Participating in the Webinar

All attendees will be muted and will remain in Listen Only Mode.

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.

How to Receive CME and MOC Points

LIVE VIRTUAL GRAND ROUNDS WEBINAR

ACG will send a link to a CME & MOC evaluation to all attendees on the live webinar.

ABIM Board Certified physicians need to complete their MOC activities by December 31, 2022 in order for the MOC points to count toward any MOC requirements that are due by the end of the year. No MOC credit may be awarded after March 1, 2023 for this activity.
MOC QUESTION

If you plan to claim MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement. THESE ANSWERS WILL BE REVIEWED.

ACG Virtual Grand Rounds

Join us for upcoming Virtual Grand Rounds!

Week 38 – September 22, 2022
Therapeutic Drug Monitoring in IBD: Why, When and How?
Faculty: Andres J. Yarur, MD, FACP
Moderator: Ryan C. Ungaro, MD, MS
Thursday, September 22, 2022 at Noon Eastern and **NEW!** 8pm Eastern!

SPECIAL EDITION – GQuIC Bite Webinar – September 28, 2022
Screening Colonoscopy Updates: What They Mean for Your Practice
Wednesday, September 28, 2022 at 8:00 PM Eastern

Visit gi.org/ACGVGR to Register
Disclosures

Nalini M. Guda, MD, FACP
Boston Scientific Corporation: Consultant
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Prabhleen Chahal, MD, FACP
BSCI: Consultant, advisory council
Medtronic: Consultant, advisory council

*All of the relevant financial relationships listed for these individuals have been mitigated*
Palliation in Pancreatic Cancer

Nalini M Guda MD, FACP
Aurora St. Luke’s Medical Center, Milwaukee, WI
Clinical Adjunct Professor of Medicine
University of Wisconsin School of Medicine & Public Health

Current Problem

• 7th highest mortality in the world and 4th in US – likely 2nd by 2030 in US
• Resectability at the time of diagnosis 20%
• 5-year survival approximately 5%
• Most common problems: Gastric outlet obstruction, Biliary obstruction, Pain control and local tumor sensitization/treatment

Palliation in Pancreatic Cancer – Endoscopist’s role

Objectives: Explain endoscopic palliation options
1. Biliary drainage – ERCP stent/EUS guided drainage
2. Gastric outlet obstruction (GOO) – Stents/Surgery/EUS guided bypass
3. Tumor localization – fiducial placement
4. Pain management
5. Local therapies- tumor regression/sensitization

Biliary drainage

• Lesions in the head of pancreas likely cause biliary obstruction – jaundice, pruritus, cholangitis
• Current concept is for upfront stenting prior to neoadjuvant therapy
• Options: Surgical, Percutaneous, Endoscopic
• Surgical – Increased recovery time, long recovery time – rarely done
• Percutaneous drainage – Not desirable – external bag, leakage, infection – last resort!!

Sharaiha et al. Gastrointestinal Endoscopy Vol. 85 Issue 5p904–914
Endoscopic Biliary drainage – should it be routine?

- Not everyone needs drainage
- Indications: HOP lesions, biliary obstruction, surgery >2 weeks, GOO needing stenting
- ERCP even with experts – 5-8% risk of complications
- For upfront surgery – No Routine preop ERCP: higher complications, delay in surgery
- Limitations: High failure rates of ERCP, high complication rates, no data on EUS intervention

Biliary stenting – ERCP

- Metal stents favored over plastic stents*
- Metal stents: longer patency, fewer complications
- Covered: less tumor ingrowth but more migration, >risk of PEP, cholecystitis
- No clear consensus for covered vs Uncovered – both can be used for neoadjuvant therapy**
- Reasons for failure of stenting: Stricture, Mass effect and angulation
- Stent PD if even unintentional cannulation
- Biliary and GOO may be synchronous/asynchronous – evaluate and proceed – double stenting when needed
- Endoscopic decompression improves QoL

References:
Van derGaag N Engl J Med 2010

Drug Eluting Stents

• Likely increase stent patency
• Improve local drug penetration without increasing systemic toxicity
• Increased patency but no survival benefit (429 vs 148 (covered)/143 (uncovered) days

Lee et al. Gastrointest Endosc 2005;61(2):296-301

EUS guided Biliary drainage

• Failure rate of ERCP 5-7%
• Three options:
  1. Biliary Rendezvous
  2. Direct Access: Choledochoduodenostomy/Hepaticogastrostomy – puncture LHD/CHD from stomach or duodenum
  3. Antegrade drainage – Stent through the liver across the ampulla

