Azienda Ospedaliera
Universitaria di Ferrara
Dipartimento Medico

La calcolosi delle vie urinarie: approccio multidisciplinare

Patologie gastro-intestinali e calcolosi delle vie urinarie

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25 Gennaio 2015

Patologie gastro-intestinali e calcolosi delle vie urinarie

- Rapporto fra calcolosi delle vie urinarie e
  - patologie gastroenteriche
  - patologie epatiche
  - Farmaci utilizzati nelle malattie gastroenterologiche
- Percorsi di prevenzione

Malattie associate allaformazione di calcoli delle vie urinarie

- Iperpartiroidismo
- Acidosi tubulare renale (completa/parziale)
- By-pass gigiuno-ileale
- Morbo di Crohn
- Resezione intestinale
- Stati di Malassorbimento
- Sarcoidosi

The prevalence of nephrolithiasis is estimated to be 5.2% in the general population.

Multiple studies established and confirmed the connection between IBD and nephrolithiasis.

Reported frequencies of nephrolithiasis ranged from 0.2% to 11.0% in non-surgical ulcerative colitis patients and from 8.4% to 40.0% in those with total colectomy with ileostomy.

Reported frequencies of nephrolithiasis in non-surgical Crohn's disease patients were noted to range from 4.0% to 5.5%, which increased to 15.0% to 30.5% after small bowel resection. In addition, patients with Crohn's disease that affected both the small and large bowels appear to have a higher risk for nephrolithiasis than those with either small bowel or large bowel disease.

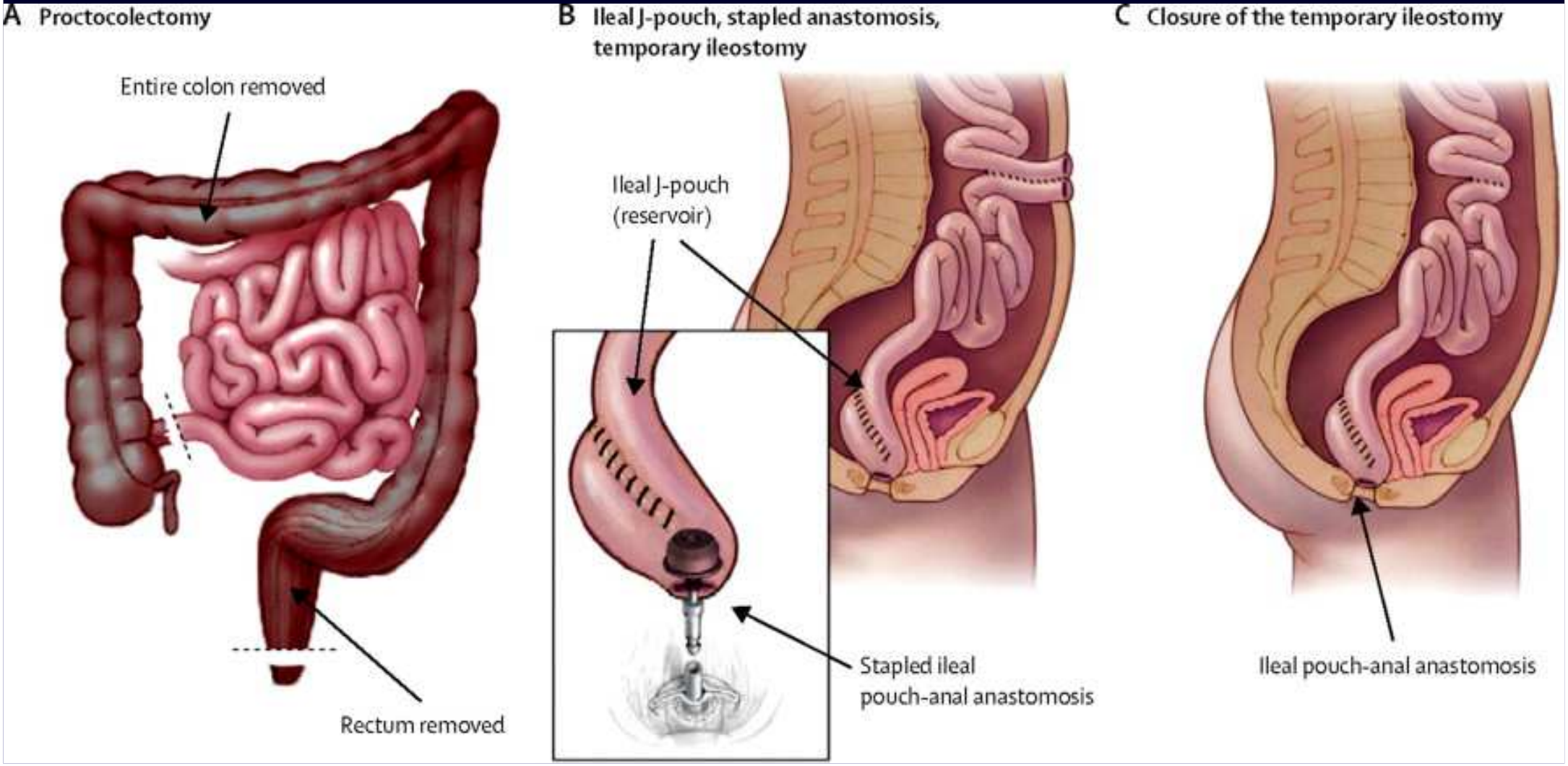
Mukewar S. et al. Journal of Crohn's and Colitis (2013) 7, 70–78

