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Importanța analizei compoziției calculilor renali în prevenirea recurenței litiazice pe rinichii ce asociază malformații congenitale.

MEMBRI ECHIPĂ PROIECT:
Șef de lucrări dr. Rașcu Ștefan
Asist. univ. dr. Proca Tudor
Asist. univ. dr. Nechita Cătălin

Rezumat

Litiaza renală reprezintă o patologie complexă, multifactorială, cu implicații semnificative asupra calității vieții și riscului de recidivă. Pacienții cu malformații renale congenitale, precum rinichiul în potcoavă (HSK) sau rinichiul ectopic pelvin (PEK), prezintă particularități anatomice ce pot modifica atât tipologia calculilor, cât și eficiența tratamentelor chirurgicale.

Studiul pe care îl prezentăm a fost realizat în două etape distincte, fiecare menită să contribuie la o înțelegere mai profundă și mai detaliată a subiectului abordat. În prima etapă, am efectuat o analiză comparativă a compoziției calculilor între două categorii de pacienți: cei care prezintă o anatomie renală normală și cei cu malformații congenitale ale rinichilor, caracterizate prin diverse anomalii structurale. Această comparație a avut scopul de a evidenția diferențele și particularitățile fiecărei situații. În a doua etapă a studiului, am urmărit evaluarea cu precizie a predictorilor recurenței litiazei, examinând influența parametrilor metabolici, precum și factorii chirurgicali, pentru a identifica eventuale corelații relevante.

Pe baza unui eșantion mixt, au fost utilizate o serie de metode spectroscopice, în special tehnica FTIR, împreună cu evaluări metabolice ale urinei pe parcursul a 24 de ore și modele de regresie statistică pentru identificarea factorilor semnificativi asociați. Rezultatele obținute au evidențiat o tendință clară către prevalența calculilor de acid uric și fosfat de calciu în cadrul grupului de pacienți cu malformații. În plus, din lista factorilor de risc, s-a remarcat faptul că volumul redus de urină pe 24 de ore și prezența fragmentelor reziduale postoperatorii mai mari de 4 mm s-au dovedit a fi indicatori independenți și predictori semnificativi ai riscului de recurență a formării calculilor.

1. Introducere

Litiaza renală este o afecțiune cu o incidență în creștere la nivel global, afectând până la 10–15% din populația adultă la un moment dat în timpul vieții. Dincolo de evenimentele acute, litiaza are un potențial semnificativ de recurență și complicații, inclusiv infecții recurente și afectare progresivă a funcției renale.

Pe lângă factorii metabolici cunoscuți (hipercalciurie, hiperuricosurie, hiperoxalurie, hipocitraturie), în ultimii ani a crescut interesul pentru influența arhitecturii anatomice renale asupra patogenezei calculilor. În mod particular, pacienții cu malformații congenitale renale, în special rinichi în potcoavă (HSK) sau rinichi ectopic pelvin (PEK), au un risc semnificativ crescut de litiază, prin mecanisme care includ drenaj urinar ineficient, stază, infecții recurente și pH urinar modificat. Aceste modificări favorizează cristalizarea și crearea unui mediu propice formării unor tipuri particulare de calculi, precum cei de fosfat de calciu sau acid uric.

Literatura de specialitate oferă date limitate referitoare la compoziția calculilor în raport cu anomaliile structurale. Majoritatea studiilor se concentrează fie pe aspecte metabolice generale, fie pe rezultatele tratamentului chirurgical al calculilor, fără a integra pe deplin aceste două dimensiuni În acest context, este pe deplin justificată adoptarea unei abordări integrate și comprehensive, care să combine tehnicile de spectroscopie prin FTIR, analiza detaliată a datelor metabolice (urină și sânge), precum și particularitățile intervențiilor chirurgicale, în special în cazul pacienților cu anatomie modificată, pentru a obține o evaluare cât mai completă.

Obiectivul general al acestui studiu a fost dublu:

(1) Compararea compoziției chimice a calculilor între pacienți cu rinichi normali și cei cu malformații congenitale (HSK și PEK).

(2) Identificarea factorilor predictivi (chirurgicali și metabolici) ai recidivei litiazei la 12 luni post-intervenție, în cadrul unui subgrup cu malformații structurale.

2. Materiale și metode

2.1. Designul studiului

Studiul a fost realizat în două etape, în cadrul Spitalului Clinic "Prof. Dr. Theodor Burghele" din Bucureşti:

- Etapa I a inclus o cohortă de 100 pacienți (studiu retrospectiv observațional) internați în perioada septembrie 2023 – august 2024, cu litiază urinară confirmată și evaluare completă a compoziției calculilor prin spectroscopie FTIR.
- Etapa II a vizat un subgrup de 50 pacienți cu malformații renale congenitale (HSK și PEK), care au beneficiat de intervenții endourologice (RIRS sau mini-PNL), evaluare metabolică completă și urmărire imagistică la 12 luni post-operator.

Toate datele au fost colectate în mod standardizat, iar protocolul a fost aprobat de comisia de etică a instituției, respectând prevederile Declarației de la Helsinki.

2.2. Criterii de includere și excludere

Au fost incluși pacienți:

- cu vârsta ≥18 ani;
- cu litiază renală sau ureterală confirmată prin CT;
- care au avut intervenție activă pentru extragerea fragmentelor (RIRS, mini-PNL, laparoscopie);
- cu evaluare metabolică completă (urinară 24h + analize serice);
- și urmărire imagistică de minimum 12 luni postoperator.

Au fost excluși pacienții cu:

- litiază exclusiv vezicală sau uretrală;
- infecție urinară activă în momentul evaluării metabolice;
- boli sistemice care influențează compoziția calculilor (hiperparatiroidism primar, cistinurie);
- date incomplete sau nevalidate statistic.

2.3. Evaluarea compoziției calculilor

Compoziția chimică a calculilor a fost analizată utilizând spectroscopie cu transformare Fourier în infraroșu (FTIR). Fragmentele au fost obținute intraoperator și păstrate în condiții sterile. Clasificarea s-a realizat conform ghidurilor EAU și Mayo Clinic:

- 50% calciu oxalat (CaOx)
- 50% acid uric sau urat de sodiu
- 10% struvit sau urat de amoniu

- 50% fosfat de calciu (brushit, carbapatit, tricalciu)
- calculi cu orice procent de cistină

2.4. Evaluarea metabolică

Toți pacienții incluși în a doua etapă a studiului, cu malformații renale congenitale, au beneficiat de o evaluare metabolică completă, conform recomandărilor ghidurilor internaționale (EAU, AUA). Aceasta a inclus:

- Analiza urinară pe 24 de ore, cu determinarea următorilor parametri:
    - Volum urinar total (ml/24h)
    - Calciu urinar (mg/24h)
    - Oxalat urinar (mg/24h)
    - Acid uric urinar (mg/24h)
    - Citrat urinar (mg/24h)
    - pH urinar mediu
- Profilul biologic seric:
    - Calcemie totală și ionizată
    - Creatinină serică
    - Uree
    - Acid uric
    - Fosfați serici

Pacienții au fost instruiți să respecte o dietă obișnuită în zilele premergătoare recoltării și să evite aportul excesiv de proteine sau lichide care ar putea influența parametrii urinari.

Valorile obținute au fost comparate cu intervalele de referință validate. Anomaliile au fost definite astfel:

- Hipercalciurie: >250 mg/24h (femei) sau >300 mg/24h (bărbați)
- Hiperoxalurie: >40 mg/24h
- Hipocitraturie: <320 mg/24h
- Hiperuricosurie: >750 mg/24h (femei), >800 mg/24h (bărbați)
- Volum urinar scăzut: <1500 ml/24h
- pH acid (<5.5) – considerat favorabil formării calculilor de acid uric

Datele au fost utilizate ulterior în analiza asocierii între profilul metabolic și tipul de calcul, precum și în evaluarea factorilor de risc pentru recidivă.

2.5. Intervențiile chirurgicale (RIRS, mini-PNL)

Toți pacienții au beneficiat de tratament activ endourologic. Alegerea tehnicii chirurgicale a fost determinată de:

- dimensiunea calculului,
- localizarea acestuia în sistemul pielocaliceal,
- anatomia renală,
- și experiența echipei operatorii.

a) RIRS – Retrograde Intrarenal Surgery

- Utilizată predominant la calculi <20 mm
- Instrumentație: ureteroscop flexibil, teacă ureterală de acces, laser Holmium:YAG
- Manevre: fragmentare (dusting, basketing), extragere cu coșuleț
- Închiderea intervenției: stent ureteral JJ 6 Ch, menținut 7–14 zile

b) Mini-PNL – Mini-Percutaneous Nephrolithotomy

- Indicație: calculi >20 mm sau localizare nefavorabilă pentru RIRS (ex. pol inferior)
- Abord percutanat sub ghidaj fluoroscopic/ecografic
- Dilatare până la 16–18 Ch, nefroscop rigid, fragmentare cu laser Holmium sau litotritor pneumatic
- Sistem miniaturizat cu presiuni scăzute pentru irigație, reducând riscul de sepsis
- Drenaj postoperator prin nefrostomie sau tubless în cazuri selectate

Procedurile au fost realizate utilizând protocoale standardizate, pentru a minimiza variabilitatea.

