



Gastroenterology Foundation
of sub Saharan Africa

Acute cholangitis, cholecystitis

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OUTLINE

Cholangitis

- Diagnosis
- Investigations
- Management

Cholecystitis

- Epidemiology
- Diagnosis
- Approach

EPIDEMIOLOGY AND RISK FACTORS

- Stasis and infection in the biliary tract
- Fever, jaundice, and abdominal pain
- Biliary calculi (28% to 70%)
- Benign biliary stricture (5% to 28%)
- Malignancy (10% to 57%)

OTHER RISK FACTORS

- Post endoscopic retrograde cholangiopancreatography
- Strictured biliary-enteric anastomosis
- Sump syndrome
- Extrinsic compression of the bile duct due to a duodenal periampullary diverticulum-Lemmel syndrome
- Mirizzi syndrome
- Biliary obstruction by blood clots, parasitic infections

PATHOGENESIS

- Sphincter of Oddi- mechanical barrier to duodenal reflux and ascending bacterial infection
- Bacteriostatic activity of bile salts
- Secretory IgA and biliary mucous

- Disruptions normal barrier mechanisms
- Increased intra-biliary pressure

MICROBIOLOGY

Isolated microorganisms from bile cultures	Proportions of isolated organisms (%)
Gram-negative organisms	
<i>Escherichia coli</i>	31–44
<i>Klebsiella</i> spp.	9–20
<i>Pseudomonas</i> spp.	0.5–19
<i>Enterobacter</i> spp.	5–9
<i>Acinetobacter</i> spp.	–
<i>Citrobacter</i> spp.	–
Gram-positive organisms	
<i>Enterococcus</i> spp.	3–34
<i>Streptococcus</i> spp.	2–10
<i>Staphylococcus</i> spp.	0 ^a
Anaerobes	4–20
Others	–

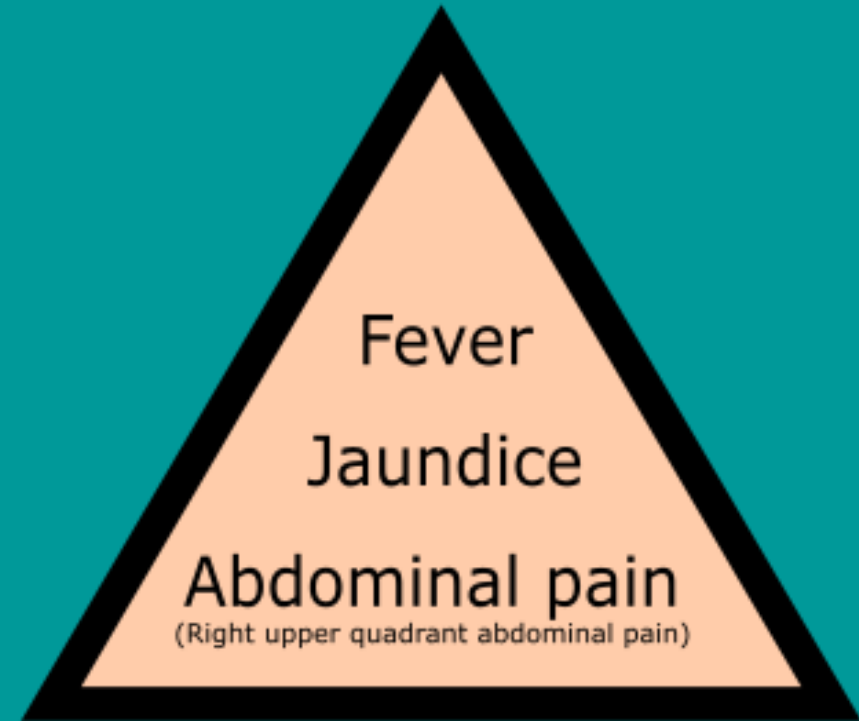
Table 2. Spectrum of biliary microbial culture and HIV infection

	HIV-positive (N=36), n (%)	HIV-negative (N=65), n (%)	Unknown (N=5), n (%)	p-value
Biliary infection	21 (58)*	33 (51)*	2 (40)	0.86
Gram-positive				
<i>Streptococcus</i> species	1 (4)	11 (22)	1	
<i>Staphylococcus aureus</i>	2 (7)	2 (4)	0	
<i>Enterococcus</i> species	4 (14)	8 (16)	0	0.18
Gram-negative				
<i>Escherichia coli</i>	4 (14)	8 (16)	0	
<i>Klebsiella pneumoniae</i>	6 (21)	12 (24)	0	
<i>Pseudomonas aeruginosa</i>	3 (11)	3 (6)	1	
<i>Citrobacter freundii</i>	2 (7)	2 (4)	0	
<i>Enterobacter cloacae</i>	2 (7)	3 (6)	0	
<i>Proteus mirabilis</i>	1 (4)	0	0	
<i>Morganella morganii</i>	1 (4)	0	0	0.18
Fungi				
<i>Aspergillus</i> species	1 (4)	0	0	
<i>Candida albicans</i>	1 (4)	0	0	0.32

*Some patients had multimicrobial infections.

CLINICAL MANIFESTATIONS

- Charcot's triad - 24 to 72% of patients
- Reynolds pentad-hypotension and altered mental state
- Complications from bacteraemia:
 1. Hepatic abscess
 2. Sepsis
 3. Multiple organ system dysfunction



Charcot's cholangitis triad

Low sensitivity (26.4%) and
High specificity (95.9%)

DIAGNOSTIC APPROACH

TG18/TG13 diagnostic criteria for acute cholangitis

A. Systemic inflammation

A-1. Fever and/or shaking chills

A-2. Laboratory data: evidence of inflammatory response

B. Cholestasis

B-1. Jaundice

B-2. Laboratory data: abnormal liver function tests

C. Imaging

C-1. Biliary dilatation

C-2. Evidence of the aetiology on imaging (stricture, stone, stent etc.)

