HHS Public Access

Author manuscript

Curr Opin Nephrol Hypertens. Author manuscript; available in PMC 2020 November 01.

Published in final edited form as:

Curr Opin Nephrol Hypertens. 2019 November ; 28(6): 621–630. doi:10.1097/MNH.0000000000000542.

Thyroid Disease in End-Stage Renal Disease

Connie M. Rhee[1]

[1]Harold Simmons Center for Chronic Disease Research and Epidemiology, University of California Irvine School of Medicine, Orange, CA.

Abstract

Purpose of Review: Hypothyroidism is a highly prevalent endocrine disorder in the end-stage renal disease (ESRD) population, yet many cases may remain latent and undiagnosed.

Recent Findings: Epidemiologic data show that there is a nearly five-fold higher prevalence of hypothyroidism in advanced chronic kidney disease (CKD) patients vs. those without CKD. Given that the metabolism, degradation, and excretion of thyroid hormone and its metabolites, as well as the regulation of the hypothalamic-pituitary-thyroid axis may be altered in ESRD, certain considerations should be made when interpreting thyroid functional tests in these patients. Growing evidence shows that hypothyroidism and other thyroid functional test derangements are associated with higher risk of cardiovascular disease, worse patient-centered outcomes, and survival in the advanced CKD population, including those with ESRD. While limited data examining treatment of hypothyroidism suggests benefit, further studies of the efficacy and safety of thyroid hormone supplementation, including clinical trials and rigorous longitudinal observational studies are needed to inform the management of thyroid dysfunction in CKD.

Summary: Given the high burden of hypothyroidism in ESRD patients and potential ill effects on their cardiovascular health, patient-centered outcomes, and survival, further research is needed to inform the optimal management of thyroid dysfunction in this population.

Keywords

Thyroid; hypothyroidism; kidney; end-stage renal disease; dialysis

Introduction

Thyroid dysfunction is a common yet under-recognized endocrine disorder in the chronic kidney disease (CKD) population, including end-stage renal disease (ESRD) patients receiving dialysis.[1–5] Hypothyroidism is the most prevalent thyroid disorder encountered in ESRD patients,[1–5] which is typically ascertained by biochemical tests including an elevated serum thyrotropin (TSH) level in conjunction with normal or low free thyroxine (FT4) concentrations (i.e., subclinical “mild-moderate” and overt “severe” hypothyroidism,

Corresponding Author and Reprint Requests: Connie M. Rhee, MD, MSc, Harold Simmons Center for Chronic Disease Research and Epidemiology, University of California Irvine School of Medicine, 101 The City Drive South, City Tower, Suite 400, Orange, CA 92868, Tel: 714-456-5142; Fax: 714-456-6034, crhee1@uci.edu.

Conflicts of Interest:
None.

respectively).[6] In the general population, given that thyroid hormone receptors are present in nearly all tissues, untreated hypothyroidism may have pervasive adverse effects on multiple organ systems, including the kidney (Figure 1).[7] In non-dialysis dependent (NDD) and dialysis-dependent CKD patients, hypothyroidism and other thyroid functional test derangements have been associated with higher risk of cardiovascular disease,[8–13] impaired health-related quality of life (HRQOL),[14] and death.[15–20] In this review, we will discuss the epidemiology, diagnostic considerations, prognostic implications, and management of thyroid dysfunction in ESRD patients.

Epidemiology of Thyroid Dysfunction in Kidney Disease

Epidemiologic data show that there is a substantially higher prevalence of hypothyroidism in advanced CKD patients compared to those without CKD (Table 1).[15, 17–19, 21–32] Similar to the non-CKD population, subclinical disease accounts for a large proportion of hypothyroidism in CKD patients.[27]

Large population-based studies show that there is an increasingly higher prevalence of hypothyroidism with incrementally lower estimated glomerular filtration rates (eGFRs).[27, 30] In a study of 14,623 participants from the Third National Health and Nutrition Examination Survey, 5%, 11%, 20%, 23%, and 23% with eGFRs of >90, 60–89, 45–59, 30–44, and <30ml/min/1.73m^2 were observed to have hypothyroidism ascertained by a TSH >4.5mIU/L and/or thyroid hormone supplementation treatment.[27] In a study of 461,607 United States (US) veterans with stages 3–5 CKD, 23% patients were found to have hypothyroidism defined by TSH levels and treatment status, and every 10ml/min/1.73m^2 decrement in eGFR was associated with an 18% higher risk of hypothyroidism independent of case-mix covariates.[30] While studies of thyroid dysfunction in the ESRD population have been comparatively smaller, a similarly high prevalence of hypothyroidism has been reported (Table 1).[15, 17–19, 21–32]

A Potential Bi-Directional Link Between Thyroid Dysfunction and Kidney Disease

Although the mechanistic link between thyroid dysfunction and kidney disease has not been fully elucidated, growing evidence suggests that the relationship may be bi-directional (Figure 2).[1–5]

Thyroid Dysfunction Leading to Kidney Disease

Experimental and clinical studies suggest that hypothyroidism may adversely impact *kidney size* and *structure* in both development and adulthood via multiple pathways. In animal models, hypothyroidism has been shown to lead to a decreased kidney-to-body weight ratio,[33, 34] truncations in tubular mass,[33, 35, 36] and various alterations in glomerular architecture (i.e., decreased glomerular basement membrane [GBM] volume and area, GBM thickening, mesangial matrix expansion, increased glomerular capillary permeability).[37–39]

It has also been proposed that hypothyroidism may lead to kidney dysfunction due to reduced cardiac output,[40, 41] intra-renal vasoconstriction resulting from reduced vasodilator synthesis and activity,[41, 42] alterations in renin-angiotensin-aldosterone activity,[40, 42–44] and altered chloride channel expression leading to increased tubuloglomerular feedback.[45] In animal studies, hypothyroidism has led to decreased single nephron glomerular filtration rate (GFR), renal plasma flow, and glomerular transcapillary hydrostatic pressure.[46, 47] In case series, patients with severe hypothyroidism due to thyroidectomy manifested reductions in plasma flow and GFR measured by both creatinine-based estimating equations and gold-standard isotopic scans, which were reversed with exogenous thyroid hormone supplementation.[41, 42, 48–50] Several large population-based studies have also corroborated the relationship between higher TSH and development of incident CKD.[51–53] Limited data also suggest that thyroid hormone supplementation may ameliorate CKD progression, including one study of 309 stage 2–4 CKD patients with subclinical hypothyroidism in whom those treated with thyroid hormone supplementation had a slower rate of annual eGFR decline vs. those who were untreated.[54]