2.6. Definirea recurenței

Recidiva litiazei a fost definită conform ghidurilor EAU: apariția unui nou calcul urinar clinic sau radiologic confirmat, în același rinichi sau contralateral, în interval de 12 luni de la intervenția inițială.

Recidiva a fost documentată prin examinări imagistice standard:

- ecografie renală
- tomografie computerizată nativă (NCCT) – la pacienții simptomatici sau cu suspiciuni clinice

Pentru analiză, pacienții au fost grupați în funcție de statusul postoperator:

- Stone-free (SFR) – fără fragmente reziduale detectabile imagistic
- FR ≤4 mm – fragmente mici, considerate clinic nesemnificative
- FR >4 mm – fragmente reziduale semnificative, cu risc crescut de recidivă

Această stratificare a fost utilizată ulterior în modelele statistice de predicție a recidivei.

2.7. Analize statistice

Datele au fost analizate cu IBM SPSS Statistics versiunea 26. Protocolul statistic a inclus:

a) Analiza descriptivă

- Medii și deviații standard pentru variabile continue
- Frecvențe și procente pentru variabile categorice

b) Testarea asocierilor

- Testul Chi-pătrat (χ^2) pentru asocieri între variabile categoriale (ex. tip calcul și malformație)
- Testul t Student sau Mann–Whitney U pentru variabile continue
- Corelații Pearson și Spearman (ex. între volum urinar și risc de recidivă)

c) Analiza multivariată

- Regresie logistică binară: predicția recidivei în funcție de fragmente reziduale, volum urinar, pH, tip calcul etc.
- Variabilele incluse au fost cele cu semnificație statistică la analiza univariată ($p < 0.10$)
- Rezultatele au fost exprimate ca Odds Ratio (OR) cu intervale de încredere 95% și prag de semnificație $p < 0.05$

d) Controlul confounderilor

- Au fost testate interacțiuni între tipul malformației, tipul intervenției și anomaliile metabolice

3. Rezultate

3.1. Caracteristicile lotului de pacienți

Grupurile de pacienți în cele două studii au fost împărțite astfel:

- Grupul 1 (control vs rinichi malformați) – 100 pacienți;
- Grupul 2 (malformații congenitale) – 50 pacienți cu rinichi în potcoavă (HSK, n=36) sau rinichi ectopic pelvin (PEK, n=14).

Distribuția demografică a fost comparabilă între grupuri:

- Vârsta medie: 48,2 ± 12,1 ani;
- Sex: 62% bărbați, 38% femei;
- Comorbidități frecvente: hipertensiune arterială (42%), diabet zaharat tip 2 (18%).

3.2. Compoziția calculilor

Toți pacienții au avut analiza compoziției calculilor efectuată prin spectroscopie FTIR. Distribuția compoziției diferă semnificativ între cele două grupuri (Tabelul 1):

Tabel 1 - Distributia compoziției calculilor al pacienților din primul studiu

Tip de calcul	Rinichi normali (%)	Rinichi malformați (%)
Oxalat de calciu (CaOx)	62%	48%
Acid uric	14%	24%
Fosfat de calciu (CaP)	9%	20%
Calculi de infecție (struvit)	2%	8%
Compoziție mixtă (CaOx+CaP)	13%	8%

La pacienții cu malformații, se constată o prevalență crescută a calculilor de acid uric și CaP, probabil corelată cu drenajul alterat și modificarea pH-ului urinar. În grupul cu rinichi normali, predomină calculii de oxalat de calciu, în concordanță cu literatura de specialitate.

3.3. Profilul metabolic urinar (24h)

La 50 de pacienți cu malformații s-a efectuat evaluare metabolică urinară completă (Tabelul 2). Doar 22% dintre pacienți au avut un profil metabolic complet normal. Majoritatea pacienților au prezentat ≥2 anomalii metabolice, justificând necesitatea unei evaluări extinse pentru toți pacienții cu litiază recidivantă sau cu anatomie particulară.

Tabel 2 - Evaluarea metabolică a pacienților cu anomalii renale

Parametru	**Prevalență (%)**	**Observații**
Hipercalciurie	48%	Frecvent în CaOx și CaP
Hiperoxalurie	28%	Asociată cu calculi oxalici
Hipocitraturie	26%	Mai frecventă la pacienții cu recidivă
Hiperuricosurie	18%	Asociată cu calculi de acid uric
Volum urinar <1500 ml/zi	54%	Asociat semnificativ cu recurența
pH acid (<5.5)	36%	Corelat cu calculi de acid uric

3.4. Intervențiile chirurgicale și clearance-ul postoperator

Tipul de intervenție:

- RIRS (n=32, 64%) – calculi ≤20 mm, acces chirurgical facil.
- Mini-PNL (n=18, 36%) – calculi >20 mm sau în pol inferior

Rezultate postoperatorii:

- Stone-free complet (SFR) – 35.5%
- Fragmente reziduale ≤4 mm – 36.5%
- Fragmente reziduale >4 mm – 28%

Pacienții tratați prin RIRS au avut o rată mai mică de clearance complet (31.3%) comparativ cu cei tratați prin mini-PNL (44.4%), însă fără semnificație statistică (p = 0.17). Prezența de FR >4 mm a fost identificată ca factor de risc major pentru recidivă.

3.5. Recidiva la 12 luni

Rate de recidivă:

- Total pacienți recidivați: 21/50 (42%)
- După status postoperator:
    - Stone-free: 6/17 (35.5%)
    - FR ≤4 mm: 7/18 (38.8%)
    - FR >4 mm: 8/11 (72.7%)

Recidiva a fost semnificativ asociată cu:

- Prezența fragmentelor >4 mm (p = 0.047)
- Volum urinar <1500 ml/24h (p = 0.018)
- pH urinar acid (<5.5)

3.6. Analiza multivariată – predictori de recidivă

Modelul de regresie logistică a identificat cei doi predictori independenți ai recurenței evidentiati in Tabelul 3. Alte variabile testate (tip intervenție, tip calcul, sex, vârstă) nu au avut influență semnificativă.

Tabel 3 - Regresie logistică multivariată pentru predicția recidivei litiazei

Variabilă	**OR (IC95%)**	**p-valoare**
Fragmente reziduale >4 mm	4.2 (1.11–16.3)	0.035
Volum urinar <1500 ml/zi	3.8 (1.03–14.1)	0.043

3.7. Corelații între parametrii urinari

Analiza corelației (matrice Pearson) a arătat:

- Nu s-au identificat corelații semnificative între volumele urinare și concentrațiile de solute (toate $r < 0.2$, $p > 0.05$).
- Calciuria și oxaluria nu s-au corelat între ele.
- Citratul urinar nu a avut relație semnificativă cu acidul uric sau pH-ul.

4. Discuții

Studiul de față oferă o analiză detaliată a compoziției calculilor și a factorilor metabolici și postoperatori implicați în recurența litiazei renale, cu un accent deosebit pe pacienții cu malformații congenitale ale rinichilor. În special, ne-am concentrat pe două entități anatomice importante: rinichiul în potcoavă (HSK) și rinichiul ectopic pelvin (PEK), ale căror prezență influențează atât dinamica urinară, cât și abordarea terapeutică.

4.1. Compoziția calculilor în contextul malformațiilor renale

Datele noastre indică o diferență clară în distribuția tipurilor de calculi între pacienții cu rinichi cu anatomie normală și cei cu malformații. În timp ce oxalatul de calciu a rămas principalul compus în ambele grupuri, s-a remarcat o creștere a prevalenței calculilor de acid uric (24%) și fosfat de calciu (20%) în grupul cu malformații. Aceste rezultate sunt conform literaturii recente, care evidențiază că drenajul urinar deficitar și modificările pH-ului favorizează formarea acestor tipuri de calculi.

Anomaliile anatomice asociate cu HSK și PEK, inclusiv rotația anormală, poziționarea calicelor și a bazinetului, precum și fluxul turbulent, contribuie la stază urinară cronică, predispunând la cristalizare și infecții recurente. Astfel, nu este surprinzător faptul că și calculii de infecție (struvit) au avut o prevalență crescută în aceste cazuri (8%).

4.2. Evaluarea metabolică

Evaluarea metabolică a identificat anomalii importante la pacienții cu malformații, cele mai frecvente fiind hipercalciuria (48%) și hipocitraturia (26%), urmate de hiperoxalurie (28%) și hiperuricosurie (18%). Aceste valori sunt în linie cu alte studii care au subliniat că profilul metabolic al pacienților cu rinichi anatomic modificat nu diferă semnificativ cantitativ, dar poate avea implicații diferite asupra riscului de formare și recidivă.

