

Prevention of post-ERCP pancreatitis. Evidence based approach.

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What is Post ERCP Pancreatitis?

- Definition Cotton:
 - Pain consistent with pancreatitis
 - Elevated amylase 3x ULN
 - Hospitalisation >24 hours
- Definition Atlanta:
 - Pain consistent with pancreatitis
 - Elevated amylase or lipase 3x ULN
 - CT evidence pancreatitis

How common is it?

Study	Number	% PEP	Mild	Moderate	Severe
Andriulli	16000	3.47	45%	44%	11%
Kapral	13513	4.2	55%	34%	11%
Sutton	886	4.4	69%	23%	8%

Andriulli A, Loperfido S, Napolitano G et al. Incidence rates of post-ERCP complications: a systematic survey of prospective studies. *Am J Gastroenterol* 2007; 102: 1781–1788

Kapral C, Mühlberger A, Wewalka F et al. Quality assessment of endoscopic retrograde cholangiopancreatography: results of a running nationwide Austrian benchmarking project after 5 years of implementation. *Eur J Gastroenterol Hepatol* 2012; 24: 1447–1454

Sutton VR, Hong MK, Thomas PR. Using the 4-hour post-ERCP amylase level to predict post-ERCP pancreatitis. *JOP* 2011; 12: 372–376

What are the risk factors for developing it?

	Adjusted odds ratios (95 % confidence intervals in parentheses except where indicated otherwise)	Pooled incidence of PEP in patients with vs. those without risk factor
Patient-related risk factors		
<i>Definite risk factors</i>		
Suspected sphincter of Oddi dysfunction (SOD)	1.91 (1.37 – 2.65)	8.6 % vs. 2.5 %
Female gender	3.5 (1.1 – 10.6)	4.0 % vs. 2.1 %*
Previous pancreatitis	2.46 (1.93 – 3.12)	6.7 % vs. 3.8 %
<i>Likely risk factors</i>		
Previous PEP	8.7 (3.2 – 23.86)	30 % vs. 3.5 %
Younger age	Range of odds ratios: 1.09 – 2.87	6.2 % vs. 2.6 %
Nondilated extrahepatic bile ducts		3.8 % vs. 2.3 %
Absence of chronic pancreatitis	1.87 (1.00 – 3.48)	4.0 % vs. 3.1 %
Normal serum bilirubin	1.89 (1.22 – 2.93)	4.15 % vs. 1.43 %
Procedure-related risk factors		
<i>Definite risk factors</i>		
Cannulation attempts duration > 10 minutes ²	1.76 (1.13 – 2.74)	3.8 % vs. 10.8 %
Pancreatic guidewire passages > 1	2.77 (1.79 – 4.30)	2.9 % vs. 9.5 %
Pancreatic injection	2.2 (1.60 – 3.01)	3.3 % vs. 1.7 %
<i>Likely risk factors</i>		
Precut sphincterotomy ³	2.3 (1.4 – 3.7)	5.3 % vs. 3.1 %
Pancreatic sphincterotomy	3.07 (1.64 – 5.75)	2.6 % vs. 2.3 %
Biliary balloon sphincter dilation	4.51 (1.51 – 13.46)	9.3 % vs. 2.6 %
Failure to clear bile duct stones	3.35 (1.33 – 9.10)	1.7 % vs. 1.6 %
Intraductal ultrasound (IDUS) ⁴	2.41 (1.33 – 4.39)	8.37 % vs. 2.76 %

Ryder's 1st evidence based rule

Run away from young women with non dilated ducts

Wherever possible send them to your surgical colleagues for laparoscopic CBD exploration so they can deal with the complications

If you have to do the ERCP what else can be done?