Kidney Disease Leading to Thyroid Dysfunction

Conversely, it has also been hypothesized that CKD may contribute to various thyroid functional test abnormalities.[1–5] First, impaired iodine clearance and retention ensuing from contrast media (i.e., angiograms, CT scans), medications (i.e., amiodarone), cleaning solutions (i.e., povidine-iodine), and dietary sources has been proposed to engender hypothyroidism via the Wolff-Chaikoff effect and hyperthyroidism via the Jod-Basedow phenomenon based on observational studies in the general population and case reports of dialysis patients.[55–60] With respect to other dietary factors, selenium deficiency frequently occurs in dialysis patients, which may lead to exacerbation of autoimmune thyroid disease.[61–63] As the vast majority of circulating thyroid hormone is bound to proteins, there have been case reports and series of thyroid hormone deficiency in patients with heavy protein losses due to nephrotic syndrome[64]; it has also been proposed that heavy protein losses in peritoneal effluent may also contribute to thyroid dysfunction in peritoneal dialysis (PD) patients.[18] Finally, metabolic acidosis,[65, 66] malnutrition, and non-thyroidal illness that develop in the uremic milieu of advanced CKD may also contribute to thyroid functional derangements (i.e., low triiodothyronine [T3] levels).[67, 68]

Interpretation of Thyroid Functional Tests in End-Stage Renal Disease

Production of thyroid hormones, namely T3 and T4, is stimulated by TSH secreted from the pituitary gland, which is regulated by thyrotropin-releasing hormone (TRH). In turn, TRH and TSH are suppressed by modest increases in T3 and T4. While T4 is solely synthesized by the thyroid gland, a large proportion of T3 is produced by 5’-deiodination of T4 to T3 in peripheral organs. In peripheral tissues, T4 is converted to T3 by type 2 5’-deiodinase (D1) and type 2 5’-deiodinase (D2), and T4-to-T3 conversion also occurs in the hypothalamus and pituitary by D2.[67, 69–71]

In ESRD, there may be alterations in the 1) metabolism, degradation, and excretion of thyroid hormone and its metabolites; 2) regulation of the hypothalamic-pituitary-thyroid

axis; and 3) performance of certain thyroid functional test assays.[1–5] Hence, there are a number of considerations that should be taken into account when interpreting thyroid functional tests in ESRD.

Thyrotropin Levels

In the general population, TSH is considered to be the most sensitive and specific single biochemical marker of thyroid status, given its inverse logarithmic relationship between circulating T3 and T4 (i.e., small changes in T3/T4 lead to exponential changes in TSH).[6] While various TSH alterations may potentially be observed in ESRD, including changes in clearance, diminished response to TRH, reduced pulsatility, impaired glycosylation, and increased half-life,[24, 72] TSH has been shown to be a more accurate metric of thyroid status vs. T3 in dialysis patients based on metabolic testing.[73] Limited data in ESRD patients also shows that TSH is suppressed with thyroid hormone supplementation, and that there is an appropriate rise in TSH with thyroidectomy, signaling an intact thyroid-pituitary feedback loop.[22] Hence, it may be inferred that TSH levels are a more reliable indicator of thyroid status compared with other existing metrics (i.e., T3 and T4).

Thyroxine Levels

Approximately 99.98% of T4 is bound to proteins, including thyroid-binding globulin, transthyretin, albumin, and lipoproteins.[74] FT4 assays, which measure the unbound, biologically-active fraction of T4, are typically used as an adjunctive test to classify the severity of hypothyroidism and hyperthyroidism.[6] Thus, assays which measure total T4 (i.e., free and protein-bound T4) may result in reduced T4 levels in conditions that lead to low protein levels, such as malnutrition, nephrotic syndrome, and heavy protein losses via peritoneal effluent.

FT4 assays (e.g., FT4 analog assay) that are routinely used in clinical practice indirectly estimate the minute fraction of non-protein bound T4, which may lead to spurious results in ESRD. The analog assay estimates FT4 according to antibody sequestration of total T4 relative to FT4 levels and are protein-hormone binding dependent.[74] In conditions where serum proteins levels are altered, or in the presence of circulating substances (e.g., uremic toxins) or medications (e.g., heparin, furosemide) that alter protein-hormone binding, results may not be accurate.[67, 74] However, direct FT4 assays are able to directly measure circulating FT4 levels by physically separating free vs. protein-bound T4 using ultrafiltration or equilibrium dialysis, followed by measurement of free hormone using radioimmunoassay or liquid chromatography tandem mass spectrometry.[74–76] Direct FT4 assays have become increasingly available for clinical and research purposes through reference laboratories, and further studies are needed to determine their utility in accurately defining thyroid status in the ESRD population.

Triiodothyronine Levels

Low T3 concentrations are the most frequently observed thyroid functional test abnormality in patients with advanced CKD.[68] For example, in cross-sectional analyses of 2284 CKD patients with normal TSH concentrations, over three-quarters of patients with eGFRs <15 ml/min/1.73m^2 had low T3 levels.[77] Notably, the majority of T3 is produced by the

peripheral deiodination of T4-to-T3, which is reduced in the setting of malnutrition, inflammation, non-thyroidal illness, and specific medications (e.g., glucocorticoids).[41, 67, 69, 78] Hence, low T3 levels in CKD may be representative of these above-mentioned factors independent of thyroid status.

Reverse Triidothyronine Levels

Reverse T3 (rT3) is a metabolically inactive form of thyroid hormone that is produced by the conversion of T4 to rT3 by the type 3 5'-deiodinase enzyme (D3). D3 is also responsible for the degradation of T3 to inactive diiodothyronine (T2).[67, 69] In hypothyroidism, rT3 levels are typically low, whereas in non-thyroidal illness rT3 levels are usually elevated due to increased conversion of T4 to rT3 and decreased clearance of rT3 to T2.[67] In kidney disease, rT3 levels are typically normal, although further studies are needed to determine their diagnostic utility and prognostic significance in ESRD patients.[24]

Anti-Thyroid Peroxidase Antibodies

Thyroid peroxidase (TPO) is a membrane-associated glycoprotein that catalyzes the iodination of tyrosine residues and their coupling to form thyroid hormones (i.e., T3 and T4) in a process known as organification. Anti-TPO antibodies are found in both the presence and absence of autoimmune thyroid disease. In the non-CKD population, the prevalence of anti-TPO antibody elevation in subclinical hypothyroidism varies according to age, sex, and race/ethnicity; however, on average ~60–80% of patients with subclinical hypothyroidism and/or elevated TSH have elevated anti-TPO antibody levels.[79–81] By comparison, existing data indicate that a small fraction (i.e., ~20–30%) of dialysis-dependent CKD patients with elevated TSH have anti-TPO antibody positivity as compared with the non-CKD population.[11, 82] However, in one study of a prospective cohort of 996 hemodialysis patients with cross-sectional anti-TPO antibody and TSH measurements, patients with elevated anti-TPO antibody levels had higher TSH levels vs. those with normal anti-TPO antibody levels.[82] These observations suggest that the high prevalence of TSH elevations among dialysis patients may only partially be explained by autoimmune causes.