Un aspect extrem de important constă în faptul că doar 22% dintre pacienți au prezentat un profil metabolic complet normal, evidențiind astfel necesitatea efectuării unei evaluări metabolice pentru toți pacienții cu litiază, în mod special în situațiile în care există malformații congenitale.

4.3. Predictori ai recidivei

Rezultatele evidențiază doi factori principali asociați independent cu recurența litiazei la 12 luni:

1. Fragmente reziduale >4 mm: acești pacienți au avut un risc de recidivă de 72,7%, comparativ cu 35,5% la cei stone-free (p = 0,047). Acest rezultat susține datele din literatură,

care indică faptul că fragmentele mici, aparent nesemnificative, pot acționa ca nucleu de cristalizare în condiții nefavorabile.

2. Volumul urinar <1500 ml/24h – pacienții cu hidratare necorespunzătoare au avut o probabilitate de recidivă de aproape patru ori mai mare de recidivă a litiazei (OR = 3,8, p = 0,043). Hidrodiluția este, probabil, cel mai eficient mod de profilaxie primară și secundară a litiazei, efect bine documentat în studii randomizate.

În mod interesant, nici tipul intervenției chirurgicale (RIRS vs. mini-PNL), nici tipul de calcul nu au fost predictori independenți ai recidivei în analiza multivariată, deși au existat tendințe diferențiate.

4.4. Implicații terapeutice și clinice

Aceste date impun o reevaluare a algoritmului de urmărire și tratament al pacienților cu malformații renale litiazice. Algoritmul propus este unul stratificat și adaptat:

- pentru calculi ≤20 mm în locații favorabile, RIRS rămâne opțiunea preferată, oferind morbiditate redusă și timp operator scurt.
- pentru calculi voluminoși sau localizați în polul inferior, mini-PNL oferă un grad mai mare de clearance, chiar și în rinichi anatomic anormal, cu un profil de siguranță crescut datorită miniaturizării instrumentarului.
- pacienții cu fragmente reziduale după intervenție necesită o monitorizare strictă și, în cazuri selectate, reintervenție timpurie pentru a reduce riscul de recidivă.
- consilierea privind aportul hidric trebuie inclusă ca parte obligatorie a managementului post-operator, întrucât hidratarea s-a dovedit a fi singurul factor metabolic modificabil cu impact major asupra recurenței.

4.5. Limitări ale studiului

Ca orice studiu observațional, și analiza de față prezintă limitări:

- număr relativ mic de pacienți în subgrupul cu PEK, care reduce puterea statistică pentru comparații detaliate;
- urmărirea de doar 12 luni poate subestima rata reală de recidivă la distanță;
- variabilitatea tehnică inter-operatorie posibilă, deși intervențiile au fost efectuate cu protocoale standardizate.

5. Concluzii

Proiectul a demonstrat că pacienții cu malformații renale congenitale prezintă particularități clare atât în compoziția calculilor, cât și în profilul metabolic, diferențe care influențează semnificativ riscul de recidivă și eficiența tratamentului chirurgical. Analiza FTIR a evidențiat o prevalență crescută a calculilor de acid uric și fosfat de calciu la pacienții cu rinichi în potcoavă sau ectopic pelvin, probabil în legătură cu drenajul deficitar și modificările pH-ului. Evaluarea metabolică a arătat că majoritatea pacienților prezintă una sau mai multe anomalii, subliniind importanța bilanțului metabolic complet în vederea prevenirii recidivei.

În ceea ce privește evoluția postoperatorie, doi factori s-au remarcat drept predictori independenți ai recurenței la 12 luni: fragmentele reziduale mai mari de 4 mm și un volum urinar sub 1500 ml/24 h. Aceste rezultate reafirmă importanța obținerii unui clearance cât mai complet în timpul intervenției, precum și asigurarea unei hidratări corespunzătoare ulterior, ambele fiind componente fundamentale în reducerea riscului de recidivă.

Alegerea strategiei chirurgicale trebuie adaptată particularităților anatomice, RIRS fiind adecvat pentru calculii mici și accesibili, iar mini-PNL oferind un grad mai mare de clearance în cazurile cu volum litiazic mare.

În ansamblu, proiectul a evidențiat valoarea unui model integrat de evaluare: spectroscopică, metabolică și chirurgicală pentru optimizarea tratamentului pacienților cu malformații renale congenitale și litiază. Rezultatele susțin adoptarea unor algoritmi personalizați de tratament și monitorizare, cu accent pe hidratare, control metabolic și rezolvarea completă a fragmentelor postoperatorii, elemente cheie pentru reducerea recurenței și îmbunătățirea prognosticului pe termen lung.

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Kidney Anatomy, Stone Type: Is There a Link?

Ștefan Rașcu[1,2], Ovidiu-Cătălin Nechita[1,2]*, Tudor Marian Proca[1,2]*, Daniel Liviu Bădescu[1,2], Cosmin-George Radu[1,2], Viorel Jinga[1,2,3]

[1]Department of Urology, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
[2]Department of Urology, Prof. Dr. Th. Burghele Clinical Hospital, Bucharest, Romania
[3]Medical Sciences Section, Academy of Romanian Scientists, Bucharest, Romania

*Corresponding author:
Ovidiu-Cătălin Nechita, MD
Department of Urology
Prof. Dr. Th. Burghele Clinical Hospital
Bucharest, Romania
E-mail: ovidiu-catalin.nechita@drd.umfcd.ro
Tudor Marian Proca, MD
Department of Urology
Prof. Dr. Th. Burghele Clinical Hospital
Bucharest, Romania
E-mail: tudor.proca@gmail.com

Abbreviations:
FTIR: Fourier-transform infrared;
HSK: Horseshoe kidney;
URS: Ureteroscopy;
PCNL: Percutaneous nephrolithotomy;
CaOx: Calcium oxalate;
EAU: European Association of Urology.

Abstract

Background: Renal anatomical anomalies are associated with altered urinary drainage and pH, which may influence urinary stone formation and composition. However, limited studies have assessed the stone composition differences in patients with abnormal versus normal renal anatomy.
Methods: This observational study included 100 patients treated between September 2023 and August 2024 in a tertiary academic center in southern

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Romania. Stone composition was assessed using Fourier-transform infrared spectroscopy and categorized into five major types. Comparative and multivariate analyses were performed to assess associations between renal morphology, comorbidities, and stone type.
Results: Uric acid (39%) and calcium oxalate (32%) were the most common stone types. Patients with horseshoe kidney and ectopic kidneys showed higher proportions of calcium phosphate stones. Diabetes and hyperuricemia were significant predictors of calcium phosphate and uric acid stones, respectively. No statistically significant association was found between renal anatomy and stone composition, though descriptive differences were observed.
Conclusions: While anatomical anomalies did not show statistically significant differences in stone composition, metabolic factors such as diabetes and hyperuricemia strongly influenced stone type. Spectroscopic analysis remains essential in guiding individualized nephrolithiasis management.

Keywords:

Introduction

Renal stone disease is a prevalent and multifactorial condition (1) affecting a significant proportion of the population globally (2). Anatomical anomalies, dietary choices, and metabolic abnormalities are some of the factors that influence the composition of kidney stones (3). The potential of renal malformations, such as horseshoe kidney (HSK), ectopic kidney, and malrotated kidney, to disrupt normal urinary drainage can lead to stasis, recurrent infections, and altered urinary pH-factors that significantly influence the formation and composition of renal lithiasis (4). Calcium oxalate and uric acid stones are the most commonly reported types in the general population (5); however, anatomical abnormalities can lead to different distributions, with a higher prevalence of uric acid or infection-related stones such as struvite (6). Despite these clinical observations, comparative studies on the specific impact of renal malformations on stone composition remain limited.

This study aims to conduct a spectroscopic analysis of kidney stone composition in patients with renal anomalies, compared to those with normal renal anatomy.

The objective is to assess the incidence of different stone compositions, examine statistical correlations between renal morphology and stone types, and identify the metabolic or anatomical mechanisms responsible for changes in stone composition.

Materials and Methods

Study Population

This is a retrospective observational study that analyzed patient data collected between September 1, 2023, and August 31, 2024, at a tertiary care academic urology center in southern Romania. We included patients aged 18 years and older who had confirmed upper urinary tract stones, identified either through spontaneous passage or retrieved during procedures such as percutaneous nephrolithotomy (PCNL), ureteroscopy (URS), or laparoscopic surgery. Patients were excluded if they presented with isolated bladder or urethral stones, if their clinical data were incomplete, or if stone composition analysis could not be performed. Data obtained included demographic variables, body mass index, urine pH, and medical history concerning diabetes mellitus, hypertension, hyperlipidemia and hyperuricemia. Medical history was determined through medical records, patient self-reports, or verification of chronic medication use. Self-reported information also covered alcohol and tobacco consumption.