• Clinical success for EUS- biliary drainage: 94% with AE of 17%
• Data suggest primary EUS guided biliary drainage to minimize complications

Giovannini M et al. Endoscopy 2001; 33: 898-900
Han SY et al. Sci Rep 2019; 9: 16551
Biliary Rendezvous. EUS guided biliary access followed by ERCP

Mallery, Shawn et al. Gastrointestinal Endoscopy, Volume 59, Issue 1, 100 - 107
Khasab et al. Gastrointestinal Endoscopy Volume 78 Issue 5 Pages 734-741

Direct Access Choledochoduodenostomy or Hepaticogastrostomy

Suresh Vasan Venkatachalapathy et al. Gastrointestinal Endoscopy Volume 94 Issue 2 Pages 321-328
Antegrade drainage – Stent through the liver across the ampulla

Khasab et al. Gastrointestinal Endoscopy Volume 82 Issue 6 Pages 993-1001
Hathorn et al. Gastrointestinal Endoscopy Vol. 95 Issue 3 pp 443–451

Will or should EUS- BD be preferred over ERCP- BD

- Three RCTs done – SEMS used
- EUS-BD comparable to ERCP – safety and patency
- No pancreatitis, reduced stent occlusion, re intervention rates
- Potential for same setting diagnosis, relief of obstruction, fiducial placement

Park J.K Gastrointest Endosc 2018; 88: pp. 277-282
Gastric outlet obstruction

- Tumor growth, related inflammation -15-25%
- Nausea, vomiting, poor oral intake
- Surrogate marker for poor survival
- Options:
  - Surgical Bypass
  - Endoscopic stenting of the duodenum
  - EUS guided gastro jejunostomy

Tendler DA. *Am J Gastroenterol* 2002;97: 4-6

Endoscopic stenting for GOO

- Seen in up to 15% of patients with pancreatic cancer
- Symptoms: Abdominal pain, early satiety, fullness, nausea, vomiting, GERD
- High technical success once you pass the wire
- Easier to deploy, good palliation, shorter LOS but HIGH recurrence of symptoms
- Compared to surgery fewer complications, shorter LOS, quicker PO intake
- Common problems:
  - Perforation
  - Bleeding
  - Tumor ingrowth
  - Difficulty in subsequent ERCP

Nagaraja V, et al. *J Gastrointest Oncol.* 2014;5:92–8
Surgical GJ vs Endoscopic stenting

- Multicenter RCT 18 in GJ and 21 to stent
- Stent placement: less time to PO intake, <LOS, lower costs
- GJ had higher patency rates
- If survival is > 2 months GJ recommended
- Similar conclusions from a retrospective propensity score matched study
- GJ probably favored with neoadjuvant therapy and improved survival


Endoscopic Ultrasound guided GJ

- EUS guided GJ alternative to stenting and surgery
- LAMS used to create connection between stomach and small bowel distal to obstruction
- Technical success rates: 92%, Clinical Success 90% and pooled AE: 12%, Reintervention rate 9%
- Impact of EUS-GJ on subsequent pancreaticoduodenectomy unclear

Tyberg A et al. Endosc Int Open 2016; 4: E276-E281
Iqbal U et al. Endosc Ultrasound 2020; 9: 16-23
Sánchez-Aidehuelo, Rubén et al. Gastrointestinal Endoscopy, Volume 0, Issue 0. In Press
Michiel Bronswijk, et al. Gastrointestinal Endoscopy Volume 94 Issue 3 Pages 526-536*
EUS GJ better than Lap GJ

EUS-GJ VS SURGICAL GJ vs ENERAL STENT

<table>
<thead>
<tr>
<th></th>
<th>EUS GJ N=241</th>
<th>ES N=142</th>
<th>Surgical GJ N=80</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technical success</td>
<td>98.3%</td>
<td>98.9%</td>
<td>100%</td>
<td>0.58</td>
</tr>
<tr>
<td>Clinical success</td>
<td>97.5%</td>
<td>90.1%,</td>
<td>85.0%</td>
<td>&lt;0.0001</td>
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<tr>
<td>Re-intervention</td>
<td>1.7%</td>
<td>14.1%</td>
<td>15%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LOS days</td>
<td>2</td>
<td>4</td>
<td>5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>AE</td>
<td>9.1%</td>
<td>39.3%</td>
<td>28.7%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**Conclusion:** This large cohort study demonstrates the long-term durability and safety of EUS-GJ as an alternative strategy for GOO palliation