Thyroid Status and Outcomes in End-Stage Renal Disease

There is a growing body of evidence showing that hypothyroidism and other thyroid functional test derangements are associated with higher mortality risk, cardiovascular disease, and worse patient-centered outcomes in the advanced CKD population, including those with ESRD (Table 2).[8, 9, 11, 14–20, 83, 84]

Mortality

Multiple studies have shown that hypothyroidism ascertained by serum TSH concentrations is associated with higher death risk in both non-dialysis and dialysis dependent CKD patients. In one of the first studies conducted to date, among 2715 dialysis patients from two tertiary care centers in Boston who underwent TSH measurement at study entry, hypothyroid patients had a higher mortality risk vs. those who were euthyroid.[15] However, in a secondary analysis of 1000 diabetic hemodialysis patients from the *Die Deutsche Diabetes Dialyse* (4D Trial), hypothyroidism (i.e., subclinical disease examined separately or in

conjunction with overt disease) at study entry was not associated with sudden cardiac death, cardiovascular events, or all-cause mortality.[84] However, it should be noted that only 1.8% of the cohort had hypothyroidism, providing limited power to detect significant associations. In addition, patients with subclinical hyperthyroidism had higher risk of sudden cardiac death.

Three subsequent studies that examined repeated measures of TSH over time have found that hypothyroidism and high-normal TSH levels are associated with higher death risk in dialysis patients. Among 8840 incident hemodialysis patients from a large US dialysis organization, in both baseline and time-varying analyses hypothyroidism as well as high-normal TSH levels >3.0mIU/L were each associated with higher mortality risk.[17] Similarly, in a prospective multi-center cohort of 541 hemodialysis patients from the *Hypothyroidism, Cardiovascular Disease, and Survival in Kidney Disease* (HyCARDS) study who underwent protocolized TSH measurements every six months, time-varying TSH levels in the highest tertile (TSH >2.11mIU/L) were associated with higher death risk.[19] Finally, among 1474 PD patients from a large US dialysis organization, both time-varying hypothyroidism and hyperthyroidism were associated with higher mortality.[18]

Cardiovascular Disease

In the general population, hypothyroidism is a known risk factor for cardiovascular disease via multiple pathways (Figure 3).[40] Given that ~40% of ESRD deaths are due to cardiovascular causes, there has been increasing interest in hypothyroidism as an under-recognized risk factor for cardiovascular disease in this population. In a cross-sectional analysis of 51 peritoneal dialysis patients from South Korea, patients with subclinical hypothyroidism had lower left ventricular ejection fractions vs. those who were euthyroid.[11] More recently, in a secondary analysis of 99 hemodialysis patients from the multi-center *Anti-Inflammatory and Anti-Oxidative Nutrition in Hypoalbuminemic Dialysis Patients* (AIONID) trial, patients with TSH levels in the highest three quartiles had worse endothelial function measured by digital thermal monitoring vs. those in the lowest quartile.[83]

Given that thyroid hormone deficiency may engender accelerated atherosclerosis and decreased production of vascular calcification inhibitors (i.e., matrix gla protein, klotho), there has been growing interest in hypothyroidism as a risk factor for coronary artery calcification (CAC) in kidney disease.[85, 86] First, in a study of 84 PD patients from Sweden, low free T3 (FT3) levels were associated with higher CAC scores measured by cardiac CT scan; while TSH levels were also measured, associations with CAC were not reported.[12] In a subsequent study of 94 ESRD patients eligible for living donor transplantation, lower FT3, FT4, and TSH levels were associated with higher CAC scores.[13] More recently, in a secondary analysis of 104 patients from AIONID trial, incrementally higher TSH levels were associated with higher CAC burden.[8, 9]

Patient-Centered Outcomes

As another potential pathway towards death, one study has examined the relationship between thyroid status with HRQOL in ESRD. In a prospective cohort of 450 hemodialysis

patients with serial protocolized TSH and SF36 assessments, higher TSH levels were associated with impaired HRQOL SF36 scores. Notably, the SF36 subscales most impaired in the setting of thyroid dysfunction were those related to physical health (i.e., energy/fatigue, physical function, role limitations due to physical health, pain).[14] Future studies are needed to determine if thyroid hormone supplementation improves the HRQOL of ESRD patients with thyroid dysfunction.

Management of Thyroid Dysfunction in End-Stage Renal Disease

Screening

Existing clinical practice guidelines lack screening recommendations for thyroid dysfunction in ESRD patients, among whom many cases may remain latent and undiagnosed due to symptom overlap with uremia (e.g., fatigue, cold intolerance, decreased cognition). In the general population, multiple professional societies have recommended thyroid functional test screening in selected subgroups (Table 3).[87–93] While extrapolation of some of these criteria may pertain to ESRD patients (i.e., presence of heart failure), further research of the prognostic implications of thyroid dysfunction and its treatment, risk factors, and magnitude of the benefits and risks of screening are needed to inform guidelines.[94]

Treatment

Data from the United States Renal Data System has shown that thyroid hormone supplementation is one of the most commonly prescribed medications in NDD-CKD and ESRD patients.[95, 96] However, there have been few studies that have examined the impact of thyroid hormone supplementation in CKD patients, including those receiving dialysis. In a study of 2715 dialysis patients in whom TSH and treatment status were measured at baseline, patients who were euthyroid on medication (i.e., presumed to be hypothyroid treated-to-target) had similar mortality risk compared to those who were spontaneously euthyroid.[15] In contrast, patients with hypothyroid-range TSH levels with or without treatment had higher death risk. In a subsequent study of 227,426 stage 3 CKD patients from the national Veterans Affairs database in whom thyroid function and treatment status were assessed at study entry, those with untreated and undertreated hypothyroidism and untreated hyperthyroidism had higher mortality risk compared to spontaneously euthyroid patients. whereas patients who were hypothyroid treated-to-target had similar to slightly lower mortality risk.[16] However, it bears mention that thyroid hormone supplementation has a potential narrow therapeutic-to-toxic window with theoretical risk of protein-energy wasting, cardiovascular events, and bone loss.[1–5, 97] Thus, further studies of the benefits and risks of thyroid hormone supplementation, including clinical trials and rigorous observational studies providing “real-world” evidence of longitudinal treatment are needed to inform the management of CKD patients with thyroid dysfunction.

Conclusion

In conclusion, there have been substantial advances in our understanding of the scope of thyroid disease in the CKD population, limitations of existing thyroid testing methods in ESRD, and the impact of hypothyroidism and other thyroid functional test abnormalities

upon cardiovascular and patient-centered outcomes and survival in these patients. However, there remains substantial uncertainty with regards to the (1) mechanistic link between thyroid and kidney disease, (2) performance characteristics and prognostic significance of novel metrics of thyroid status assessment, and (3) efficacy and safety of thyroid hormone supplementation, including target TSH ranges, in this population. Given the high prevalence of hypothyroidism in ESRD, as well as high rates of cardiovascular disease, impaired HRQOL, and mortality in these patients, there is compelling need for further investigation of how to optimally manage thyroid dysfunction in this population.

Financial Support and Sponsorship:

The author is supported by research grants from the NIH/NIDDK including K23-DK102903, R03-DK114642, and R01-DK122767; and philanthropic grants from Dr. Joseph Lee.