Risk factors for nephrolithiasis in patients with ileal pouches ☆

Saurabh Mukewar [a], Phillip Hall [b,*], Bret A. Lashner [c], Rocio Lopez [d], Ravi P. Kiran [e], Bo Shen [c,*]

Frequenza di nefrolitiasi nei pazienti sottoposti a IPAA 37%

Mukewar S. et al. Journal of Crohn's and Colitis (2013) 7, 70–78



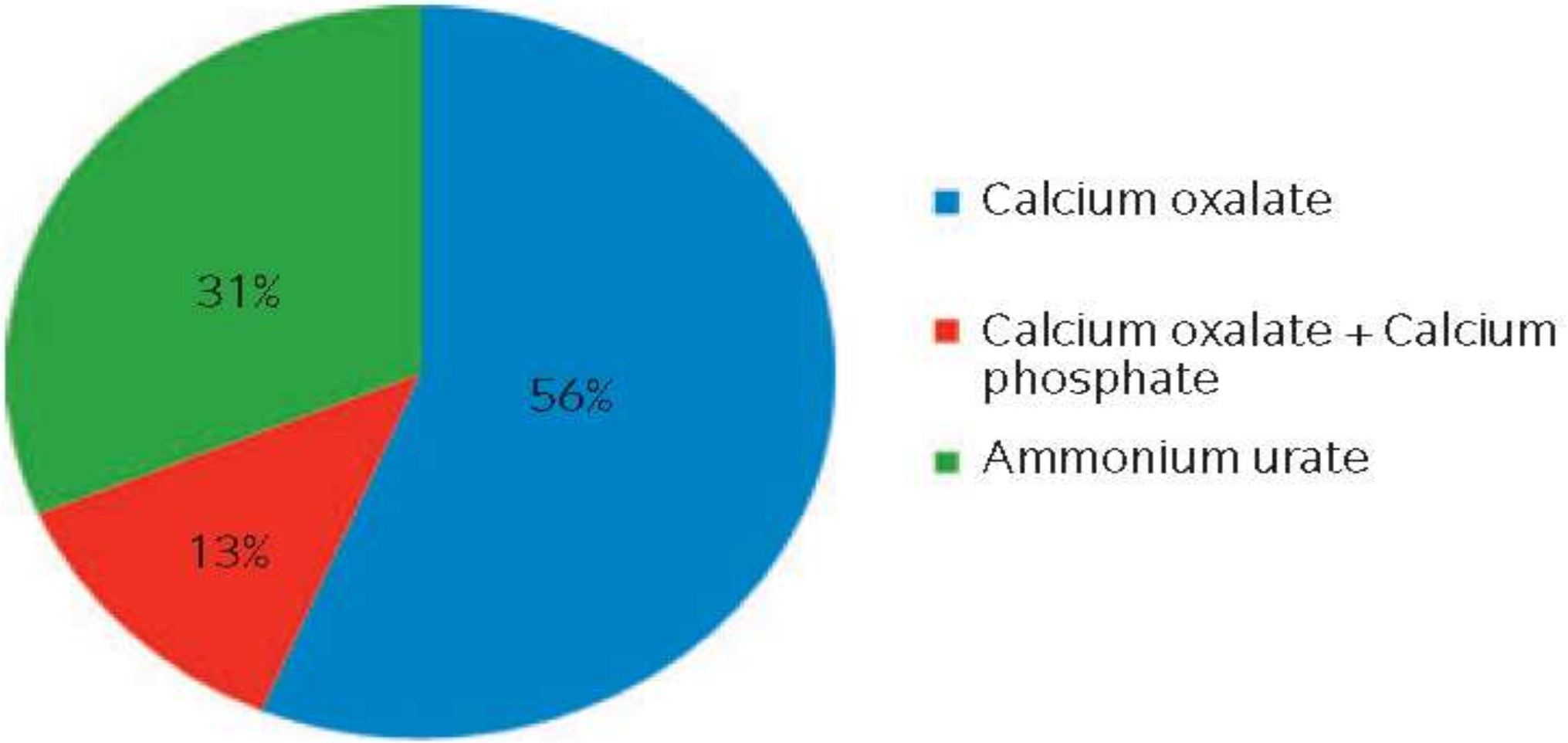
IPAA patients: multivariable analysis for risk factors associated with nephrolitiasis

Factor	Odds ratio (95% Confidence Interval)	*p*-Value
Extra-intestinal manifestations	2.9 (1.4, 5.8)	*0.003*

