Hypoparathyroidism and Renal Function

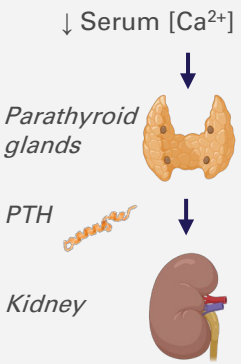
Renal pathophysiology in chronic hypoparathyroidism

Intact PTH axis

PTH increases renal tubular Ca^{2+} reabsorption and PO_4^{3-} excretion[1,2]

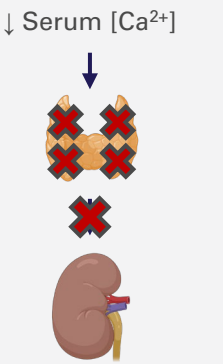
PTH stimulates renal 25(OH)D 1α-hydroxylase (CYP27B1) enzyme, which promotes conversion of calcidiol to **calcitriol (1,25-dihydroxyvitamin D)**[1,2]

Calcitriol increases intestinal absorption of dietary calcium via the vitamin D receptor[1,2]



↑ Ca^{2+} Reabsorption
↑ PO_4^{3-} Excretion
↑ Calcitriol

Hypoparathyroidism



PTH insufficiency may cause an increase in renal fractional excretion of Ca^{2+} (FECa), decrease in PO_4^{3-} excretion, and decrease in calcitriol, which lead to[1-4]:

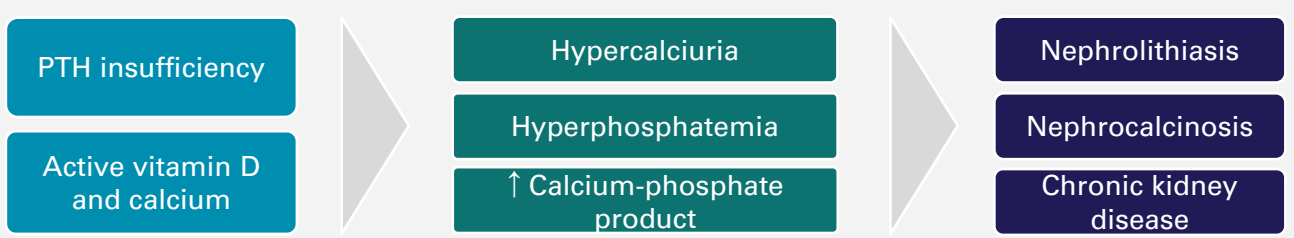
- Hypocalcemia
- Hyperphosphatemia

↓ Ca^{2+} Reabsorption
↓ PO_4^{3-} Excretion
↓ Calcitriol

Conventional therapy (active vitamin D and calcium) for chronic hypoparathyroidism

- Conventional therapy aims to alleviate hypocalcemia but does not address insufficient PTH levels[5]
- Conventional therapy may lead to increased renal filtered load of Ca^{2+}, hypercalciuria, and nephrotoxic effects[1,4]

Factors associated with renal complications in individuals with chronic hypoparathyroidism who are managed with conventional therapy[a]



The pathophysiological mechanisms of renal complications in chronic hypoparathyroidism are not well established and likely reflect a variety of factors, including PTH insufficiency and adverse renal responses to conventional therapy[a,12,13]

[a]active vitamin D and calcium

Abbreviations: Ca^{2+}, calcium; PO_4^{3-}, phosphate; PTH, parathyroid hormone

References: 1. Mannstadt M, et al. *Nat Rev Dis Primers* . 2017;3:17055. 2. Shoback D. *N Engl J Med* . 2008;359(4):391-403. 3. Brandi ML, et al. *J Clin Endocrinol Metab* . 2016;101(6):2273-83. 4. Khan AA, et al. *J Bone Miner Res* . 2022;37(12):2568-2585. 5. Khan AA, et al. *Eur J Endocrinol* . 2019;180(3):P1-p22. 6. Rubin MR. *F1000Res* . 2020;9. 7. Shoback DM, et al. *J Clin Endocrinol Metab* . 2016;101(6):2300-2312. 8. Gosmanova EO. *Rev Endocr Metab Disord* . 2021;22(2):297-316. 9. Smith A, et al. Presented ESPE & ESE. May 2025. 10. Reddy NL et al. *Endocr Metab Sci* . 2025.11. Noori W, et al. *Adv Ther.* 2025. 12. Mitchell, D.M., et al. *J Clin Endocrinol Metab*, 2012. 97(12): p. 4507–14. 13. Hamdy, N.A.T., et al., *J Endocrinol Invest*, 2021. 44(7): p. 1437–1446.