References:

1. Rhee CM. Abnormalities of Thyroid Function in Chronic Dialysis Patients. In Nissenson Handbook of Dialysis Therapy, 5th edition, edited by Nissenson A Philadelphia: Saunders Elsevier, 2016.
2. Kalim S, Rhee CM. Thyroid Status in Chronic Renal Failure – A Non-Thyroidal Illness Syndrome. In Textbook of Nephro-Endocrinology: Hormones in Kidney Disease, 2nd edition, edited by Singh A, Williams G. New York: Elsevier, 2017.
3. Rhee CM, Brent GA, Kalantar-Zadeh K. Thyroid Dysfunction and Outcomes in Kidney Disease. Diagnosis and Treatment of Endocrine Disorders in Kidney Disease, 1st edition, edited by Rhee CM, Brent GA, Kalantar-Zadeh K. New York: Springer Science, 2019.
4. Rhee CM. The interaction between thyroid and kidney disease: an overview of the evidence. Curr Opin Endocrinol Diabetes Obes 2016;23(5):407–15. [PubMed: 27428519]
5. Rhee CM, Brent GA, Kovesdy CP, et al. Thyroid functional disease: an under-recognized cardiovascular risk factor in kidney disease patients. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association. 2015;30(5):724–37.
6. Ladenson PW. Diagnosis of Hypothyroidism. In Werner and Ingbar's The Thyroid, 10th edition, edited by Braverman LE, Cooper DS. Philadelphia: Lippincott Williams and Wilkins, 2013.
7. McDermott MT. Overview of the Clinical Manifestations of Hypothyroidism. In Werner and Ingbar's The Thyroid, 10th edition, edited by Braverman LE, Cooper DS. Philadelphia: Lippincott Williams and Wilkins, 2013.
8. Rhee CM, Budoff MJ, Novoa A, et al. Thyroid Status: A Novel Coronary Artery Calcification Risk Factor in Hemodialysis Patients. Abstract presented at the 2018 American Heart Association Scientific Sessions November 2018.
9. Rhee CM, Novoa A, You AS, et al. Thyroid Status and Coronary Artery Calcification in a Prospective Hemodialysis Cohort. Abstract presented at the 2018 American Society of Nephrology Kidney Week Meeting.
10. You AS, Budoff MJ, Zeb I, et al. Thyroid Status and Endothelial Function in Hemodialysis Patients. Abstract presented at the 2019 National Kidney Foundation Spring Clinical Meeting.
11. Kang EW, Nam JY, Yoo TH, et al. Clinical implications of subclinical hypothyroidism in continuous ambulatory peritoneal dialysis patients. American journal of nephrology. 2008;28(6):908–13. [PubMed: 18580053]
12. Meuwese CL, Carrero JJ, Cabezas-Rodriguez I, et al. Nonthyroidal illness: a risk factor for coronary calcification and arterial stiffness in patients undergoing peritoneal dialysis? Journal of internal medicine. 2013;274(6):584–93. [PubMed: 23815158]
13. Meuwese CL, Olauson H, Qureshi AR, et al. Associations between Thyroid Hormones, Calcification Inhibitor Levels and Vascular Calcification in End-Stage Renal Disease. PloS one. 2015;10(7):e0132353. [PubMed: 26147960]

14. Rhee CM, Chen Y, You AS, et al. Thyroid Status, Quality of Life, and Mental Health in Patients on Hemodialysis. Clinical journal of the American Society of Nephrology : CJASN 2017;12(8):1274–83. [PubMed: 28705886]

15. Rhee CM, Alexander EK, Bhan I, Brunelli SM. Hypothyroidism and Mortality among Dialysis Patients. Clinical journal of the American Society of Nephrology : CJASN 2013;8(4):593–601. [PubMed: 23258793]

**16. Rhee CM, Kalantar-Zadeh K, Ravel V, et al. Thyroid Status and Death Risk in US Veterans With Chronic Kidney Disease. Mayo Clin Proc 2018;93(5):573–85. [PubMed: 29728200] This is one of the largest studies conducted to date showing that hypothyroidism and high-normal thyrotropin levels are associated with higher death risk in US veterans with non-dialysis dependent chronic kidney disease (NDD-CKD).

17. Rhee CM, Kim S, Gillen DL, et al. Association of thyroid functional disease with mortality in a national cohort of incident hemodialysis patients. The Journal of clinical endocrinology and metabolism. 2015;100(4):1386–95. [PubMed: 25632971]

18. Rhee CM, Ravel VA, Streja E, et al. Thyroid Functional Disease and Mortality in a National Peritoneal Dialysis Cohort. The Journal of clinical endocrinology and metabolism. 2016;101(11):4054–61. [PubMed: 27525529]

19. Rhee CM, You AS, Nguyen DV, et al. Thyroid Status and Mortality in a Prospective Hemodialysis Cohort. The Journal of clinical endocrinology and metabolism. 2017;102(5):1568–77. [PubMed: 28324018]

**20. You AS, Sim JJ, Kovesdy CP, et al. Association of thyroid status prior to transition to end-stage renal disease with early dialysis mortality. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association. Epub 10 8, 2018.This study showed that there is a long-term “legacy effect” of higher thyrotropin levels >5.0 mIU/L during the pre-end-stage renal disease (ESRD) period with post-ESRD mortality risk among US veterans with advanced kidney disease.

21. Bando Y, Ushiogi Y, Okafuji K, et al. Non-autoimmune primary hypothyroidism in diabetic and non-diabetic chronic renal dysfunction. Exp Clin Endocrinol Diabetes. 2002;110(8):408–15. [PubMed: 12518252]

22. Carrero JJ, Qureshi AR, Axelsson J, et al. Clinical and biochemical implications of low thyroid hormone levels (total and free forms) in euthyroid patients with chronic kidney disease. Journal of internal medicine. 2007;262(6):690–701. [PubMed: 17908160]

23. Chonchol M, Lippi G, Salvagno G, et al. Prevalence of subclinical hypothyroidism in patients with chronic kidney disease. Clinical journal of the American Society of Nephrology : CJASN 2008;3(5):1296–300. [PubMed: 18550654]

24. Kaptein EM. Thyroid hormone metabolism and thyroid diseases in chronic renal failure. Endocrine reviews. 1996;17(1):45–63. [PubMed: 8641223]

25. Kutlay S, Atli T, Koseogullari O, et al. Thyroid disorders in hemodialysis patients in an iodine-deficient community. Artif Organs 2005;29(4):329–32. [PubMed: 15787628]

26. Lin CC, Chen TW, Ng YY, et al. Thyroid dysfunction and nodular goiter in hemodialysis and peritoneal dialysis patients. Peritoneal dialysis international : journal of the International Society for Peritoneal Dialysis. 1998;18(5):516–21. [PubMed: 9848631]

27. Lo JC, Chertow GM, Go AS, Hsu CY. Increased prevalence of subclinical and clinical hypothyroidism in persons with chronic kidney disease. Kidney international. 2005;67(3):1047–52. [PubMed: 15698444]

28. Meuwese CL, Dekker FW, Lindholm B, et al. Baseline levels and trimestral variation of triiodothyronine and thyroxine and their association with mortality in maintenance hemodialysis patients. Clinical journal of the American Society of Nephrology : CJASN 2012;7(1):131–8. [PubMed: 22246282]

29. Ng YY, Wu SC, Lin HD, et al. Prevalence of clinical and subclinical thyroid disease in a peritoneal dialysis population. Peritoneal dialysis international : journal of the International Society for Peritoneal Dialysis. 2012;32(1):86–93. [PubMed: 21532003]

30. Rhee CM, Kalantar-Zadeh K, Streja E, et al. The relationship between thyroid function and estimated glomerular filtration rate in patients with chronic kidney disease. Nephrology, dialysis,

transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association. 2015;30(2):282–7.

