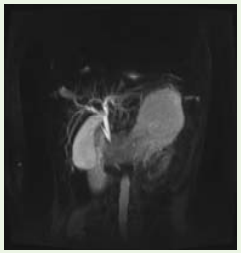
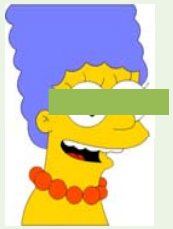
EXTRAHEPATIC MALIGNANT COMMON BILE DUCT STRICTRES

Dr Wim LALEMAN (KUL LEUVEN)



Case 1: Sabina, a 51-years old female

- 10-2010: mastectomy for a breastCa - curative
- 11-2010 till 3-2011: adjuvant chemotherapy
- 7-2011: jaundice without pain but with substantial pruritus
- Bilirubine 9 g% - AF 699 IU/L
- Abdominal ultrasound : dilated intra- en extrahepatic bile ducts till mid-CBD



Case 2: Jozef, a 64-year old male

- No medical history
- Jaundice since 3 weeks, no other symptoms except loose stools
- Bilirubine 12mg% - alkaline phosphatase 1850
- Abdominal ultrasound : dilated intra- en extrahepatic bile ducts up to distal CBD, multiple liver metastasis

Q1 : what would you consider a *pathologically* dilated common bile duct ?

A. More than 10mm
B. More than 8mm
C. No idea
D. Size alone is not enough criteria alone

Question 1

25% 1. Answer A
25% 2. Answer B
25% 3. Answer C
25% 4. Answer D

10

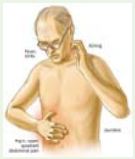
"The bile duct is dilated"

- Image modality influences reported duct diameter
  - EUS : CBD > 6-8mm, CHD > 6mm, IH > 2mm
  - CT : CBD > 8-10mm
- CBD diameters increase with age
- CBD diameters may vary with time of day, respiration, patient positioning, status post-CCE

Baron RL, et al Radiol Clin North Am 2002
Perret RS et al J Ultrasound Med 2000
Wu et al J Clin Ultrasound 1984

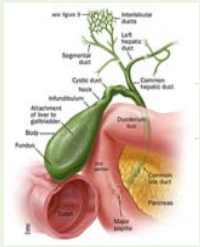
"The bile duct is pathologically dilated"

- ***Dilated bile duct***
  - CBD > 6-8mm, CHD > 6mm, IH > 2mm
- ***Clinical features*** suggesting obstruction
  - Jaundice (hepatic postmicrosomal/posthepatic)
  - *Painful – painless*
  - *Pruritus*
  - *Cholangitis (Charcot)*
  - *Constitutional*
- ***Biochemical features*** suggesting obstruction
  - Cholestatic parameters : AF, bilirubin
  - Liver associated enzymes : AST, ALT

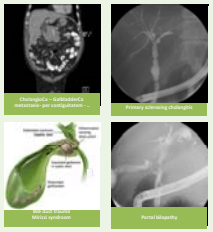


Green RM et al Gastroenterology 2002
Van Santvoort HC et al Endoscopy 2011
Selfert H et al Lancet 2000

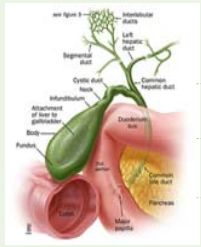
Causes of extrahepatic bile duct obstruction



Suprapancreatic

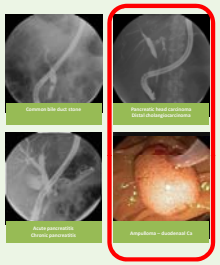


Causes of extrahepatic bile duct obstruction



Suprapancreatic

Intrapancreatic



Identify etiology

- Consider possible causes and confirm obstruction
- Define location, extension and cause
- Tools:
  - Non-invasive : US – CT – MRI
  - Invasive : EUS, ERCP, (cholangioscopy)

Green RM et al Gastroenterology 2002

Q2 : what <u>is the most sensitive</u> non-invasive method to diagnose CBD dilatation, locate the obstruction and determine the cause of obstruction ?