Stone Composition Grouping

The composition of the stones was analyzed using a Fourier-transform infrared (FTIR) spectrometer. Stone compositions were categorized into five groups following the recommendations of the European Urological Association and the Mayo Clinic classification: (1) groups containing more than 50% calcium oxalate (CaOx); (2) groups containing more than 50% uric acid, uric acid dihydrate, or sodium; (3) groups containing any amount of cystine; (4) groups characterized by infection stones (>10% struvite or ammonium acid urate); and (5) groups containing more than 50% tricalcium phosphate, brushite, or carbapatite.

Statistical Analysis

The study comprised 100 patients, divided into two groups based on renal morphology: patients with kidney anomalies (such as HSK, ectopic kidney, or malrotated kidney) and those with normal renal anatomy, who served as the control group. Patients with only bladder or urethral stones were excluded from the study. The statistical analysis was conducted out using IBM SPSS Statistics version 26®, which includes descriptive statistics, comparative analysis (Chi-square and t-tests), and logistic regression. A significance level of $p < 0.05$ was set.

Ethics Approval

The study was conducted in accordance with the Declaration of Helsinki and was approved by the institutional ethics review board. All patient data were anonymized to maintain confidentiality and ensure compliance with data protection regulations.

Results

There were 100 patients in the study with complete data, of which 55 were male. The mean age of the patients was 50.20 years, with a range of 18-82 years. However, the difference between the mean age of males (48.80 years) and females (51.91 years) was not statistically significant ($p = 0.417$). In terms of comorbidities, the most frequent were hyperlipidemia (55%), followed by diabetes mellitus (43%), hyperuricemia (25%), hypertension (24%), and urinary tract infections (25%).

Stone Composition

The quantitative analysis revealed an average stone count of 2.65 per patient, ranging from 1 to 4, and a mean stone size of 17.67 mm. The compositional study revealed that uric acid stones were the most common (39%), followed by calcium oxalate (32%), and calcium phosphate stones (20%). Cystine (6%) and struvite stones (3%) were among the less common components.

Gender-specific patterns revealed that males had a greater incidence of uric acid stones (41.8%) and calcium oxalate stones (34.5%), whereas females had a higher prevalence of calcium phosphate (24.4%) and cystine stones (8.9%). However, statistical testing indicated no significant association between sex and stone composition [$\chi^2(4) = 2.607$, $p = 0.625$].

Underlying Comorbidities

There were notable correlations found between the composition of stones and specific comorbidities. Hyperuricemia was highly associated with uric acid stones ($p = 0.006$), while diabetes mellitus was strongly related to calcium phosphate stones ($p = 0.021$). Calcium phosphate and struvite stones were both influenced by urinary tract infections ($p = 0.038$), with the latter highlighting its well-established link to infection-related lithogenesis, as shown in *Table 1.*

Table 1. Association of clinical variables with primary stone composition.

Variable	Calcium oxalate (n)	Uric acid (n)	Cystine (n)	Struvite (n)	Calcium phosphate (n)	Total (n)	p-value
Hypertension							0.777
- Yes	7	11	2	1	3	24	
- No	25	28	4	2	17	76	
Diabetes mellitus							0.021
- Yes	13	11	3	3	13	43	
- No	19	28	3	0	7	57	
Hyperlipidemia							0.344
- Yes	20	17	4	1	13	55	
- No	12	22	2	2	7	45	
Hyperuricemia							0.006
- Yes	2	17	2	1	3	25	
- No	30	22	4	2	17	75	
Urinary infection							0.038
- Yes	6	8	0	2	9	25	
- No	26	31	6	1	11	75	
Family history							0.933
- Yes	11	12	1	1	7	32	
- No	21	27	5	2	13	68	

On the other hand, there were no significant correlations found between stone composition and hypertension ($\chi^2(4) = 1.775$, $p = 0.777$), hyperlipidemia ($\chi^2(4) = 4.486$, $p = 0.344$), or family history ($\chi^2(4) = 0.844$, $p = 0.933$), suggesting that these variables may not have a direct impact on stone type.

Age and Stone Composition

The association between age and urinary stone types was investigated by grouping patients into seven age groups, as shown in *Table 2*. Stone composition was examined within these age groups and further classified by kidney anatomy, which included normal anatomy, HSK, ectopic kidney, and malrotated kidney. Although there was no statistically significant association between age groups and stone composition ($p = 0.440$), descriptive patterns have been identified.

As illustrated in *Figs. 1, 2*, calcium oxalate stones were most common in the elderly, particularly those aged 68 to 75 years, accounting for 46.2% of cases. Uric acid stones were more common in younger age groups, particularly those aged 28-37 and 38-47 years, whereas calcium phosphate stones were most common in middle-aged patients, particularly those aged 48-57 years, which corresponded to a higher incidence of metabolic conditions such as diabetes mellitus in this population.

The univariate analysis assessed the influence of age group and kidney anatomy on the type of primary stone composition. The data demonstrated no statistically significant effect of age group [$F(6,92) = 1.058$, $p=0.394$] or kidney anatomy [$F(1,92) = 1.713$, $p=0.194$] on stone composition. With a significant intercept [$F(1,92) = 50.331$, $p < 0.001$] and low explanatory power ($R2 = 0.086$, adjusted $R2 = 0.017$), the model's findings suggest that neither age group as well as anatomical features are significant predictors of stone composition in this cohort.

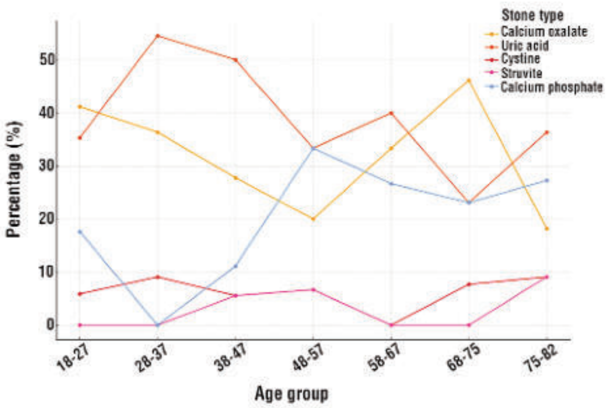

Figure 1. Distribution of stone types across age groups.

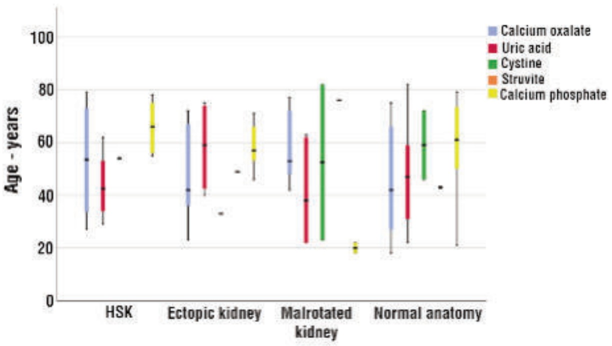

Figure 2. Stone composition in relation to age and kidney anatomy.

Kidney Anatomy and Stone Composition

The association between kidney anatomy and urinary stone composition was explored by dividing patients into four anatomical subgroups: normal anatomy, HSK, ectopic kidney, and malrotated kidney. Across all groups, uric acid stones were the most prevalent, followed by calcium oxalate and calcium phosphate stones, as

Table 2. Stone composition by age group.

Age group (years)	Calcium oxalate (%)	Uric acid (%)	Cystine (%)	Struvite (%)	Calcium phosphate (%)	Total (n)
18-27	41.2	35.3	5.9	0.0	17.6	17
28-37	36.4	54.5	9.1	0.0	0.0	11
38-47	27.8	50.0	5.6	5.6	11.1	18
48-57	20.0	33.3	6.7	6.7	33.3	15
58-67	33.3	40.0	0.0	0.0	26.7	15
68-75	46.2	23.1	7.7	0.0	23.1	13
75-82	18.2	36.4	9.1	9.1	27.3	11

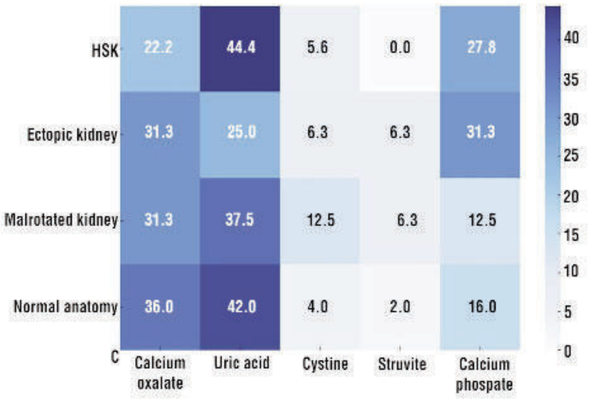

Figure 3. Heatmap of stone composition by kidney anatomy.

represented in *Fig. 3*. However, specific tendencies were detected based on anatomical variances. In patients with normal renal anatomy, a higher prevalence of uric acid stones (42%) and calcium oxalate stones (36%) was observed, reflecting the distribution typically seen in the general population.