31. Shantha GP, Kumar AA, Bhise V, et al. Prevalence of Subclinical Hypothyroidism in Patients with End-Stage Renal Disease and the Role of Serum Albumin: A Cross-Sectional Study from South India. Cardiorenal medicine. 2011;1(4):255–60. [PubMed: 22096457]
32. Targher G, Chonchol M, Zoppini G, et al. Prevalence of thyroid autoimmunity and subclinical hypothyroidism in persons with chronic kidney disease not requiring chronic dialysis. Clin Chem Lab Med 2009;47(11):1367–71. [PubMed: 19769543]
33. Canavan JP, Holt J, Easton J, et al. Thyroid-induced changes in the growth of the liver, kidney, and diaphragm of neonatal rats. Journal of cellular physiology. 1994;161(1):49–54. [PubMed: 7929607]
34. Slotkin TA, Seidler FJ, Kavlock RJ, Bartolome JV. Thyroid hormone differentially regulates cellular development in neonatal rat heart and kidney. Teratology. 1992;45(3):303–12. [PubMed: 1631783]
35. Bentley AG, Madsen KM, Davis RG, Tisher CC. Response of the medullary thick ascending limb to hypothyroidism in the rat. The American journal of pathology. 1985;120(2):215–21. [PubMed: 4025510]
36. Salomon MI, Di Scala V, Grishman E, et al. Renal lesions in hypothyroidism: a study based on kidney biopsies. Metabolism: clinical and experimental. 1967;16(9):846–52. [PubMed: 6072218]
37. Bradley SE, Coelho JB, Sealey JE, et al. Changes in glomerulotubular dimensions, single nephron glomerular filtration rates and the renin-angiotensin system in hypothyroid rats. Life sciences. 1982;30(7–8):633–9. [PubMed: 7040895]
38. Rodriguez-Gomez I, Banegas I, Wangensteen R, et al. Influence of thyroid state on cardiac and renal capillary density and glomerular morphology in rats. The Journal of endocrinology. 2013;216(1):43–51. [PubMed: 23048210]
39. Wheatley T, Edwards OM. Mild hypothyroidism and oedema: evidence for increased capillary permeability to protein. Clinical endocrinology. 1983;18(6):627–35. [PubMed: 6684003]
40. Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. The New England journal of medicine. 2001;344(7):501–9. [PubMed: 11172193]
41. Mariani LH, Berns JS. The renal manifestations of thyroid disease. Journal of the American Society of Nephrology : JASN 2012;23(1):22–6. [PubMed: 22021708]
42. Basu G, Mohapatra A. Interactions between thyroid disorders and kidney disease. Indian journal of endocrinology and metabolism. 2012;16(2):204–13. [PubMed: 22470856]
43. Ichihara A, Kobori H, Miyashita Y, et al. Differential effects of thyroid hormone on renin secretion, content, and mRNA in juxtaglomerular cells. The American journal of physiology. 1998;274(2):E224–31. [PubMed: 9486151]
44. Vargas F, Rodriguez-Gomez I, Vargas-Tendero P, et al. The renin-angiotensin system in thyroid disorders and its role in cardiovascular and renal manifestations. The Journal of endocrinology. 2012;213(1):25–36. [PubMed: 22043064]
45. Vargas F, Moreno JM, Rodriguez-Gomez I, et al. Vascular and renal function in experimental thyroid disorders. European journal of endocrinology / European Federation of Endocrine Societies. 2006;154(2):197–212.
46. Bradley SE, Stephan F, Coelho JB, Reville P. The thyroid and the kidney. Kidney international. 1974;6(5):346–65. [PubMed: 4431166]
47. Falk SA, Buric V, Hammond WS, Conger JD. Serial glomerular and tubular dynamics in thyroidectomized rats with remnant kidneys. American journal of kidney diseases : the official journal of the National Kidney Foundation. 1991;17(2):218–27. [PubMed: 1992665]
48. Karanikas G, Schutz M, Szabo M, et al. Isotopic renal function studies in severe hypothyroidism and after thyroid hormone replacement therapy. American journal of nephrology. 2004;24(1):41–5. [PubMed: 14685006]
49. Kreisman SH, Hennessey JV. Consistent reversible elevations of serum creatinine levels in severe hypothyroidism. Archives of internal medicine. 1999;159(1):79–82. [PubMed: 9892334]

50. Villabona C, Sahun M, Roca M, et al. Blood volumes and renal function in overt and subclinical primary hypothyroidism. The American journal of the medical sciences. 1999;318(4):277–80. [PubMed: 10522555]
51. Chuang MH, Liao KM, Hung YM, et al. Abnormal Thyroid-Stimulating Hormone and Chronic Kidney Disease in Elderly Adults in Taipei City. J Am Geriatr Soc 2016;64(6):1267–73. [PubMed: 27321605]
*52. Toda A, Hara S, Kato M, et al. Association of Thyrotropin Concentration with Chronic Kidney Disease in a Japanese General Population Cohort. Nephron 2019;142(2):91–7. [PubMed: 30799424] This study demonstrated that higher serum thytrotopin levels are associated with higher risk of developing de novo chronic kidney disease in a large longitudinal cohort of Japanese patients.
53. Zhang Y, Chang Y, Ryu S, et al. Thyroid hormone levels and incident chronic kidney disease in euthyroid individuals: the Kangbuk Samsung Health Study. International journal of epidemiology. 2014;43(5):1624–32. [PubMed: 25011453]
54. Shin DH, Lee MJ, Kim SJ, et al. Preservation of renal function by thyroid hormone replacement therapy in chronic kidney disease patients with subclinical hypothyroidism. The Journal of clinical endocrinology and metabolism. 2012;97(8):2732–40. [PubMed: 22723335]
55. Brough R, Jones C. Iatrogenic iodine as a cause of hypothyroidism in infants with end-stage renal failure. Pediatr Nephrol 2006;21(3):400–2. [PubMed: 16385388]
56. Lee SY, Rhee CM, Leung AM, et al. A review: Radiographic iodinated contrast media-induced thyroid dysfunction. The Journal of clinical endocrinology and metabolism. 2015;100(2):376–83. [PubMed: 25375985]
57. Moisey RS, McPherson S, Wright M, Orme SM. Thyroiditis and iodide mumps following an angioplasty. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association. 2007;22(4):1250–2.
58. Rhee CM, Bhan I, Alexander EK, Brunelli SM. Association between iodinated contrast media exposure and incident hyperthyroidism and hypothyroidism. Archives of internal medicine. 2012;172(2):153–9. [PubMed: 22271121]
59. Sanai T, Inoue T, Okamura K, et al. Reversible primary hypothyroidism in Japanese patients undergoing maintenance hemodialysis. Clinical nephrology. 2008;69(2):107–13. [PubMed: 18218304]
60. Takeda S, Michigishi T, Takazakura E. Iodine-induced hypothyroidism in patients on regular dialysis treatment. Nephron 1993;65(1):51–5. [PubMed: 8413791]
61. Napolitano G, Bonomini M, Bomba G, et al. Thyroid function and plasma selenium in chronic uremic patients on hemodialysis treatment. Biol Trace Elem Res 1996;55(3):221–30. [PubMed: 9096850]
62. Schomburg L. Selenium, selenoproteins and the thyroid gland: interactions in health and disease. Nature reviews Endocrinology. 2011;8(3):160–71.
63. Tonelli M, Wiebe N, Hemmelgarn B, et al. Trace elements in hemodialysis patients: a systematic review and meta-analysis. BMC Med 2009;7:25. [PubMed: 19454005]
*64. Li LZ, Hu Y, Ai SL, Cheng L, Liu J, Morris E, et al. The relationship between thyroid dysfunction and nephrotic syndrome: a clinicopathological study. Sci Rep 2019;9(1):6421. [PubMed: 31015507] This study showed that higher levels of urine protein in patients with nephrotic syndrome are an independent risk factor for thyroid dysfunction.
65. Brungger M, Hulter HN, Krapf R. Effect of chronic metabolic acidosis on thyroid hormone homeostasis in humans. The American journal of physiology. 1997;272(5 Pt 2):F648–53. [PubMed: 9176376]
66. Wiederkehr MR, Kalogiros J, Krapf R. Correction of metabolic acidosis improves thyroid and growth hormone axes in haemodialysis patients. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association. 2004;19(5):1190–7.
67. Langton JE, Brent GA. Nonthyroidal illness syndrome: evaluation of thyroid function in sick patients. Endocrinology and metabolism clinics of North America. 2002;31(1):159–72. [PubMed: 12055987]