A. Abdominal ultrasound
B. CT scan
C. MRI
D. CT or MRI, doesn't matter

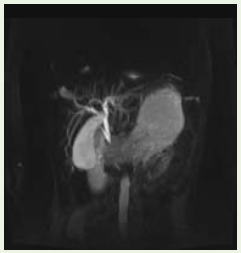
Question 2

25%	1.	Answer A
25%	2.	Answer B
25%	3.	Answer C
25%	4.	Answer D

Radiological work-up

Sensitivity	*US*[1,2]	*CT*[3,4]	*MRCP*[5,6]
Diagnosis dilatation	90%	96%	91-97%
Location obstruction	27-95%	88-97%	87-98%
Determine cause	23-81%	70-95%	84-94%
CDL	32%	56-72%	92%
Malignant stenosis[7,8]	-	77%	81-85%

[1]Songur Y et al. J Clin Gastroenterol 2001
[2]blackbourne LH et al. Am Surg 1994
[3]Baron RL Semin Roentgenol 1997
[4]Kim HC et al Abdom Imaging 2004
[5]Romagnuolo J, et al Ann Intern Med 2003
[6]Magnuson TH et al J Am Coll Surg 1999
[7]Rösch T et al. GI Endosc 2002
[8]Park MS et al Radiology 2004



Q3 : What would be your approach in the further work-up of a highly suspicious distal biliary stenosis upon non-invasive imaging (*without* evidence of metastasis or local inoperability)?

A. Go for tissue-diagnosis via ERCP with brush and blind biopsy
B. Send immediately for surgery provided patient is fit
C. Go for tissue-diagnosis via EUS + FNA
D. Go for tissue diagnosis via EUS-FNA and ERCP with brush/bx

Question 3

25% 1. Answer A
25% 2. Answer B
25% 3. Answer C
25% 4. Answer D

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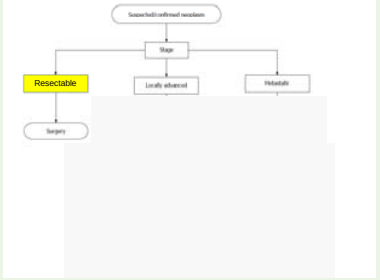
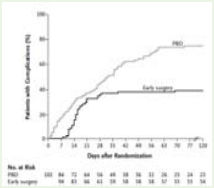
Therapeutic algorithm for malignant extrahepatic biliary obstruction



Boulay et al. WJG 2014

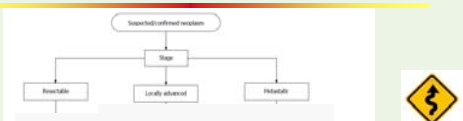
To drain or not to drain preoperatively ?

- Preoperative biliary drainage before PPD incorporated in many surgical programs (5% mortality – 40-60% morbidity PPD)
- Principle : PBD may restore synthetic and clearance function of the liver and mucosal intestinal barrier
  → improved outcome after surgery
- Before 2010 : low quality trials : evidence "equivocal"
- DROP-trial (NEJM 2010)
  - ERCP failure rate 25%, complication rate 46% (26% cholangitis in PBD)



Kimmings AN et al. Gut 2000
Mezhir JJ et al. Gastrointest Surg 2009
Wang Q et al Cochrane Database Syst Rev 2008
Sewnath ME et al. Ann Surg 2002
Van der Gaag NA et al NEJM 2010 + editorials
Fang Y et al Cochrane Database Syst Rev 2012.

Therapeutic algorithm for malignant extrahepatic biliary obstruction



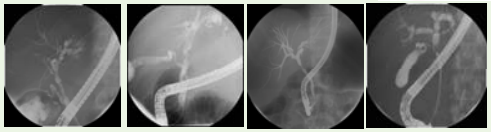
What in case of ***uncertain diagnosis*** ? Upgrading of diagnostics (ERCP, EUS, sampling, ...)

What in case of ***unresectable lesion*** ? Tissue diagnosis and drainage

Boulay et al. WJG 2014

Endoscopical work-up : ERCP

- cholangiogram



Green RM et al Gastroenterology 2002

Q4 : Which of the following cholangiograms shows a malignant stenosis ?

Question 4

25% 1. Answer A
25% 2. Answer B
25% 3. Answer C
25% 4. Answer D

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Q5 : What would you consider to have the highest yield for establishing a diagnosis in suspected malignant biliary obstruction ?