Factor	Nephrolithiasis (*N*=64)	No nephrolithiasis (*N*=137)	*p*-Value
Co-morbidities [a]	14 (22.2)	8 (5.8)	*<0.001*
Chronic obstructive pulmonary disease	2 (3.2)	0	*0.036*
Renal insufficiency	8 (12.7)	1 (0.7)	*<0.001*
Extra-intestinal manifestations	38 (59.4)	56 (40.9)	*0.014*
Arthralgia/arthropathy	33 (51.6)	48 (35.0)	*0.026*

Mukewar S. et al. Journal of Crohn's and Colitis (2013) 7, 70–78

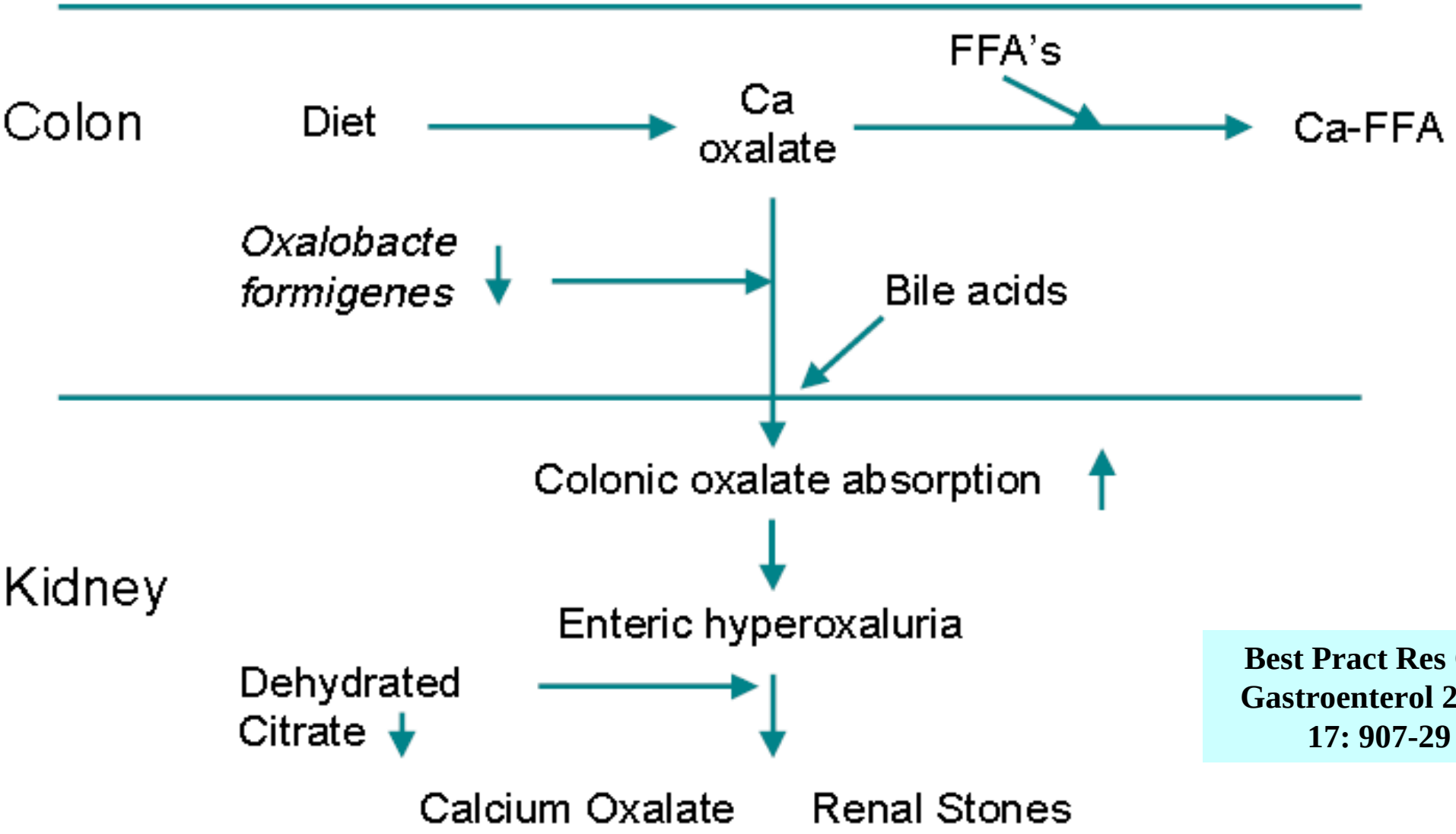
Composition of stone in Crohn's disease patients



Risk factors for kidney stones in patients with bowel disease
Uric acid stones
Low urine volume due to GI water and sodium loss
Low urine pH
Calcium stones
Low urine volume
Decreased urinary ionic strength
Hypocitraturia due to malabsorption
Hypomagnesuria
Hyperoxaluria
Hypercalciuria due to steroid use, immobilization, acidosis
Ammonium acid urate stones
Low urine volume
Bicarbonate loss in stool with metabolic acidosis
Sodium depletion
Potassium depletion
Any stones
Obstruction
Urinary tract infection

Worcester EM. Stome from bowel disease. Endocrinol Metabol Clin N Am 2002; 31: 979-99.