In contrast, patients with HSKs, revealed a similarly high incidence of uric acid stones (44.4%) but a considerably enhanced occurrence of calcium phosphate stones (27.8%). Ectopic kidneys revealed a reasonably even distribution of calcium oxalate (31.3%) and calcium phosphate stones (31.3%), with uric acid stones being significantly less frequent (25%). Patients with malrotated kidneys showed a distinct distribution of stone types in our cohort, with uric acid stones accounting for 37.5% and an unexpectedly high proportion of cystine stones at 12.5%. Although these figures are noteworthy, the small number of cases in this subgroup limits the ability to draw firm conclusions. As such, these observations should be seen as preliminary and interpreted with caution, particularly in the absence of statistical significance.

Despite these descriptive variations, statistical analysis did not demonstrate a significant link between kidney anatomy and stone composition [$\chi^2(12) = 7.567$, $p = 0.818$].

Predictors of Stone Composition

Multinomial logistic regression analysis identified significant predictors of stone composition, as detailed in *Table 3*. Diabetes mellitus emerged as a significant predictor of calcium phosphate stones ($p = 0.039$), while hyperuricemia substantially increased the likelihood of uric acid stones ($p = 0.030$). Urinary infections were associated with higher odds of both calcium oxalate ($p = 0.026$) and uric acid stones ($p = 0.050$).

The model demonstrates moderate explanatory power, with pseudo R-squared values ranging from 18.7% (McFadden) to 42.1% (Nagelkerke).

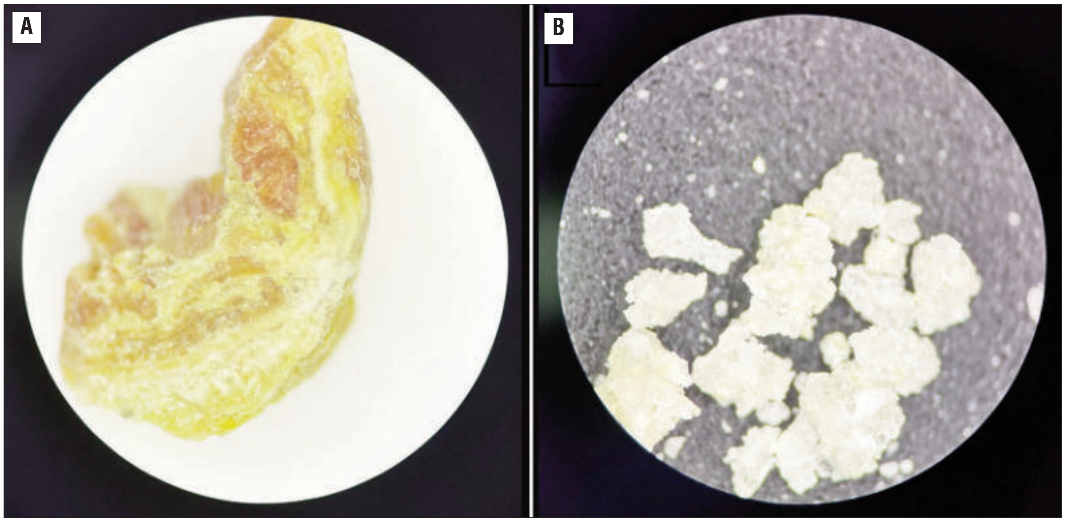

Figure 4. **(A)** Bright-field observation of uric acid kidney stones, highlighting their amber to orange-brown coloration, relatively smooth surfaces, and subtle layered architecture. (B) Microscopic images of calcium oxalate renal calculi, revealing translucent, pale-yellow crystalline aggregates with irregular, granular surfaces under bright-field illumination.

Table 3. Multivariate and univariate logistic regression analysis of predictors for stone composition.

Predictor	Stone type	B	SE	Wald	OR (Exp(B))	95% CI for Exp(B)	p-Value
Age (years)							
Calcium oxalate	-0.016	0.021	0.539	0.984	0.944 – 1.027	0.463	
Uric acid	-0.021	0.021	1.003	0.979	0.940 – 1.020	0.317	
Cystine	-0.016	0.032	0.249	0.984	0.924 – 1.048	0.618	
Struvite	-0.074	0.061	1.457	0.929	0.823 – 1.047	0.227	
Hypertension							
Calcium oxalate	-0.563	0.831	0.459	0.569	0.112 – 2.902	0.498	
Uric acid	-0.662	0.847	0.612	0.516	0.098 – 2.712	0.434	
Cystine	-0.903	1.154	0.612	0.405	0.042 – 3.894	0.434	
Struvite	-0.371	1.552	0.057	0.690	0.033 – 14.444	0.811	
Diabetes mellitus							
Calcium oxalate	0.720	0.788	0.835	2.055	0.438 – 9.633	0.361	
Uric acid	1.652	0.799	4.282	5.220	1.091 – 24.968	0.039	
Cystine	0.748	1.188	0.396	2.113	0.206 – 21.708	0.529	
Struvite	-17.381	1676.866	0.000	2.83E-8	-	0.992	
Hyperuricemia							
Calcium oxalate	0.929	1.008	0.848	2.532	0.351 – 18.270	0.357	
Uric acid	-1.787	0.824	4.706	0.167	0.033 – 0.842	0.030	
Cystine	-0.931	1.156	0.648	0.394	0.041 – 3.801	0.421	
Struvite	-2.068	1.986	1.084	0.126	0.003 – 6.200	0.298	
Urinary infection							
Calcium oxalate	1.550	0.697	4.942	4.711	1.201 – 18.474	0.026	
Uric acid	1.437	0.732	3.850	4.207	1.002 – 17.670	0.050	
Cystine	17.591	0.000	-	4.36E7	-	-	
Struvite	-2.191	2.258	0.942	0.112	0.001 – 9.337	0.332	
Hyperlipidemia							
Calcium oxalate	0.362	0.672	0.291	1.437	0.385 – 5.365	0.590	
Uric acid	1.015	0.681	2.220	2.759	0.726 – 10.482	0.136	
Cystine	0.359	1.058	0.115	1.432	0.180 – 11.387	0.734	
Struvite	0.594	1.597	0.138	1.811	0.079 – 41.406	0.710	
Family history							
Calcium oxalate	-0.319	0.689	0.214	0.727	0.189 – 2.803	0.643	
Uric acid	-0.059	0.714	0.007	0.943	0.232 – 3.824	0.934	
Cystine	0.418	1.293	0.105	1.519	0.121 – 19.134	0.746	
Struvite	0.665	1.611	0.170	1.944	0.083 – 45.715	0.680	

However, instability was noted in predicting rare stone types, such as struvite, likely due to limited data availability and potential multicollinearity among the predictors.

Discussion

This study presents an inquiry into the composition of urinary stones in patients from southern Romania, applying FTIR spectroscopy for exact categorization and analysis. Supported by the EAU and AUA, routine stone composition analysis offers vital insights into the metabolic and environmental factors behind stone formation, paving the way for targeted prevention and treatment strategies (7).

Two basic procedures are available for stone analysis: the chemical spot test and FTIR spectroscopy (8). While chemical approaches are still extensively employed because to their simplicity and cost-effectiveness (9), they often offer only approximate information regarding the basic structure of mixed stones. These approaches have considerable drawbacks, including subjectivity in interpreting results (10), inability to detect rare or unidentified elements, and the requirement for relatively large sample volumes (10-15 mg), which can be difficult when evaluating small stones (11).

Alternatively, FTIR spectroscopy offers a more sophisticated option, characterized by lower cost of operation, partial automation, quick analysis (12), and the ability to recognize organic and non-crystalline substances (13).

This research highlights descriptive patterns suggesting a possible relationship between renal structural differences and stone composition. However, given the lack of statistical significance, these findings should be interpreted with caution and regarded as preliminary hypotheses that warrant further investigation in larger, prospective cohorts.

Patients with normal renal architecture had stone compositions similar with earlier findings

(14), which were uric acid (42%) and calcium oxalate (36%) stones, assessing the theory that metabolic processes are the primary determinants of stone formation in structurally normal kidneys.

In our cohort, patients with HSKs demonstrated a stone composition pattern characterized by relatively high proportions of uric acid (44.4%) and calcium phosphate stones (27.8%). Although these differences did not reach statistical significance, they are in line with previously published data, suggesting that such patterns may be consistent in this subgroup. However, given the limited sample size and reduced statistical power, these findings should be interpreted with caution and considered as hypothesis-generating rather than conclusive(15). The increased incidence of calcium phosphate stones may be linked to urinary stasis and impaired drainage, hallmark features of HSK, which promote an alkaline urinary environment conducive to calcium phosphate crystallization (16). Conversely, the elevated proportion of uric acid stones might reflect a combination of metabolic factors, such as hyperuricosuria or intermittent urine acidification, which can occur in these patients despite the anatomical abnormalities (16). Additionally, metabolic disorders typically linked with HSK - such as hyperparathyroidism, hypercalciuria, and hypocitraturia - further increase the risk of stone development (17).

