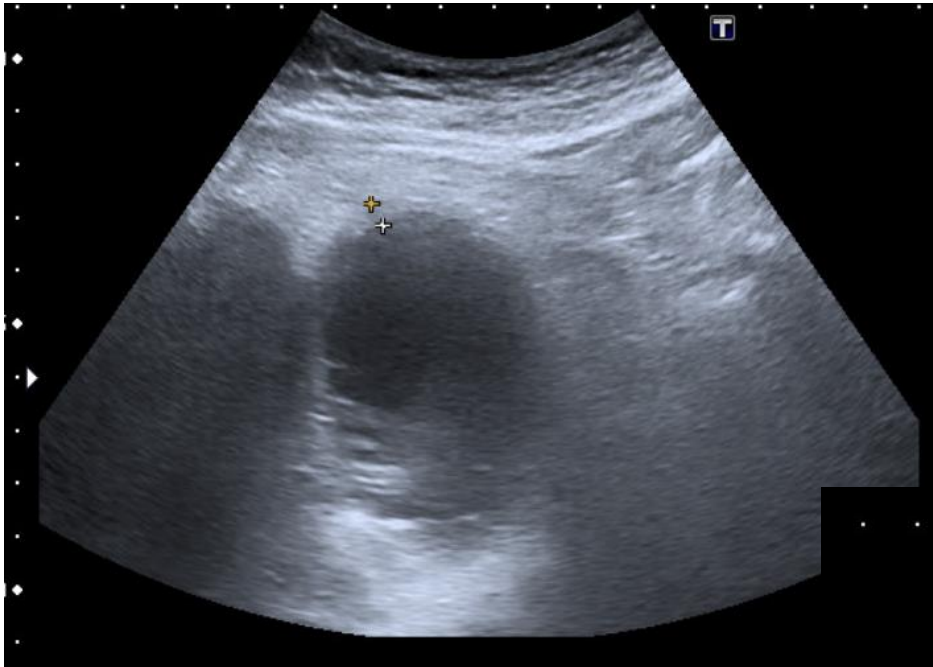


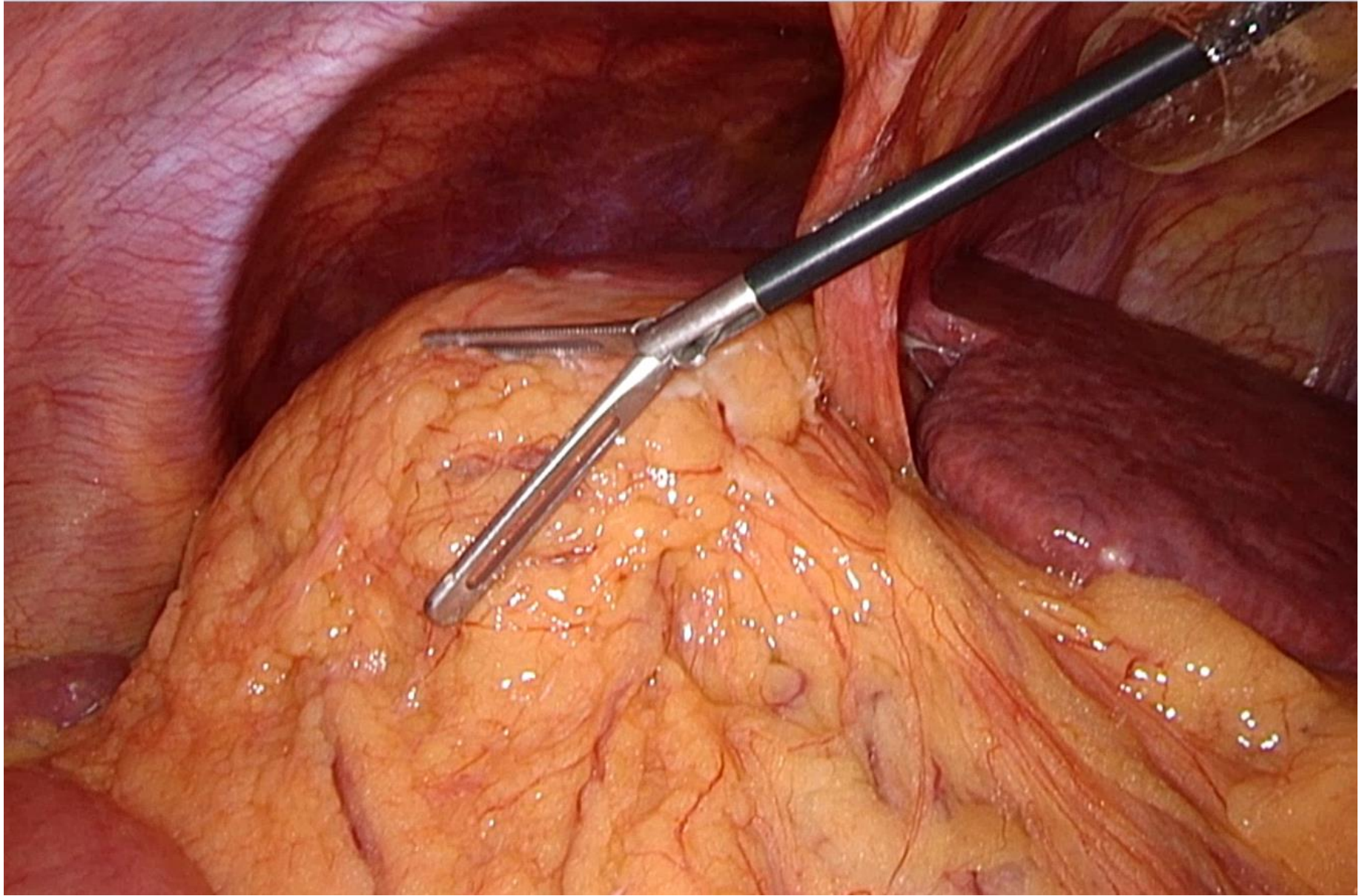
# Acute cholecystitis, acute cholangitis

Cursorisch onderwijs in maag-darm-leverziekten  
NVGE. Spoedeisende MDL zorg  
8 juni 2020, 14:55 vanuit Utrecht