Mechanisms of stone formation appear to be different in CD and UC. Resection of the small bowel in CD patients may result in bile acid malabsorption and steatorrhea (fat malabsorption).



Best Pract Res Clin Gastroenterol 2003; 17: 907-29

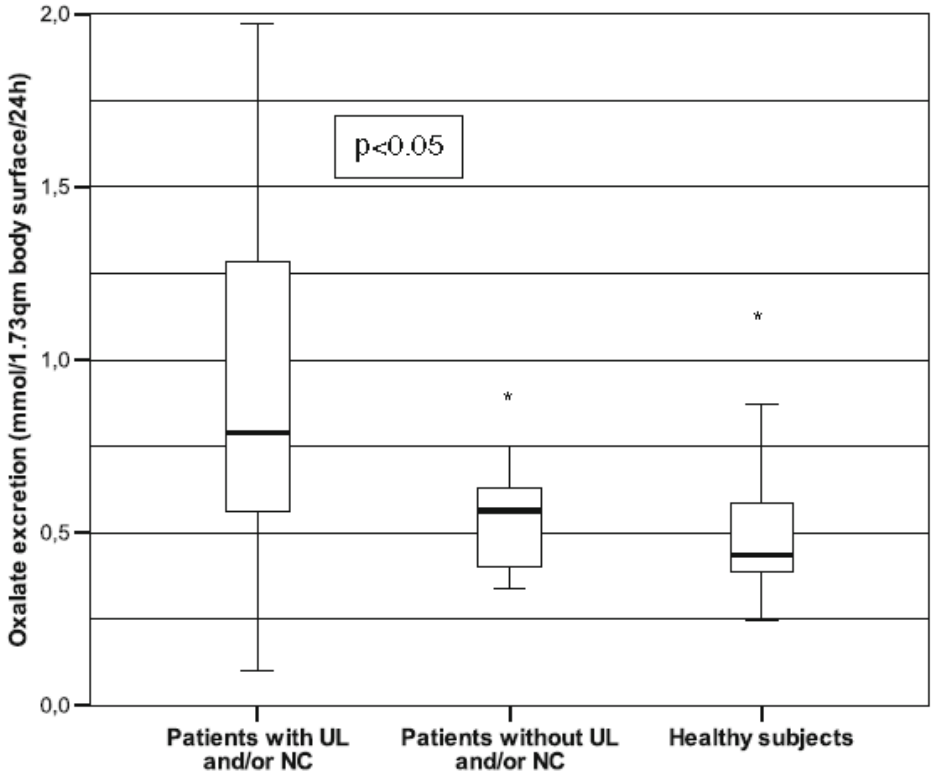


Fig. 1 Significantly higher urinary oxalate excretion (*$p < 0.05$) in Crohn's patients with compared with those without urolithiasis or oxalosis/nephrocalcinosis and with normal subjects (under standardized dietary conditions of oxalate absorption test). *Bold bars* in columns indicate median values. *UL* urolithiasis, *NC* nephrocalcinosis