- Rectal NSAIDs/GTN/Octreotide
- Pancreatic stenting
- Guidewire cannulation

Rectal NSAIDs

- Evidence from 4 RCTs
 - 2 with inometacin 100mg pre-procedure
 - 2 with diclofenac 100mg post procedure
- 6 meta analyses!
 - Include up to 10 studies in each

Elmunzer NEJM 2012;366:1414

Indomethacin
Placebo

27/295
52/307

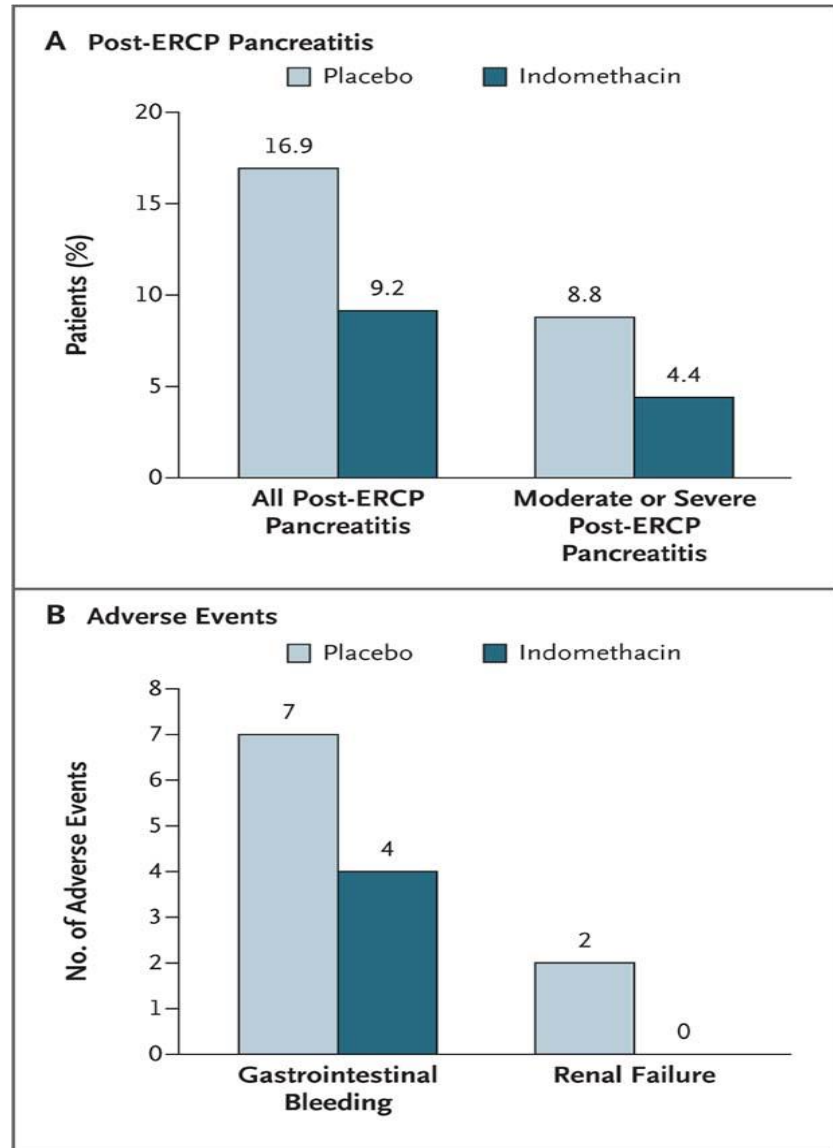


Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Indomethacin (N=295)	Placebo (N=307)
Age — yr	44.4±13.5	46.0±13.1
Female sex — no. (%)	229 (77.6)	247 (80.5)
Clinical suspicion of sphincter of Oddi dysfunction — no. (%)†		
Any	248 (84.1)	247 (80.5)
Type 1	38 (12.9)	43 (14.0)
Type 2	139 (47.1)	135 (44.0)
Type 3	71 (24.1)	69 (22.5)
Documented on manometry	155 (52.5)	160 (52.1)
History of post-ERCP pancreatitis — no. (%)	47 (15.9)	49 (16.0)
History of recurrent pancreatitis — no. (%)	85 (28.8)	94 (30.6)
Difficult cannulation (>8 attempts) — no. (%)	79 (26.8)	77 (25.1)
Precut sphincterotomy — no. (%)‡	15 (5.1)	17 (5.5)
Pancreatography		
Patients — no. (%)	249 (84.4)	260 (84.7)
Median no. of injections of contrast agent into pancreatic duct	2	2
Therapeutic pancreatic sphincterotomy — no. (%)	172 (58.3)	170 (55.4)
Pancreatic acinarization — no. (%)§	15 (5.1)	12 (3.9)
Therapeutic biliary sphincterotomy — no. (%)	172 (58.3)	171 (55.7)
Ampullectomy — no. (%)	9 (3.1)	9 (2.9)
Placement of pancreatic stent — no. (%)	246 (83.4)	250 (81.4)
Trainee involvement in ERCP — no. (%)	142 (48.1)	140 (45.6)

* Plus–minus values are means ±SD. There were no significant between-group differences in any baseline characteristic.