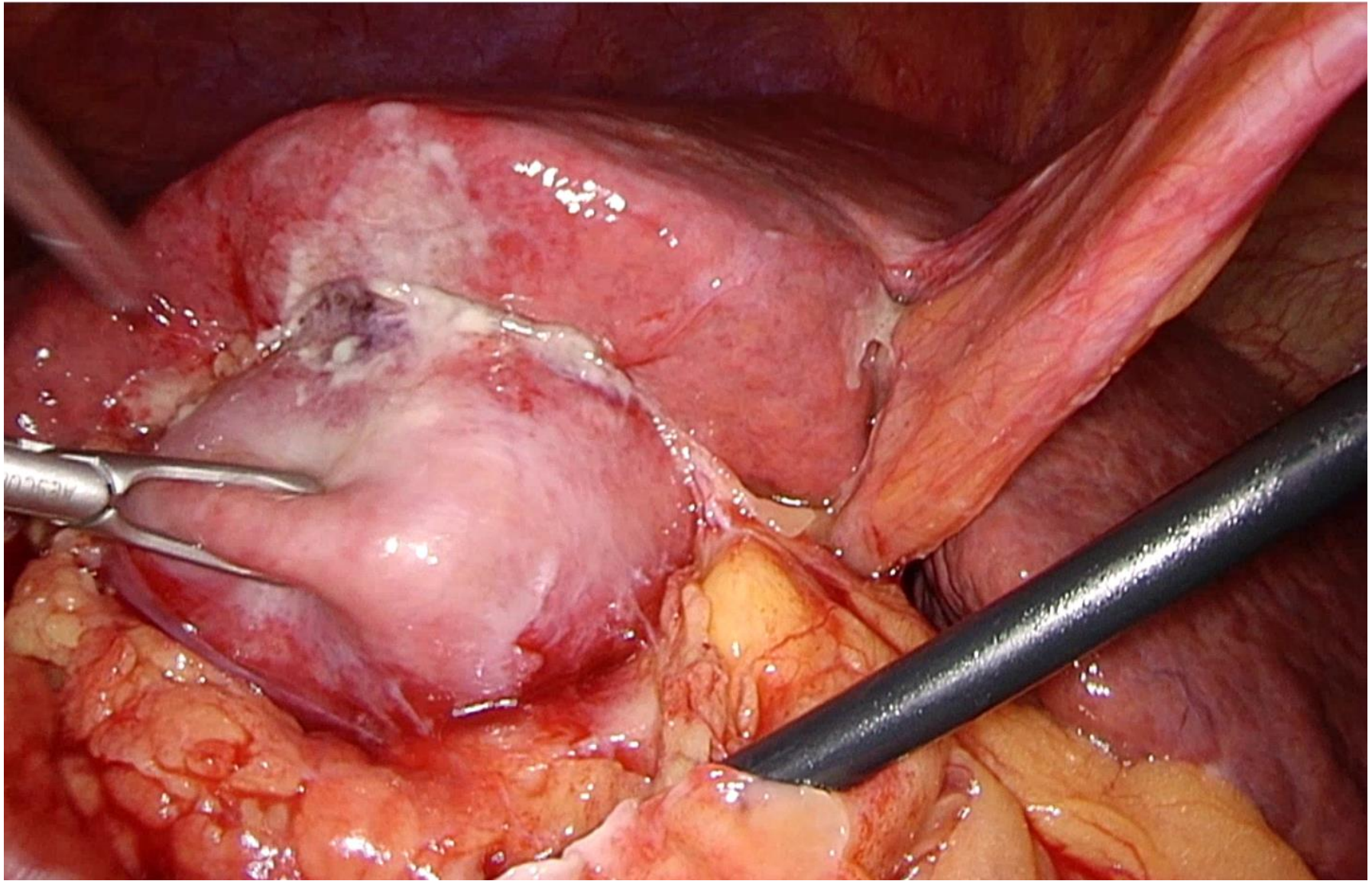
*Philip de Reuver, chirurg*



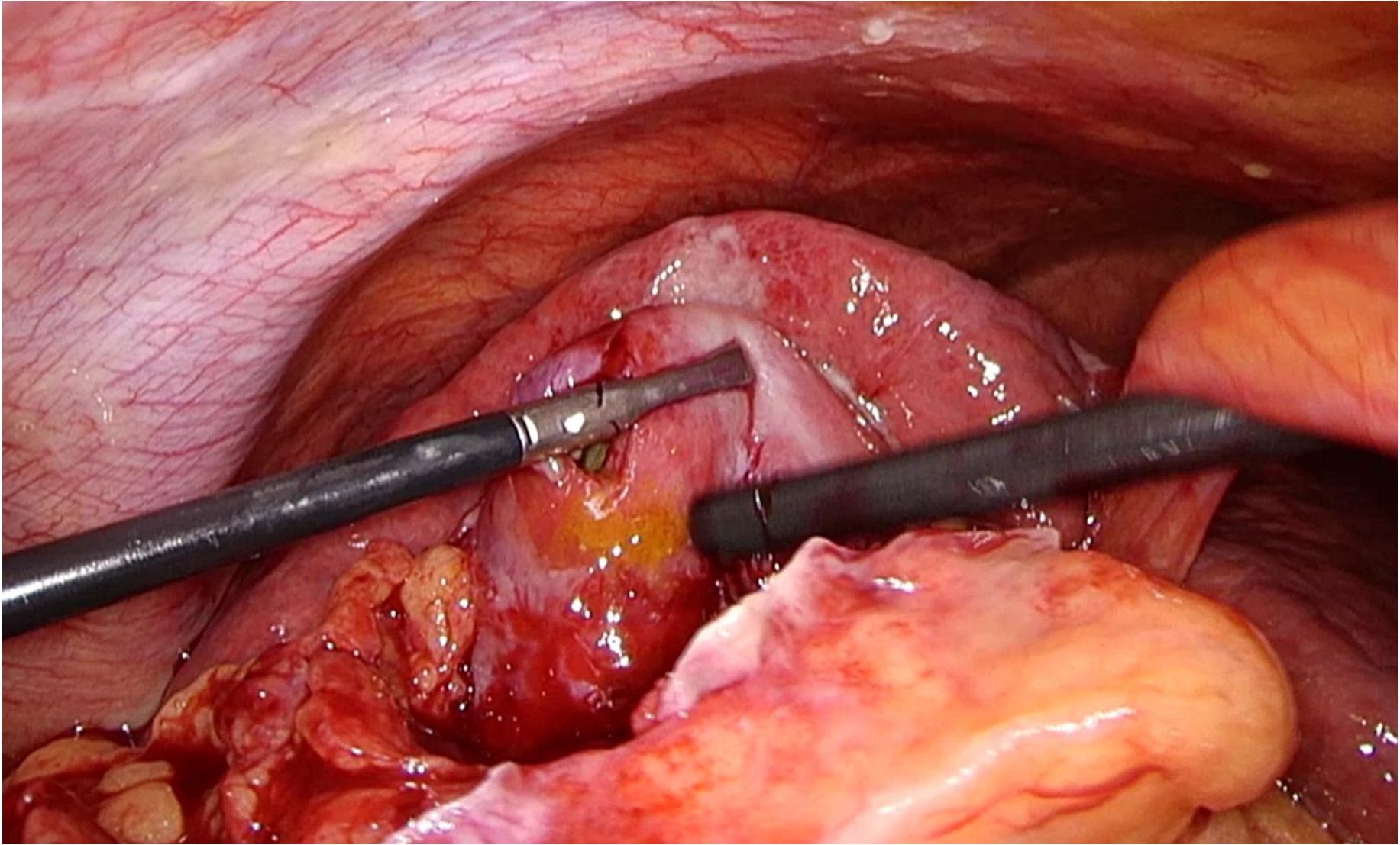
Conclusie:  
Verdikte galblaaswand met omliggende vetinfiltratie en stenen.  
Dubieus drukpijn (meest sensitieve teken in combinatie met galstenen).  
Beeld kan radiologisch goed passen bij een cholecystitis.



