. <https://doi.org/10.1053/ajkd.2001.27432>
 - [32] Tominaga, Y., Tanaka, Y., Sato, K., Nagasaka, T. and Takagi, H. (1997) Histopathology, Pathophysiology, and Indications for Surgical Treatment of Renal Hyperparathyroidism. *Seminars in Surgical Oncology*, **13**, 78-86. [https://doi.org/10.1002/\(sici\)1098-2388\(199703/04\)13:2<78::aid-ssu3>3.0.co;2-z](https://doi.org/10.1002/(sici)1098-2388(199703/04)13:2<78::aid-ssu3>3.0.co;2-z)
 - [33] Schneider, R., Slater, E.P., Karakas, E., Bartsch, D.K. and Schlosser, K. (2012) Initial Parathyroid Surgery in 606 Patients with Renal Hyperparathyroidism. *World Journal of Surgery*, **36**, 318-326. <https://doi.org/10.1007/s00268-011-1392-0>
 - [34] Pattou, F.N., Pellissier, L.C., Noël, C., Wambergue, F., Huglo, D.G. and Proye, C.A.G. (2000) Supernumerary Parathyroid Glands: Frequency and Surgical Significance in Treatment of Renal Hyperparathyroidism. *World Journal of Surgery*, **24**, 1330-1334. <https://doi.org/10.1007/s002680010220>
 - [35] Zhu, J., Wu, Y., Huang, T., Jiang, G. and Yang, Z. (2023) Efficacy and Safety of Total Parathyroidectomy with Autotransplantation vs. Subtotal Parathyroidectomy for Secondary Hyperparathyroidism: A Retrospective Study. *Heliyon*, **9**, e15752. <https://doi.org/10.1016/j.heliyon.2023.e15752>
 - [36] Li, C., Lv, L., Wang, H., Wang, X., Yu, B., Xu, Y., *et al.* (2017) Total Parathyroidectomy

- versus Total Parathyroidectomy with Autotransplantation for Secondary Hyperparathyroidism: Systematic Review and Meta-Analysis. *Renal Failure*, **39**, 678-687. <https://doi.org/10.1080/0886022x.2017.1363779>
- [37] Chang, L., Liu, S. and Liang, T. (2023) Neck Reoperation for Recurrent or Persistent Renal Hyperparathyroidism. *World Journal of Surgery*, **47**, 2784-2791. <https://doi.org/10.1007/s00268-023-07172-5>
- [38] Mikhail, A.R., Williams, R.A., Son, L.S., Danos, D.M., Samuel, J., Kleinpeter, K.P., *et al.* (2023) Total Parathyroidectomy without Autotransplantation for ESRD Patients with Secondary Hyperparathyroidism; an Effective Alternative. *The American Surgeon*, **89**, 5349-5354. <https://doi.org/10.1177/00031348221148364>
- [39] Liu, M., Qiu, N., Zha, S., Du, Z., Wang, Y., Wang, Q., *et al.* (2017) To Assess the Effects of Parathyroidectomy (TPTX versus TPTX + AT) for Secondary Hyperparathyroidism in Chronic Renal Failure: A Systematic Review and Meta-Analysis. *International Journal of Surgery*, **44**, 353-362. <https://doi.org/10.1016/j.ijssu.2017.06.029>
- [40] Ohe, M.N., Santos, R.O., Kunii, I.S., Carvalho, A.B., Abrahão, M., Neves, M.C.D., *et al.* (2013) Intraoperative PTH Cutoff Definition to Predict Successful Parathyroidectomy in Secondary and Tertiary Hyperparathyroidism. *Brazilian Journal of Otorhinolaryngology*, **79**, 494-499. <https://doi.org/10.5935/1808-8694.20130088>
- [41] Zhang, L., Xing, C., Shen, C., Zeng, M., Yang, G., Mao, H., *et al.* (2016) Diagnostic Accuracy Study of Intraoperative and Perioperative Serum Intact PTH Level for Successful Parathyroidectomy in 501 Secondary Hyperparathyroidism Patients. *Scientific Reports*, **6**, Article No. 26841. <https://doi.org/10.1038/srep26841>
- [42] Khan, A.A., Bilezikian, J.P., Brandi, M.L., Clarke, B.L., Gittoes, N.J., Pasiaka, J.L., *et al.* (2022) Evaluation and Management of Hypoparathyroidism Summary Statement and Guidelines from the Second International Workshop. *Journal of Bone and Mineral Research*, **37**, 2568-2585. <https://doi.org/10.1002/jbmr.4691>

Abbreviations

AAES	American Association of Endocrine Surgeons
CKD	chronic kidney disease
CKD-MBD	chronic kidney disease-mineral and bone disorder
CT	computed tomography
ECG	electrocardiogram
HBS	hungry bone syndrome
iPTH	intact parathyroid hormone
KDIGO	Kidney Disease: Improving Global Outcomes
KDOQI	Kidney Disease Outcomes Quality Initiative
PET/CT	positron emission tomography/computed tomography
PTH	parathyroid hormone
SHPT	secondary hyperparathyroidism
SPECT/CT	single-photon emission computed tomography/computed tomography