John A. Martin, MD

Endoscopic Approach to Malignant Pancreaticobiliary Strictures

ACG Midwest Regional Postgraduate Course
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Malignant pancreaticobiliary strictures: etiologies

• Pancreatic malignancies
  - Adenocarcinoma
  - Neuroendocrine tumor
  - Cystic lesions
  - IPMN

• Biliary malignancies
  - Cholangiocarcinoma

• Ampullary malignancies
  - Ampullary carcinomas

• Metastatic lesions
Malignant pancreaticobiliary strictures: general concepts

- Malignant pancreatic strictures
  - Usually involve a mass lesion or IPMN
  - Diagnostic workup: tissue acquisition directed toward mass rather than stricture specifically
  - Therapy: symptom management rarely directed toward the stricture itself
- Malignant biliary strictures
  - May or may not involve a mass lesion
  - Diagnostic workup: tissue acquisition frequently directed toward stricture itself in addition to mass if present
  - Therapy: symptom management often directed toward stricture itself, which is often source of symptoms and frequently source of presenting symptoms / signs

Malignant pancreaticobiliary strictures: diagnostic modalities

- CT scan
- MRI / MRCP
- EUS
- ERCP
- Tumor markers
- Cytology
- Histology
- Enhanced tissue diagnostics

*The major conundrum: malignancy vs benignity*
PSC: Prototypical example of the conundrum

Statistics

- Cholangiocarcinoma: annual incidence 1.5%; up to 15% lifetime risk
- Limitations of modalities available to identify malignancy requires
  - Multimodal approach: imaging and tissue acquisition
  - Multiple interventions
  - Invasive approaches with added risk

MRI / MRCP in PB strictures

The game changer

- High-quality MRCP/protocolled MRI
  - Introduced early- mid- ‘90’s
    - Noninvasive, risk-free imaging
    - Better visualization of prestenotic radicles, side-branches
    - Pre-ERCP mapping & "staging" for better-directed ERCP
    - Required better hardware / software
      - Ultrafast, single-breathhold sequences
      - Thin slice images; multiple projections
      - 3D MIP reconstructions, contrast retention protocols
MRI / MRCP in PB strictures

- Image 1: MRI/MRCP showing a stricture in PB.
- Image 2: Another MRI/MRCP image with a different view of the PB stricture.

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MRI / MRCP in PB strictures

MRI / MRCP in PB strictures
**MRI / MRCP in PB strictures**

*High-impact imaging*

- Combination of MRI + MRCP
  - Exploits physiologic characteristics of neoplasia
  - Accurately demonstrates the level of obstruction
- Excellent visualization of pre-stenotic radicles
  - Visualizes radicles likely to be under-opacified at ERC
  - Fully depicts saccular dilatations, bile lakes with debris
- Detailed depiction of stricture complexity
- Allows for 3D reconstruction

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**ERCP in PB strictures**

*Why it remains robust*

- MR allows no *tissue acquisition*
- MR does not always identify all strictures well
  - May rely on prestenotic dilatation
  - Duct fibrosis may limit prestenotic duct ectasia
- ERCP allows for *therapy*
  - Stricture dilation
  - Stent placement
  - Direct visualization (choledochoscopy)
Diagnostic ERCP in PB strictures

Why it’s imperfect

• Technical pitfalls in cholangiography
  - Importance of occlusion cholangiography
  • Strictures = high gradients to flow
  • PSC may be limited to peripheral radicles
  • CHD or IHD strictures may lead to excessive GB filling
  • Prior sphincterotomy may lead to incomplete opacification
• Technical limitations in tissue acquisition
  - Suboptimal tissue characteristics for existing technology
  - Limitations in today’s technologies and techniques
Diagnostic ERCP in PB strictures

Tissue acquisition modalities

- Brush cytology
  - Limited cytologic yield
  - Utility of pre-dilation
- Intraductal forceps biopsy
  - Technically challenging
  - Accuracy and precision
- Choledochoscopic biopsy
  - Time-intensive; requires adequate duct diameter
  - Fixed costs and recurrent costs
# Diagnostic ERCP in PB strictures

Cytology brushes

Biliary Aspiration Needle

Intraductal forceps

*Clinical Gastrointestinal Endoscopy 2005*

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### Diagnostic ERCP in PSC

**Comparison of tissue-acquisition techniques**

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<th>Technique</th>
<th># Reports</th>
<th># Patients</th>
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<th>Spec</th>
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*deBellis M, Sherman S, et al. GIE 2002*
**Diagnostic ERCP in PSC**

*Triple tissue sampling at ERCP: Positive sampling frequency when all atypia considered equiv to CA*

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<th>Panc Cancer N=46</th>
<th>CholangioCa N=30</th>
<th>Amp Cancer N=13</th>
<th>Metastases N=15</th>
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**Diagnostic ERCP in PB strictures**

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Diagnostic ERCP in PB strictures

![Image of ERCP procedure]