† The definitions of type 1, 2, and 3 sphincter of Oddi dysfunction are provided in the Supplementary Appendix.

‡ Precut sphincterotomy is performed to facilitate biliary access when standard cannulation techniques are unsuccessful.

§ Pancreatic acinarization occurs when excessive injection of contrast agent into the pancreatic duct results in opacification of pancreatic acini.

Sethi S et al Pancreas 2014;43:190

- 7 RCTs of rectal NSAID
- 2133 patients
- OR 0.44 with NNT 11
- No difference between diclofenac and indomethacin
- No adverse effects from NSAIDs

Levenich et al Gastroenterology 2016;150:911

- Indomethacin v placebo
- 449 consecutive patients
- 70% average risk
- 16/223 Indomethacin 7.2%
- 11/226 placebo 4.9%
- Stopped for futility

Ryder's 2nd evidence based rules

- If you do mad stuff rectal NSAIDS seem to help
- If you do normal stuff at best the effect is modest
- Given its safe why wouldn't you-it makes you feel better about life, we can forget about Brexit, pretend we are French and wheel out the suppositories.

Guidewire cannulation



Gidewire cannulation

- Switch from long wire systems to short
- Control by endoscopists may be easier
- Many studies suggested that cannulation rates better and took shorter time
- Does this reduce PEP rates?

Recent studies

Mariani, Gastrointest Endoscopy 2012;75:339

RCT of contrast injection vs GWC
1249 patients in single centre

PEP 35/678 (5.2%) in GWC
PEP 25/571 (4.4%) in contrast

No significant effect
GWC faster with less fluoroscopy
PEP risk increased with >10 cannulation attempts