Suspected diagnosis: 1 item in A + 1 item in either B or C

Definite diagnosis: 1 item in A, 1 item in B and 1 item in C

Sensitivity 91.8%
and
Specificity (77.7%)

IMAGING

Ultrasound

- 1st line-Identification of the cause of acute cholangitis
- Detect choledocholithiasis in 30% of cases

CT abdomen

- Not affected by gas, detect choledocholithiasis 42% of cases
- Clear identification of bile duct dilatation and biliary stenosis
- Aid in exclusion of differential diagnosis and complications

MRI/MRCP

- Reserved with diagnostic dilemma
- 82.2% accuracy in detecting choledocholithiasis

DIFFERENTIAL DIAGNOSIS

- Acute cholecystitis
- Biliary leak
- Acute pancreatitis
- Liver abscess/ Acute hepatitis
- Pyelonephritis
- Acute right sided diverticulitis

TG18/TG13 - SEVERITY ASSESSMENT CRITERIA FOR ACUTE CHOLANGITIS

Grade III (severe) acute cholangitis is associated dysfunction at least in any one of the following

1. Cardiovascular dysfunction: hypotension requiring dopamine ≥ 5 mcg/kg per min, norepinephrine
2. Neurological dysfunction
3. Respiratory dysfunction: PaO₂/FiO₂ ratio < 300
4. Renal dysfunction: oliguria, serum creatinine > 177 mmol/l
5. Hepatic dysfunction: PT-INR > 1.5
6. Haematological dysfunction: platelet count $< 100,000$ /mm³

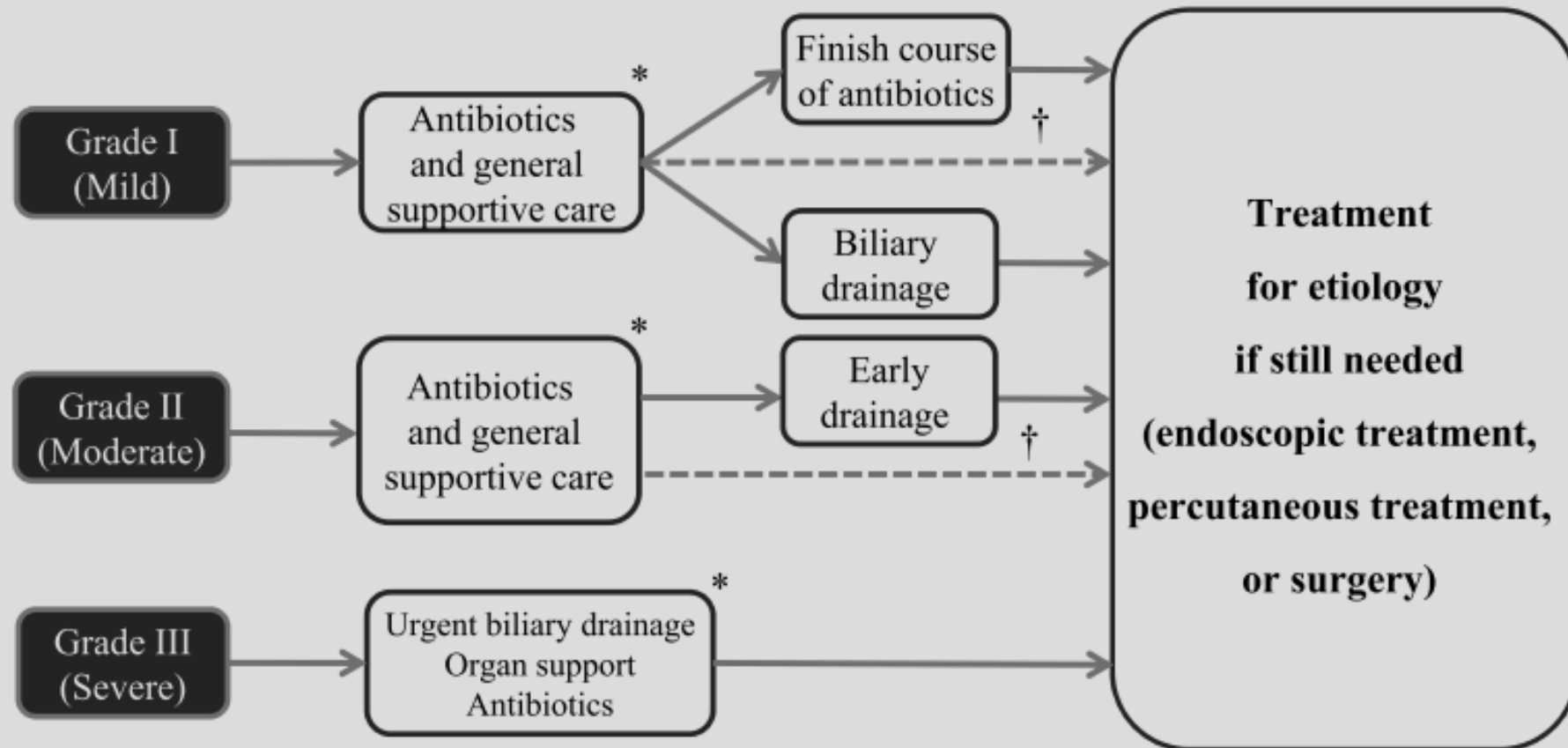
Grade II (moderate) acute cholangitis is associated with any 2