Diagnostic ERCP in PB strictures

![Image of ERCP procedure]
Diagnostic ERCP in PB strictures

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Diagnostic ERCP in PB strictures

Biliary Introducer

Intraductal FNA with biliary introducer

Clinical Gastrointestinal Endoscopy 2005

Image courtesy B. Peterson, M. Topazian

Single-operator choledochoscopy
Diagnostic ERCP in PB strictures


Diagnostic ERCP in PB strictures

CCD-video choledochoscopy with NBI

Diagnostic ERCP in PB strictures
CCD-video choledochoscopy with NBI

Image courtesy Professor Takao Itoi, MD, Tokyo Medical University
Diagnostic ERCP in PB strictures

Direct-video choledochoscopy

Larghi and Waxman, GIE 2006;63:853.

Diagnostic ERCP in PB strictures

CCD-video choledochoscopy with NBI

Image courtesy Irving Waxman, MD, University of Chicago
Diagnostic ERCP in PB strictures
Deep-enteroscopic ERC

Tissue acquisition: improving diagnostic yield

- Fluorescence in-situ hybridization (FISH)
  - Increased sensitivity
  - No decrease in specificity
- Digital Image Analysis (DIA)
  - DNA stained: DNA quantitation
  - Computer-assisted measurement of cell DNA content
- Increased sensitivity
- Minimal impact on specificity

Diagnostic ERCP in PSC


TABLE 1. Definitive and Indeterminate Diagnostic Criteria for Cholangiocarcinoma in Primary Sclerosing Cholangitis

Definitive diagnostic criteria
- Biopsy
- Positive cytology
- Mass lesion
- Dominant stricture and CA 19.9 > 100 U/mL and/or FISH polymerase and/or DIA > 1.89

Indeterminate diagnostic criteria
- FISH trisomy 7
- Dysplasia
- DIA > 1.13 and < 1.89
- FISH polymerase in absence of dominant stricture
- Dominant stricture in absence of mass, positive cytology, biopsy, elevated CA 19.9, or FISH polymerase

Abbreviations: CA 19.9, carbohydrate antigen 19-9; DIA, digital image analysis; and FISH, fluorescence in situ hybridization.
**EUS in PSC**

*Tissue acquisition, local imaging*

- **EUS**
  - Local staging of stricture/mass and regional lymph nodes
  - EUS/FNA more sensitive than ERCP/brush cytology
  - Distal CBD; role in proximal biliary tree to be defined

- **IDUS**
  - Role of IDUS in PSC yet to be determined
  - Appears to add information regarding stricture morphology
  - Does not appear to have greater accuracy than ERCP
  - No biopsy possible but may help direct biopsy

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**What’s coming up?**

*The future…*
Malignant Pancreaticobiliary Strictures: endoscopic therapy

Palliation of Pancreaticobiliary CA

The nature of the disease

- Pancreaticobiliary malignancies
  - Pancreatic adenocarcinoma
  - Cholangiocarcinoma
  - Gallbladder carcinoma
- Highly lethal; poor prognosis
  - Surgery is only curative treatment
  - Advanced stage at diagnosis
  - Minority are surgical candidates for cure
  - Many patients operated for cure have residual disease

Image courtesy Professor Takao Itoi, MD, Tokyo Medical University
Palliation of Pancreaticobiliary CA

Situations in which we are asked to help

• Unresectable malignancy
  - Anatomically unresectable
  - Metastatic disease
  - Locally extensive
  - Medically unresectable
  • Surgeon says “no”: patient medically unfit for surgery
  • Decidedly unresectable
  • Patient says “no”: patient does not want surgery
• Residual / recurrent malignancy after surgery
• Progression of disease after prior palliation

Malignant disorders we frequently manage

• Pancreatic carcinoma
  - Bile duct obstruction
  - Gastric outlet, intestinal obstruction
  - Pain
  - Pancreatic maldigestion
• Cholangiocarcinoma
  - Bile duct obstruction
  - Gastric outlet obstruction, intestinal obstruction
  - Pain
• Gallbladder carcinoma, ampullary carcinoma
Palliation of Pancreaticobiliary CA

Symptoms we manage

• Bile duct obstruction
  - Jaundice
  - Pruritus
• Gastric outlet obstruction
  - Nausea, vomiting
  - Malnutrition, dehydration
• Intestinal obstruction
• Pain
• Pancreatic duct obstruction
  • May be after surgical resection

Procedures we perform

• Bile duct obstruction
  - ERCP since 1968/1972
  • Stent
  • Ablation
• Gastric outlet obstruction
  - Gastroduodenal stent
  - Feeding tube
  - Decompressing G-tube
• Intestinal obstruction
  • After surgical resection: enteroscopic techniques
Palliation of biliary obstruction

Malignant biliary drainage: stents

Where the big impact began

- Hardware: overall excellent devices
  - Plastic stents
  - Self-expanding metallic stents
- Software: tough issues
  - Stent patency: stent diameter
  - Hilar stenting: max drainage
  - Access issues: “getting there”
- Tumor: EUS-guided rendezvous access
- Post-surgical anatomy: enteroscopic access
John A. Martin, MD