68. Rhee CM. Low-T3 Syndrome in Peritoneal Dialysis: Metabolic Adaptation, Marker of Illness, or Mortality Mediator? Clinical journal of the American Society of Nephrology : CJASN 2015;10(6):917–9. [PubMed: 25979973]
69. Bianco AC, Salvatore D, Gereben B, et al. Biochemistry, cellular and molecular biology, and physiological roles of the iodothyronine selenodeiodinases. Endocrine reviews. 2002;23(1):38–89. [PubMed: 11844744]
70. Fonseca TL, Correa-Medina M, Campos MP, et al. Coordination of hypothalamic and pituitary T3 production regulates TSH expression. J Clin Invest 2013;123(4):1492–500. [PubMed: 23524969]
71. Gereben B, Zavacki AM, Ribich S, et al. Cellular and molecular basis of deiodinase-regulated thyroid hormone signaling. Endocrine reviews. 2008;29(7):898–938. [PubMed: 18815314]
72. Carrero JJ, Stenvinkel P, Lindholm B. Endocrine Aspects of Chronic Kidney Disease In Taal Brenner and Rector's The Kidney, 9th edition, edited by Taal MW, Chertow GM, Marsden PA, Skorecki K, Yu AS, Brenner BM. Philadelphia: Elsevier Saunders, 2012.
73. Spector DA, Davis PJ, Helderman JH, Bell B, Utiger RD. Thyroid function and metabolic state in chronic renal failure. Ann Intern Med 1976;85(6):724–30. [PubMed: 999108]
74. Soldin OP. Measuring serum thyroid-stimulating hormone, thyroid hormones, thyroid-directed antibodies, and transport proteins In Werner and Ingbar's The Thyroid, 10th edition, edited by Braverman LE, Cooper DS. Philadelphia: Lippincott Williams and Wilkins, 2013.
75. Soldin OP, Soldin SJ. Thyroid hormone testing by tandem mass spectrometry. Clinical biochemistry. 2011;44(1):89–94. [PubMed: 20691174]
76. Soldin SJ, Soukhova N, Janicic N, Jonklaas J, Soldin OP. The measurement of free thyroxine by isotope dilution tandem mass spectrometry. Clinica chimica acta; international journal of clinical chemistry. 2005;358(1–2):113–8. [PubMed: 16018881]
77. Song SH, Kwak IS, Lee DW, et al. The prevalence of low triiodothyronine according to the stage of chronic kidney disease in subjects with a normal thyroid-stimulating hormone. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association. 2009;24(5):1534–8.
78. Lim VS. Thyroid function in patients with chronic renal failure. American journal of kidney diseases : the official journal of the National Kidney Foundation. 2001;38(4 Suppl 1):S80–4. [PubMed: 11576928]
79. Fatourechi V Subclinical hypothyroidism: an update for primary care physicians. Mayo Clin Proc 2009;84(1):65–71. [PubMed: 19121255]
80. Hoogendoorn EH, Hermus AR, de Vegt F, et al. Thyroid function and prevalence of anti-thyroperoxidase antibodies in a population with borderline sufficient iodine intake: influences of age and sex. Clinical chemistry. 2006;52(1):104–11. [PubMed: 16254196]
81. Parle JV, Franklyn JA, Cross KW, et al. Prevalence and follow-up of abnormal thyrotrophin (TSH) concentrations in the elderly in the United Kingdom. Clinical endocrinology. 1991;34(1):77–83. [PubMed: 2004476]
82. Rhee CM, Brent GA, You AS, et al. Anti-Thyroid Peroxidase Antibodies and Serum Thyrotropin Levels in a Prospective Hemodialysis Cohort. Abstract presented at the 2019 World Congress Nephrology meeting.
83. You AS, Budoff MJ, Zeb I, Ahmadi N, et al. Thyroid Status and Endothelial Function in Hemodialysis Patients. Abstract presented at the 2019 National Kidney Foundation Spring Clinical Meeting.
84. Drechsler C, Schneider A, Gutjahr-Lengsfeld L, et al. Thyroid function, cardiovascular events, and mortality in diabetic hemodialysis patients. American journal of kidney diseases : the official journal of the National Kidney Foundation. 2014;63(6):988–96. [PubMed: 24315768]
85. Mizuno I, Takahashi Y, Okimura Y, et al. Upregulation of the klotho gene expression by thyroid hormone and during adipose differentiation in 3T3-L1 adipocytes. Life sciences. 2001;68(26):2917–23. [PubMed: 11411791]
86. Sato Y, Nakamura R, Satoh M, et al. Thyroid hormone targets matrix Gla protein gene associated with vascular smooth muscle calcification. Circ Res 2005;97(6):550–7. [PubMed: 16100044]
87. American Academy of Family Physicians. Summary of policy recommendations for periodic health examinations. Leawood, KS: American Academy of Family Physicians, 2002.

88. Institute of Medicine (US) Committee on Medicare Coverage of Routine Thyroid Screening. Editors Stone MB, Wallace RB. Washington DC: National Academies Press, 2003.