1. Abnormal WBC count ($> 12,000$ /mm³, $< 4,000$ /mm³)
2. High fever ($\geq 39^{\circ}\text{C}$)
3. Age (≥ 75 years old)
4. Hyperbilirubinemia (total bilirubin ≥ 85.5 umol/l)
5. Hypoalbuminemia

Grade I (mild) acute cholangitis

MANAGEMENT OF ACUTE CHOLANGITIS

J Hepatobiliary Pancreat Sci (2018) 25:31–40



EMPIRIC ANTIBIOTIC REGIMENS FOR HIGH-RISK COMMUNITY-ACQUIRED INTRA-ABDOMINAL INFECTIONS IN ADULTS

Single-agent regimen

Imipenem-cilastatin	500 mg IV every 6 hours
Meropenem	1 g IV every 8 hours
Doripenem	500 mg IV every 8 hours
Piperacillin-tazobactam	4.5 g IV every 6 hours

Combination regimen with metronidazole

ONE of the following:

Cefepime	2 g IV every 8 hours
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OR

Ceftazidime	2 g IV every 8 hours
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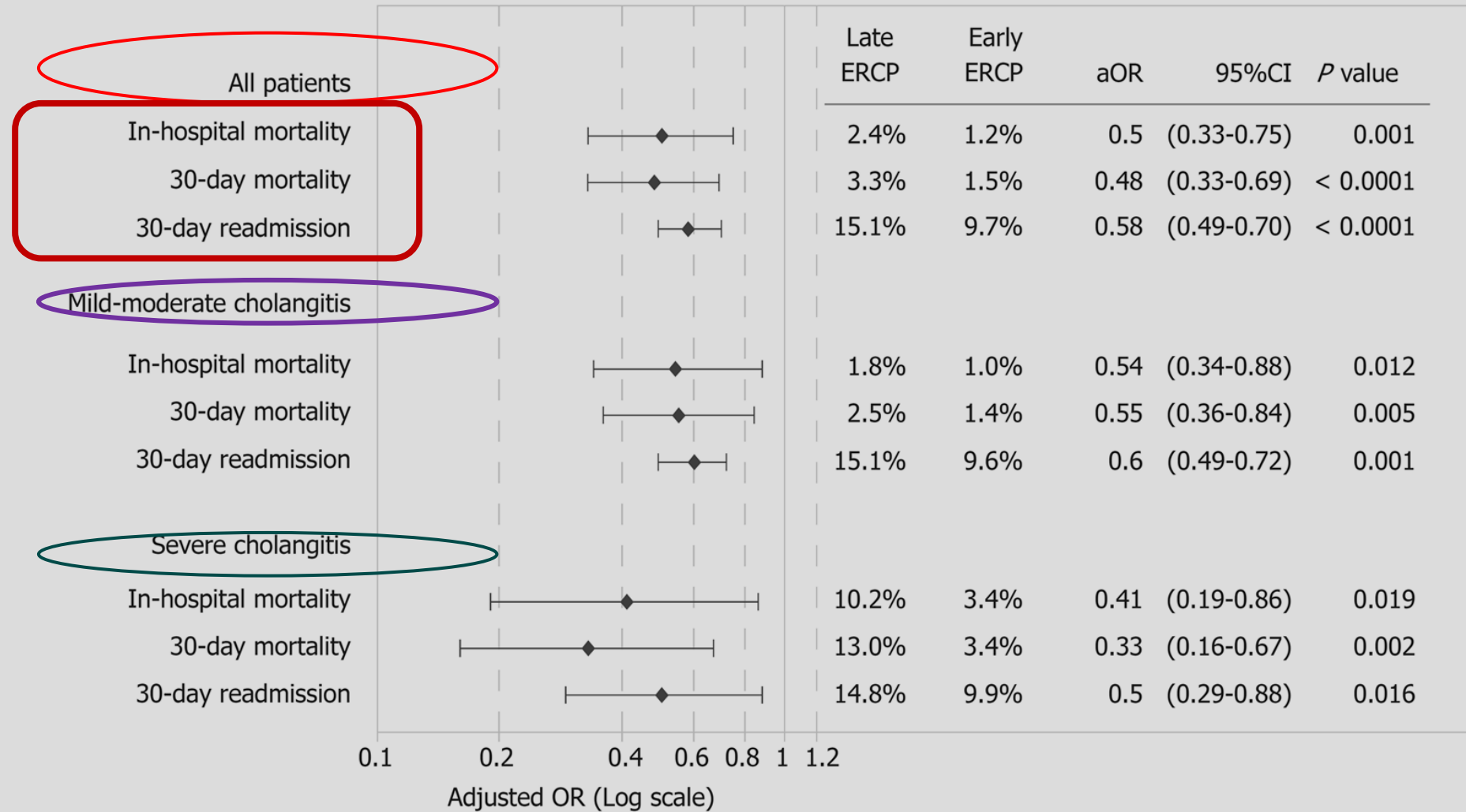
PLUS:

Metronidazole	500 mg IV or orally every 8 hours
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Early vs late endoscopic retrograde cholangiopancreatography in patients with acute cholangitis: A nationwide analysis

A Retrospective Study

Ramzi Mulki, Rushikesh Shah, Emad Qayed



DECOMPRESSION

1 - Decompression alone versus more extensive endoscopic therapy

- Reduce hospitalization
- Risk of haemorrhage
- Hemodynamically unstable patients
- Coagulopathic and/or are receiving antithrombotic agents