In comparison, patients with ectopic kidneys revealed a more balanced distribution of stone types, with calcium oxalate 31.3% and uric acid stones accounting for 25%.

Sex-related variations were also identified, with a male-to-female ratio of 1.22:1. Males had a higher frequency of calcium oxalate and uric acid stones, likely explained by increasing testosterone levels and lower urine pH (18). In contrast, females showed a larger proportion of calcium phosphate stones, perhaps due to anatomical vulnerability to urinary tract infections and their connection with alkaline urine (19).

Age-related tendencies further confirmed recent findings, suggesting a decreasing frequency of calcium oxalate stones with advancing age. Comorbidity study found high prevalence of diseases such as hyperlipidemia (55%), diabetes mellitus (43%), and chronic renal disease (49%), all of which significantly impact stone development. Specifically, diabetes mellitus has been associated with a higher incidence of calcium phosphate stones, while hyperuricemia was considerably linked to uric acid stone formation.

Multivariate analysis identified diabetes, hyperuricemia, and urinary infections as significant predictors of stone composition, highlighting the importance of incorporating metabolic examinations into routine clinical practice. While the predicted accuracy of the model was moderate (57%), this indicates the need for further improvement of predictive tools by integrating more factors or applying different modeling strategies.

Clinically, these findings show the necessity of a multidisciplinary approach to kidney stone treatment, integrating the knowledge of endocrinologists, nephrologists, and dietitians. Prevention efforts should prioritize metabolic management, hydration optimization, and dietary changes. Anatomical anomalies, despite not significantly affecting stone composition, require specialized surgical planning and imaging.

Despite its contributions, the study has limitations. The sample size, while sufficient for descriptive research, may lack the ability to identify subtle relationships. The cross-sectional design excludes causal inferences, and the absence of data on diets, hydration intake, genetic variables, and biochemical markers limits the depth of study. Additionally, self-reported comorbidities may induce recall bias, especially in retrospective circumstances.

Beyond anatomical considerations, recent literature increasingly emphasizes the need to interpret stone formation through a broader biochemical and epidemiological lens. This perspective aligns with our findings and supports the importance of advanced analytical techniques in uncovering clinically relevant compositional patterns.

Emerging evidence from large-scale cohort studies reinforces the importance of compositional heterogeneity in kidney stones. A recent German investigation analyzing over 42,000 stones found that more than half exhibited mixed composition, with calcium oxalate-phosphate combinations accounting for 33.8%, while uric acid stones made up only 7.6% of cases. These results illustrate the biochemical complexity of stone formation and highlight the clinical utility of FTIR spectroscopy in detecting even minor stone constituents - details that are often missed by conventional chemical analysis methods (20).

A regional study conducted in Austria analyzed over 300 kidney stones using FTIR spectroscopy and found that calcium oxalate was the most commonly identified component, followed by calcium phosphate, uric acid, struvite, and cystine. This pattern aligns well with global epidemiologic data and further supports the value of FTIR as a diagnostic standard. Its ability to accurately detect both crystalline and amorphous phases makes it especially useful in identifying mixed stones or rare compositions that might be overlooked by more traditional chemical methods (21).

Our observations in patients with horseshoe kidneys are in line with findings from a recent meta-analysis, which reported a 36% prevalence of nephrolithiasis among adults with this anomaly. Most stones in that group were calcium-based - specifically calcium oxalate (64.2%) and calcium phosphate (18.8%) - while uric acid stones were relatively uncommon, at just 3.8%. This distribution is comparable to what we noted in our cohort and may reflect the distinct urodynamic environment associated with HSK, where impaired drainage and urinary stasis could promote the formation of certain stone types (22).

Recent clinical data also point to the strong influence of systemic metabolic conditions on stone composition. For example, individuals with diabetes appear more prone to forming uric acid and calcium phosphate stones, likely due to chronic changes in urinary pH and solute handling. Similarly, patients with hyperuricemia or gout often develop uric acid stones as a direct consequence of elevated uric acid levels. These associations are consistent with our multivariate analysis, which identified diabetes, hyperuricemia, and urinary infections as independent predictors of stone type. Taken together, these findings support a more integrated clinical approach that addresses metabolic factors alongside anatomical considerations (23).

Conclusion

This study analyzed kidney stone composition in patients with renal malformations, revealing that uric acid and calcium phosphate stones were notably prevalent. While anatomical anomalies such as horseshoe and malrotated kidneys showed distinct compositional trends, only metabolic factors - especially hyperuricemia, diabetes, and urinary infections - were statistically associated with stone type. These findings highlight the importance of FTIR spectroscopy and metabolic assessment in managing stone disease in anatomically abnormal kidneys.

Conflicts of Interest

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Title: Metabolic and surgical predictors of recurrence in horseshoe and pelvic ectopic kidneys

Authors: Ștefan Rașcu[1][2], Ovidiu-Cătălin Nechita[1][2], Tudor Marian Proca[1][2], Daniel Liviu Bădescu[1][2], George-Sabin Popescu[1][2], Viorel Jinga[1][2][3]

Affiliations

[1] Department of Urology, "Prof. Dr. Theodor Burghele" Clinical Hospital, Bucharest, Romania
[2] Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
[3] Romanian Academy of Scientists, Bucharest, Romania

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Corresponding author

Ovidiu-Cătălin Nechita
Department of Urology
"Prof. Dr. Theodor Burghele" Clinical Hospital
20 Panduri Street
050653 Bucharest
Romania
Phone: +40 766-292-270
Email: ovidiu-catalin.nechita@drd.umfcd.ro,

Key words

horseshoe kidney, pelvic ectopic kidney, nephrolithiasis, metabolic evaluation, stone recurrence

Ethics approval and consent to participate

Ethical approval for this retrospective study was obtained from the Ethics Committee of “Prof. Dr. Theodor Burghele” Clinical Hospital in Bucharest (approval no. 8506 / 09/05/2024).

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and analyzed during this study are not publicly available because of patient privacy and institutional data protection policies. However, they can be obtained from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

SR: study concept and design, data collection, surgical data acquisition, critical revision of the manuscript.OCN: study design, data curation, statistical analysis, interpretation of results, manuscript drafting.TMP: imaging review, validation of surgical classifications, contribution to manuscript writing and editing.DLB: metabolic data acquisition and verification, contribution to data interpretation, manuscript editing.GSP: clinical data collection, database management, and contribution to manuscript revision.VJ: supervision, methodological guidance, validation of final analyses, and critical review of the manuscript.

All authors have read and approved the final version of the manuscript and accept responsibility for all aspects of the work.

Further information

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Introduction

Congenital anomalies of the kidney and urinary tract (CAKUT) represent a diverse group of structural malformations with significant implications for renal physiology and urological health. Horseshoe kidney (HSK) and pelvic ectopic kidney (PEK) are two of the most frequently encountered entities, resulting from disrupted embryologic ascent and fusion processes [1,2]. These anomalies alter calyceal orientation, impair urinary drainage, and predispose to recurrent infections and nephrolithiasis [3].

The prevalence of kidney stones in patients with HSK and PEK is notably higher than in the general population, with estimates ranging from 20% to 60% depending on diagnostic criteria and imaging modality [4,5]. Anatomic factors, such as malrotation, ureteropelvic obstruction, and aberrant vasculature, contribute to urinary stasis and compromise the effectiveness of standard surgical approaches [6].

While retrograde intrarenal surgery (RIRS) has gained popularity due to its minimally invasive nature, its efficacy in the setting of congenital anomalies is limited by altered anatomy and restricted access to calyces [7]. In contrast, percutaneous nephrolithotomy (PNL) provides higher stone-free rates (SFR), particularly for complex or larger stones, albeit with a higher morbidity profile [8,9]. Emerging data suggest that laparoscopy and robotic-assisted techniques may offer additional tools for selected patients with challenging anatomy [10].

Metabolic factors also play a significant role in stone formation, with hypercalciuria, hypocitraturia, and hyperoxaluria frequently reported among stone formers [11,12]. However, metabolic data specific to HSK and PEK populations remain limited, and it is unclear whether these anomalies confer unique biochemical risk profiles [13]. Stone recurrence is particularly concerning in these patients due to impaired drainage and fragment clearance [14].

This study aims to assess the surgical and metabolic outcomes in a well-defined cohort of patients with HSK and PEK, with a focus on predictors of postoperative clearance and stone recurrence.

Materials and methods

This retrospective observational study included 50 patients with congenital renal malformations and associated urolithiasis who underwent surgical treatment in a single tertiary urology center over a continuous 12-month period. All anatomical anomalies were confirmed preoperatively by contrast-enhanced CT urography, with MRI reserved for patients in whom iodinated contrast was contraindicated. Stone composition was determined by Fourier-transform infrared spectroscopy of intraoperatively retrieved fragments.