89. Clinical guideline, part 1. Screening for thyroid disease. American College of Physicians. Ann Intern Med 1998;129(2):141–3. [PubMed: 9669976]

90. Garber JR, Cobin RH, Gharib H, et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Thyroid : official journal of the American Thyroid Association. 2012;22(12):1200–35. [PubMed: 22954017]

91. Hunt SA, Baker DW, Chin MH, et al. ACC/AHA Guidelines for the Evaluation and Management of Chronic Heart Failure in the Adult: Executive Summary A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1995 Guidelines for the Evaluation and Management of Heart Failure): Developed in Collaboration With the International Society for Heart and Lung Transplantation; Endorsed by the Heart Failure Society of America. Circulation. 2001;104(24):2996–3007. [PubMed: 11739319]

92. LeFevre ML, Force USPST. Screening for thyroid dysfunction: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2015;162(9):641–50. [PubMed: 25798805]

93. Rugge JB, Bougatsos C, Chou R. Screening and treatment of thyroid dysfunction: an evidence review for the U.S. Preventive Services Task Force. Ann Intern Med 2015;162(1):35–45. [PubMed: 25347444]

**94. Stan MN, Drake MT. Failing Kidneys and Thyroid Dysfunction-An Undesirable Synergy. Mayo Clin Proc 2018;93(5):555–7. [PubMed: 29728198] This editorial highlights specific areas warranting further research in the area of thyroid dysfunction in kidney disease, including future studies that investigate the potential need for public health policy in which thyroid monitoring is routinely conducted in non–dialysis-dependent chronic kidney disease and therapeutic approaches that ameliorate hypothyroid-related mortality risk.

95. United States Renal Data System. USRDS 2018 Annual Data Report: Atlas of End-Stage Renal Disease in the United States. Bethesda, MD; 2018.

96. United States Renal Data System. USRDS 2012 Annual Data Report: Atlas of End-Stage Renal Disease in the United States. Bethesda, MD; 2012.

97. Wartofsky L Levothyroxine: therapeutic use and regulatory issues related to bioequivalence. Expert Opin Pharmacother 2002;3(6):727–32. [PubMed: 12036412]

Key Points:

- Hypothyroidism is a common endocrine disorder in the end-stage renal disease (ESRD) population, yet many cases may remain latent and undiagnosed due to the overlap of its symptoms with uremia.
- Emerging data show that hypothyroidism is associated with higher risk of cardiovascular disease, worse patient-centered outcomes, and survival in the advanced chronic kidney disease (CKD) population, including those with ESRD.
- Further studies of the efficacy and safety of thyroid hormone supplementation, including clinical trials and rigorous longitudinal observational studies, are needed to inform the management of thyroid dysfunction in CKD.

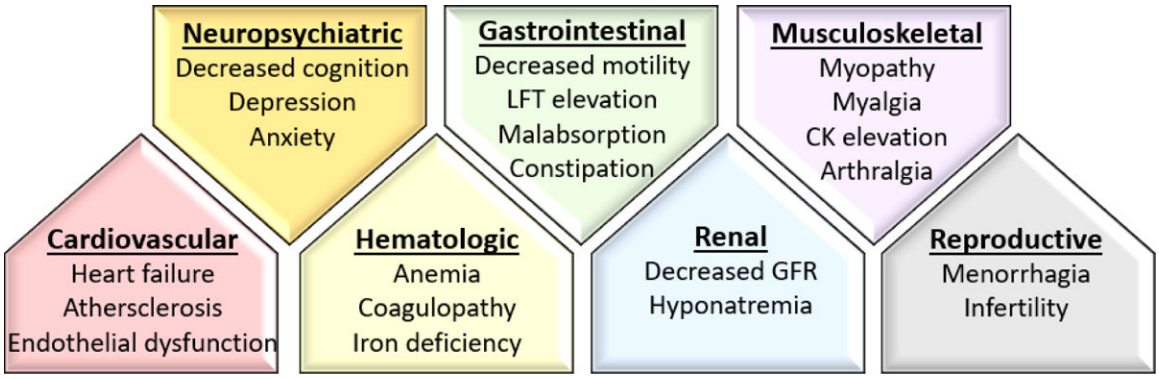

Figure 1.
Clinical manifestations of hypothyroidism.

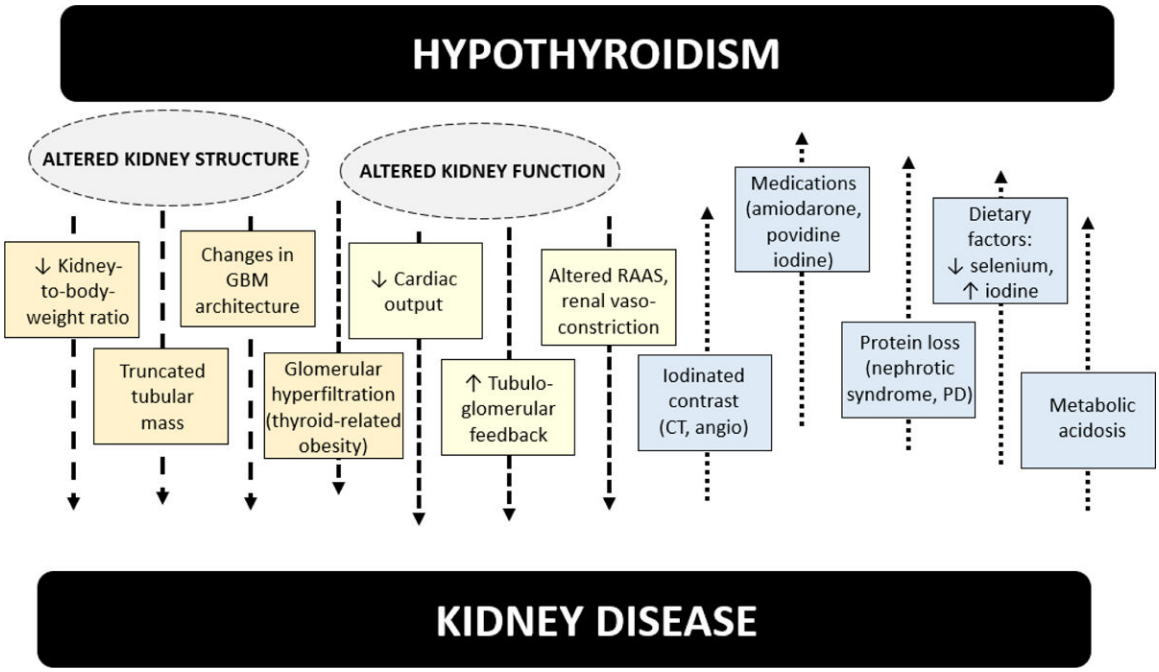

Figure 2.
Pathways between hypothyroidism and kidney disease.