2 - ERCP versus PTBD for compression

- ERCP-reduced length of stay, adverse events, and better patient values
- PTBD- Difficult anatomy, failed ERCP, Sick patients

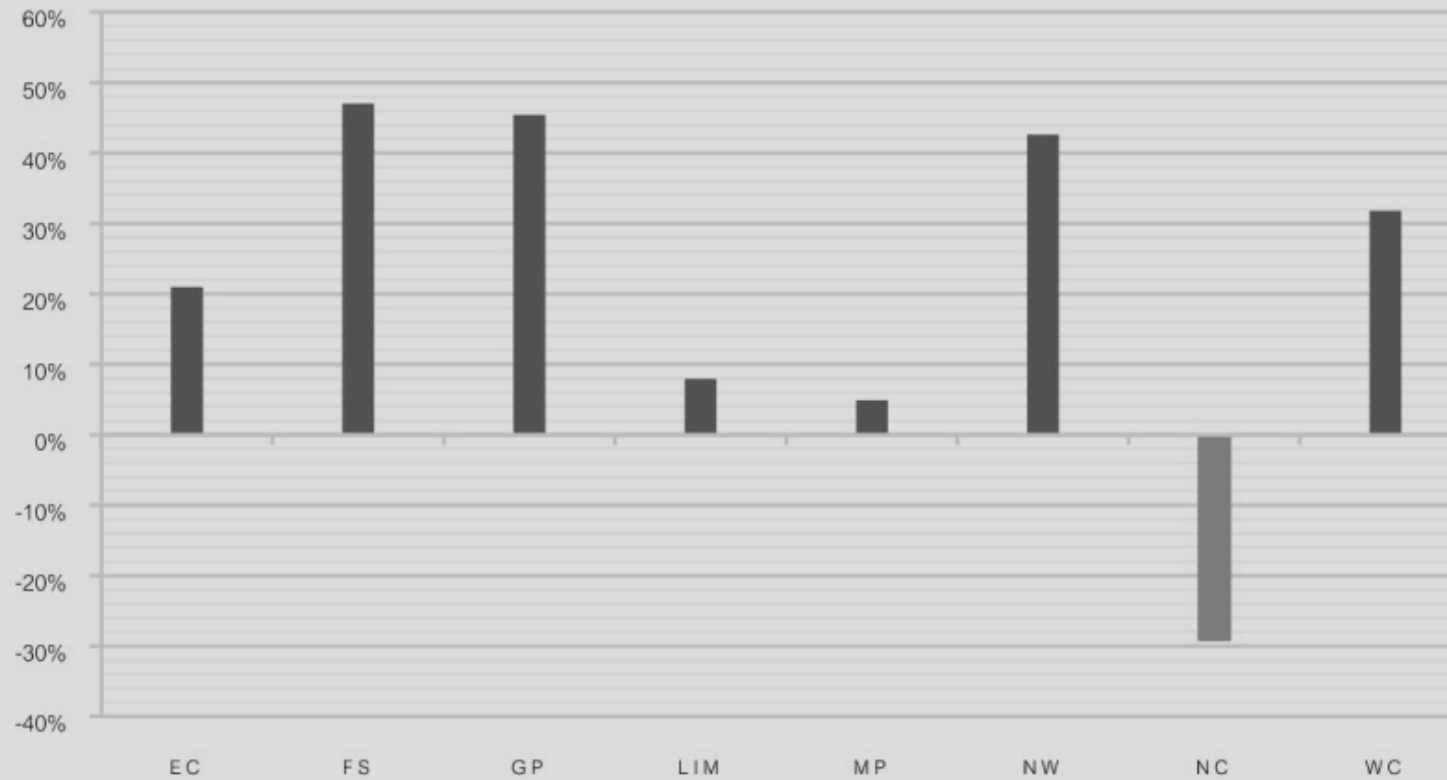
3 - EUS guided biliary drainage

CHOLECYSTITIS

- Right upper quadrant pain, fever, and leucocytosis associated with gallbladder inflammation
- Acalculous cholecystitis 5 to 10% of cases
- Acute calculous cholecystitis-cystic duct obstruction
- Production of lysolecithin
- Escherichia coli, Enterococcus, Klebsiella, and Enterobacter
- Mild oedema and acute inflammation to necrosis and gangrene