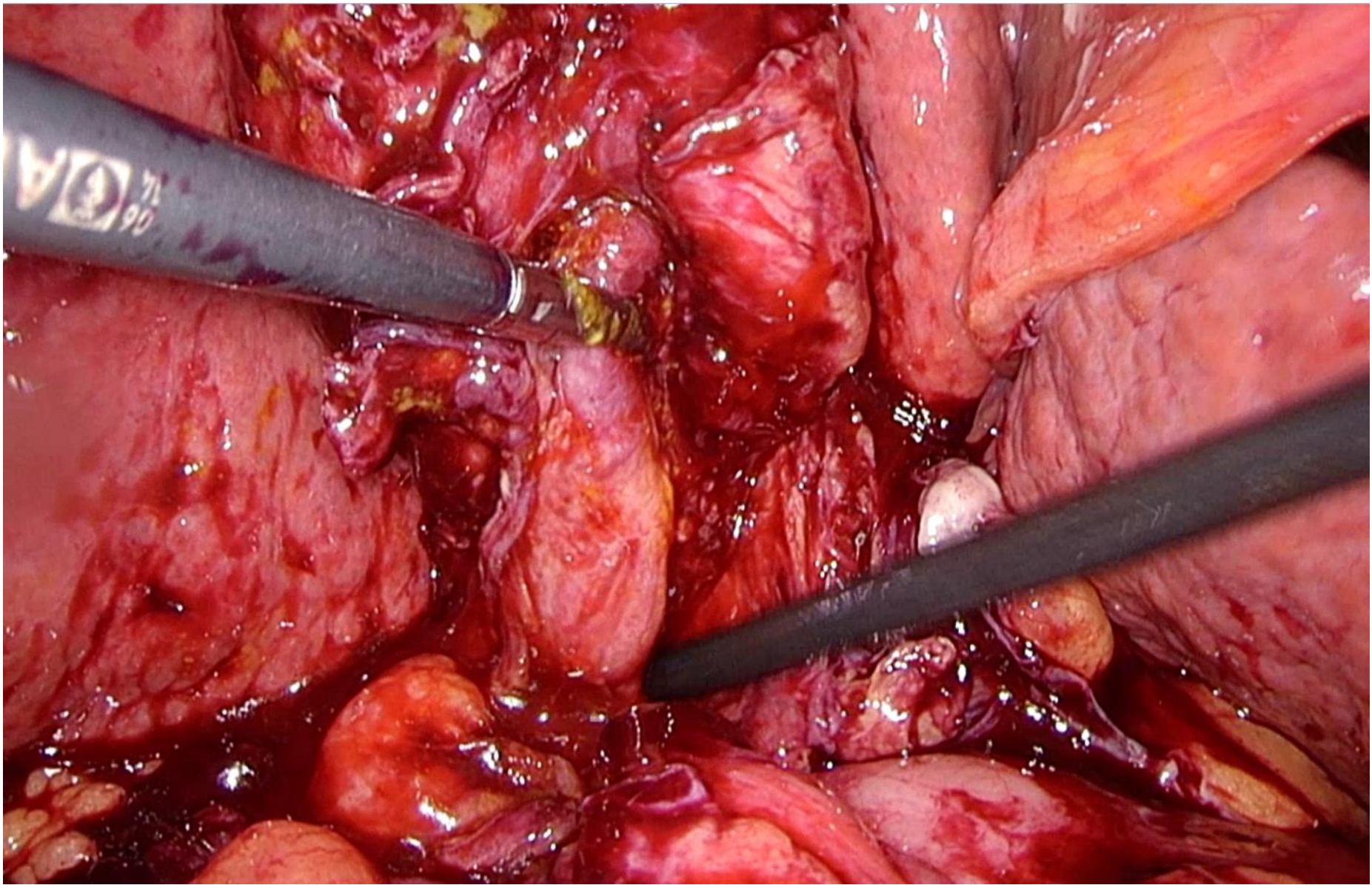
**Radboudumc**



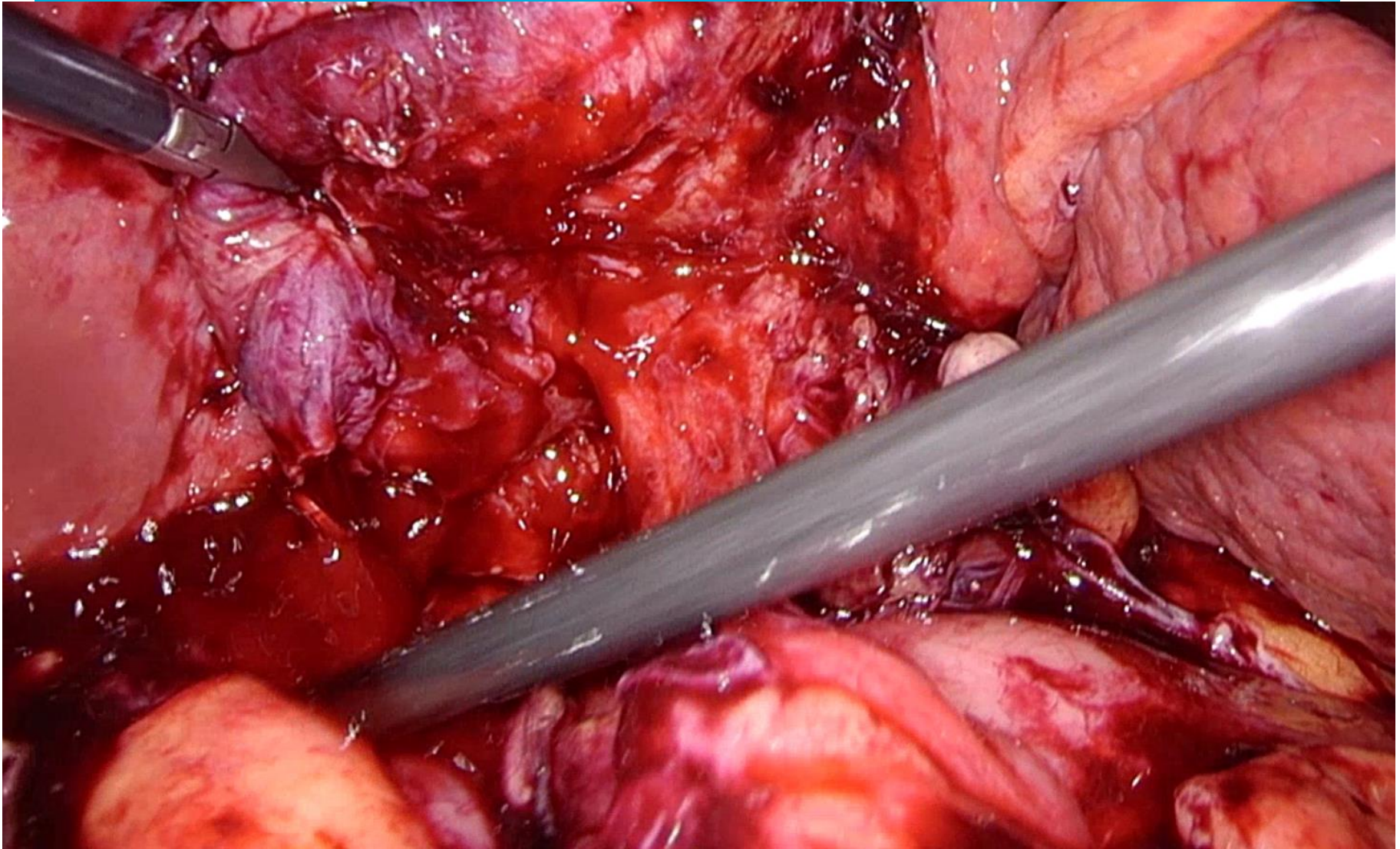
Radboudumc



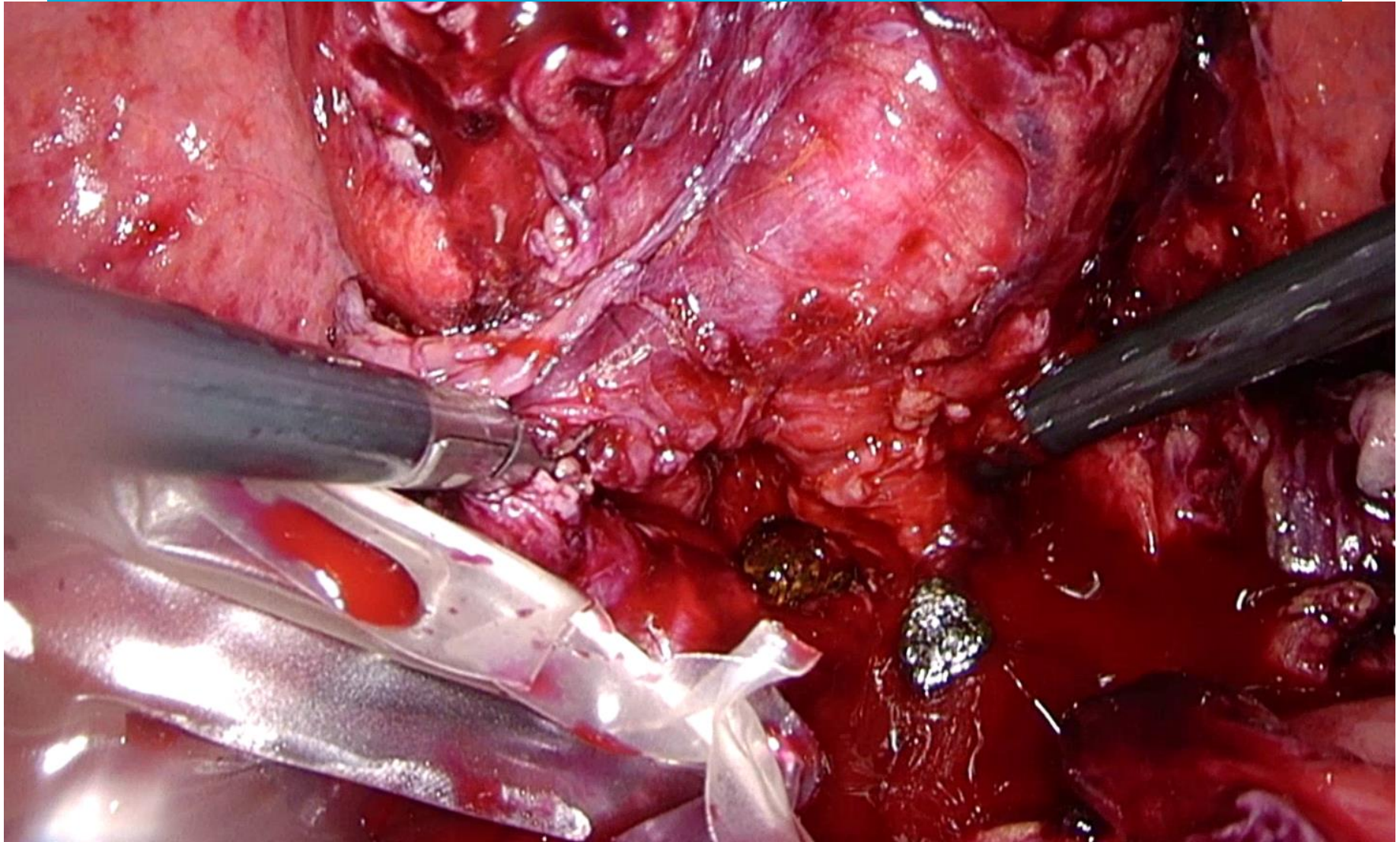
**Radboudumc**



Radboudumc



**Radboudumc**



**Radboudumc**



---

# Acute Cholecystitis

- Veel voorkomende SEH diagnose
- 5% van patiënten met acute buikpijn
- Klinische diagnose i.c.m. beeldvorming
- Kliniek: pijn RBB, Murphy's sign
- koorts, CRP, leucocytose
- Verschuiving in richtlijnen

---

# *NVvH –richtlijn galsteenlijden*

- NVvH<sup>1</sup>
  - Een acute cholecystitis dient **bij voorkeur direct** geopereerd te worden (**binnen 1 week**)
  - Percutane galblaasdrainage is een waardevolle alternatieve behandeling voor operatie, met name bij **inoperabele patiënten** (ASA IV)

---

# Tokyo Guidelines 2018

J Hepatobiliary Pancreat Sci (2018) 25:55–72  
DOI: 10.1002/jhbp.516

---

GUIDELINE

**Tokyo Guidelines 2018: flowchart for the management of acute cholecystitis**

Update richtlijn 2013 en 2007

**Table** diagnostic criteria for acute cholecystitis

---

A. Local signs of inflammation, etc.:

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

B. Systemic signs of inflammation, etc.:

(1) Fever, (2) elevated CRP, (3) elevated WBC count

C. Imaging findings:

Imaging findings characteristic of acute cholecystitis

Suspected diagnosis: One item in A + one item in B

Definite diagnosis: One item in A + one item in B + C

---

*Graad I, milde cholecystitis*

*Graad II, matige cholecystitis*

1. Leucocytose ( $>18,000/\text{mm}^3$ )
2. Palpabele massa
3. Klachten langer dan  $>72$  h
4. Lokale ontsteking op echo (gangreneuze cholecystitis, abscess, peritonitis)

*Graad III, ernstige cholecystitis*

1. Cardiovasculair
2. Neurologisch
3. Respiratoir
4. Nier functie
5. Lever functie
6. Stolling

# Gradering AC en opname duur

References	Year	<i>n</i>	Grade I	Grade II	Grade III	<i>P</i> -value
Cheng [44]	2014	103	7.3 ± 3.5	9.2 ± 3.9	15.2 ± 8.5	<0.05
Kamalapurkar <sup>a</sup> [11]	2014	84		5 (4–8)	12 (8–16)	<0.001
Wright <sup>a</sup> [10]	2015	445	3 (1–16)	4 (1–33)	7 (1–60)	<0.001
Ambe <sup>b</sup> [13]	2015	138	6.0 ± 2.7	7.8 ± 3.3	10.4 ± 6.1	0.02
Amirthalingam <sup>c</sup> [12]	2016	149	4.46 (2–14)	6.24 (1–41)	9.31 (3–21)	<0.001
Hayasaki [17]	2016	171	4.3 ± 2.5	11.0 ± 11.6	20.8 ± 13.5	<0.001

Yokoe M, J Hepatobiliary Pancreat 2017

# Gradering AC en conversie

References	Year	<i>n</i>	Grade I	Grade II	Grade III	<i>P</i> -value
Asai [45]	2014	225	7/105 (6.7%)	22/119 (18.5%)	0/1 (0%)	0.0279
Kamalapurkar [11]	2014	84		1/60 (1.7%)	4/24 (16.7%)	0.006
Wright [10]	2015	445	7/92 (7.0%)	31/121 (25.6%)	9/26 (34.6%)	0.001
Ambe [13]	2015	138	5/79 (6.3%)	5/33 (15.2%)	9/26 (34.6%)	0.001
Amirthalingam [12]	2016	149	2/84 (2.4%)	6/49 (12.2%)	0/16 (0%)	0.03

# Gradering AC en Morbiditeit

References	Year	<i>n</i>	Grade I	Grade II	Grade III	<i>P</i> -value
Cheng [44]	2014	103	3/31 (9.7%)	7/25 (28.0%)	9/20 (45.0%)	<0.05
Wright [10]	2015	445	4/137 (2.9%)	6/191 (3.1%)	13/117 (11.1%)	0.003
Ambe [13]	2015	138	7/79 (8.9%)	5/33 (15.2%)	12/26 (46.2%)	0.01



# Gradering AC en mortaliteit

---

## Severity grading

---

	Grade I <i>n</i> = 1,339	Grade II <i>n</i> = 1,702	Grade III <i>n</i> = 680	<i>P</i> -value
--	-----------------------------	------------------------------	-----------------------------	-----------------

---

30-day mortality	15 (1.1%)	13 (0.8%)	37 (5.4%)	<0.001
------------------	-----------	-----------	-----------	--------

---

## Survival analysis

### 30-day mortality in patients with Grade I and Grade II acute cholecystitis

Survivor (n = 2,677) vs Non-survivor (n = 21)

Variabele	Univariate	Multivariate OR (95% CI)
Leeftijd	+	
BMI	+	0.241 (0.088–0.659)
Performance status	+	
Charlson comorbidity index >6	+	4.433 (1.816–10.822)
Niet geassocieerd zijn: Geslacht, Icterus, CRP, WBC, Palpabele massa, Klachten >72 uur, Echo		

Survival analysis, 30-day mortality, Grade III

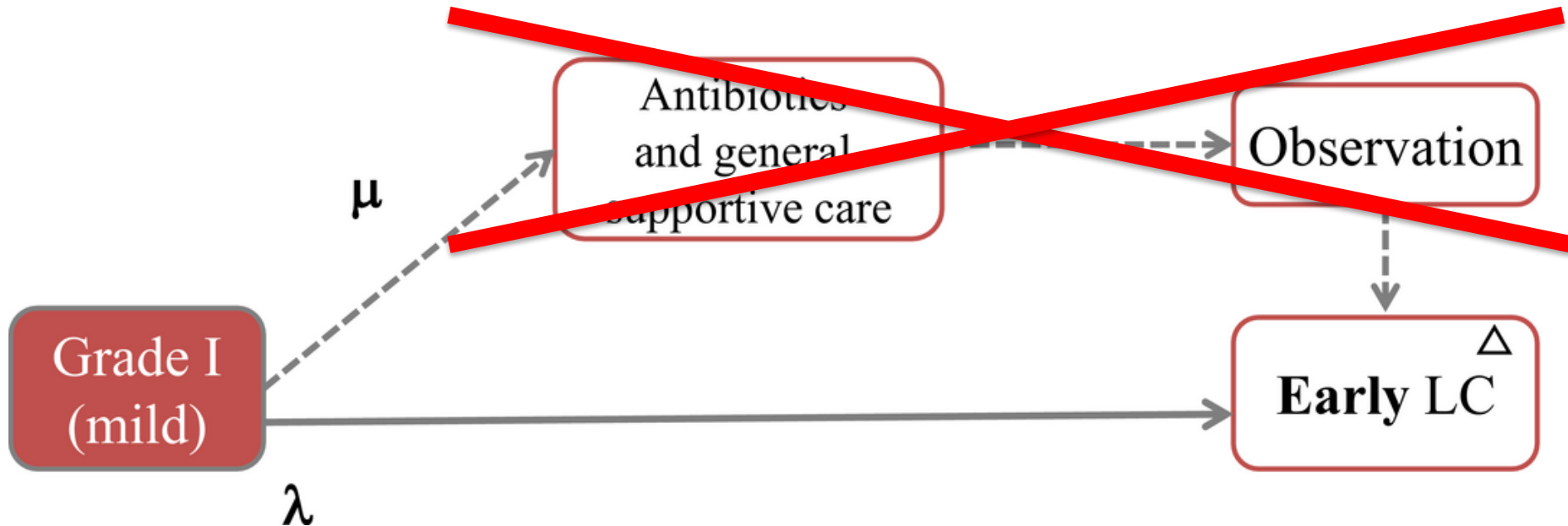
Survivor (n = 591) vs Non-survivor (n = 20)