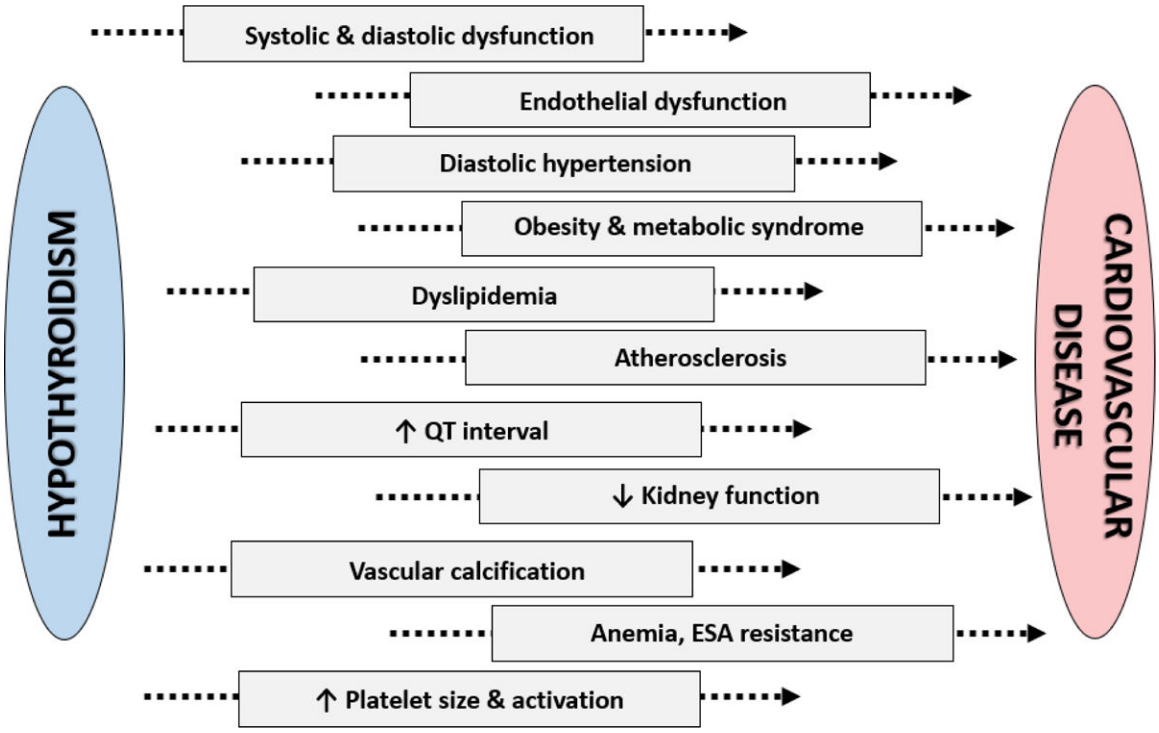

Figure 3.
Pathways between hypothyroidism and cardiovascular disease.

Table 1.

Selected studies of the prevalence of hypothyroidism in the end-stage renal disease and non-dialysis dependent chronic kidney disease populations.

Study (Year)	Cohort (N)	Prevalence
End-Stage Renal Disease		
TSH Elevation		
Lin et al. (1998)[26]	HD/PD (221)	14.9%
Kutlay et al. (2005)[25]	HD (87)	23.1%
Rhee et al. (2013)[15]	HD/PD (2715)	12.9%
Rhee et al. (2015)[17]	National incident HD from LDO (8840)	21.8%
Rhee et al. (2016)[18]	National PD from LDO (1484)	18.0%
Rhee et al. (2017)[19]	Prospective HD (541)	10.5%
Subclinical Hypothyroidism		
Shantha et al. (2011)[31]	HD (137)	24.8%
Ng et al. (2012)[29]	PD (122)	15.6%
Rhee et al. (2013)[15]	HD/PD (2715)	8.9%
Rhee et al. (2015)[17]	National incident HD from LDO (8840)	8.9%
Rhee et al. (2016)[18]	National PD from LDO (1484)	11.7%
Overt Hypothyroidism		
Kaptein (1998)[24]	HD (306)	2.6%
Lin et al. (1998)[26]	HD/PD (221)	8.9%
Kutlay et al. (2005)[25]	HD (87)	3.4%
Meuwese et al. (2012)[28]	HD (218)	5.0%
Rhee et al. (2013)[15]	HD/PD (2715)	4.3%
Rhee et al. (2015)[17]	National incident HD from LDO (8840)	8.9%
Rhee et al. (2016)[18]	National PD from LDO (1484)	6.5%
Non-Dialysis Dependent Chronic Kidney Disease		
TSH Elevation		
Bando et al. (2002)[21]	DM and non-DM (63)	24.0%
Lo et al. (2005)[27]	NHANES III (14,523)	See text
Rhee et al. (2015)[30]	US veterans (461,607)	23.3%
Subclinical Hypothyroidism		
Carrero et al. (2007)[22]	Stage 5 CKD (210)	8.1%
Chonchol et al. (2008)[23]	Stage 3–5 CKD (277)	17.9%
Targher et al. (2009)[32]	Stage 3–5 CKD (53)	26.0%

Abbrev.: HD, hemodialysis; PD, peritoneal dialysis; LDO, large dialysis organization; DM, diabetes; NHANES III, Third National Health and Nutrition Examination Survey.

Table 2.

Selective studies of hypothyroidism and outcomes in the end-stage renal disease and non-dialysis dependent chronic kidney disease populations.

Study (Year)	Cohort (N)	TSH (mIU/L)	Outcome
Mortality			
Rhee et al. (2013)[15]	Retrospective HD patients in Boston (2715)	≥3.0	↑ All-cause mortality
Dreschler et al. (2014)[84]	Prospective diabetic HD patients from *Die Deutsche Diabetes Dialyse* (4D Trial)	N/A	No association with cardiovascular events, sudden cardiac death, or all-cause death
Rhee et al. (2015)[17]	Retrospective HD patients from national LDO (8840)	≥3.0	↑ All-cause mortality
Rhee et al. (2016)[18]	Retrospective PD patients from national LDO	>5.0	↑ All-cause mortality
Rhee et al. (2017)[19]	Prospective HD patients in Southern California	>2.1	↑ All-cause mortality
Rhee et al. (2018)[16]	Retrospective NDD-CKD cohort in US (232,524)	>3.0	↑ All-cause mortality
You et al. (2018)[20]	Retrospective NDD-CKD cohort transitioning to ESRD (15,335)	>5.0	↑ All-cause mortality
Cardiovascular Disease			
Kang et al. (2008)[11]	Prospective PD patients in South Korea (51)	>5.0	↓ Left ventricular function
Rhee et al. (2018)[8, 9]	Prospective HD patients in Southern California (104)	>3.0	↑ Coronary artery calcification
You et al. (2018)[83]	Prospective HD patients in Southern California (99)	>1.2	↓ Endothelial function
Patient-Centered Outcomes			
Rhee et al. (2017)[14]	Prospective HD patients in Southern California (450)	>2.1	↓ Health-related quality of life

Abbrev.: TSH, thyrotropin; HD, hemodialysis; LDO, large dialysis organization; PD, peritoneal dialysis; NDD-CKD, non-dialysis dependent chronic kidney disease; ESRD, end-stage renal disease.

Table 3.

Screening recommendations for thyroid functional testing in non-chronic kidney disease populations.

Professional Society	Recommendations
American College of Cardiology/American Heart Association[91]	Patients with newly diagnosed congestive heart failure
American College of Physicians[89]	Women >50 years old
American Academy of Family Physicians[87]	Periodic screening in older women
American Thyroid Association[90]	Screening if at high-risk: • Type 1 diabetes • Autoimmune disease • Family history of thyroid disease • Neck radiation • History of thyroid surgery
American Association of Clinical Endocrinologists[90]	
Institute of Medicine[88]	Lack of information to make assessment of economic costs of screening
United States Preventative Services Task Force[92, 93]	Does not recommend routine screening in children or adults