SHORT COMMUNICATION

Glucagon-like peptide-1 receptor agonists, weight loss, and urolithiasis: what urologists should know

Stamatios Katsimperis[1,2], Lazaros Tzelves[1,2], Begoña Ballesta Martinez[2,3], Theodoros Spinos[2,4], Angelis Peteinaris[2,4], Amelia Pietropaolo[5], Andreas Skolarikos[1]

[1]*Second Department of Urology, Sismanogleio Hospital, National and Kapodistrian University of Athens, Greece*
[2]*EAU Young Academic Urologists (YAU) Urolithiasis and Endourology Working Group Arnhem, Arnhem, The Netherlands*
[3]*Department of Urology, University Hospital del Vinalopo, Alicante, Spain*
[4]*Department of Urology, University of Patras, Greece*
[5]*Department of Urology, University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom*

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Corresponding author
Stamatios Katsimperis
Sismanogliou 1,
Athens, Greece,
stamk1992@gmail.com

Introduction Obesity and type 2 diabetes mellitus are closely linked to urolithiasis risk through adverse urinary chemistry, including lower urine pH and higher lithogenic supersaturation. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are increasingly used for glycemic control and weight loss, creating a need to clarify their implications for stone-forming patients.

Material and methods A narrative mini-review was performed using targeted searches of PubMed and screening of reference lists of relevant articles for studies evaluating GLP-1RA therapy in stone formers or reporting changes in 24-hour urine parameters. Evidence was summarized qualitatively with emphasis on urinary risk factors, and clinical outcomes.

Results Across cohorts of stone formers receiving GLP-1RAs, urinary parameters show an overall neutral pattern, with no consistent, clinically meaningful shifts in urine volume, pH, citrate, or supersaturation indices. Some datasets report favorable changes in selected markers, including higher urinary citrate in diabetic stone formers and reduced stone growth signals in imaging-based analyses, but these findings remain hypothesis-generating due to retrospective designs and potential confounding. Evidence for effects on hard clinical outcomes such as new stone formation, recurrence, or need for intervention is limited.

Conclusions Current evidence suggests GLP-1RAs can be incorporated into the management of patients with urolithiasis who require pharmacologic weight loss or diabetes therapy, without a consistent signal of increased lithogenic risk. Clinical focus should remain on established prevention strategies, particularly maintaining urine volume during treatment initiation and gastrointestinal adverse effects, while prospective studies with standardized imaging and stone endpoints are needed.

Key Words: GLP-1 receptor agonists ‹› GLP-1Ras ‹› urolithiasis ‹› nephrolithiasis ‹› kidney stone disease ‹› obesity ‹› type 2 diabetes mellitus ‹› weight loss pharmacotherapy

INTRODUCTION

The burden of kidney stone disease is rising alongside obesity and type 2 diabetes mellitus (T2DM) [1–3]. This convergence matters because obesity and insulin resistance influence several established lithogenic pathways, including lower urinary pH, higher urinary uric acid, and dietary patterns that increase acid load and sodium intake [4, 5]. At the same time, glucagon-like peptide-1 receptor agonists (GLP-1RAs) have become cornerstone treatments for obesity and T2DM, producing clinically meaningful weight loss and cardiometabolic benefit, so urologists are increasingly encountering stone formers receiving these agents [6, 7]. In this narrative mini-review, we examine whether GLP-1–based

weight loss alters urinary stone risk or stone outcomes in ways relevant to counseling and follow-up in urology and metabolic stone clinics.

We searched PubMed/MEDLINE until January 2026, using terms related to GLP-1RAs and nephrolithiasis. Reference lists were also screened. Clinical studies reporting urinary parameters or stone-related outcomes were included, and findings were synthesized descriptively.

EVIDENCE ON URINARY RISK FACTORS AND CLINICAL IMPLICATIONS

Mechanistically, GLP-receptor agonists could influence nephrolithiasis through both indirect metabolic improvements and direct renal or gastrointestinal effects. Indirectly, substantial weight loss may improve insulin resistance, potentially mitigating the propensity toward acidic urine that underlies uric acid stone formation. Appetite suppression and dietary shifts during GLP-1RA therapy may reduce animal protein intake, lowering dietary acid load and altering urinary sulfate and ammonium excretion, markers often used as proxies for net endogenous acid production. In theory, these changes could favour higher urinary citrate or higher urine pH, thereby lowering calcium stone and uric acid stone risk, respectively. Direct renal mechanisms have also been proposed. Experimental and clinical observations suggest GLP-1 signalling may influence proximal tubular sodium handling (including effects on the sodium–hydrogen exchanger NHE3) and may modulate urate physiology [8]. In the real-world URISEMA study of oral semaglutide, reductions in serum urate were observed, with a more pronounced effect among those with higher baseline urate levels [9]. Although intriguing, changes in serum urate do not automatically translate to clinically relevant changes in urinary uric acid supersaturation, which depends heavily on urine pH and urine volume. Counterbalancing any theoretical lithoprotective effects is the most clinically tangible hazard of GLP-1RAs for stone formers: gastrointestinal adverse effects. Nausea, vomiting, diarrhea, and early satiety can reduce fluid intake or increase extrarenal fluid losses, leading to lower urine volume and higher supersaturation, conditions that can precipitate colic in predisposed patients even if solute excretion remains stable.