Variabele	Univariate	Multivariate OR (95% CI)
BMI >20	+	
Performance status	+	
Charlson comorbidity index >6	+	
Icterisch	+	6.470 (2.446–17.110)
Neurologisch dysfunctie	+	4.346 (1.640–11.515)
Respiratoire dysfunctie	+	5.843 (2.052–16.635)

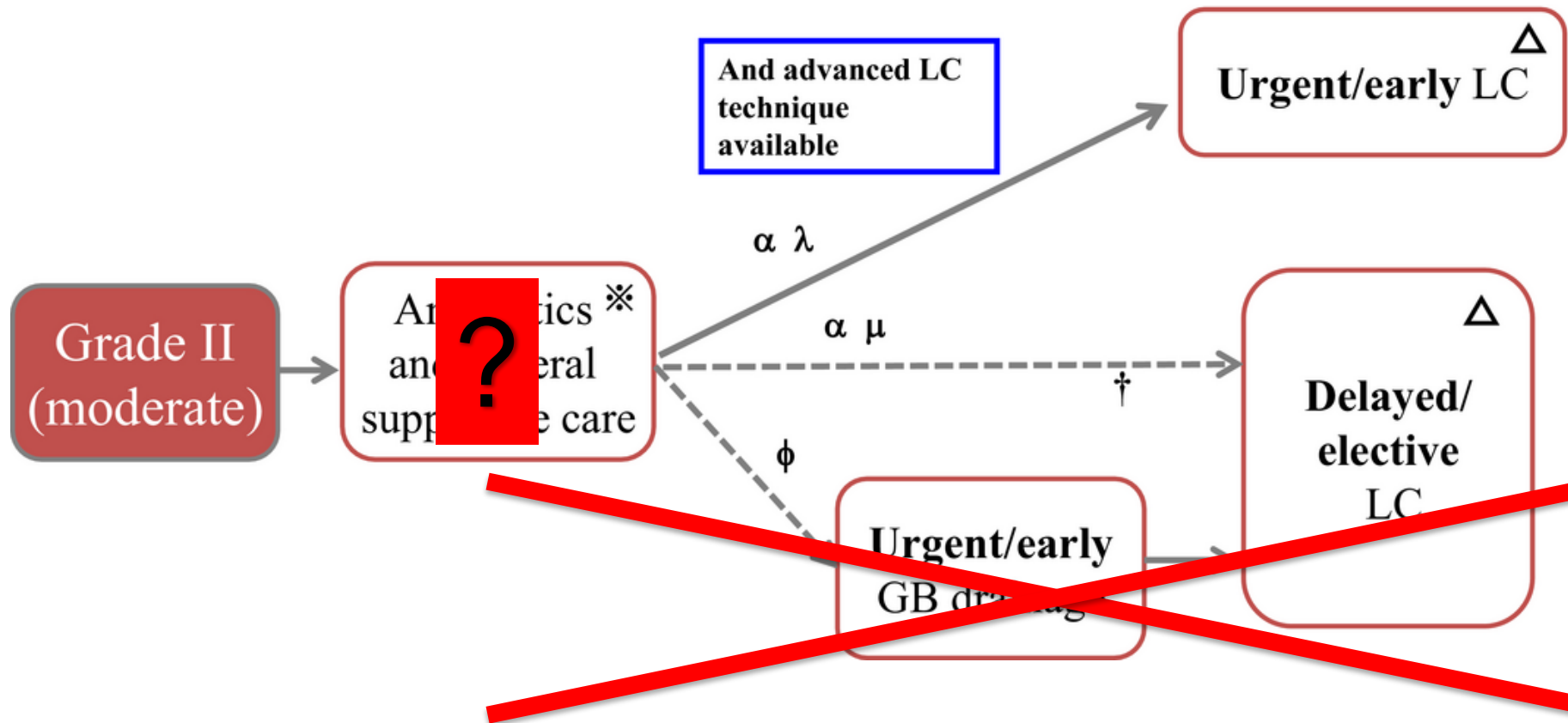
Niet geassocieerd zijn:

Leeftijd, Geslacht, Icterus, Charlson comorbidity index, CRP, WBC,

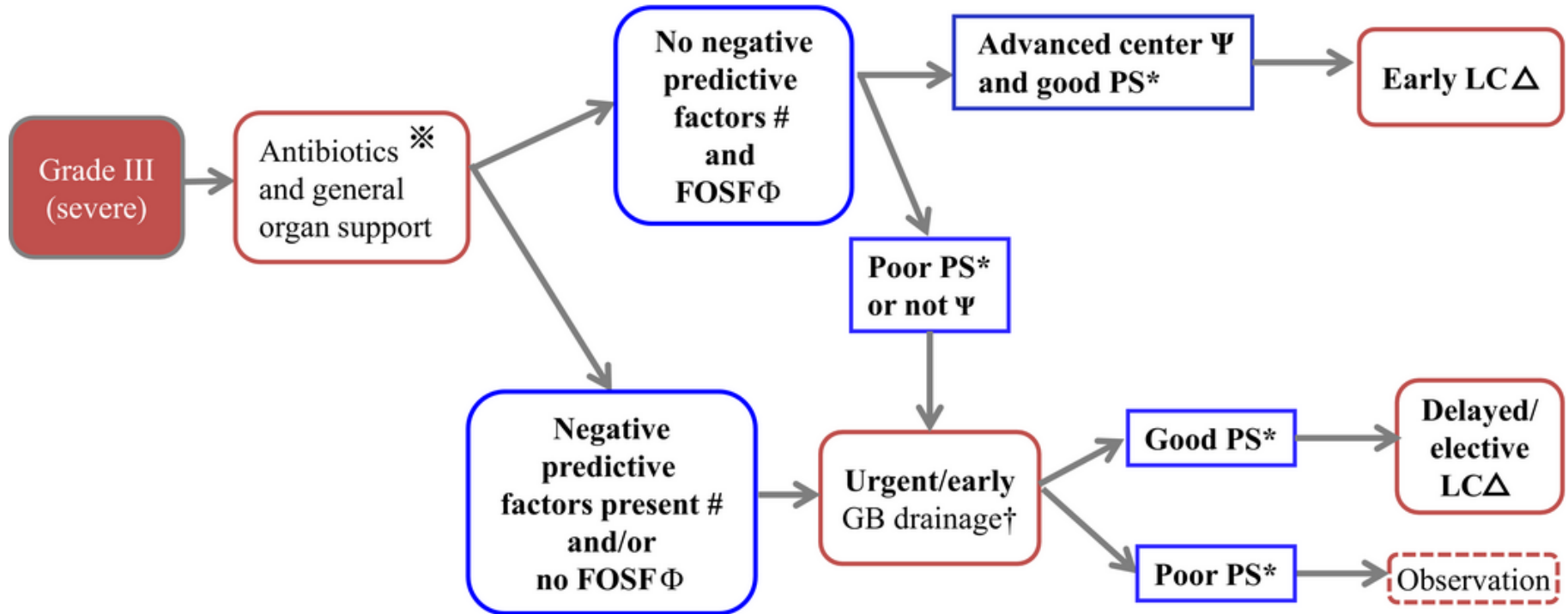
# Behandeling AC graad I



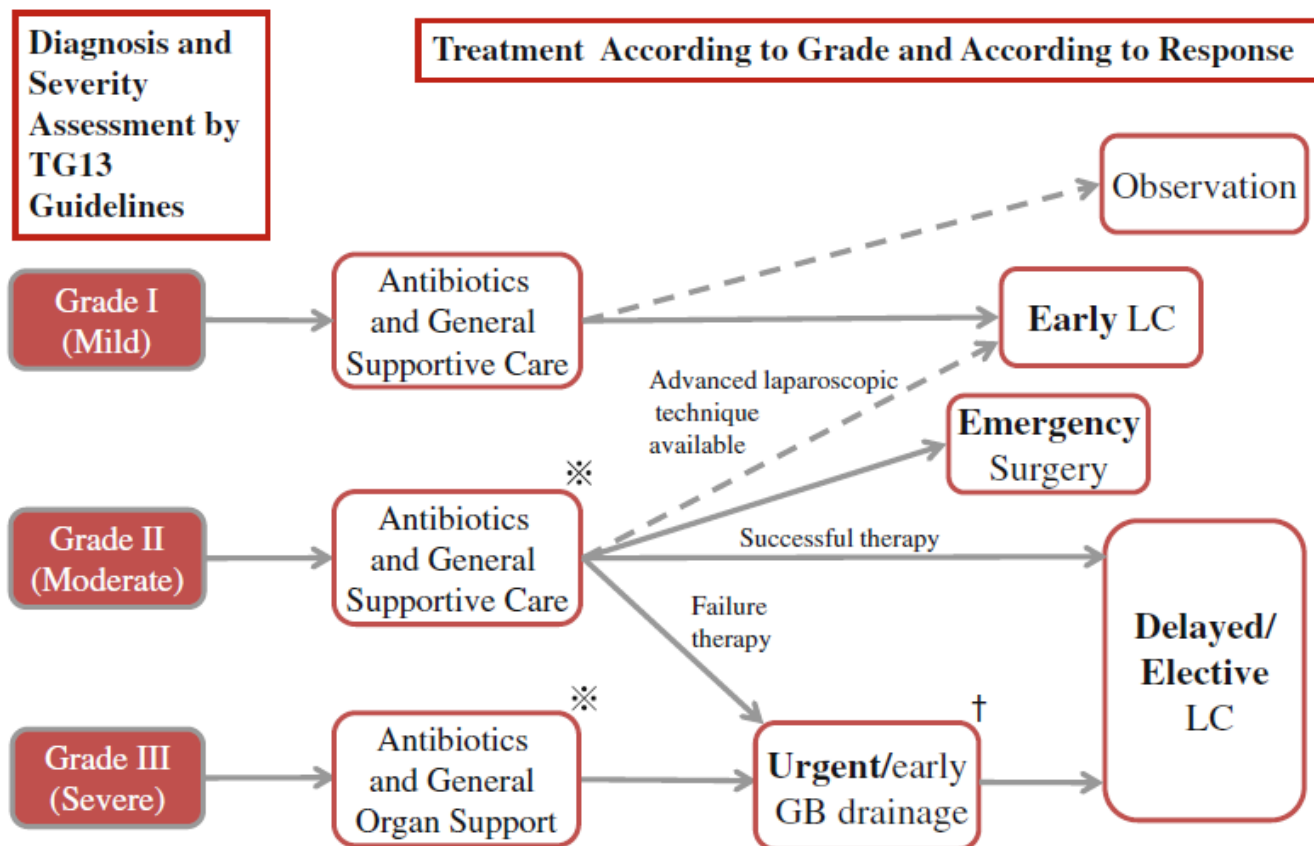
# Behandeling AC graad II



# Behandeling AC graad III



# Behandeling cholecystitis



# Timing

Hoelang kan een cholecystectomie voor acute cholecystitis worden uitgesteld?