EPIDEMIOLOGY

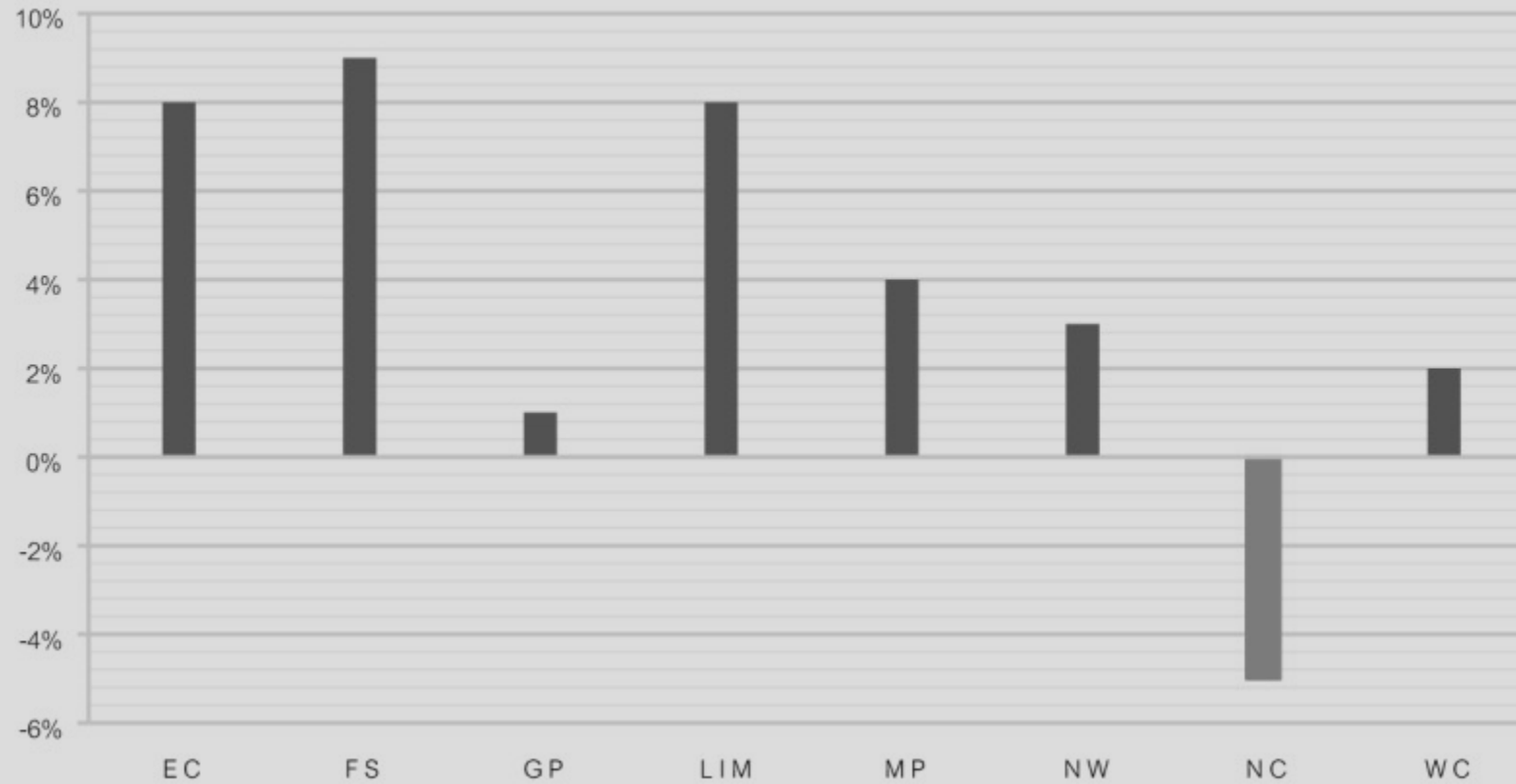
CHANGE IN CHOLECYSTECTOMY RATES: 2009-2013 vs 2004-2008



Percentage change in cholecystectomy rates in the last decade per province

EPIDEMIOLOGY

CHANGE IN URBANIZATION PER PROVINCE: 2001-2011



Percentage change in urbanization in the nine South African provinces

TG18/TG13 DIAGNOSTIC CRITERIA FOR ACUTE CHOLECYSTITIS

A - Local signs of inflammation

1 - Murphy's sign, 2-RUQ mass/pain/tenderness

B - Systemic signs of inflammation

1 - Fever, 2-elevated CRP, 3-elevated WBC count

C - Imaging findings characteristic of acute cholecystitis

Suspected diagnosis: 1 item in A+1 item in B

Definite diagnosis: 1 item in A= 1 item in B+C

Diagnostic accuracy ranges from 60.4% to 94.0%

TG18/TG13 SEVERITY GRADING FOR ACUTE CHOLECYSTITIS

Grade III (severe) acute cholecystitis

1. Cardiovascular dysfunction: hypotension requiring treatment with dopamine ≥ 5 g/kg per min, or norepinephrine
2. Neurological dysfunction: decreased level of consciousness
3. Respiratory dysfunction: PaO₂/FiO₂ ratio < 300
4. Renal dysfunction: oliguria, creatinine > 177 micmol/l
5. Hepatic dysfunction: PT-INR > 1.5
6. Haematological dysfunction: platelet count $< 100,000/mm^3$

Grade II (moderate) acute cholecystitis

1. Elevated WBC count ($> 18,000/mm^3$)
2. Palpable tender mass in the right upper abdominal quadrant
3. Duration of complaints > 72 h
4. Marked local inflammation (gangrenous cholecystitis, pericholecystic abscess, hepatic abscess, biliary peritonitis, emphysematous cholecystitis)