A. Plasmatic markers
B. ERCP with brush and blind biopsy
C. EUS + FNA
D. ERCP+brush/bx and EUS-FNA are equally accurate

Question 5

25% 1. Answer A
25% 2. Answer B
25% 3. Answer C
25% 4. Answer D

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Endoscopical work-up : ERCP (2)

- No exclusive cholangiographic criteria
- Yield brushing cytologie : 27-56%

Green RM et al Gastroenterology 2002

Endoscopical work-up : ERCP (3)

- No exclusive cholangiographic features
- Yield brushing cytologie : 27-56%
- Yield intraductale "blind" biopsies : 30-56%
- Combination brush + biopsy: 63%
- (Ancillaire cytological techniques: FISH)

Green RM et al Gastroenterology 2002
Fritchner et al Am J Gastro 2011

Endoscopische work-up : EUS-FNA vs ERC+brush/bx

- n=51, suspect of malignant biliary obstruction
- prospective, comparative design

	Sensitivity, %			Accuracy, %		
	EUS-FNA	ERCP	*P* value	EUS-FNA	ERCP	*P* value
Overall (N = 51)	94	50	<.0001	94	53	<.0001
Pancreatic mass (n = 36)	100	38	<.0001	100	42	<.0001
Biliary mass or stricture (n = 15)	79	79	NS	80	80	NS
Indeterminate stricture (n = 15)	80	67	NS	80	67	NS

Conclusion: EUS-FNA is superior to ERCP tissue sampling in evaluating suspected malignant biliary obstruction, particularly for pancreatic masses. EUS-FNA appears similar to ERCP sampling for biliary tumors and indeterminate strictures. Given the superior performance characteristics of EUS-FNA and the higher incidence of pancreatic cancer compared with cholangiocarcinoma, EUS-FNA should be performed before ERCP in all patients with suspected malignant biliary obstruction. (Clinical trial registration number: NCT01356030.) (Gastrointest Endosc 2014;80:97-104.)

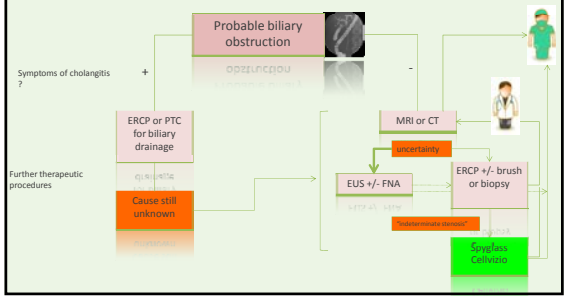
Weilert F, Bhat YM, Binmoeller K, et al GI Endosc 2014

Endoscopische work-up : EUS

First author	Publication year	Study design	All biliary strictures (no.)	Hilar strictures (no.)	Mass seen on radiologic imaging (%)	Mass seen on EUS (%)	Sensitivity of EUS-FNA for all biliary strictures (%)	Sensitivity of EUS-FNA for proximal extrahepatic biliary strictures (%)	Sensitivity of EUS-FNA for distal biliary strictures (%)
Fritscher-Ravens[1]	2000	Prospective	10	10	NR	100	80	80	NA
Fritscher-Ravens[2]	2004	Prospective	44	44	NR	98	89	89	NA
Eloubeidi[3]	2004	Prospective	28	15	33	89	75	NR	NR
Byrne[4]	2004	Retrospective	35	3	NR	71	86	NR	NR
Lee[5]	2004	Retrospective	40	1	0	25	47	NR	NR
Rösch[6]	2004	Prospective	50	11	NR	NR	43	25	60
Meara[7]	2006	Prospective	46	NR	NR	NR	87[1]	NR	NR
Dewitt[8]	2006	Prospective	24	24	39	96	77	77	NA
Mohamadnejad[9]	2011	Prospective	81	30	36 (CT), 42 (MRI)	94	73[1]	59[1]	81
					34%	81%	81%	66%	70%

Khasab MA, Fockens P et al GI Endosc 2012

Diagnostic algorithm obstructed bile duct

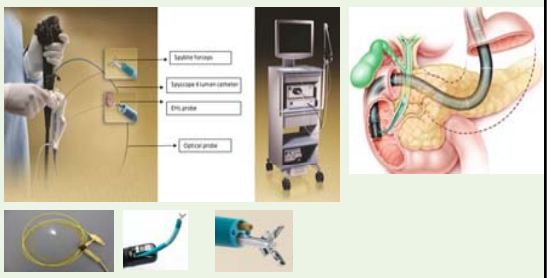


Confocal endomicroscopie
Cellvizio platform

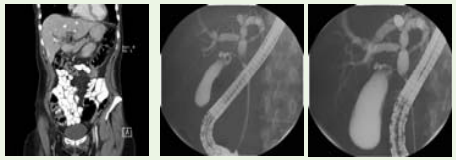
Accuracy: 81% - 90%

Meining A et al. Clin Gastroenterol Hepatol 2011
Meining A et al GI Endosc 2011

Peroral single-operator retrograde cholangioscopy:
SPYGLASS-SOC-platform (Boston-Scientific)