The strongest available evidence for stone-related effects comes not from randomized trials with stone endpoints, but from observational analyses of 24-hour urine chemistry in stone formers. In a paired pre/post cohort of 44 obese stone formers receiving GLP-1–based therapy, Feghali and colleagues reported a significant reduction in urinary oxalate (40 to 32 mg/d, $p = 0.002$) and decreases in urinary sulfate and ammonium after treatment, while most other standard urinary risk factors, including urine volume, calcium, citrate, uric acid, and pH, did not change significantly [10]. Supersaturation indices for calcium oxalate (2.76 ± 3.01 to 2.24 ± 2.17, $p = 0.27$), calcium phosphate, and uric acid did not show a significant shift suggesting the clinical magnitude of solute changes was modest. This pattern is reassuring because it argues against a consistent pro-lithogenic effect of GLP-1–based pharmacologic weight loss and suggests at least one potentially favorable signal. The oxalate finding is particularly notable because some weight-loss strategies, especially those involving malabsorption, can increase oxalate absorption and urinary oxalate excretion. While the mechanism of oxalate reduction in this cohort is not definitively established, it is plausible that diet quality changes, altered intake patterns, or reduced gastrointestinal oxalate exposure play a role.

Schaub et al. [11] analyzed Medicare claims linked to Litholink 24-hour urine collections in diabetic stone formers, evaluating both cross-sectional comparisons of GLP-1RA users vs matched controls ($n = 349$ users vs 349 controls) and longitudinal pre/post comparisons ($n = 154$) within GLP-1RA users [11]. Across these analyses, the authors did not identify robust, consistent differences in urinary parameters once multiple comparisons were addressed, including no reproducible improvements in urine volume or citrate. Unadjusted or less conservative analyses suggested possible trends in uric acid–related measures, but these were not stable after correction, reinforcing the conclusion that any GLP-1RA effect on urine chemistry is likely modest, heterogeneous, or confounded by real-world variability in diet and comorbidity [11]. In practice, this means GLP-1RAs should not be expected to reliably normalize classic urinary risk factors in stone formers, particularly the highest-yield targets in prevention such as urine volume, citrate in hypocitraturia, and urine pH in uric acid stone disease.

Hard clinical endpoints such as new stones, recurrence, growth on imaging, and need for procedures, remain insufficiently studied. Existing signals come mainly from retrospective institutional datasets and meeting abstracts. In a retrospective institutional cohort, published as a preliminary abstract, ($n = 174$), semaglutide was associated with lower CT-defined stone growth compared with other GLP-1RAs ($p = 0.024$), without differences in new stones or surgical intervention, although these findings remain hypothesis-generating given the

retrospective design [12]. In another retrospective analysis (conference abstract) of 510 stone formers (86 with T2DM), GLP-1 agonist use among diabetic patients was associated with substantially higher urinary citrate compared with both diabetic non-users (927.9 vs 544.6 mg/day, $p = 0.007$) and non-diabetic patients (566.6 mg/d, $p < 0.0001$), without differences in BMI or HbA1c between diabetic users and non-users; GLP-1 agonist users also did not demonstrate a higher rate of uric acid stones compared with non-diabetic patients [13].

These observations are interesting but cannot establish causality due to potential confounders. Patients prescribed certain agents may differ in baseline stone activity, imaging intensity, diet counseling, adherence, comorbidity burden, or concurrent medications. Until prospective studies with standardized imaging and adjudicated stone outcomes are available, urine chemistry remains the principal evidence base and points toward neutrality rather than a strong protective or harmful effect. Overall, the current evidence base for hard clinical endpoints is of low certainty.

Renal safety considerations intersect with stone risk mainly through volume status. Broadly, GLP-1RAs have demonstrated kidney benefits in meta-analyses of cardiovascular outcome trials, often driven by improvements in albuminuria and composite kidney endpoints [14]. In the SELECT trial, kidney outcomes have been evaluated without a prominent signal suggesting intrinsic nephrotoxicity as a dominant concern, while gastrointestinal tolerability remains the major limiting factor [15]. While large-scale trial data do not currently identify an increased risk of acute kidney injury (AKI) specifically tied to GLP-1RA therapy, the potential for prerenal injury exists in the setting of severe gastrointestinal-induced volume depletion.