Jaruvongvanich, Veeravich et al. Gastrointestinal Endoscopy, Volume 95, Issue 6, AB508 - AB509
EUS GJ vs SURGICAL GJ

<table>
<thead>
<tr>
<th></th>
<th>EUS GE (N=97)</th>
<th>Surgical GE (N=64)</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Technical Success</td>
<td>96.9%</td>
<td>100%</td>
<td>0.156</td>
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<tr>
<td>Clinical Success</td>
<td>93.8%</td>
<td>96.9%</td>
<td>0.382</td>
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<tr>
<td>Resumption of chemotherapy</td>
<td>23.1 days</td>
<td>41.1 days</td>
<td>&lt;0.001</td>
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<tr>
<td>Pre procedure Albumin</td>
<td>2.9</td>
<td>3.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AE</td>
<td>16.5%</td>
<td>32.8%</td>
<td>0.016</td>
</tr>
</tbody>
</table>

Conclusions: EUS-GE can be performed among nutritionally deficient patients and allows earlier resumption of chemotherapy

de Gooyer, Peter et al. Gastrointestinal Endoscopy, Volume 95, Issue 6, AB493
Sánchez-Aldehuelo, Rubén et al. Gastrointestinal Endoscopy, Volume 0, Issue 0 In Press*

Tumor Localization – Fiducial placement

- Image guided radiotherapy – precise deliver of radiation to target lesion
- Allows local tumor control with decreased radiation toxicity
- Placement of gold radio opaque markers by EUS to delineate the tumor
- Technical success 96%, AE 5%

Tchelebi et al. Cancer 2020; 126: 2120-2131
Patel et al. World J Gastrointest Endosc 2020; 12: 231-240
EUS – Injection therapies

- Small studies – animal/human
- Mostly feasibility studies
- No definite data on outcomes/survival advantage
- Studies include concomitant therapy – radiation/chemo and not local injection as standalone – unlikely
- Likely tumor sensitizing agents – minimize toxicity and increase response to systemic therapies

Injectable therapies

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Malignancy</th>
<th>Injection Therapy</th>
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<tbody>
<tr>
<td>Chang et al., 2000</td>
<td>Phase I trial</td>
<td>Pancreatic adenocarcinoma</td>
<td>Cytoimplant</td>
</tr>
<tr>
<td>Hecht et al., 2003</td>
<td>Phase I trial</td>
<td>Pancreatic adenocarcinoma</td>
<td>ONYX-015</td>
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<tr>
<td>Gan et al., 2005</td>
<td>Pilot study</td>
<td>Cystic pancreatic lesions</td>
<td>Ethanol lavage</td>
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<tr>
<td>Meenan et al., 2007</td>
<td>Early phase clinical trial</td>
<td>Pancreatic cancer</td>
<td>32P Bismuth</td>
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<tr>
<td>DeWitt et al., 2009</td>
<td>Randomized, double-blind study</td>
<td>Cystic lesions</td>
<td>Ethanol lavage + paclitaxel</td>
</tr>
<tr>
<td>Yang et al., 2009</td>
<td>Prospective study</td>
<td>Pancreatic cancer</td>
<td>Ethanol</td>
</tr>
<tr>
<td>Oh et al., 2011</td>
<td>Prospective study</td>
<td>Cystic lesions</td>
<td>Ethanol lavage + paclitaxel</td>
</tr>
<tr>
<td>Levy et al., 2011</td>
<td>Prospective study</td>
<td>Pancreatic cancer</td>
<td>Gemcitabine</td>
</tr>
<tr>
<td>Hecht et al., 2012</td>
<td>Phase I trial</td>
<td>Pancreatic adenocarcinoma</td>
<td>TNF-α</td>
</tr>
<tr>
<td>Levy et al., 2012</td>
<td>Prospective study</td>
<td>Pancreatic adenocarcinoma</td>
<td>Ethanol lavage</td>
</tr>
<tr>
<td>Herman et al., 2013</td>
<td>Phase I trial</td>
<td>Pancreatic adenocarcinoma</td>
<td>TNF-α</td>
</tr>
<tr>
<td>Levy et al., 2017</td>
<td>Prospective study</td>
<td>Pancreatic cancer</td>
<td>Gemcitabine</td>
</tr>
<tr>
<td>Nishimura et al., 2017</td>
<td>Open-label study</td>
<td>Pancreatic cancer</td>
<td>STXMM1 (double-stranded RNA oligonucleotide)</td>
</tr>
</tbody>
</table>