Grade I (mild) acute cholecystitis

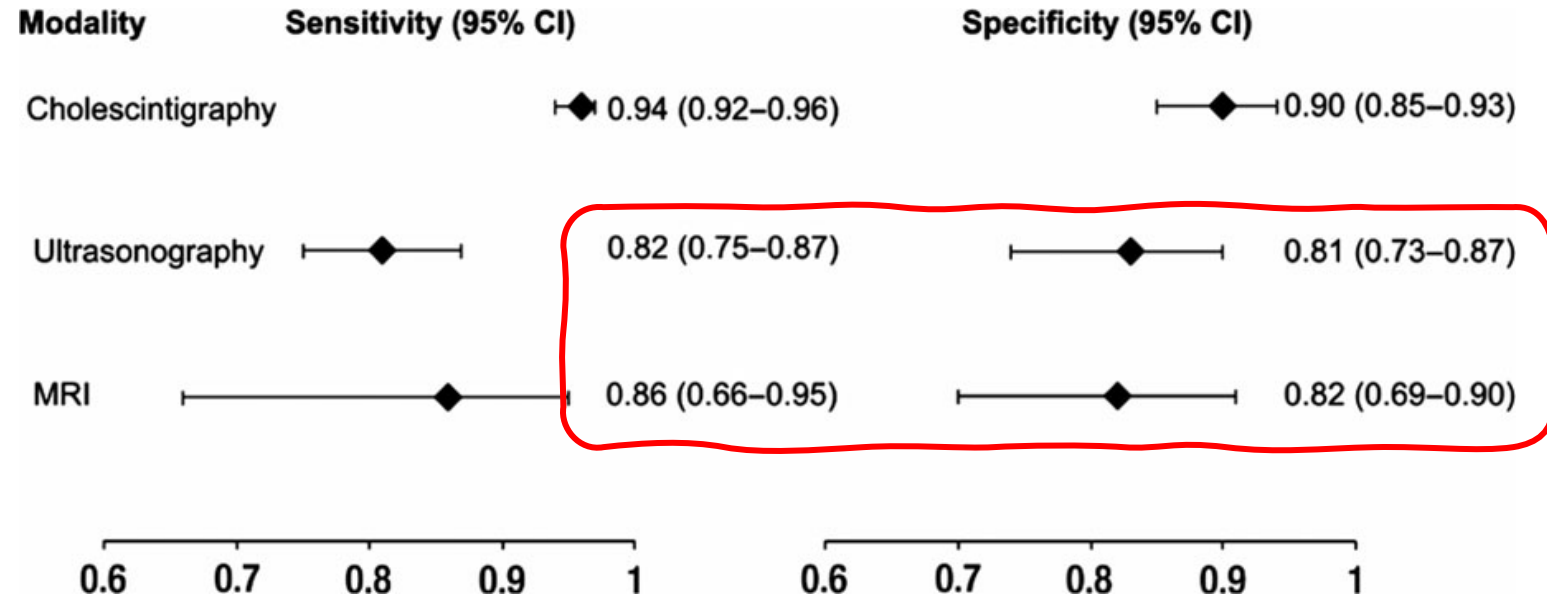
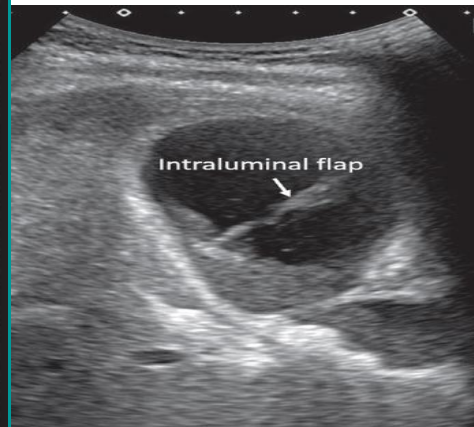
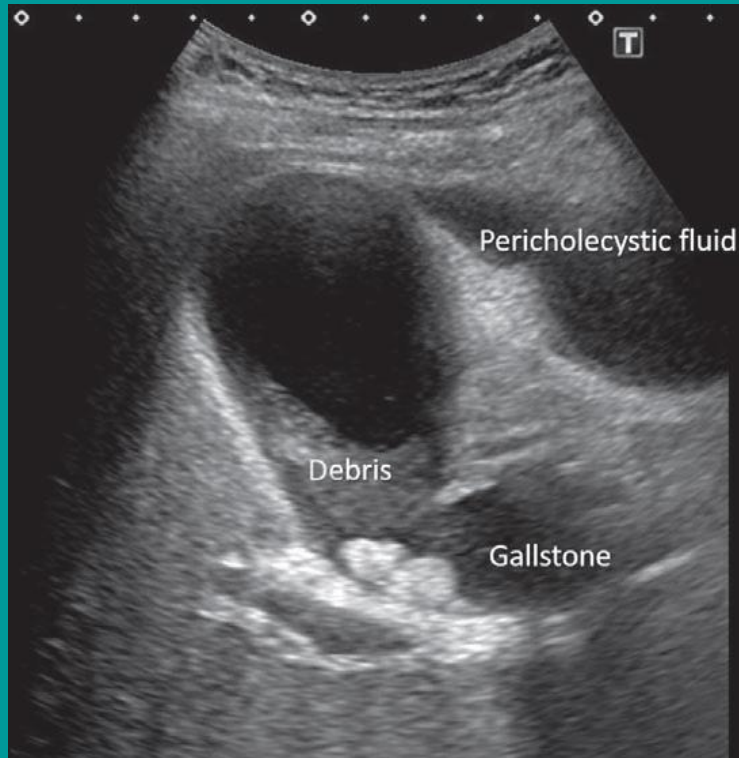
RELATIONSHIP BETWEEN SEVERITY GRADE AND 30-DAY OVERALL MORTALITY

SEVERITY GRADING				
	Grade I	Grade II	Grade III	P-value
	n = 1,339	n = 1,702	n = 680	
30-day mortality	15 (1.1%)	13 (0.8%)	37 (5.4%)	< 0.001