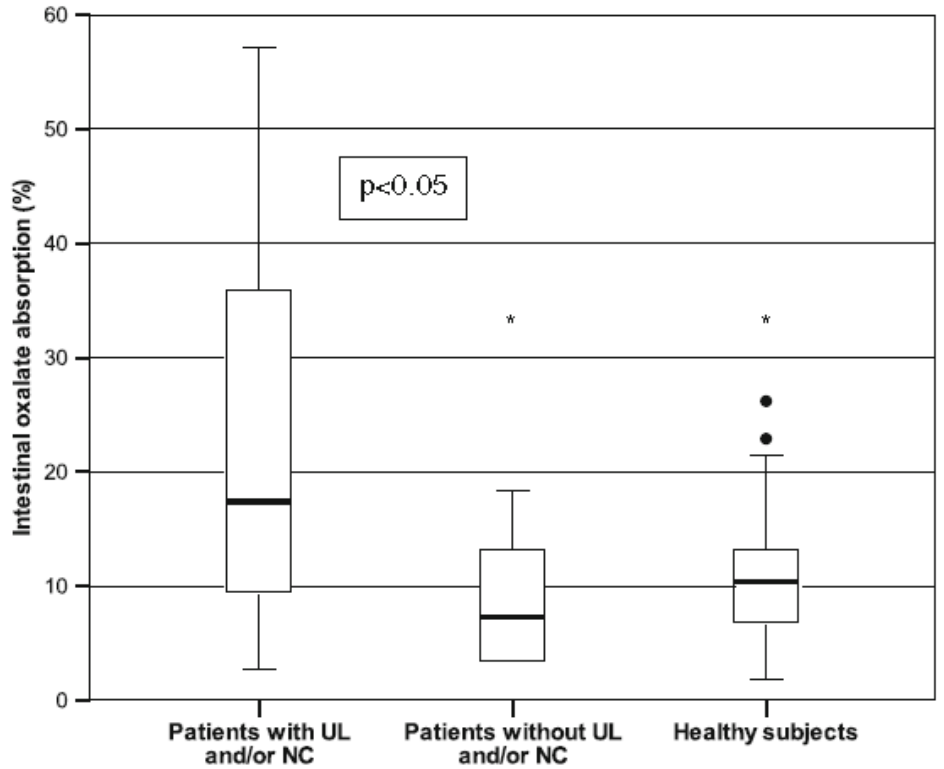


Fig. 2 Significantly higher intestinal oxalate absorption (%) in patients with Crohn's disease with compared with those without urolithiasis or oxalosis/nephrocalcinosis and compared with normal subjects (*$p < 0.05$). The two *dots* over the healthy subject bar indicate statistical outliers. *UL* urolithiasis; *NC* nephrocalcinosis

Hueppelshaeuser R et al. Pediatr Nephrol (2012) 27:1103–1109

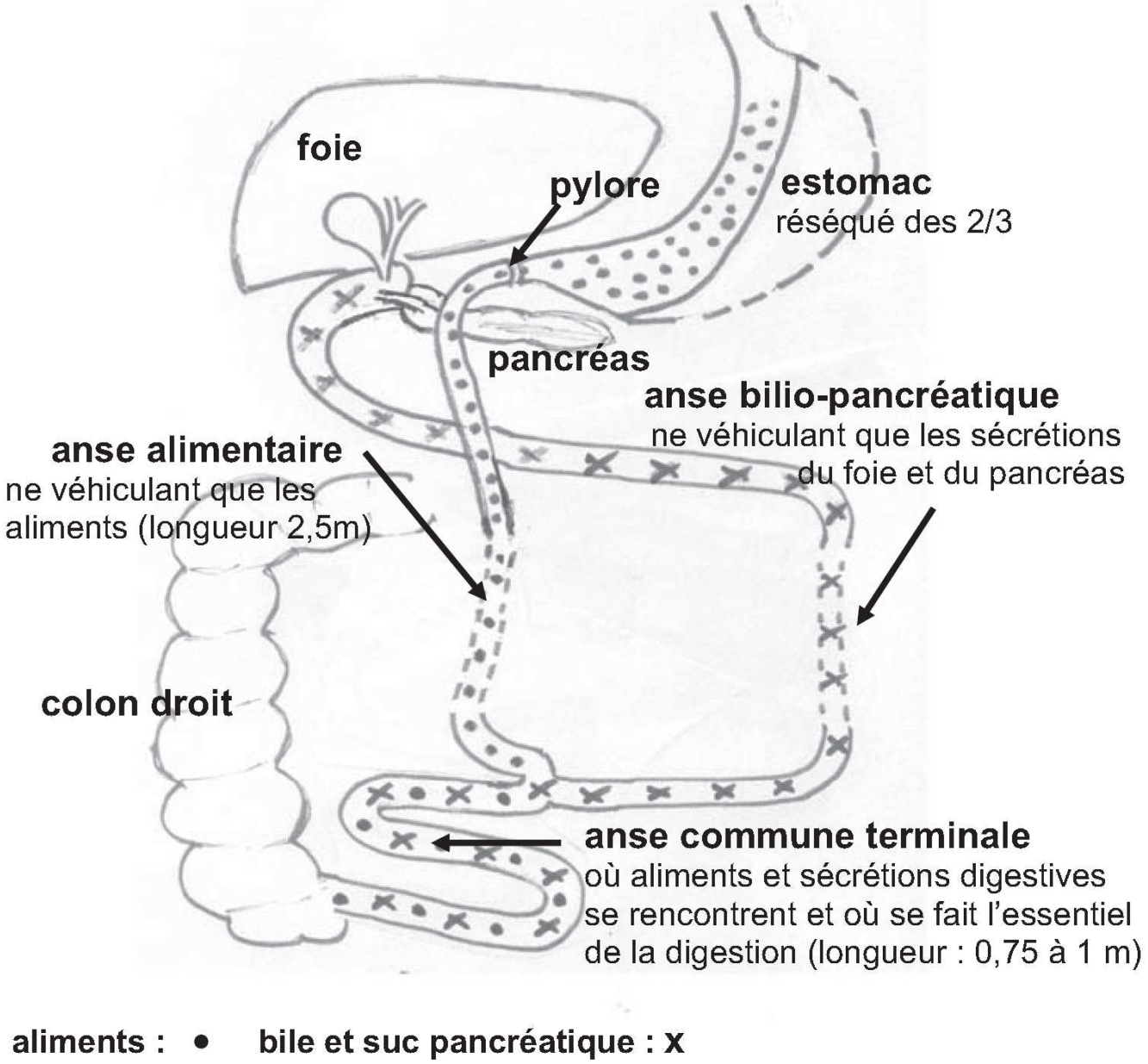


Fig. 1. Schéma de la gastrectomie longitudinale « *sleeve gastrectomy* » et de la dérivation biliopancréatique « *switch* duodénal ».