Patients were included if they had a CT-confirmed diagnosis of HSK or PEK, at least one renal stone requiring active intervention, a predefined 24-hour urinary metabolic profile, and at least 12 months of imaging follow-up. Patients were excluded if the metabolic assessment was incomplete, if they had an active urinary tract infection during the metabolic work-up, or if they had a documented systemic disorder known to affect stone formation, including primary hyperparathyroidism or cystinuria.

All patients underwent a standardized metabolic evaluation based on a 24-hour urine collection, which included measurements of urinary volume, calcium, oxalate, citrate, uric acid, and urinary pH. Serum uric acid levels were obtained on the same day as the urine sample.

Metabolic abnormalities were defined according to standard reference values used in 24-hour urine analysis. Hypercalciuria was defined as urinary calcium >250 mg/24 h in women or >300 mg/24 h in men. Hyperoxaluria corresponded to urinary oxalate >45 mg/24 h. Hypocitraturia was defined as urinary citrate <320 mg/24 h. Hyperuricosuria was defined as uric acid >750 mg/24 h in women or >800 mg/24 h in men. [11]

In addition to solute-specific metabolic abnormalities, two lithogenic parameters were systematically recorded and analyzed: 24-hour urinary volume and urinary pH. Low urinary volume was defined as <1.5 L per 24 hours. Low urinary pH was defined as pH <5.4, a threshold associated with uric acid supersaturation in standard metabolic stone evaluation.[12,14]

Urine collections followed a uniform protocol that provided written instructions on diet and hydration and included verification of completeness upon return to limit day-to-day variation. The protocol used to minimize inter-individual variability is detailed in Appendix 1.

Surgical management consisted of either RIRS or miniaturized PNL (mini-PNL), selected based on stone size, location, and the feasibility of endoscopic access determined by the underlying renal anomaly. RIRS was performed using flexible digital ureteroscopes in combination with holmium laser lithotripsy, with all procedures carried out under general anesthesia in the lithotomy position. Mini-PNL was conducted through a sub-20 Fr tract obtained under fluoroscopic guidance, using controlled dilation and a mini-nephroscope system. Stone fragmentation was achieved using pneumatic or ultrasonic lithotripsy, depending on equipment availability and surgeon preference.

Stone clearance was assessed using a standardized low-dose non-contrast CT protocol performed one month after surgery. Residual stone burden was classified into three categories: stone-free, residual fragments measuring ≤4 mm, and fragments >4 mm. Measurements were based on the largest diameter of any identifiable fragment; in cases with multiple fragments, classification was determined by the largest one. All CT scans were reviewed by an experienced urologist, with radiological confirmation obtained when findings were equivocal.

Recurrence was defined as the appearance of new stones on scheduled imaging or the occurrence of clinically confirmed stone-related events during follow-up. These events included documented renal colic, new-onset obstruction, or urinary tract infection attributed to calculi based on clinical or imaging findings. The follow-up schedule included renal ultrasound at 6 and 12 months, with non-contrast CT reserved for symptomatic patients or when ultrasound could not reliably exclude small residual fragments or early obstruction.

Statistical analysis was conducted using IBM SPSS Statistics version 26. The distribution of continuous variables was assessed with the Shapiro–Wilk test. Normally distributed variables were reported as means and standard deviations, while non-normally distributed variables were summarized as medians and interquartile ranges; in both cases, minimum and maximum values were provided. Categorical variables were described using frequencies and valid percentages. Missing data were minimal and addressed through case-wise deletion.

Group comparisons were performed using Pearson's Chi-square test or Fisher's exact test, where appropriate, based on expected cell frequencies. Postoperative outcomes were analyzed either as a binary endpoint (stone-free vs. any residual fragment) or as an ordinal, three-level variable (stone-free, residual fragments ≤4 mm, residual fragments >4 mm), depending on the analytical framework. Binary and ordinal logistic regression models were used to identify predictors of postoperative stone clearance and 12-month recurrence. Variable selection followed a predefined enter method, and multicollinearity was assessed using tolerance and variance inflation factor (VIF) values. Model performance was evaluated using the −2 log-likelihood, Nagelkerke R^2, and the Hosmer–Lemeshow goodness-of-fit test. For binary models, discriminatory ability was assessed using receiver operating characteristic (ROC) analysis and the area under the curve (AUC). Statistical significance was defined as a p-value <0.05, while values between 0.05 and 0.10 were interpreted as suggestive but not conclusive.

Results

Baseline demographic and clinical characteristics

Out of the 50 patients included in the study cohort, a substantial majority were male (74%), indicating a clear gender asymmetry. All cases included in the analysis had confirmed structural anomalies, with HSK slightly more prevalent (58%) than PEK (42%). The sample size was evenly distributed between the two anomaly types with respect to other baseline variables, suggesting no initial systematic bias.

As illustrated in **Table 1**, the clinical parameters show a relatively homogenous metabolic profile, albeit with a wide interindividual dispersion. No missing data were recorded, and all 50 patients had complete metabolic and postoperative follow-up data, allowing for full-case analysis without the need for imputation strategies.

Procedural outcomes

All patients underwent surgical treatment for stone disease, most commonly through RIRS, as shown in Table 1. Mini-PNL was performed in fewer cases, generally in patients with larger stones that would likely have required more than one flexible ureteroscopy session.

Stone-free status was achieved in just over half of the patients, while the remainder had either small, clinically insignificant fragments or larger residual ones detectable on follow-up imaging.

Although descriptive data suggested a higher clearance rate in the mini-PNL group (80% vs. 57.5% for RIRS), this difference did not reach statistical significance (p = 0.262), likely due to the small sample size and procedural allocation bias.

The presence of residual stone fragments, particularly those exceeding 4 mm, was associated with an increased likelihood of recurrence during follow-up, as will be detailed in the following subsection. It is noteworthy that residual fragments ≤ 4 mm were observed exclusively in patients treated with RIRS, which may reflect differences in fragmentation efficacy or intraoperative visualization.

A comprehensive schematic of the study structure, from inclusion to endpoint evaluation, is presented in Figure 1.

Association between stone composition and metabolic abnormalities

Among patients with uric acid stones, hyperuricosuria was more frequent (42.9%) than among those with calcium oxalate stones (12.9%). Although a numerical difference was observed, the association did not reach statistical significance (Pearson's Chi-square, p = 0.164), a result likely attributable to the limited sample size rather than a true absence of effect. Similarly, hyperoxaluria was most frequent in patients with pure calcium oxalate stones (38.7%) and was not identified in those with uric acid stones. While the trend appeared consistent, statistical significance was not achieved (p = 0.151), though the likelihood ratio (p = 0.067) suggested a near-significant association.

Low urinary volume was identified in 16% of patients, predominantly among those with calcium oxalate and uric acid stones. In contrast, markedly acidic urine was observed in 6 of 7 patients with uric acid stones (85.7%), whereas no cases were observed in any other stone category. Because of the low expected frequencies, Fisher's exact test was used, revealing a very strong link between uric acid stones and acidic urine (p < 0.000001).

Hypocitraturia was most prevalent in calcium oxalate stone formers (35.5%), but the association was not statistically significant (p = 0.212). With a uniform distribution across stone types (40–52%), hypercalciuria emerged as a non-specific finding, unlikely to aid in differentiating stone composition within this population.

Although 14 patients had a history of recurrent urinary tract infections, all preoperative urine cultures were negative at the time of intervention, as procedures were postponed until microbiological clearance. No struvite stones were detected. All calcium phosphate stones were hydroxyapatite, including the phosphate component of mixed CaOx + CaP stones, with no brushite or infection-related apatite profiles identified. Detailed distribution of metabolic abnormalities by stone composition is presented in Table 2 below.

Predictors of postoperative outcome and stone recurrence

At one-month follow-up, complete stone clearance was achieved in 62% of patients. The presence of residual fragments ≥4 mm was strongly associated with an unfavorable postoperative profile and represented a clinically relevant predictor for subsequent stone recurrence. Postoperative outcomes were not significantly affected by malformation type (p = 0.890) or surgical technique (p = 0.670) in univariate analysis. Multivariate analysis identified age as the only independent predictor of stone-free status, with older age associated with reduced likelihood of complete clearance (B = –0.069, p = 0.011).

At 12-month follow-up, 44% of patients experienced stone recurrence, as defined by either radiological evidence of new stones or clinical events attributed to lithiasis. Recurrence was strongly influenced by postoperative stone status: the lowest rate (35.5%) was observed in stone-free patients, while the highest (72.7%) was observed in patients with residual fragments ≥4 mm (p = 0.047). Although the recurrence risk was comparatively lower, patients with residual fragments ≤4 mm still demonstrated an elevated likelihood of recurrence.

Binary logistic regression confirmed that postoperative stone status was an independent predictor of recurrence (OR = 2.04, p = 0.051), with a near-significant p-value. Importantly, 24-hour urinary volume emerged as the only significant biochemical predictor, with higher volumes associated with a reduced likelihood of recurrence (OR = 0.243, p = 0.039). None of the other metabolic variables (Figure 2) showed significant associations with recurrence in either univariate or multivariable analyses. Additionally, neither the type of malformation nor the type of surgical approach was associated with recurrence at 12 months.