Tse F et al, Endoscopy 2013;45:605

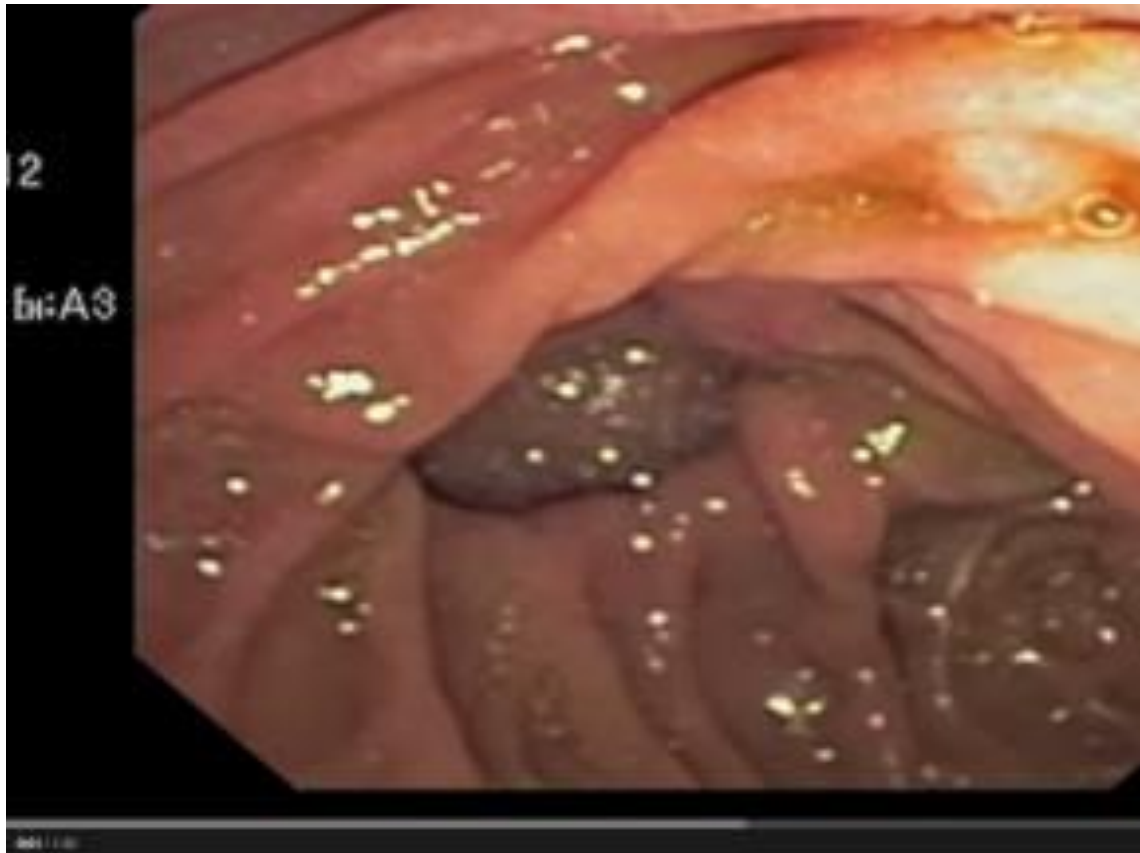
- Meta analysis of 12 trials (RCT)
- 3450 patients
- GWC vs contrast
- PEP reduced R/R 0.51 (0.32-0.82)
- Successful CBD cannulation increased (R/R 1.07)
- Reduction in pre-cut sphincterotomy (R/R 0.75)

Ryder's 3rd evidence based rule

- Gidewire cannulation better (quicker) than contrast
- Less faffing about probably irritates your pancreas less

What is the definition of faffing about (difficult biliary cannulation)?

- 2 studies looked at factors which endoscopists perceive as difficult biliary cannulation
- Halttunen (Scand J Gastro 2014;49:752)
- 904 biliary cannulations in 10 centres
- Prospectively collected data on attempts and quantified factors
- Wang (Am J Gastro 2009;104:31)
- 880 cannulations in 12 centres



What makes a difficult cannulation?