Bariatric surgery patients

Six and 12 months after RYGB surgery, plasma oxalate and urine calcium oxalate supersaturation increased significantly compared to similar measurements obtained prior to surgery (P values all ≤0.02). Fecal fat excretion at 6 and 12 months was increased (P-value, 0.026 and 0.055, 0 vs 6 and 12 months).
An increase in urine oxalate excretion after an oral dose of oxalate was observed at 6 and 12 months (P-values ≤0.02 each).

Surgery 2011; 149: 654-61.

Determinants of Urolithiasis in Patients With Intestinal Fat Malabsorption

Roswitha Siener, Julia Petzold, Norman Bitterlich, Birgit Alteheld, and Christine Metzner

OBJECTIVE To investigate the determinants of urinary stone formation in patients with fat malabsorption, because, although the prevalence of urolithiasis is greater in patients with intestinal diseases, the

Increased urinary oxalate and decreased citrate excretion, probably resulting from pancreatic and/or bowel resection with mainly preserved colon, were identified as the most crucial urinary risk factors for stone formation in patients with fat malabsorption.

The findings suggest that hyperoxaluria predominantly results from increased colonic permeability for oxalate due to disturbed bile acid metabolism. The impaired status of fat-soluble antioxidants b-carotene and vitamin E indicates severe malabsorptive states associated with an enhanced stone-forming propensity.

disturbed bile acid metabolism. The impaired status of fat-soluble antioxidants β-carotene and vitamin E indicates severe malabsorptive states associated with an enhanced stone-forming propensity. UROLOGY 81: 17–24, 2013. © 2013 Elsevier Inc.

Diseases associated with enteric hyperoxaluria

Disease involving small bowel mucosa

- Crohn's disease
- Celiac sprue

Surgical interruption

- Jejunoileal bypass
- Ileal resection

Other causes of malabsorption and steatorrhea

- Pancreatic insufficiency or resection
- Biliary obstruction or diversion
- Bacterial overgrowth
- Blind loop syndrome

Endocrinol Metabol Clin N Am 2002; 31: 979-99.

Background

Urinary stone disease is a mal-absorptive disorder that is a significant health problem because of its high prevalence and incidence. However, there are few population-based studies on the risk of urinary stone disease in patients with coeliac disease (CD).

Aim

To examine the risk of urinary stone disease in CD.

Methods

Population-based cohort study. Using small intestinal biopsy report data from 1969 to 2008 obtained from all Swedish pathology departments (n = 28), we identified [redacted] atrophy). Patients w[redacted] year to 142 177 re[redacted] We used Cox regres[redacted] tone dis-ease and c[redacted] ORs) for urinary sto[redacted] ary stone disease we[redacted] ster that contains da[redacted]

27% increased risk of urinary stone disease

Results

During follow-up, 314 individuals with CD and 1142 reference individuals developed urinary stone disease. This corresponded to a 27% increased risk of urinary stone disease in CD [95% confidence interval (CI) = 1.12 1.44]. CD patients had an absolute risk of urinary stone disease of 107/100 000 person-years (excess risk of 23/100 000). Risk estimates were similar in men and women, and did not differ according to age at CD diagnosis. Conditional logistic regression found that patients with CD were at a slightly increased risk also of prior urinary stone disease (OR = 1.19; 95% CI = 1.06 1.33).