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Hypoparathyroidism and Renal Function

Individuals with chronic hypoparathyroidism who are managed with conventional therapy have an increased risk of renal complications vs. the general population[1-4]

Nephrolithiasis and nephrocalcinosis[a,1]

For those with chronic hypoparathyroidism, nephrolithiasis has been reported in up to 36% of individuals and nephrocalcinosis has been reported in up to 38% of individuals

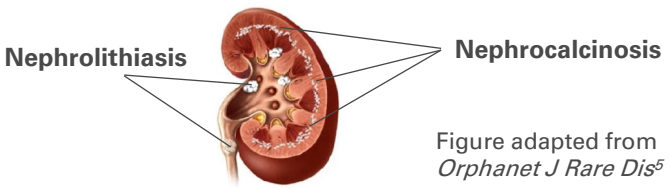
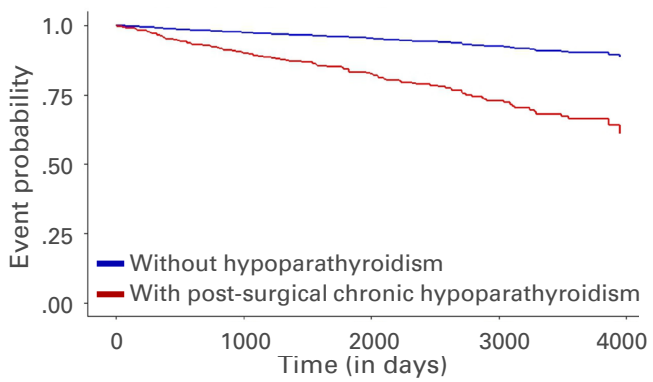


Figure adapted from *Orphanet J Rare Dis*[5]

Composite renal complications[b,c,2]

Individuals with post-surgical chronic hypoparathyroidism have a higher probability of composite renal complications

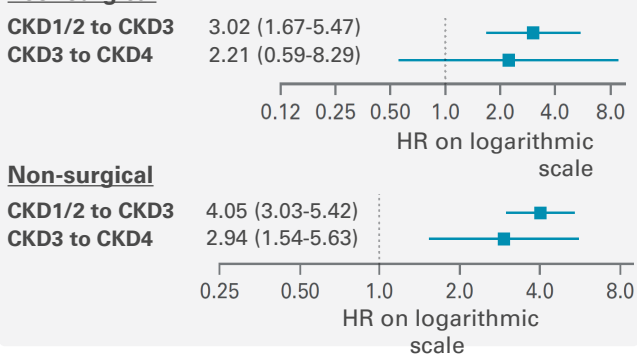


Individuals with post-surgical chronic hypoparathyroidism vs. patients without hypoparathyroidism

	Hazard ratio (95% CI)	*P* value
Composite renal complications	**4.10 (2.25-7.46)**	**<.001**

Chronic kidney disease (CKD) progression[d,3]

Individuals with chronic hypoparathyroidism who are managed with conventional therapy[e] have an increased risk of CKD progression



CKD has been reported in up to 41% of individuals with chronic hypoparathyroidism[a,1]

Risk of hospitalization for CKD

Individuals with chronic hypoparathyroidism compared with matched controls[f,6]

	Hazard ratio (95% CI)	*P* value
Chronic hypoparathyroidism	**3.49 (2.84-4.30)**	**<.001**
Postsurgical	3.34 (2.64-4.23)	<.001
Nonsurgical	3.96 (2.76-5.68)	<.001

Individuals with hypoparathyroidism have an increased risk of hospitalization due to renal complications, such as CKD and renal failure, compared with age- and sex-matched controls[5,6]

[a]In systematic review of 13 manuscripts, nephrolithiasis and nephrocalcinosis were assessed by diagnostic codes, CT scans, or self-reporting; CKD defined as eGFR <60 mL/min/1 .73 m^2, ≥ stage 3 classification, ICD codes, or self-reporting. [b]Retrospective matched cohort study in England (2007–2020); post-surgical hypoparathyroidism (n=215) matched to patients without hypoparathyroidism (n=2,149) in adjusted cox proportional hazards regression model. [c]composite = renal insufficiency, nephrocalcinosis and nephrolithiasis; [d]Retrospective matched cohort study in England (2008–2019); post-surgical (n=215) or non-surgical (n=730) hypoparathyroidism matched to controls (1:10) in cox proportional hazards regression model adjusted for age, sex, and cardiovascular disease. [e]In post-surgical patients, 71% were managed with calcitriol (≥0.50 µg/day); 73% were managed with calcium (≥600 mg/day). In non-surgical patients, 40% were managed with calcitriol (≥0.50 µg/day); 67% were managed with calcium (≥600 mg/day). [f]Swedish cohort study (1997-2018); Chronic hypoparathyroidism without preexisting CKD (n=1562) matched to controls (n=15620) in cox proportional hazards regression, adjusted for myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic pulmonary disease, diabetes, and hypertension.

Abbreviations: CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HR, hazard ratio; PTH, parathyroid hormone

References: 1. Gosmanova EO. *Rev Endocr Metab Disord*. 2021;22(2):297-316. 2. Reddy NL et al. *Endocr Metab Sci*. 2025. 3. Smith A, et al. Presented ESPE & ESE. 2025. 4. Díez JJ, et al. *Endocrine*. 2025;88(3):826–835; 5. Cipriani C, et al. *J Endocrinol Invest*. 2024 Aug;47(8):2021-2027; 6. Swartling O, et *al. J Clin Endocrinol Metab*. 2022 Sep 28;107(10):e4098-e4105.

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