Cited from Yokoe et al

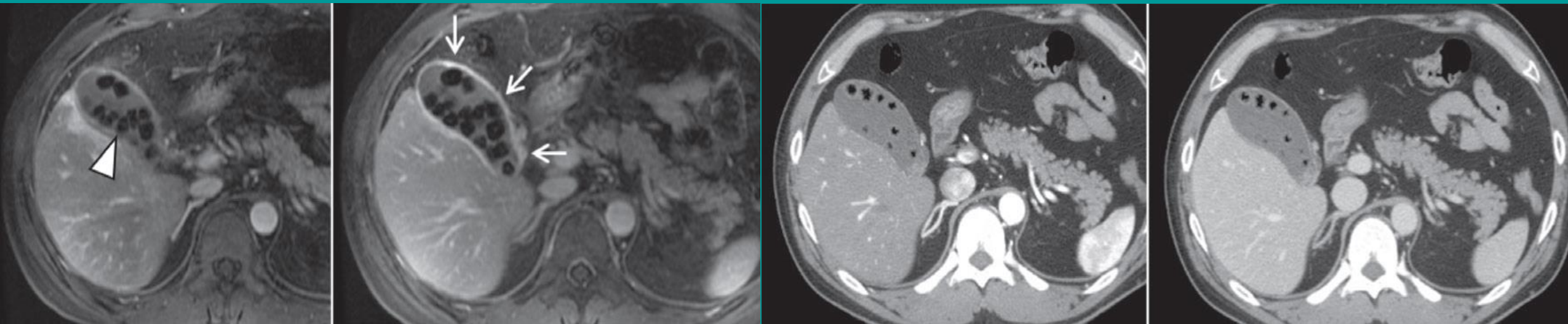
IMAGING

- Ultrasound- first-choice imaging method



Forest plot adapted from TG 2018 guidelines

IMAGING



Adapted from TG 18

- MRI/MRCP if abdominal US does not provide a definitive diagnosis
- Gall bladder wall (≥ 4 mm)
- Enlargement of the gallbladder (long axis ≥ 8 cm, short axis ≥ 4 cm)
- Gallstones or retained debris
- Fluid accumulation around the gallbladder

ASSOCIATED COMMON BILE DUCT STONES

- Choledocholithiasis occur in 10% to 20% of gallstone cases and 5 to 15 %, in case of ACC
- Recommend against the use of elevated LFTs or bilirubin as the only method to identify CBDS in patients with ACC

High risk

- The presence of a CBD stone on US or cross-sectional imaging
- Acute cholangitis

Intermediate risk

- Abnormal liver biochemical tests
- >55
- Dilated CBD on ultrasound or cross-sectional imaging

Low risk

- Age
- No predictors present

TREATMENT OF CBDS IN PATIENTS WITH ACC

- Preoperative ERCP with sphincterotomy
- Intraoperative ERCP with sphincterotomy
- Laparoscopic or open common bile duct exploration
- Post-operative ERCP with sphincterotomy
- No differences in morbidity, mortality and success rate

TIMING OF CHOLECYSTECTOMY IN PEOPLE WITH ACC

- Early Laparoscopic Cholecystectomy(ELC) -7 days from admission and within 10 days of symptoms
- Intermediate laparoscopic Cholecystectomy(ILC) - 7 days of admission to 6 weeks
- Delayed LC (DLC)- between 6 weeks and 3 months
- ELC > DLC > ILD

ACUTE CHOLECYSTITIS

Early Versus Delayed Cholecystectomy, A Multicentre Randomised Trial (ACDC Study, NCT00447304)

Carsten et al. 2013

Secondary Efficacy Outcomes	Group ILC (n = 304)	Group DLC (n = 314)	<i>P</i>
⇒ Morbidity score on day 75,* mean [95% CI]	0.53 [0.10–0.96]	1.12 [0.66–1.58]	<0.001
Conversion rate to open surgery, n (%) [95% CI]	30 (9.9) [6.5–13.2]	33 (11.9) [8.1–15.7]	0.44
⇒ Adverse events, n (%) patients [95% CI]	43 (14.1) [10.2–18.1]	127 (40.4) [35.0–45.9]	<0.001
Change of antibiotic treatment, n (%)	22 (7.2)	31 (9.9)	0.24
Mortality rate, n (%)	1 (0.3)	1 (0.3)	0.98
⇒ Total hospital stay, mean (interquartile range) [95% CI], d	5.4 (4–6) [5.08–5.71]	10.03 (7–12) [9.36–10.69]	<0.001
Duration of hospitalization after cholecystectomy, mean (interquartile range) [95% CI], d	4.68 (3–6) [4.36–5.00]	4.89 (3–6) [4.26–5.51]	0.57
Total hospital costs, mean (interquartile range) [95% CI], €	2919 (2651–2651) [2812–3026]	4262 (3021–4724) [4029–4494]	<0.001
Cost-effectiveness ratio, † mean, € per successful cholecystectomy	3300	6206	—

*Fifteen patients had a missing or implausible morbidity score.

†Ratio based on ITT population without patients with unassessed morbidity status.

Early Versus Delayed Cholecystectomy for Acute Cholecystitis, Are the 72hrs still the rule?