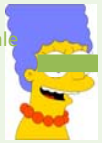
Case 1: Sabina, a 51-years old female



EUS and CT indeterminate

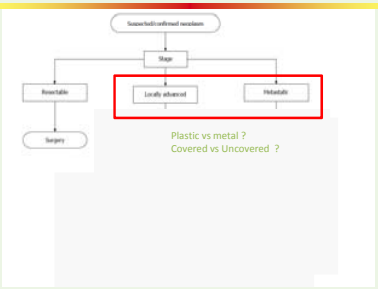
Case 1: Sabina, a 51-years old female

Case 1: Sabina, a 51-years old female



Spybite biopsy: adenocarcinoma
Surgical resection : pTisN0 ductal carcinoma in situ

Therapeutic algorithm for malignant extrahepatic biliary obstruction



Q6 : What would be your therapeutic approach in the further work-up of a suspicious distal biliary stenosis (*with* evidence of local inoperability) upon non-invasive imaging ?

A. ERCP with metallic stenting (uncovered)
B. ERCP with plastic stenting
C. ERCP with metallic stenting (partially covered)`
D. ERCP with metallic stenting (never mind which type)

Question 6

25% 1. Answer A
25% 2. Answer B
25% 3. Answer C
25% 4. Answer D

10

Q7 : What would be your therapeutic approach in the further work-up of a suspicious distal biliary stenosis (*with* evidence of metastasis) upon non-invasive imaging ?

A. ERCP with plastic stenting
B. ERCP with metallic stenting (uncovered)
C. ERCP with metallic stenting (partially covered)`
D. ERCP with metallic stenting (never mind which type)

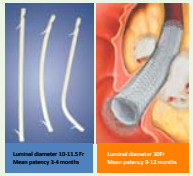
Question 7

25% 1. Answer A
25% 2. Answer B
25% 3. Answer C
25% 4. Answer D

10

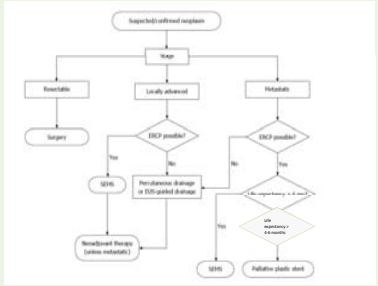
Therapeutic algorithm for malignant extrahepatic biliary obstruction

- Plastic vs Metal (SEMS)?
- SEMS: Covered vs Uncovered ?
- Determining factors
  - Technical aspects (placement, efficiency, patency, removability, reintervention)
  - Economic (cost stent, procedure and reintervention)
  - Patient factors (socioeconomic, life expectancy, level of obstruction)
- Analysis based on meta-analysis, retrospective trials
- Consensus : SEMS are superior to plastic stents when survival is expected > 4 months



Boulay BR et al. WJG 2014
Moss AC et al Eur J Gastroenterol Hepatol 2007
Telford JJ et al GIE 2010
Saleem A et al. GIE 2011
Arguedas MR et al Am J Gastroenterol 2002