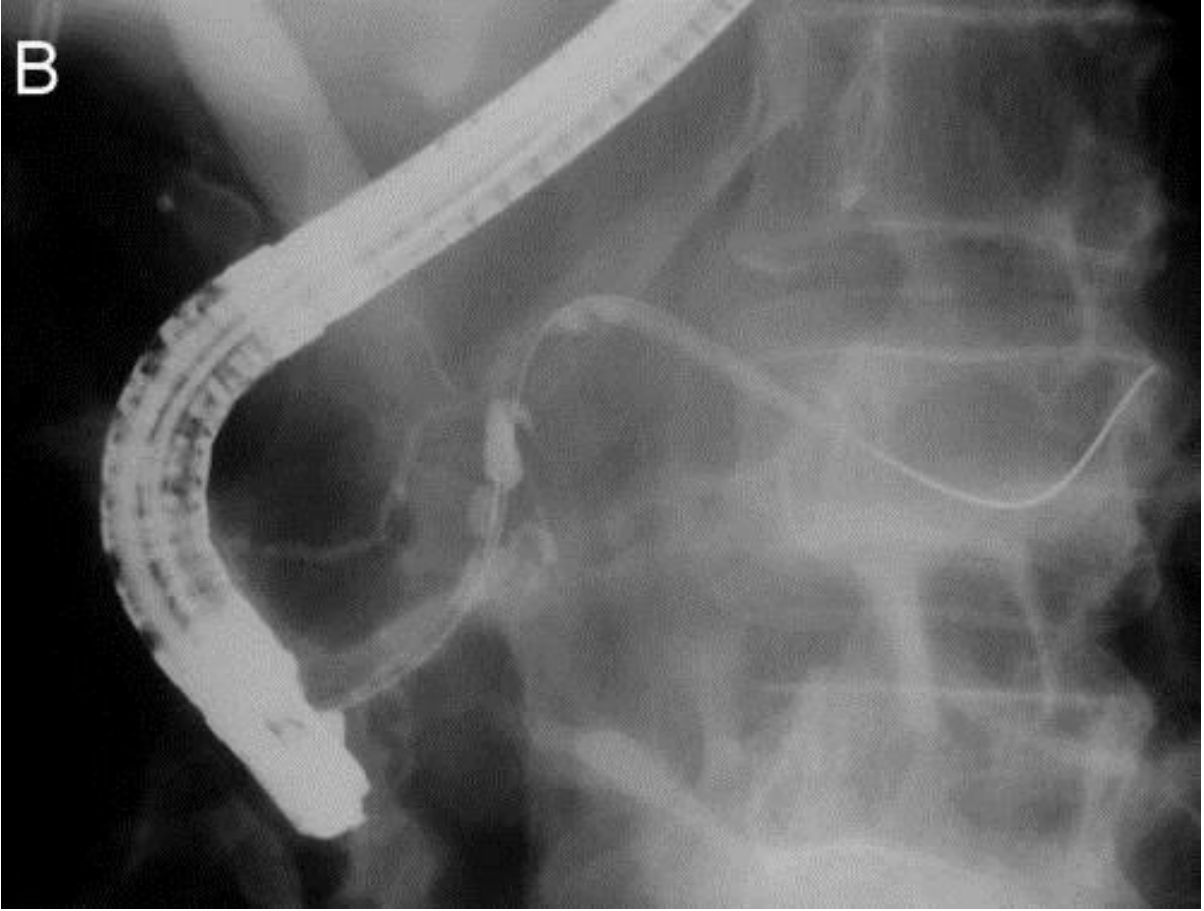
- PEP risk rises to 10% if:
 - >5 minutes to cannulation
 - >5 attempts to cannulate
 - >2 guidewire cannulations of pancreatic duct

Ryder's 4th evidence based rule

- Know how long you have been trying and how many goes
- Einstein's principle that a definition of insanity is doing the same thing over and over again and expecting different results works for ERCP too

OK its difficult-what next?

- Pancreatic guidewire-good or bad?
- Pre-cut sphincterotomy-scary but safer?
- Pancreatic stents-out of jail free?



Pancreatic guidewire

- Herreros de Tejada Gast Endosc 2009;70:700
- 188 difficult cannulations (5+ attempts)
- RCT double guidewire v continue

	DGW	STD
N=	97	91
CBD+	47%	56%
PEP	17%	8%

Pre-cut vs Einstein

- Cennamo V, Endoscopy 2010; 42: 381–388
- Meta analysis of 6 RCTs
- After 5 attempts pre-cut or keep on going