Vroeg of laat opereren?

Wat is vroeg en laat?



---

# RCT na 2012

## ❑ Methode:

- ❑ 35 centra (Duitsland & Slovenie)
- ❑ 618 gerandomiseerd => Immediate LC of Delayed LC
- ❑ ILC <24u operatie, DLC 7 – 45 dagen de operatie
- ❑ 58% vrouw
- ❑ 56 jaar
- ❑ BMI 29

	<b>Group ILC</b>	<b>Group DLC</b>	
Persistent abdominal pain >72 h	7 (2.3)	30 (10.0)	<0.001
Persistent fever >72 h	1 (0.33)	10 (3.33)	0.006

	<b>Group ILC</b>	<b>Group DLC</b>	
Cholangitis/cholecystitis	4 (1.32)	31 (10.33)	<0.001

	<b>Group ILC</b>	<b>Group DLC</b>	
Bile leak	3 (0.99)	1 (0.33)	0.31

---

	<b>Group ILC</b>	<b>Group DLC</b>	<b><i>P</i></b>
Conversion rate to open surgery	30 (9.9) [6.5–13.2]	33 (11.9) [8.1–15.7]	0.44

	<b>Group ILC</b>	<b>Group DLC</b>	<b><i>P</i></b>
Total hospital stay	5.4 [5.08–5.71]	10.03 [9.36–10.69]	<0.001
Total hospital costs, €	2919	4262	<0.001

---

## □ Conclusie:

- Direct laparoscopische cholecystectomie
  - Minder morbiditeit
  - Zelfde risico op galwegletsel of conversie
  - Korter in ziekenhuis
  - Minder kosten

---

# Early or delayed Cholecystectomy

Systematic review:

- ❑ 6 RCT's van goede kwaliteit geïncludeerd
- ❑ Totaal 501 patiënten gerandomiseerd (488 geopereerd)
- ❑ Gemiddelde leeftijd 57 jaar (57% vrouw)
- ❑ Vroege Lap Chol < 7 dagen
- ❑ Late Lap Chol > 6 weken

# Results

## Comparison 1. Early versus delayed laparoscopic cholecystectomy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
Bile duct injury	5	438	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.49 [0.05, 4.72]
Conversion to open cholecystectomy	6	488	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.63, 1.25]
Hospital stay	4	373	Mean Difference (IV, Fixed, 95% CI)	-4.12 [-5.22, -3.03]
Operating time	6	488	Mean Difference (IV, Fixed, 95% CI)	-1.22 [-3.07, 0.64]

Bile duct injury: 1 (0.4%) versus DLC 2 (0.9%)

Conversie: 49 (20%) versus DLC 54 (22%)

---

# Conclusions

- ❑ Geen verschil chirurgische complicaties
- ❑ Geen verschil conversie
- ❑ Langere opname duur in late groep
- ❑ Toename morbiditeit in late groep

---

# Conclusions

- Directe cholecystectomie leidt tot minder morbiditeit, kortere opnameduur, sneller herstel

LEVEL 1a

- Geen verschil in operatieve complicaties en conversie

LEVEL 1a

- Minder kosten

LEVEL 1b

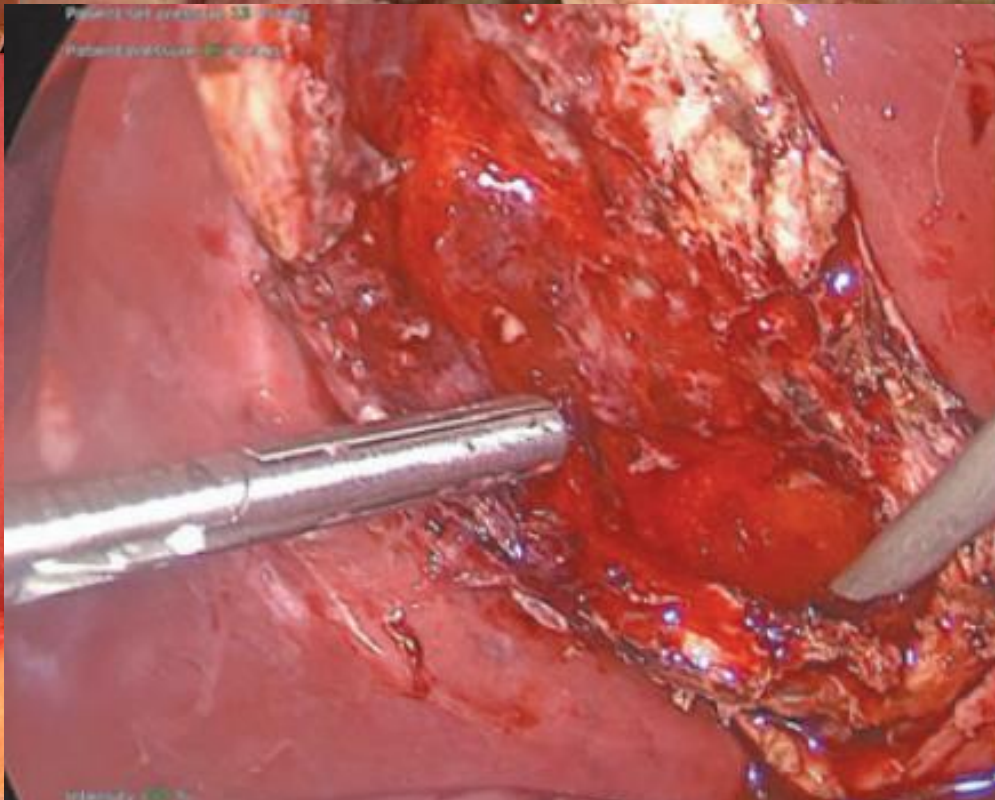
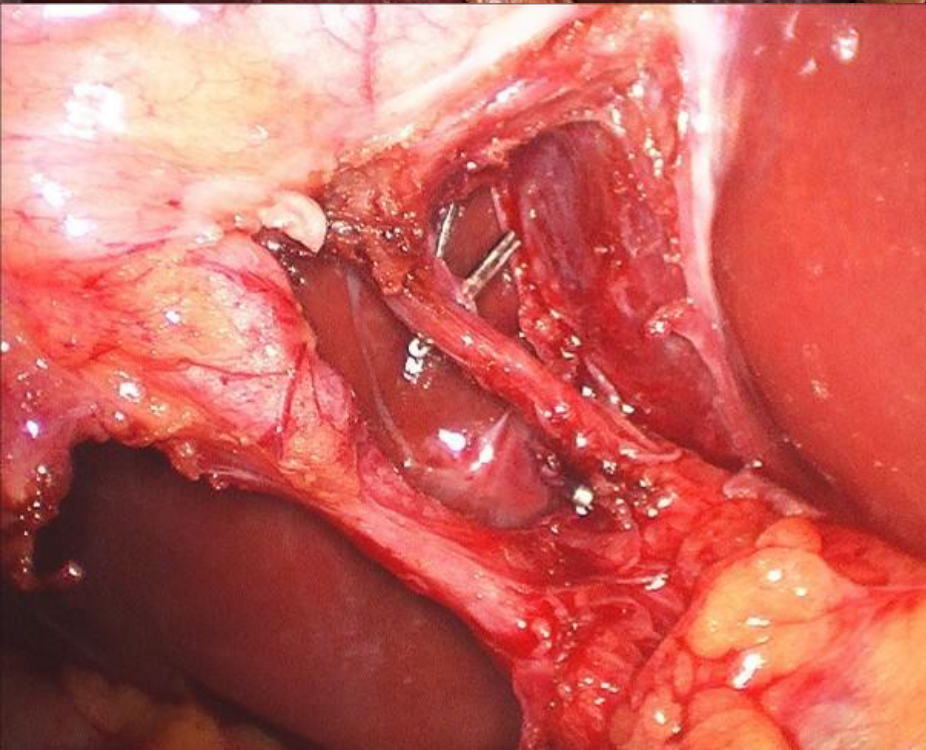
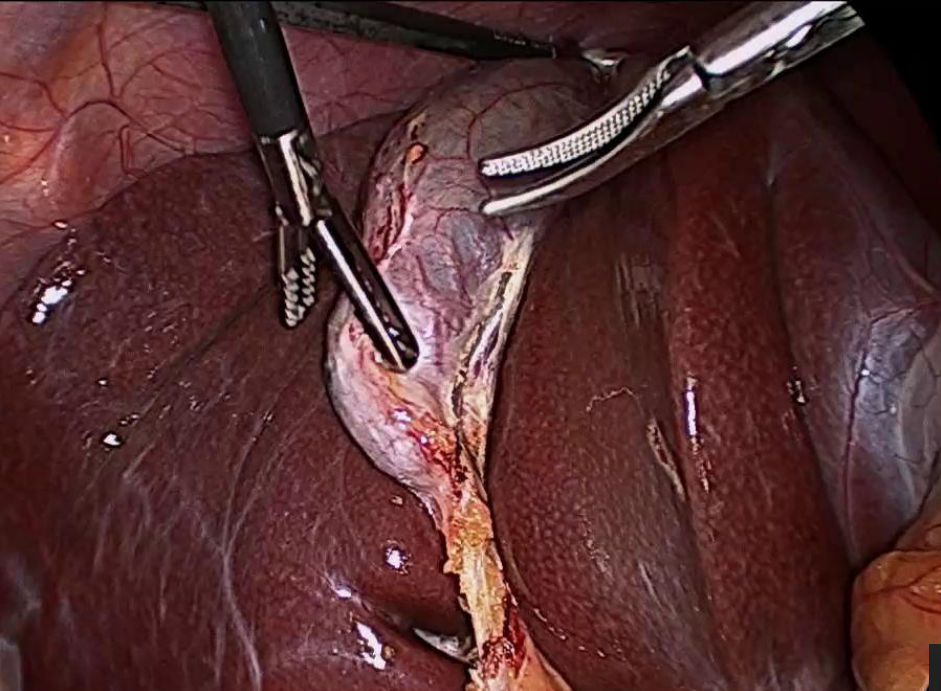


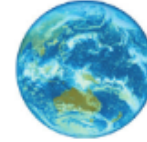
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## Tokyo Guidelines 2018: the management of acute cholecystitis:


*Even if there are benefits to early surgery, this does not mean that urgent surgery after hours should be performed.*

*Ideally, surgery should be performed by surgeons experienced in laparoscopy or at facilities with a long history of laparoscopic procedures*





## Predicting operative difficulty of laparoscopic cholecystectomy in patients with acute biliary presentations

Sarah Z. Wennmacker ,\*† Nazim Bhimani,† Aafke H. van Dijk,‡ Thomas J. Hught§ and Philip R. de Reuver\*

\*Department of Surgery, Radboud University Medical Center, Nijmegen, The Netherlands

†Department of Upper Gastrointestinal Surgery, Royal North Shore Hospital, Sydney, New South Wales, Australia

‡Department of Surgery, Academic Medical Center, Amsterdam, The Netherlands and

§Discipline of Surgery, The University of Sydney, Sydney, New South Wales, Australia

N=257

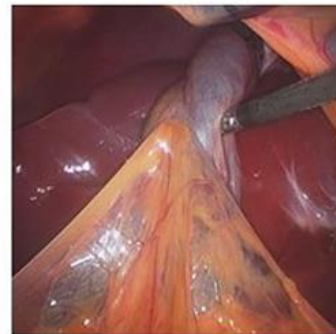
Prospectieve data verzameling

Alle patienten met eerste presentatie SEH ivm acuut galsteenlijden



Grade 1

Thin walled, normal appearing GB  
No adhesions



Grade 2

Mildly abnormal appearing GB  
(slightly thick walled or distended)  
And/or thin-filmy GB adhesion



Grade 3

Moderately abnormal appearing GB  
(thick walled, oedematous, with  
mucocele, or large distended  
gallbladder)  
And/or overlying moderate adhesions



Grade 4

Severely inflamed or grossly abnormal  
appearing GB (e.g. necrotic or perforated)  
And/or extensive or dense adhesions

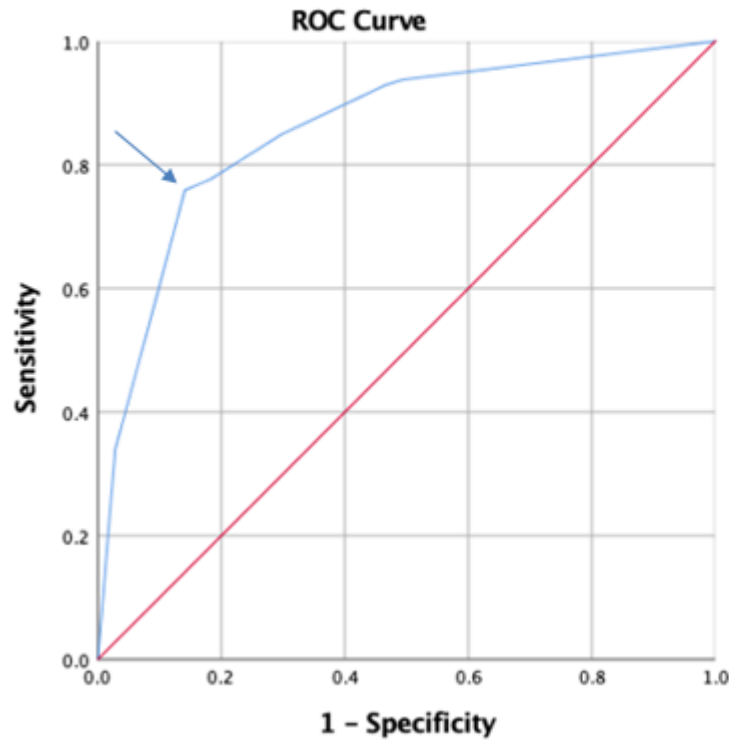
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**Table 2** Univariable and multi-variable analysis

Variable	'Straightforward' LC	'Complicated' LC	Univariable OR (95% CI)	P-value	Multivariable OR (95% CI)	P-value	Regression coefficient	Points Prediction model
Acute cholecystitis†, <i>n</i> (%)	18 (25.0)	94 (83.2)	14.84 (7.18–30.69)	<0.001	8.33 (3.78–18.36)	<0.001	2.12	2
Murphy's sign positive, <i>n</i> (%)	19 (26.4)	59 (52.2)	3.05 (1.61–5.79)	0.001				
CRP >10.5 mg/L, <i>n</i> (%)	23 (32.4)	84 (75.0)	6.26 (3.25–12.06)	<0.001	3.85 (1.78–8.34)	0.001	1.35	1.5
Pericholecystic fluid, <i>n</i> (%)	9 (12.5)	54 (47.8)	6.41 (2.91–14.12)	<0.001	2.77 (1.11–6.95)	0.029	1.02	1
Impacted stone GB neck, <i>n</i> (%)	12 (16.8)	47 (41.6)	3.56 (1.73–7.34)	<0.001				
Neutrophils >8 × 10 <sup>9</sup> /L, <i>n</i> (%)	24 (33.3)	73 (64.6)	3.65 (1.96–6.81)	<0.001				
US diagnosis AC, <i>n</i> (%)	19 (26.4)	69 (61.1)	4.37 (2.29–8.35)	<0.001				
Age >50 years, <i>n</i> (%)	26 (36.1)	70 (61.9)	2.88 (1.56–5.32)	0.001				
First episode, <i>n</i> (%)	22 (30.6)	48 (42.5)	1.68 (0.90–3.14)	0.104				
Symptoms >24 h prior to ER, <i>n</i> (%)	31 (43.1)	68 (60.2)	2.00 (1.10–3.64)	0.024				
WBC >9.5 × 10 <sup>9</sup> /L, <i>n</i> (%)	35 (48.6)	80 (70.8)	2.56 (1.39–4.73)	0.003				
GB wall >4 mm, <i>n</i> (%)	23 (31.9)	64 (56.6)	2.78 (1.50–5.17)	<0.001				

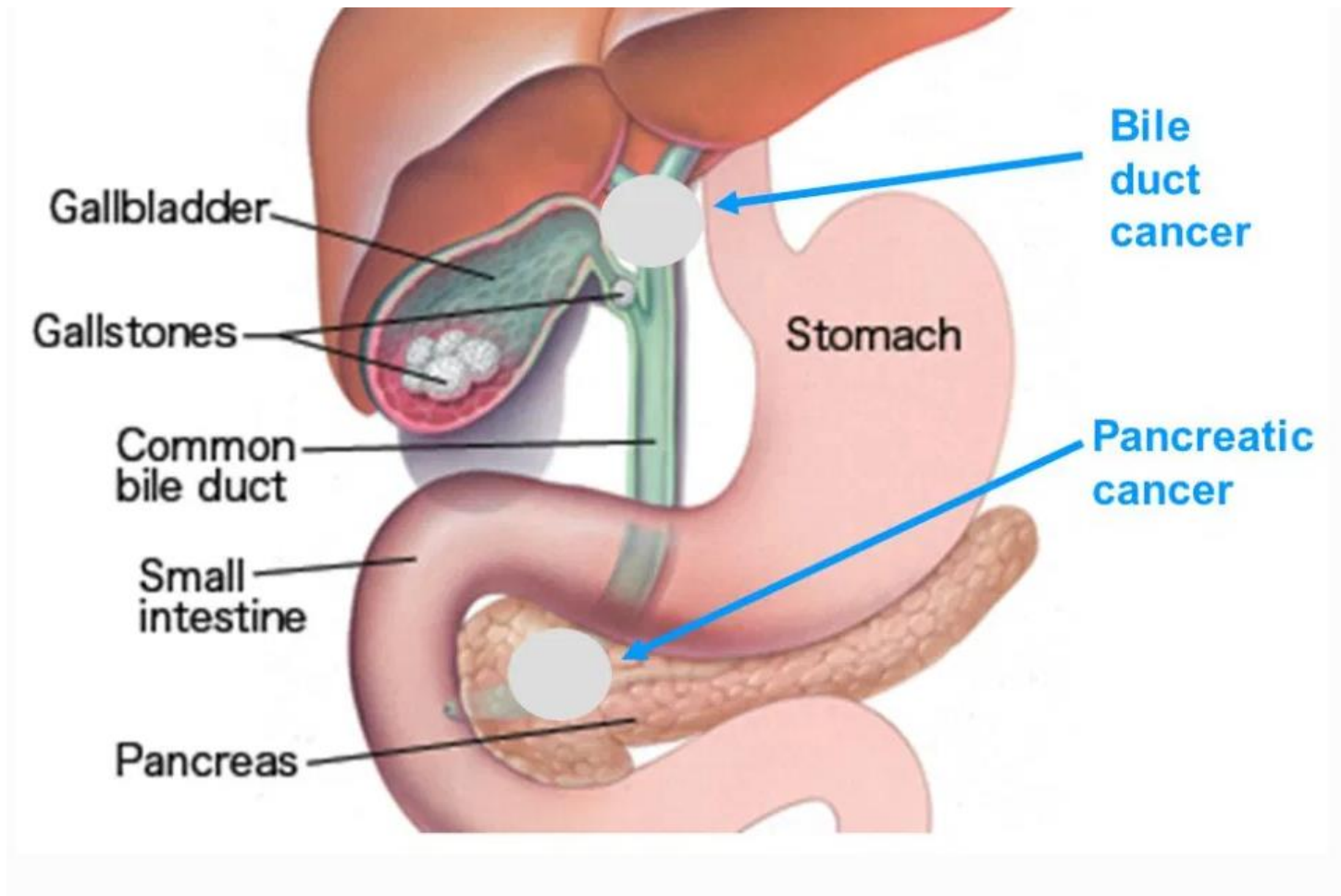
†Including three patients with biliary sepsis based on cholecystitis. AC, acute cholecystitis; CI, confidence interval; CRP, C-reactive protein; ER, emergency room; GB, gallbladder; OR, odds ratio; US, ultrasound; WBC, white blood cell count.

## Supporting Figure S2. ROC-curve prediction model



Score  $\geq 2.5$   
Sensitivity: 0.78  
Specificity: 0.82  
AUC 0.86 (0.80-0.91,  
P<0.001)

# Cholangitis



By continuing to use this website, you agree to their use.