Age was also analyzed as a continuous predictor of recurrence. The average age did not differ significantly between patients with and without recurrence (p = 0.761), and the variance was consistent.

Correlations between biochemical urinary parameters

The interrelationships between urinary biochemical variables were assessed using both parametric and non-parametric correlation coefficients. No statistically significant correlations emerged from either method, and all observed coefficients were weak, with absolute *r* or *p* values consistently below 0.20.

Specifically, 24-hour urinary volume demonstrated no meaningful association with the excretion of calcium, oxalate, citrate, or uric acid, nor with urinary pH. Likewise, no significant linear or monotonic relationships were identified between urinary calcium and oxalate, or between citrate and uric acid, suggesting that these solutes vary independently within the cohort.

Discussion

The surgical treatment of nephrolithiasis in patients with congenital renal anomalies, particularly HSK and PEK, remains a nuanced clinical challenge due to altered anatomy, atypical calyceal distribution, and impaired drainage. Our findings align with the broader literature in underscoring that while both RIRS and PNL are feasible, their efficacy is context-dependent and should be guided by anatomical and stone-related factors.

RIRS has emerged as a preferred approach for select patients with HSK due to its minimally invasive nature and lower complication profile. Bansal et al. reported that flexible ureteroscopy in HSK achieved acceptable SFRs for stones ≤20 mm, though operative times were longer and access to upper-pole calyces was frequently limited [15]. Similarly, Lavan et al. found that stone clearance in HSK was significantly affected by the degree of renal malrotation, with lower pole calculi being more difficult to access via ureteroscopy [16]. These anatomical constraints contribute to higher retreatment rates and explain why complete clearance in a single session is often elusive [17].

In contrast, PNL offers the advantage of direct access to renal cavities and is particularly effective for large or complex calculi. Zhiqiang et al. demonstrated that modified PNL techniques in HSK achieved an SFR of 85.3% with acceptable morbidity, highlighting the importance of precise calyceal puncture planning using fluoroscopic and ultrasonographic guidance. [18]. Khadgi et al. further reported that mini-PNL in anomalous kidneys resulted in fewer complications compared to standard PNL, without compromising efficacy [19]. Notably, ultrasound-guided puncture and tract dilation have been shown to reduce the risk of injury to aberrant vessels in HSK [20].

PEK presents a different set of challenges, primarily due to its low pelvic position and anterior rotation. Wu et al. reported that RIRS in PEK is limited by ureteral angulation and reduced working space, resulting in incomplete stone access [21]. For this reason, laparoscopic pyelolithotomy has gained traction in PEK cases where both stone burden and anatomy preclude effective RIRS or PNL [22].

Stone recurrence is a major concern, particularly in cases with residual fragments postoperatively. Purkait et al. demonstrated that residual fragments >4 mm in anomalous kidneys were associated with a twofold increase in recurrence at 12 months, underscoring the importance of complete clearance [23]. Our findings support this observation, indicating that residual burden is a significant predictor of recurrence.

Metabolic abnormalities also raise the risk of recurrence. According to the work of Duvdevani and colleagues, a significant number of patients with congenital renal anomalies exhibit at least one metabolic disturbance, most often hypercalciuria or hypocitraturia [24]. Notably, metabolic risk was independent of anatomical anomaly, underscoring the need for systematic biochemical screening in all stone formers, regardless of structural abnormality [25].

Urinary volume was the only metabolic parameter significantly associated with recurrence in our cohort, corroborating the findings of Daudon et al., who reported that patients with daily urine output <2 L had substantially higher recurrence rates, even when stone-free initially [26].

Interestingly, neither the type of malformation nor surgical modality was a significant predictor of recurrence in multivariate models, supporting the view that anatomical anomaly alone is not a sufficient risk stratifier. This aligns with a study by Shpitzer et al., which emphasized the multifactorial nature of recurrence and advocated for risk-adapted surveillance strategies [27].

Conclusion

In the light of our findings and the current literature, a stratified treatment algorithm is warranted: RIRS remains ideal for small, accessible stones; PNL (preferably mini-PNL) should be considered for larger or lower-pole stones; and laparoscopic interventions should be reserved for select PEK cases. Adjunct metabolic evaluation and structured follow-up are indispensable to long-term success [28,29].

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Table 1. Baseline demographic, anatomical, metabolic, and clinical characteristics of the study population

Variable	**Category**	**n (%)**
Sex	Male	37 (74.0%)
	Female	13 (26.0%)
Renal malformation type	HSK	29 (58.0%)
	PEK	21 (42.0%)
Surgical intervention	RIRS	40 (80.0%)
	mini-PNL	10 (20.0%)
Stone composition	Calcium oxalate (CaOx)	31 (62.0%)
	Mixed CaOx + CaP	7 (14.0%)
	Uric acid	7 (14.0%)
	Calcium phosphate (CaP)	5 (10.0%)
Metabolic abnormalities	Hypercalciuria	24 (48.0%)
	Hyperoxaluria	14 (28.0%)
	Hypocitraturia	13 (26.0%)
	Hyperuricosuria	9 (18.0%)
Recurrent UTIs	Present	14 (28.0%)
Postoperative SFR status	Stone-free	31 (62.0%)
	Residual ≤ 4 mm	8 (16.0%)
	Residual ≥ 4 mm	11 (22.0%)
Recurrence at 12 months	Yes	22 (44.0%)

	No	28 (56.0%)

Table 2. Distribution of urinary metabolic abnormalities by stone type

Stone type	Hypercalciuria n (%)	Hyperoxaluria n (%)	Hypocitraturia n (%)	Hyperuricosuria n (%)	Low urinary volume n (%)	Low urinary pH (pH<5.4) n (%)
CaP	2 / 5 (40.0%)	1 / 5 (20.0%)	1 / 5 (20.0%)	0 / 5 (0.0%)	0 / 5 (0.0%)	0 / 5 (0.0%)
CaOx	16 / 31 (51.6%)	12 / 31 (38.7%)	11 / 31 (35.5%)	4 / 31 (12.9%)	5 / 31 (16.1%)	0 / 31 (0.0%)
Uric acid	3 / 7 (42.9%)	0 / 7 (0.0%)	1 / 7 (14.3%)	3 / 7 (42.9%)	2 / 7 (28.6%)	6 / 7 (85.7%)
Mixed CaOx+ CaP	3 / 7 (42.9%)	1 / 7 (14.3%)	0 / 7 (0.0%)	2 / 7 (28.6%)	1 / 7 (14.3%)	0 / 7 (0.0%)
Total	24 / 50 (48.0%)	14 / 50 (28.0%)	13 / 50 (26.0%)	9 / 50 (18.0%)	8 / 50 (16.0%)	6 / 50 (12.0%)

Figure 1. Study design

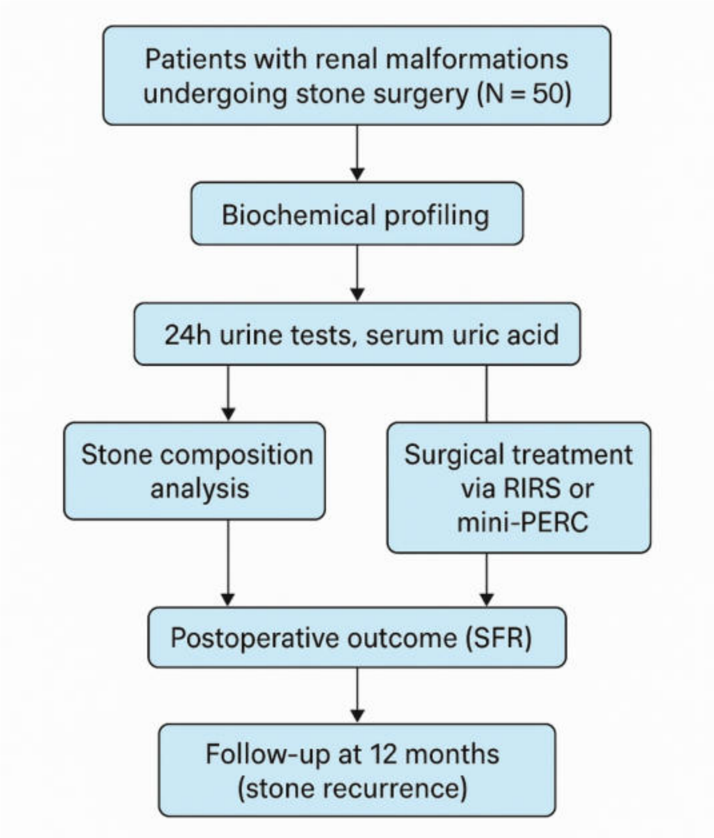

Figure 2. Forest plot of predictors for recurrence