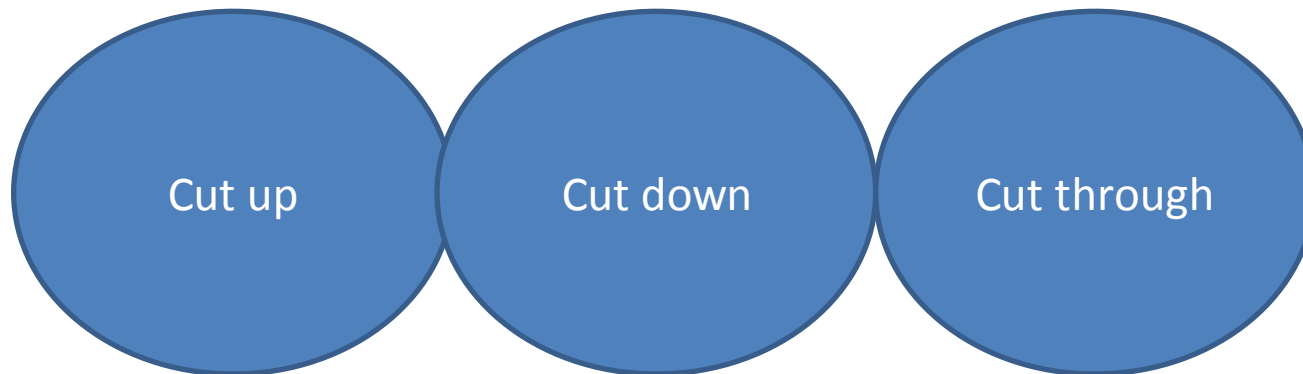
Technique	CBD+	PEP	Overall complication
Pre-cut	90%	2.5%	5%
KOG	90%	5.3%	6.3%