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# Cholangitis, symptomen

- Buikpijn
- Icterus
- Koorts (Charcot's triad)
  
- Koude rillingen

Tokyo guidelines 2018  
J Hepatobiliary Pancreat Sci (2018) 25:17–30



---

# Cholangitis

**Table 3.** Diagnostic criteria for acute cholangitis

A. Clinical context and clinical manifestations	1. History of biliary disease 2. Fever and/or chills 3. Jaundice 4. Abdominal pain (RUQ or upper abdominal)
B. Laboratory data	5. Evidence of inflammatory response <sup>a</sup> 6. Abnormal liver function tests <sup>b</sup>
C. Imaging findings	7. Biliary dilatation, or evidence of an etiology (stricture, stone, stent etc)
Suspected diagnosis	Two or more items in A
Definite diagnosis	(1) Charcot's triad (2 + 3 + 4) (2) Two or more items in A + both items in B and item C

<sup>a</sup> Abnormal WBC count, increase of serum CRP level, and other changes indicating inflammation

<sup>b</sup> Increased serum ALP, r-GTP (GGT), AST, and ALT levels

Tokyo guidelines 2018  
J Hepatobiliary Pancreat Sci (2018) 25:17–30

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# Grading Cholangitis

**Table 5.** Criteria for severity assessment of acute cholangitis

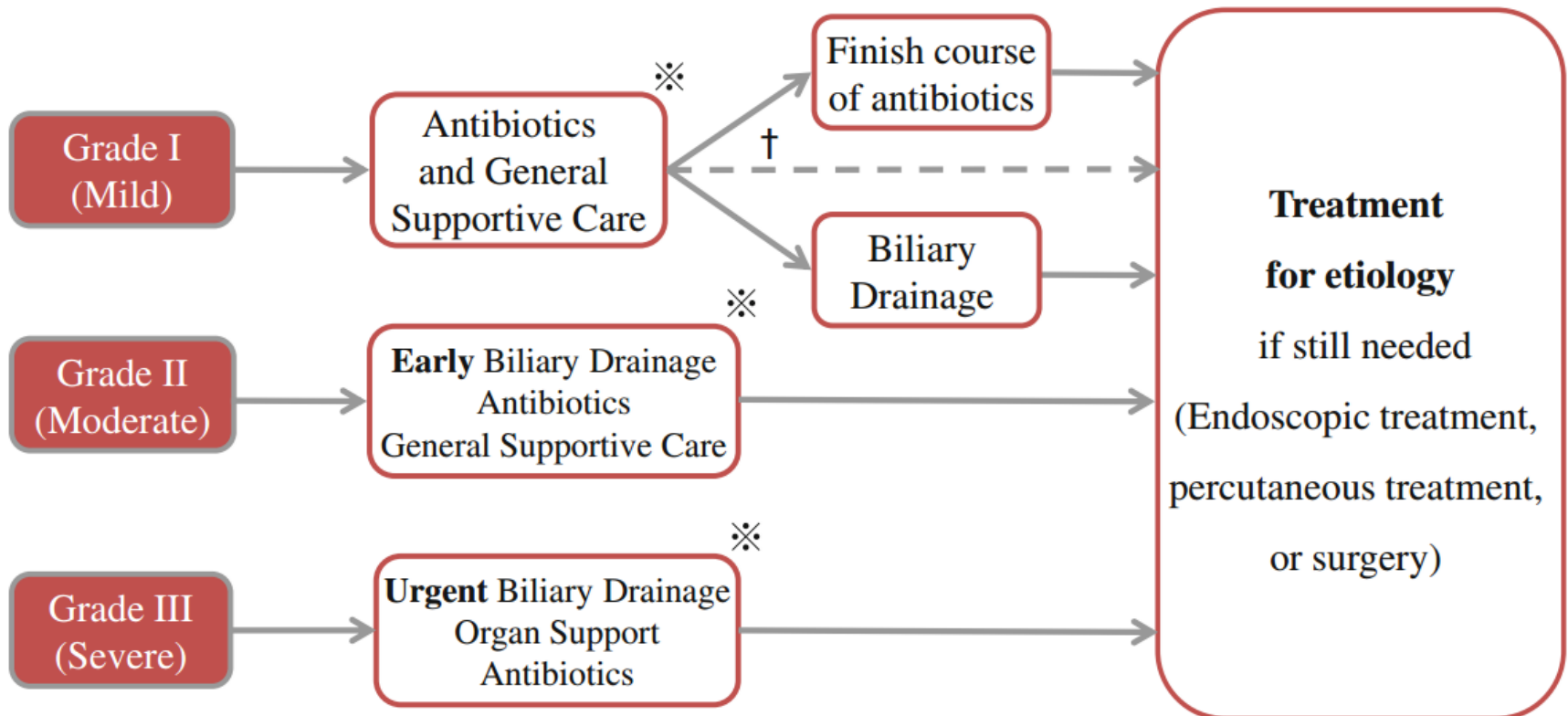
Criterion	Severity of acute cholangitis		
	Mild (grade I)	Moderate (grade II)	Severe (grade III)
Onset of organ dysfunction	No	No	Yes
Response to initial medical treatment <sup>a</sup>	Yes	No	No

<sup>a</sup> Consisting of general supportive care and antibiotics

Tokyo guidelines 2018  
J Hepatobiliary Pancreat Sci (2018) 25:17–30

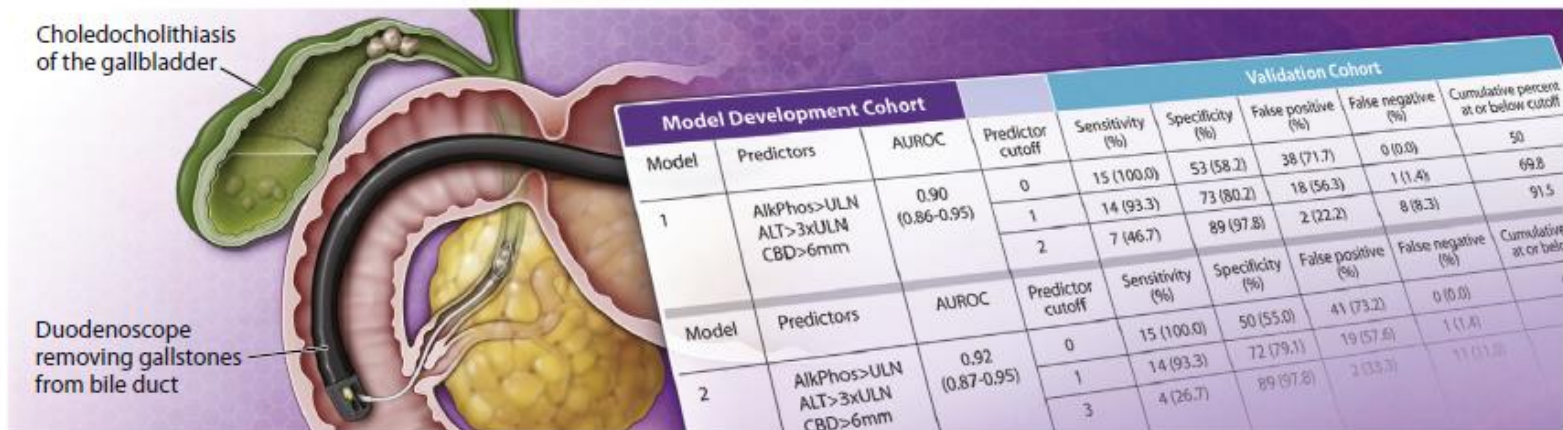
# Tokyo Guidelines 2018

**Treatment According to Grade, According to Response, and According to Need for Additional Therapy**



# Richtlijnen en kliniek

## 68 jarige man met beeld van cholecystitis acuta en leverfunctie stoornissen



Chisholm GI Endoscopy 2019, Collin  
Ann Surg 2004, Chen ANZJ Surg 2019

# Cholecystitis en leverfunctie stoornissen

- Leverfunctiestoornissen bij +/- 30-60 % van de patiënten met cholecystitis acuta
- Meestal hoger bij CBD steen, maar niet altijd...
- Mogelijke oorzaken
  - Sepsis
  - Gepasseerde steen
  - Compressie hydropisch ontstoken galblaas op CBD
  - Steatohepatitis
  - Aspecifieke, reactieve hepatitis galblaasbed

# Percentage choledocholithiasis?

- Bij presentatie met acute cholecystitis heeft 10-20% van de patiënten ook choledocholithiasis

**Table 1** Characteristics of included studies

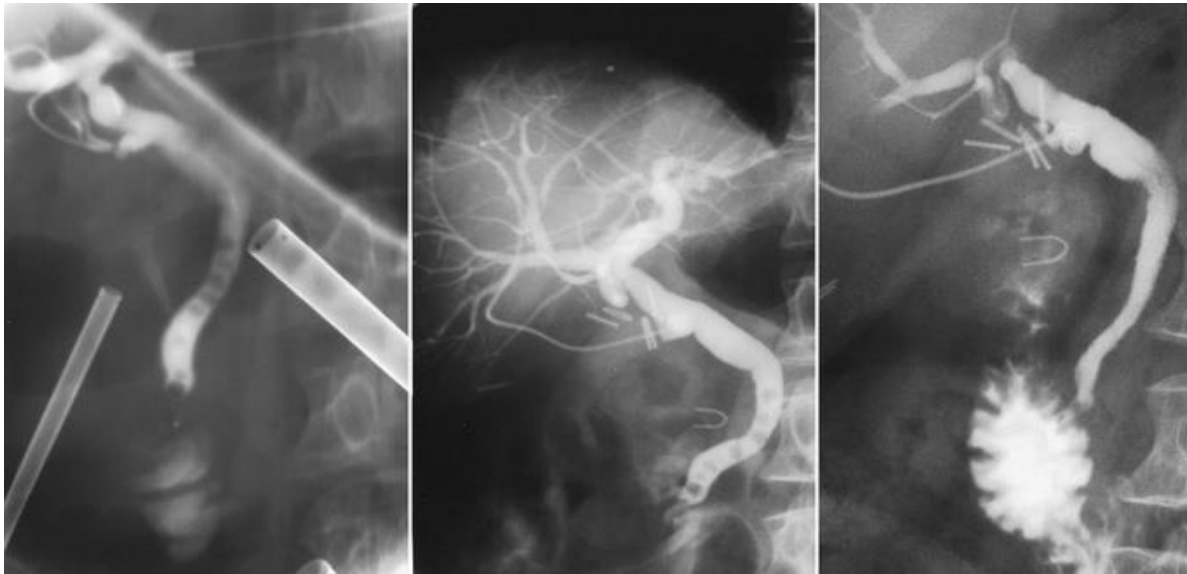
Study ID	Patients with AC	Patients with CBD stones	Incidence of CBD stones in AC patients (%)
Spence	116	17	14.70
Song	1178	246	20.90
Wong	57	7	12.28
Videhult	323	28	8.67
Stryker	256	33	12.90
Cheung	41	1	2.40
Peng	216	28	13
Nikfarjam	290	60	21
Borzellino	295	47	15.93
Regan	45	9	20
Grau-Talens	78	7	8.97
Grinberg	321 802	73 648	23
Hsieh	64	16	25
Kim	248	48	19.3
Kelly	140	17	12.10
Oszan	149	5	3.36
Paran	54	5	9.26
Philips	25	4	16
Shin	334	42	12.60
Yang	672	85	12.60
Ahn	654	98	15

AC, acute cholecystitis; CBD, common bile duct.

# Is dat een reden om niet direct te opereren?

---

- Spontane steenpassage: 60-90% van de patiënten!