For stone formers, this framing is helpful. The medication is unlikely to directly injure kidneys in a way that increases stones, but dehydration, especially during dose escalation, can quickly lower urine volume and promote supersaturation. This is especially relevant in patients with recurrent stones, prior low urine output, chronic kidney disease, solitary kidney, or those taking concomitant agents that increase osmotic diuresis or reduce effective circulating volume. These data translate into a practical clinical approach. GLP-1RAs are generally compatible with stone prevention, and concerns about weight loss causing stones should be nuanced because pharmacologic GLP-1–based weight loss does not resemble malabsorptive bariatric surgery in its typical urinary signature [16]. Available data do not show consistent pro-lithogenic changes. At the same time, GLP-1RAs are not a substitute for standard prevention. Patients with uric acid stones still require urine alkalinization strategies, because urine pH is not consistently improved by GLP-1RAs in available datasets. Patients with calcium stones still benefit most from adequate urine volume, sodium moderation, maintaining normal dietary calcium, and targeting hypocitraturia or hypercalciuria when present. The most actionable intervention around GLP-1 initiation is hydration. Stone formers benefit from proactive counseling about maintaining fluid intake during the titration phase and during episodes of nausea, vomiting, or diarrhea. Clinicians should recommend a practical daily urine volume target of 2.0–2.5 l to offset potential fluid losses during the titration phase.

Selective metabolic monitoring remains reasonable. Not every patient starting a GLP-1RA needs repeat 24-hour urine testing, but it is sensible for recurrent stone formers with frequent events, patients with high-risk phenotypes, those with CKD or a solitary kidney, and individuals with sustained gastrointestinal symptoms that plausibly reduce urine output. A pragmatic strategy is to ensure a baseline 24-hour urine is available and to repeat testing within several months if symptoms, diet, or stone activity changes substantially. Stable patients with controlled risk factors can follow usual clinic intervals.

Several limitations should temper interpretation. The bulk of evidence is observational and subject to confounding by diet, comorbidities, and concurrent medications, while real-world adherence and counseling intensity are rarely captured. Many studies rely on single pre/post urine comparisons or laboratory databases without standardized dietary recording. Most importantly, urine chemistry is a surrogate, and changes in supersaturation do not perfectly predict stone events. The field needs prospective studies that track recurrence, imaging-defined stone growth, and procedural outcomes with standardized protocols. Priorities include repeated urine collections during dose escalation and stable maintenance, stratification by stone phenotype, and comparisons across incretin agents, including dual incretin agonists, to determine whether certain molecules or dose ranges have distinct urinary signatures.

Findings from key clinical studies, are summarized in Table 1.

CONCLUSIONS

GLP-1RAs and dual incretin agonists appear compatible with urolithiasis prevention in patients with obesity or T2DM. Current low-certainty evidence suggests these agents are metabolically safe but should not replace standard preventive principles.

Table 1. *Summary of key studies evaluating GLP-1RAs and urolithiasis risk*

Study	Design and Population	Sample size (n)	Key urinary and stone findings	Clinical magnitude and interpretation
Feghali et al. (2024) [10]	Retrospective pre/post; obese stone formers	44	↓ Urinary oxalate (40 to 32 mg/d; p = 0.002), ↓ sulfate, and ↓ ammonium	Modest: no significant change in SI indices (SI CaOx 2.76 to 2.24; p = 0.27), pH, or volume
Schaub et al. (2025) [11]	Retrospective medicare cohort; diabetic stone formers	349 (cross-sectional) /154 (longitudinal)	Neutral: no significant differences in 24-h urinary parameters after Bonferroni correction	Safe: no consistent signal of increased lithogenic risk identified in a large cohort
Thiagarajan et al. (2025) [12]	Retrospective institutional; GLP-1RA users	174	Semaglutide associated with ↓ risk of CT-defined stone growth vs other GLP-1RAs (p = 0.024)	Promising: Suggests potential agent-specific benefits on stone progression
Zhao et al. (2023) [13]	Retrospective institutional; diabetic stone formers	510 (86 with T2DM)	GLP-1RA use associated with ↑ urinary citrate (928 vs 545 mg/d; p = 0.007) vs diabetic non-users	Lithoprotective: Potential benefit for UA stone rates independent of BMI or HbA_{1c}

BMI – body mass index; SI – supersaturation index; CaOx – calcium oxalate; CT – computed tomography; GLP-1RA – glucagon-like peptide-1 receptor agonist; HbA_{1c} – hemoglobin A_{1c}; Retro – retrospective; T2DM – type 2 diabetes mellitus; UA – uric acid.

Practically, urologists should focus on preserving urine volume during dose escalation and gastrointestinal side effects through individualized counseling. While nearly half of early stone-forming cohorts included dual agonists like tirzepatide, prospective studies with standardized imaging are needed to clarify if distinct incretin-based signatures meaningfully influence stone recurrence or progression.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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ETHICS APPROVAL STATEMENT

The ethical approval was not required.

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