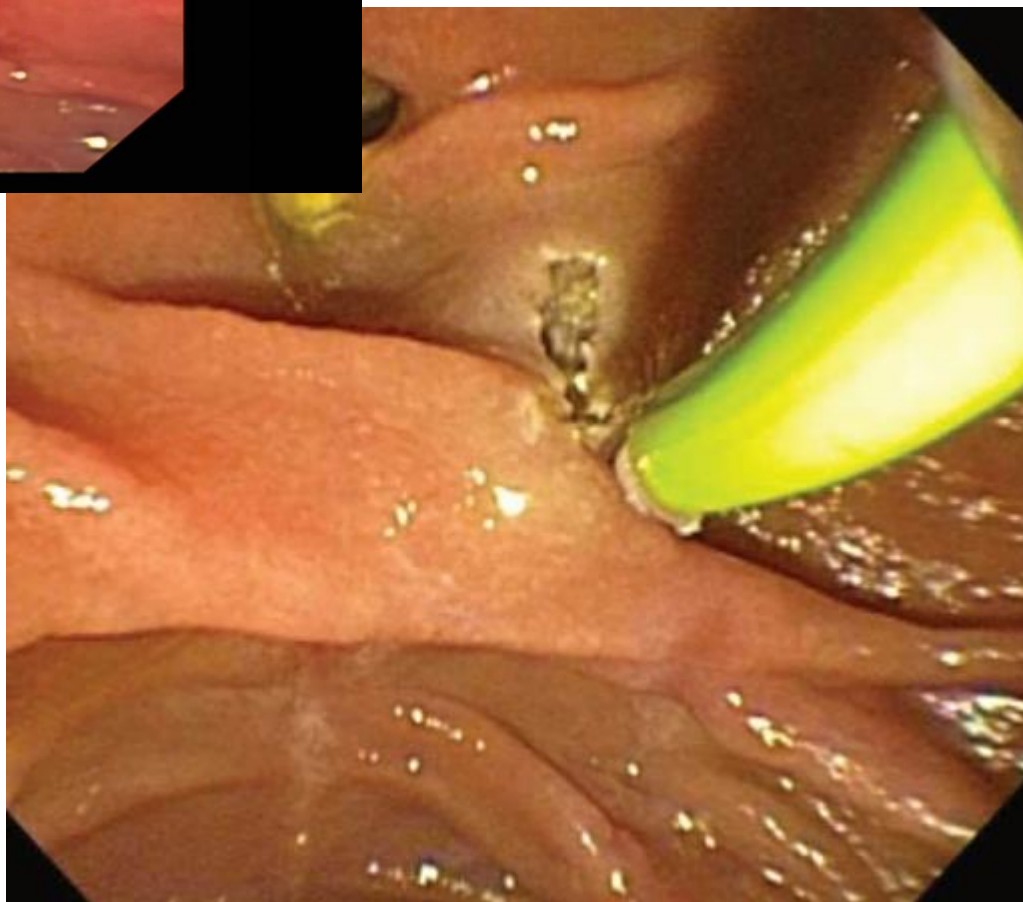
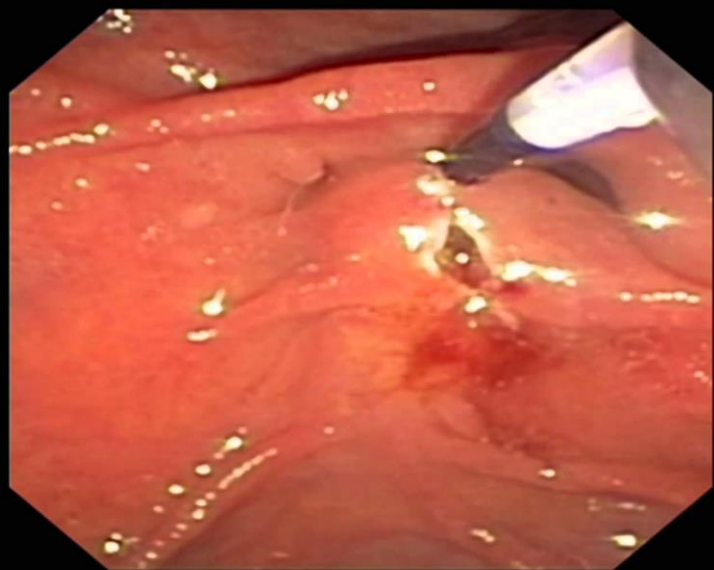
Pre-cut vs Einstein 2

- Sundarlingam P et al Clin Gastro Hep 2015;13:1722
- Meta analysis 5 studies 523 patients
- R/R CBD+ 1.32
- PEP 0.29 (in experienced ERCPists)

Pre-cut- You don't mean that do you?

- Katsinelos P, Gkagkalis S, Chatzimavroudis G et al. Comparison of threetypes of precut technique to achieve common bile duct cannulation:a retrospective analysis of 274 cases. Dig Dis Sci 2012; 57: 3286





Technique	PEP rate
Fistulotomy	2.6%
Pre-cut	21%
Pancreatic septotomy	22%

Pancreatic stenting

- Mazaki T, Mado K, Masuda H et al. Prophylactic pancreatic stent placement and post-ERCP pancreatitis: an updated meta-analysis. J Gastroenterol 2014; 49: 343–355
- Meta analysis 14 RCTs with 1541 patients
- 760 patients stented, 781 not
- PEP R/R for stenting 0.30

Sex: Age:

D.O.B.:

10/06/2014

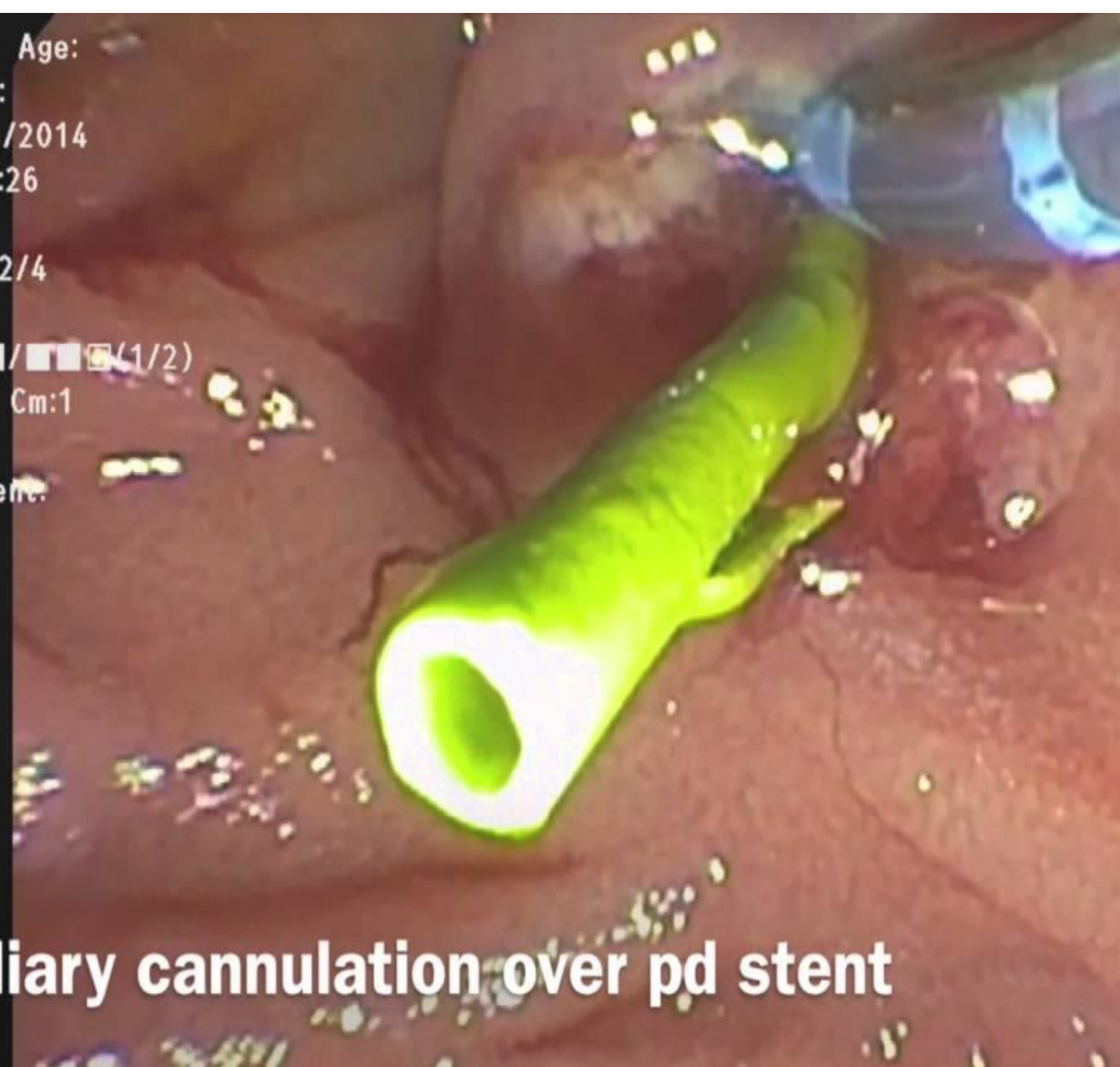
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CVP:A2/4

■■■/■■■(1/2)

Eh:A5 Cm:1

Comment:



wire-guided biliary cannulation over pd stent

Ryder's 5th evidenced based rule

(s)

- If you put a wire in the pancreas more than twice stent it
- If you don't put a wire in it do a fistulotomy
 - Cut down not up and don't cut through unless you have put a stent in it already

Conclusions

- 5 laws enough for anyone
- Techniques now well described which have evidence to support
- Yet to have definitive evidence that pancreatitis rates are lower!