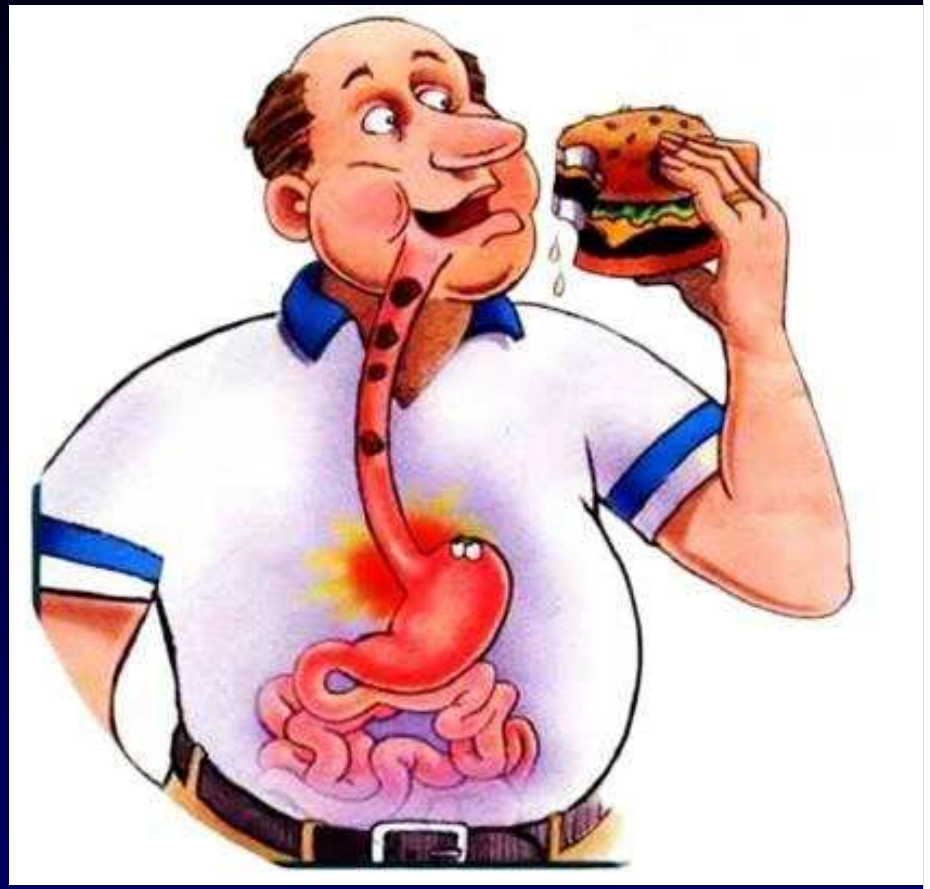
Conclusion

In this study, coeliac disease was associated with a moderately increased risk of urinary stone disease both before and after coeliac disease diagnosis.

Moderately increased risk of urinary stone disease in patients with biopsy-verified coeliac disease.

Ludvigsson JF et al.
Aliment Pharmacol Ther
2012; 35: 477-84:

Il diabete mellito, l'ipertensione arteriosa, la cardiopatia ischemica e l'ulcera peptica si associano ad una maggior frequenza della malattia litiasica ma senza una significatività statistica



Italian Guideline on Urinary Stones 2009; Anatol T 2005, Meydan N 2003

Farmaci con meccanismo metabolico

calcoli radiopachi	calcoli radiotrasparenti
supplementi di calcio/vit. D	idrossido di alluminio
inibitori anidrasi carbonica	lassativi
furosemide	uricosurici
idrossido di magnesio	allopurinolo
nimesulide	bicarbonato di sodio o potassio
corticosteroidi	farmaci acidificanti il pH urinario
acido ascorbico	
carbonato o farmaci contenenti carbonato	
antibatterici	
farmaci alcalinizzanti	

Italian Guideline on Urinary Stones 2009

Farmaci cristallizzanti nelle urine

antibatterici	sulfamidici cefalosporine	aminopecilline chinolonici
inibitori proteasi	indinavir	nelfinavir
analgesici	glafenina floctafenina	antrafenina
antipertensivi	triamterene	
antiacidi	trisilicio di magnesio idrossido di alluminio	colloidi di silicio
altri	primidone guaiafenasina sulfasalazina	methotrexate allopurinolo

Italian Guideline on Urinary Stones 2009

Mesalazione: a rare constituent of urinary tract concretions.

Hasan M, Tiselius HS. Urolithiasis 2013; 41: 271-2.

Case presentation

A 32-year-old woman presented at the emergency unit with right-sided abdominal and flank pain. The pain episode was subsequently followed by urgency and painful micturition, symptoms similar to those seen with mild urinary tract infection (UTI). There was no vomiting, nausea or fever.

At the examination, she reacted with pain when the renal area was slapped and mild pain also was demonstrated upon abdominal palpation. Microscopic haematuria was observed. The condition was preliminary interpreted as a UTI and she was accordingly treated with ciprofloxacin. Citodon was prescribed to treat the pain.

The patient revisited the department the following day because of recurrent severe pain for which the citodon regimen was inefficient. After a while, the pain subsided and she was discharged with Spasmofen™ suppositories; this pharmaceutical agent is a combination of narcotic analgeticum and spasmolyticum. At this second hospital visit, it was assumed that the pain was caused by a ureteral stone.

One month later, the patient again presented at the emergency unit with severe pain (VAS 10) and macroscopic haematuria. She then reported a history of seven pain episodes: two right-sided and five left-sided. On the CT images, there was no stone observed and no obstruction (Fig. 1).

After admittance, several concrements were voided, the largest with a diameter of 6 7 mm. After that, VAS was reduced to level 1 2. A cystoscopy was carried out with normal findings.

The laboratory findings were normal all the time with a normal plasma creatinine, CRP and urinary pH between 5.5 and 6.

It was of note that the patient recently had been diagnosed with ulcerative colitis, but the treatment with Pentasa™ had resulted in a successful remission and she had no bowel disturbances associated with the described pain episodes.

Some of the retrieved concrements were sent to a Swedish laboratory for analyses, but the analytical result did not disclose any urinary stone constituents. Remaining concrements were, therefore, sent to Louis C. Herring and Company, Orlando, Florida and the analytical result showed mesalamine; $C_7H_7NO_3$.