A Randomised Trial

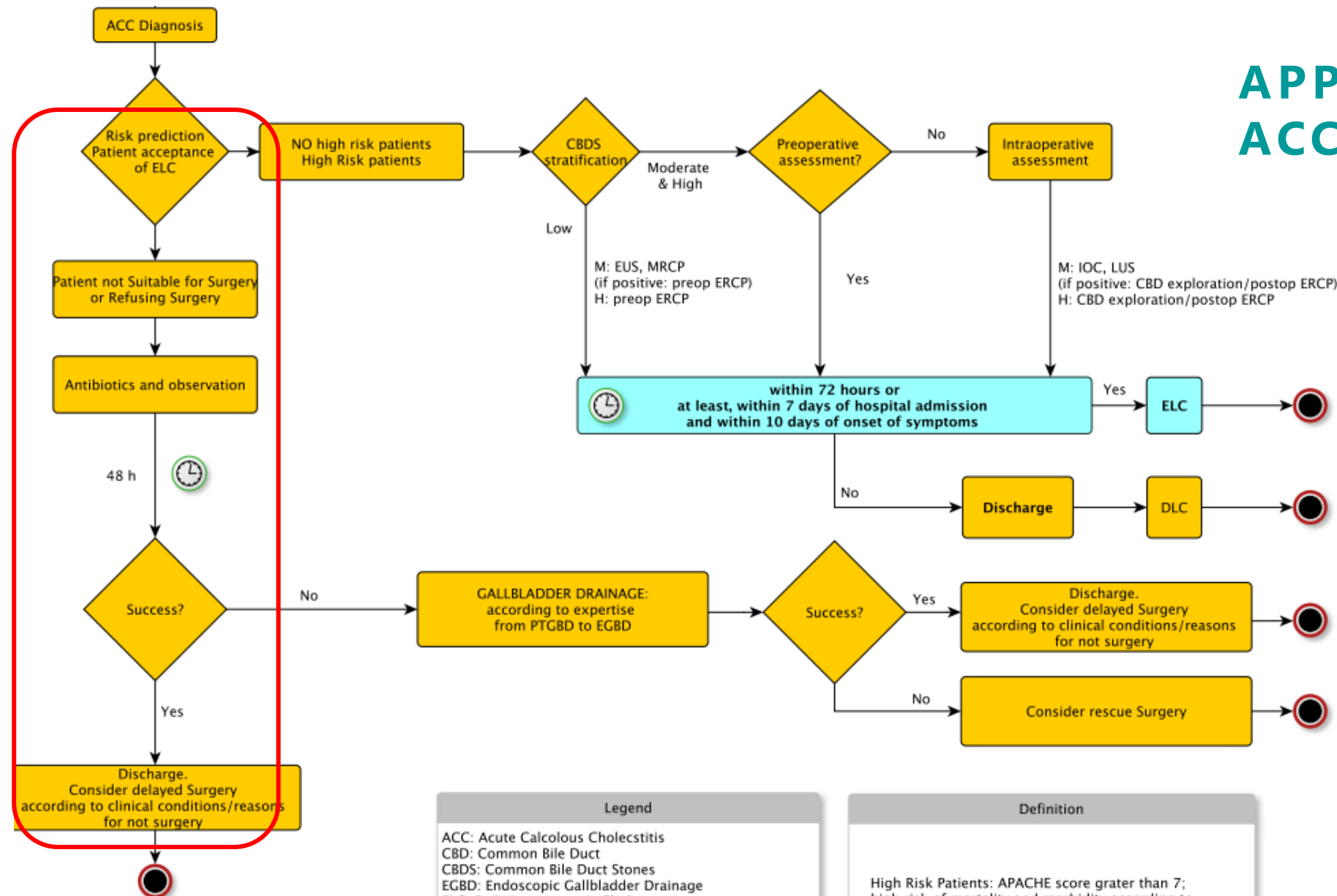
Roulin et al. 2016

Outcomes	ELC (n = 42)	DLC (n = 44)	OR (95% CI)	P
Overall morbidity, n (%)	6 (14.3)	17 (38.6)*	0.26 (0.0–0.76)	0.015
Failure of initial treatment	0 (0)	3 (6.8)	0.14 (0–2.79)	0.242
Unplanned readmission/emergency consultation awaiting delayed cholecystectomy	0 (0)	10 (22.7)	0.04 (0–0.68)	0.001
Posoperative complications	6 (14.3)	7 (15.9)	0.88 (0.27–2.88)	1.000
Total antibiotic duration, median (IQR), d	2 (1–5)	10 (10–14)	—	<0.001
Total hospital length of stay, median (IQR), d	4 (3–4)	7 (5–11)	—	<0.001
Total hospital costs, mean cost per patient (95% CI), €	9349 (7865–11,142)	12,361 (10,753–14,253)	—	0.018

*Three patients with unplanned readmission while awaiting DLC also presented with postoperative complications.

CI indicates confidence interval; OR, odds ratio.

APPROACH TO ACC



Legend
ACC: Acute Calculous Cholecystitis
CBD: Common Bile Duct
CBDS: Common Bile Duct Stones
EGBD: Endoscopic Gallbladder Drainage
ELC: Early Laparoscopic Cholecystectomy
ERCP: Endoscopic Retrograde Cholangiopancreatography
EUS: Endoscopic Ultrasound
DLC: Delayed Laparoscopic Cholecystectomy
IOC: Intraoperative Cholangiography
LUS: Laparoscopic Ultrasound
MRCP: Magnetic Resonance Cholangiopancreatography
PTGBD: Percutaneous Transhepatic Gallbladder Drainage
M: Moderate (risk of CBDS)
H: High (risk of CBDS)

Definition
High Risk Patients: APACHE score greater than 7; high risk of mortality and morbidity according to local use of clinical score and local clinical agreement.
Patients Not Suitable for Surgery: different than "common high risk patients"; according to specific surgeon judgment, patients not fit for surgery due to clinical conditions not classifiable by clinical score.

ANTIMICROBIAL REGIMENS SUGGESTED FOR ACC

Good penetration efficiency Antibiotics Bile/serum (>=5)	Low penetration efficiency Antibiotics Bile/serum (<1)
Piperacillin/tazobactam	Cefotaxime
Tigecycline	Meropenem
Amoxicillin/clavulanate	Ceftazidime
Ciprofloxacin	Vancomycin
Ampicillin/Sulbactam	Amikacin
Ceftriaxone	Gentamicin
Levofloxacin	Cefepime
Penicillin G	Imipenem

Gram-negative aerobes- Escherichia coli and Klebsiella pneumonia
Anaerobes-Bacteroides fragilis

Take home message

- Biliary drainage and antibiotics
- Mortality acute cholangitis is less than 10% after biliary drainage
- Pre-ERCP era mortality >50%

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