Lefemine Hepatobil Panc Dis Int 2011 Collins Ann Surg 2004,  
Tranter Ann R Coll Surg Engl 2003 Spence Am Surg 2017 Kohn Surg Endosc 2018

# Maar soms niet, en dat kan leiden tot

- Cholangitis
- Pancreatitis
- ESGE richtlijn: 25% van de bewezen galwegstenen gaat op enig moment een complicatie geven
- En.... geven mogelijk een grotere kans op conversie of galwegletsel!

Surg Endosc (2018) 32:1184–1191

	Odds ratio	95% confidence interval		<i>p</i> value
ASA class	1.65	0.61	4.49	0.3254
Previous ERCP	1.98	0.37	10.76	0.4272
Intraoperative choledocholithiasis	<b>6.63</b>	<b>1.05</b>	<b>41.78</b>	<b>0.0439</b>

Statistically significant values are in bold

Lefemine Hepatobil Panc Dis Int 2011 Collins Ann Surg 2004, Tranter Ann R Coll Surg Engl 2003 Spence Am Surg 2017 Julie Kohn Surg Endosc 2018, n=786. BDI n=7, 4 type A-tjes ESGE guideline Endoscopy 2019

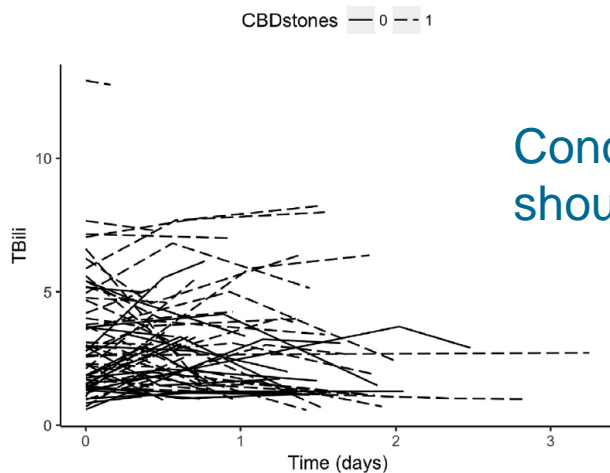


# ...En als we het lab vervolgen?

---

- Afwijkend lab zal wat dalen, maar kan je er echt op varen?
- Zie onder: 60% van de patiënten met stijgend bilirubine had een steen in de CBD....

1481 patiënten met cholecystolithiasis, choledocholithiasis of een biliare koliek  
98 patiënten met verhoogd Bili  
30 patiënten maar eenmalige verhoging! Zijn geexcludeerd  
38 patiënten met CBDS



Conclusion: Patients with elevated serum bilirubin, should undergo immediate imaging or procedural intervention.

# Wanneer eerst een ERCP ?

TABLE 15. Proposed strategy to assign risk of choledocholithiasis and manage patients with symptomatic cholelithiasis based on clinical predictors

Probability	Predictors of choledocholithiasis	Recommended strategy
High	Common bile duct stone on US/cross-sectional imaging <i>or</i> Clinical ascending cholangitis <i>or</i> Total bilirubin >4 mg/dL and dilated common bile duct on US/cross-sectional imaging	Proceed to ERCP
Intermediate	Abnormal liver biochemical tests <i>or</i> Age >55 years <i>or</i> Dilated common bile duct on US/cross-sectional imaging	EUS, MRCP, laparoscopic IOC, or intraoperative US
Low	No predictors present	Cholecystectomy with/without IOC or intraoperative US

US, Ultrasound; IOC, intraoperative cholangiography.

- Ja, maar die zijn NIET gevalideerd bij acute cholecystitis!
- M.n veel 'vals-positieven', met tot **42% negatieve ERCP's**
- ERCP heeft een 10-15% kans op complicaties, m.n pancreatitis

ASGE guideline GI endoscopy 2019, Chisholm GI

# Cholelithiasis bij acute cholecystitis

## Systematic literature review and meta-analysis till 2018

**Table 1** Characteristics of included studies

Study ID	Patients with AC	Patients with CBD stones	Incidence of CBD stones in AC patients (%)	Country where study was conducted	How AC is confirmed	Average age
Spence	116	17	14.70	UK	Unknown	Unknown
Song	1178	246	20.90	South Korea	Unknown	57.4
Wong	57	7	12.28	Taiwan	Clinical	55.79
Videhult	323	28	8.67	Sweden	Clinical	Unknown
Stryker	256	33	12.90	USA	Histological	54.7
Cheung	41	1	2.40	USA	Histological	54
Peng	216	28	13	Britain	Histological/radiological	54
Nikfarjam	290	60	21	Australia	Histological	61
Borzellino	295	47	15.93	Italy	Histological	66.1
Regan	45	9	20	USA	Clinical/histological	Unknown
Grau-Talens	78	7	8.97	Spain	Histological	62.4
Grinberg	321 802	73 648	23	USA	Unknown	Unknown
Hsieh	64	16	25	Taiwan	Clinical	55.2
Kim	248	48	19.3	South Korea	Radiological	Unknown
Kelly	140	17	12.10	Unknown	Unknown	59.3
Oszan	149	5	3.36	Turkey	Clinical	46.3
Paran	54	5	9.26	Israel	Clinical	61
Philips	25	4	16	USA	Clinical	Unknown
Shin	334	42	12.60	South Korea	Unknown	Unknown
Yang	672	85	12.60	South Korea	Unknown	Unknown
Ahn	654	98	15	South Korea	Clinical	58.2

AC, acute cholecystitis; CBD, common bile duct.

The pooled incidence of CBDS was 13.7% (95% confidence interval 11.8–15.9).

Hongyi Chen et al. ANZ J Surg (2019)

# Voorspellers voor stenen specifiek bij acute cholecystitis

ORIGINAL ARTICLE: Clinical Endoscopy

## Preoperative predictors of choledocholithiasis in patients presenting with acute calculous cholecystitis

Phillip R. Chisholm, MD,<sup>1</sup> Arpan H. Patel, MD,<sup>1</sup> Ryan J. Law, DO,<sup>1</sup> Allison R. Schulman, MD, MPH,<sup>1</sup> Arti O. Bedi, MD,<sup>1</sup> Richard S. Kwon, MD, MS,<sup>1</sup> Erik J. Wamsteker, MD,<sup>1</sup> Michelle A. Anderson, MD, MS,<sup>1</sup> Grace H. Elta, MD,<sup>1</sup> Shail M. Govani, MD, MSc,<sup>1,3,4,\*</sup> Anoop Prabhu, MD<sup>1,2,\*</sup>

Ann Arbor, Michigan; San Antonio, Texas, USA

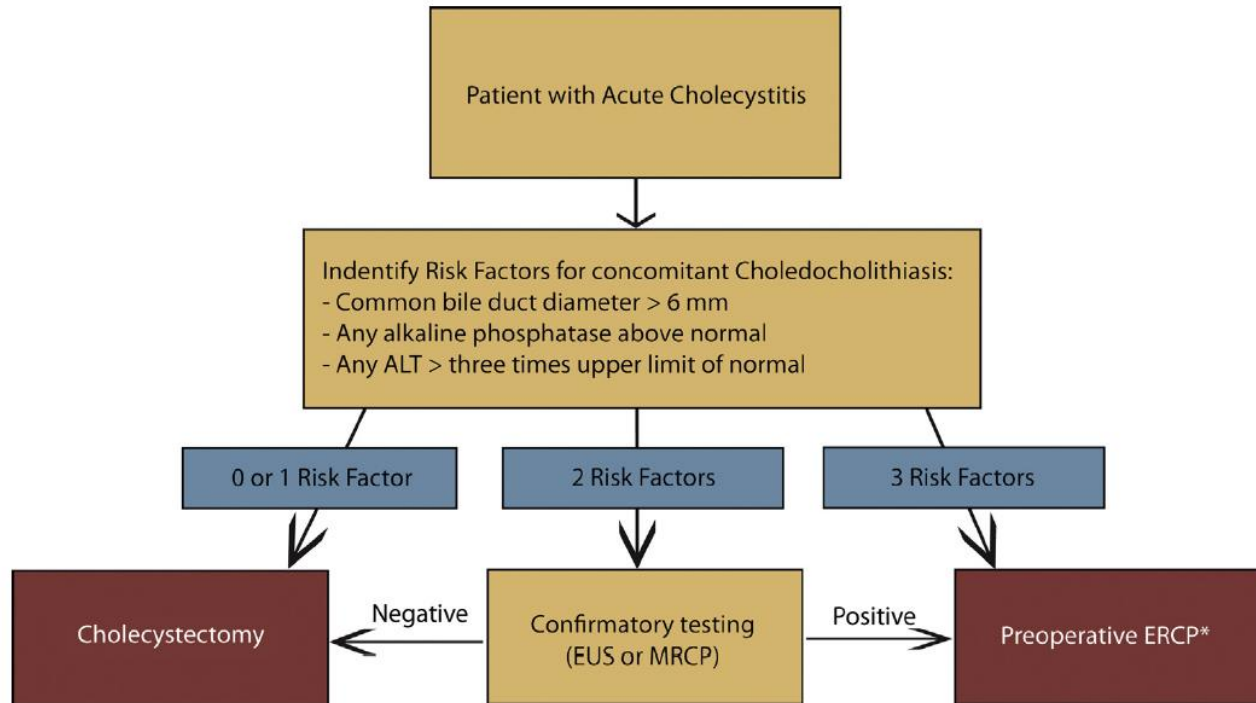
- N = 366 ptn met cholecystitis acute, waarvan uiteindelijk 65 (17.8%) met stenen

TABLE 4. Performance characteristics of multivariable model based on presence of cumulative risk factor cutoffs in the validation cohort

Model development cohort			Validation cohort					
Model	Predictors	AUROC	Predictor cutoff*	Sensitivity (%)	Specificity (%)	False positive (%)	False negative (%)	Cumulative percentage at or below cutoff
1	AlkPhos > ULN, ALT > 3× ULN, CBD >6 mm	0.90 (0.86-0.95)	0	15 (100.0)	53 (58.2)	38 (71.7)	0 (0.0)	50
			1	14 (93.3)	73 (80.2)	18 (56.3)	1 (1.4)	69.8
			2	7 (46.7)	89 (97.8)	2 (22.2)	8 (8.3)	91.5

Chisholm GI Endoscopy  
2019

Radboudumc



\*Confirmatory test (MRCP or EUS) can be considered prior to preoperative ERCP when appropriate

70% van de patiënten!

## Take home message

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- Bij acute cholecystitis:
  - 30-60% leverfunctiestoornissen
  - Ongeveer 20% choledocholithiasis
  - CBD steen passeert meestal spontaan.  
Zonder passage toegenomen kans op complicaties bij cholecystectomie
  - Voorspellen van choledocholithiasis is lastig, vaar niet op 1 modaliteit!
  - Twijfel: EUS/MRCP
  - Alleen ERCP bij **bewezen steen** op transabdominale echo, niet o.b.v lab-uitslagen of een verwijde galweg