Brachytherapy

- Seeds/microparticles/liquids placed directly into or adjacent to the tumor
- Steady exposure of target tissue to low-energy gamma, Xrays/ Beta particles
- Leads to localized tissue injury and ablation
- EUS to delivery the radioactive seeds – phosphorus 32, iodine, gold, iridium and yttrium
- Goal is to downstage tumor for resection


Radiofrequency ablation

- RFA generates high temperatures and causes local coagulative necrosis
- Possible stimulation of immune response – Abscopal effect
- Potential complications: Pancreatitis, PD strictures, bowel perforation, peritonitis, bleeding

Tatli S et al. Diagn Interv Radiol 2012; 18: 508-516
Kaminski JM et al. Cancer Treat Rev 2005; 31: 159-172
Pain Control

• Pain/analgesia ladder – escalation based on symptoms
  • Mild: Acetaminophen, NSAIDs
    • Complementary approaches – acupuncture, massage, mindfulness etc.,
  • Moderate: Adjuvant meds – Duloxetine, amitriptyline, gabapentin, tizanidine, baclofen etc..
    • Mild/Moderate opioids
  • Severe: Stronger opioids (morphine, oxycodone, hydromorphone etc.,)
    • EUS- CPB
    • EUS – CPN
    • video-thoracoscopic splanchnicectomy (VSPL)
    • intrathecal drug delivery systems (IDDS)

Celiac Plexus block & Neurolysis

• CPN used in treatment of pain
  • Injection : central location, bilateral or into the celiac ganglion
  • Overall response rates 68% (CI 61-74%) at week 2 and 53 % (95% CI 45-62%) at week 4
  • No difference in injection techniques
  • Complications higher in central injection
Celiac Plexus neurolysis with RFA

- RFA: Proven efficacy in splanchnic nerve blockade in chronic abdominal pain due to chronic pancreatitis/malignancies
- RCT of 28 patients CPN (14) RFA (12)
- At 4 weeks pain scores lower in RFA group
- No difference in opiate use
- Preliminary data favor RFA over CPN


Non endoscopic options

- Nausea
  - Serotonin receptor antagonists +/- dopamine-receptor antagonists
  - Antipsychotics
- Dyspnea
  - Opiates
- Abdominal distension (peritoneal metastases + Ascites)
  - Paracentesis (drain placement)/diuretics/Peritoneovenous shunt
- Constipation
  - Multiple drug regimens (different mechanism of action)
- Behavioral health
  - Pain control, anxiolytics, anti depressants, psychological support

Thromboembolic disease

- >27%. 4 times > other cancers and >50 times to average individuals
- VTE poor prognostic factor for mortality
- PE and VTE second leading cause of death in PDAC
- Consider LMWH, DOACs

Yousuke Nakai et al. Surgical Oncology Clinics of North America, 2021-10-01, Volume 30, Issue 4, Pages 639-65

Nutrition in Pancreatic Cancer

- Weight loss and cachexia seen in up to 80%
- Leads to decrease QOL
- Frequent small meals, well balanced, low fat, simple carbs
- Avoid excess alcohol
- Panc Enzyme Replacement Therapy (PERT) – improves malabsorption, pain, steatorrhea and QoL. Symptom correlation is poor.
- Consider appetite stimulants: Megestrol, synthetic tetrahydrocannabinol

Landers A et al. Palliative care 2019;12:1178224218825270
Malignant Afferent Limb Syndrome

- Seen post pancreaticoduodenectomy
- Complete or partial obstruction of the afferent (pancreaticobiliary) limb
- Common causes: Radiation enteropathy, tumor recurrence
- Incidence: up to 13% in one year
- Treatment options: Surgical bypass or EUS –GE/enteral stent
- EUS-GE – technically feasible, natural way for biliary and pancreatic drainage

Yusuke Nakai et al. Surgical Oncology Clinics of North America, 2021-10-01, Volume 30, Issue 4, Pages 639-65

In summary:

1. Endoscopic biliary drainage superior and favorable to surgical or percutaneous approaches
2. If ERCP drainage not feasible consider EUS drainage or EUS first approach is preferable as well.
3. Consider Biliary drainage at the time of stenting of GOO
4. EUS- GJ preferable over surgical approach and maybe superior to transpyloric stenting
5. Early Celiac plexus neurolysis may be beneficial in pain control
6. Local injection therapies, brachytherapy, RFA are still experimental in treatment of pancreatic cancer
7. Consider prophylaxis for VTE, nutrition and enzyme replacement
Questions and Answers

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