Inasmuch as mesalamine (5-aminosalicylic acid) is the main constituent of Pentasa™, the treatment dose was reduced from 6 to 2 g per day together with recommendations to maintain a high fluid intake. After that change in the therapeutic regimen, no more pain episodes were encountered.

Preventive treatment in calcium stone disease

Preventive treatment in patients with calcium stone disease should be started with conservative measures.

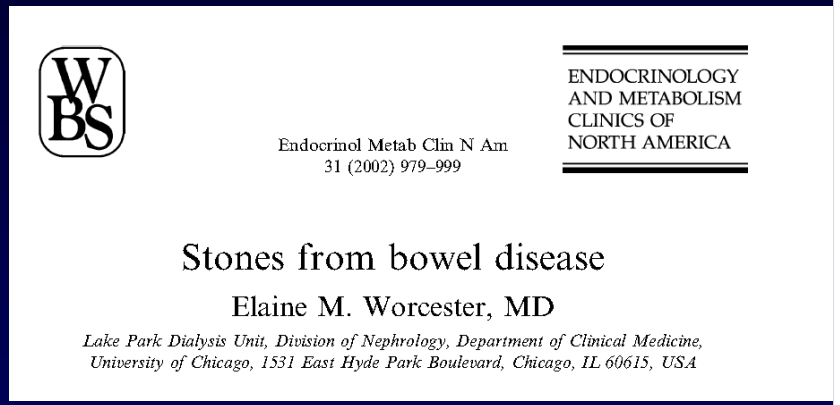
Pharmacological treatment should be instituted only when the conservative regimen fails. Patients should be encouraged to have a high fluid intake.

- restricted intake of oxalate-rich foods;
- restricted fat intake;
- calcium supplementation at meal times to enable calcium oxalate complex formation in the intestine ;
- sufficient fluid intake to balance intestinal loss of water caused by diarrhoea;
- alkaline citrates to raise urinary pH and citrate

ALIMENTI RICCHI DI OSSALATO DI CALCIO DA ELIMINARE DALLA DIETA CONTENUTO DI OSSALATO (mg%)	ALIMENTI A MEDIO CONTENUTO DA USARE CON MOLTA MODERAZIONE contenuto medio grammi 0,10	ALIMENTI PROIBITI CHE NON HANNO OSSALATO MA POSSONO PRODURLO NEL METABOLISMO	ALIMENTI A BASSO CONTENUTO DA USARE CON MODERAZIONE contenuto medio grammi 0,05
bietole mg.690 spinaci mg.676 cacao mg.400 acetosella mg.390 the' nero mg. 370 barbabietole rosse mg.338 pepe nero mg.300 rabarbaro mg.250	pomidoro da insalata mg.7,5 sedano mg.50 prugne secche mg.10 cicoria mg.10 infuso di caffè mg.13 carote mg.33 cavolfiore mg.60 piselli mg.52 melanzane mg. 13 fagiolini verdi mg.30 fagioli mg.32 indivia mg.27 cicoria mg.27 cetrioli mg.25 scarola mg.27 cavolfiore mg.24 peperoni mg.16 fichi secchi mg.30 cocomero mg.25 lattuga mg.7 asparagi mg.5,2 caffè	carne in scatola in gelatina brodi di carne carne ricca di collageno(tendini, cartilagine compresse di vitamina C eccessivo uso di farinacei (pasta e pane)	patate agrumi carote carciofi sedano rape melenzane ceci ciliege fragole pere mele
			ALIMENTI NON PROIBITI
			Pane, Pasta carne pesce sugo di pomodoro uova lattE, formaggi frutta fresca in piccola quantità vino in piccola quantità

Treatment of stones in patients with enteric hyperoxaluria

- General measures
  - Increased fluid intake
  - Non-specific methods for control of diarrhea
- Treatment of hyperoxaluria
  - Bile acid malabsorption (minimal steatorrhea)
    - Cholestyramine
  - Fatty acid malabsorption (moderate to marked steatorrhea)
    - Low fat diet
    - Medium chain triglycerides
    - Calcium supplements
    - Specific therapies of steatorrhea in certain conditions:
      - gluten-free diet (celiac sprue)
      - pancreatic enzyme replacement (pancreatic insufficiency)
      - antibiotics (bacterial overgrowth)
  - All causes
    - Low oxalate diet
- Treatment of other abnormalities
  - Hypocitraturia
    - Potassium citrate
    - Magnesium replacement
  - Magnesium deficiency or hypomagnesuria
    - Magnesium supplements
  - Uric acid crystallization
    - Alkali therapy (such as citrate)



Conclusioni

- **Le malattie infiammatorie croniche, le sindrome da malassorbimento, sindromi da resezione ileale o colica e i pazienti sottoposti a terapia bariatrica sono correlate ad un aumento dell'incidenza di urolitiasi**
- **La fisiopatolgia dell'urolitiasi in questi pazienti è multipla e complessa**
- **E' essenziale impostare una terapia preventiva basata sia su basi dietetico-alimentari e in caso di insuccesso anche farmacologica**