Therapeutic algorithm for malignant extrahepatic biliary obstruction



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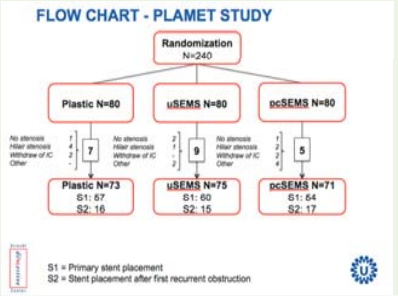
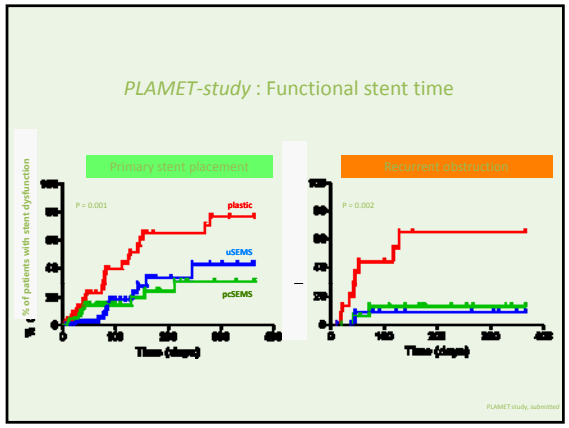
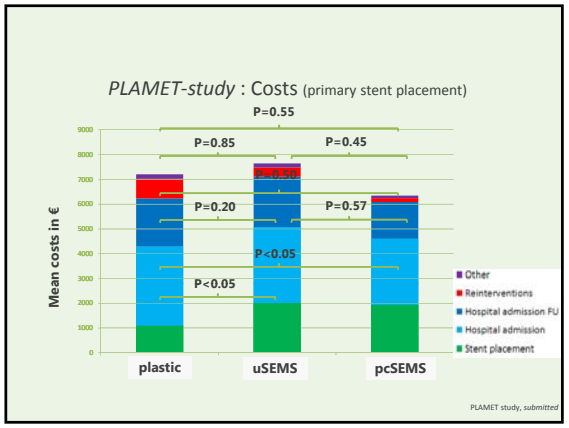
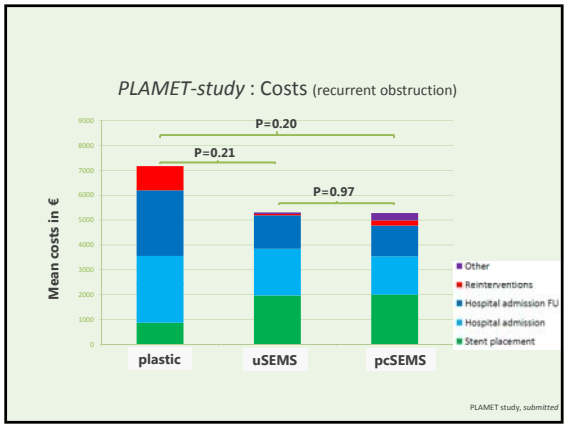
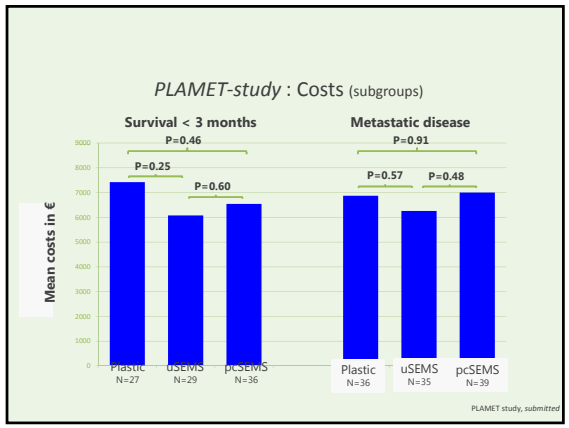


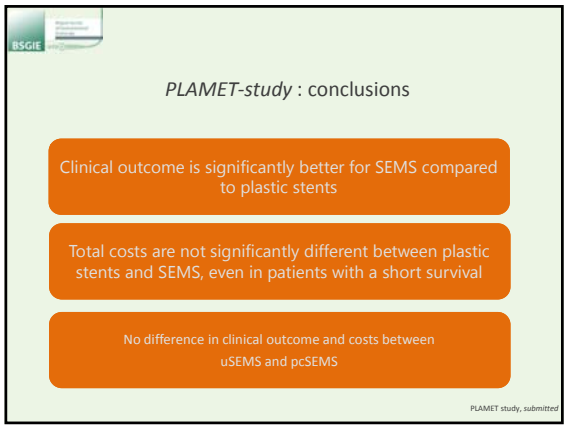
18 centers Belgium & The Netherlands


PLAMET-study : Functional stent time
Primary stent placement
Recurrent obstruction
% of patients with stent dysfunction
plastic
uSEMS
pcSEMS
P = 0.001
P = 0.002
Time (days)
PLAMET study, submitted


PLAMET-study : Costs (primary stent placement)
Mean costs in €
P=0.55
P=0.85
P=0.45
P=0.50
P=0.20
P=0.57
P<0.05
P<0.05
Other
Reinterventions
Hospital admission FU
Hospital admission
Stent placement
plastic
uSEMS
pcSEMS
PLAMET study, submitted


PLAMET-study : Costs (recurrent obstruction)
Mean costs in €
P=0.20
P=0.21
P=0.97
Other
Reinterventions
Hospital admission FU
Hospital admission
Stent placement
plastic
uSEMS
pcSEMS
PLAMET study, submitted


PLAMET-study : Costs (subgroups)
Survival < 3 months
Metastatic disease
Mean costs in €
P=0.46
P=0.25
P=0.60
P=0.91
P=0.57
P=0.48
Plastic N=27
uSEMS N=29
pcSEMS N=36
Plastic N=36
uSEMS N=35
pcSEMS N=39
PLAMET study, submitted


PLAMET-study : conclusions
Clinical outcome is significantly better for SEMS compared to plastic stents
Total costs are not significantly different between plastic stents and SEMS, even in patients with a short survival
No difference in clinical outcome and costs between uSEMS and pcSEMS
PLAMET study, submitted