Making palliation durable…

Stent patency: it’s still size that matters

*Increasing Stent Diameter*

- 7F ➔ 10F: Benefit
- 8F ➔ 10F: Benefit
- 10F ➔ 12F: No Benefit

*Poiseuille’s law will always apply…*

*Speer et al, GIE 1988*
Self-expanding metallic stents for malignant strictures

- Prolonged patency
  - Mean 180 days
- Cost effective when life expectancy > 3 mos (one stent exchange)
- Majority require no further intervention
- Improved QOL

SEMS for malignant strictures below the hilum: size matters

Multicenter RCT comparing a new nitinol-based SEMS to routine therapy (MOZART Study Group)

- Assess patency rates of nitinol SEMS vs stainless steel SEMS in a three arm RCT: 6mm + 10mm Zilver; 10mm Wallstent
- Determine frequency, timing, and mechanism of occlusion
- Measure and compare complications, accuracy and ease of placement, success of re-intervention, and overall patient survival

Mid-study Interim analysis

Randomization to the 6mm Zilver arm was closed


Total Occlusion: Study End

Mechanism of Stent Occlusion


Hilar stenting: metal or plastic?

Prospective, multicenter

Prospective, multicenter

n = 62, 11 centers acad/non

SEMS pts: worse anatomy, more w/mets

Similar technical success

Adverse outcomes plastic > SEMS

Malignant biliary drainage: stents
Malignant biliary drainage: stents
ERCP in post-surgical anatomy
Deep-enteroscopic ERC
ERCP in post-surgical anatomy
Deep-enteroscopic ERC

Palliation of gastric outlet obstruction
Gastroduodenal stents

*Recent arrival, big impact*

- Sir Charters J. Symonds London
  - 1885: first metallic esophageal prosthesis
- SEMS: late 1980’s
- TTS SEMS: early 1990’s
- Covered SEMS: late 1990’s
- **Duodenal stent: late 1999**
- SEPS: 2003
- Fully covered SEMS: mid-2000’s

Gastroduodenal stents: do they work? The literature says yes…

- Overall technical success: 85-95%
- Overall clinical success: 80-85%
- Compared to surgical bypass
  - Faster symptom relief
  - Lower overall cost
Effective. But cost-effective?
RCT in 2006 says “yes to both”…

Prospective randomized trial of laparoscopic gastrojejunostomy versus duodenal stenting for malignant gastric outflow obstruction

S. Mehta,1 A. Hindmarsh,1 E. Cheong,1 J. Cockburn,2 J. Sazda,2 R. Tighe,2 M. P. N. Lewis,1 M. Rhodes1

1 Department of Upper Gastrointestinal Surgery, Norfolk and Norwich University Hospital, Colney Lane, Norwich, England, United Kingdom
2 Department of Radiology, Norfolk and Norwich University Hospital, Colney Lane, Norwich, England, United Kingdom

- Less pain
- Resumed diet sooner
- Shorter hospitalizations
- Better QOL at 1 month
- Overall more cost-effective


Also, 2007 decision analysis confirmed prior claims that stents are more cost-effective than surgery
- Less clearly dominant with longer patient life


Gastroduodenal stenting: angulation, length, scope passage, contrast injection
Gastroduodenal stenting in biliary obstruction

Why is this so important?

• 44% of these patients will develop biliary obstruction
• Some will develop biliary obstruction before GOO
• Others will develop biliary obstruction after GOO: PTC or ERCP?

Gastroduodenal stenting in biliary obstruction

What to do…

• Evaluate for biliary obstruction first
• Prior biliary stent does not preclude duodenal stent placement
• Duodenal stent placement can facilitate ERCP

Baron & Topazian, GIE 2009;69:166.
Intestinal stenting beyond the gastroduodenum

Ross, et al., GIE 2006;64:835.

Gastroduodenal and intestinal stenting in 2012: the upshot

• Effective, cost-effective, and durable in context of patient life expectancy
• Concomitant biliary obstruction surmountable in expert hands but preferably addressed first
• Deeper deployment possible with deep enteroscopy but requires extra steps and non-TTS deployment
Feeding tubes

When all else fails…
skills to remember

• Decompressing tube
  - G-tube
  - NG tube
• Feeding jejunostomy
  - NJ
  - Bridling
  - PEG-J
  - D-PEJ (only when you can get there)

Summary and conclusion

Bad cancers, but good news…

• There is always something we can do
  - Biliary obstruction
  - GOO
• Stents are an extremely successful technology
  • All work very well (except Bismuth 4, some 3)
  • Excellent technical and clinical success rates
  • Effective, cost-effective, and demonstrated QOL impact
• Technique is as important as technology
  - Post-surgical anatomy (enteroscopy)
  - Complex anatomy including biliary + GD obstruction (EUS)
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