

Supplementary Doc 1

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Supplementary Table 1 Studies on EUS-LB in patients with NAFLD

| Study | Design of the study | Patients | Technical success (%) | Diagnostic yield (%) | Specimen length (median, range) (mm) | CPT (median, range) | Needle used for EUS-LB | Needle passes (median) | Complications (n (%)) |
|-------------------------|---------------------------|----------|-----------------------|----------------------|--------------------------------------|---------------------|------------------------|------------------------|-----------------------|
| Saab et al (a) | Retrospective case series | 47 | 100 | 100 | 65 (46-80) | 18 (14-24) | 19 G (SharkCore) | 1 | 2(4.2) |
| Bazerbachi et al (b) | Prospective (RCT) | 27 | 100 | 100 | 24 (20-27.5) | 26 (7-62) | 22 G (SharkCore) | 2 | 6(7) |
| DeWitt et al (66) | Prospective case series | 9 | 100 | 77.8 | 8 (1-13) | 2 (0-9) | 19 G (SharkCore) | 3 | 0 |
| Gleeson et al (65) | Retrospective case series | 6 | 100 | 100 | 11.5 (8-27) | 7 (5-8) | 19 G (QuickCore) | 2(1-3) | 0 |
| Gor et al (60) | Retrospective case series | 4 | 100 | 100 | 11 (6-23) | 6.5 (6-14) | 19 G (FNA) | - | 0 |
| Stavropoulos et al (50) | Prospective case series | 5 | 100 | 100 | 32.2 (12.5-58.7) | 9 (4-13) | 19 G (FNA) | 1 | 0 |
| Shah et al (61) | Retrospective study | 11 | 100 | 100 | 71.1 (17.1-167.4) | 33 (23-85) | 19 G (SharkCore) | 2 (1-3) | - |

Abbreviations: NAFLD: nonalcoholic fatty liver disease; EUS-LB: endoscopic ultrasound guided liver biopsy; CPT: complete portal triads; RCT: randomized controlled trial; G: gauge; FNA: fine needle aspiration

- a) Saab S, Phan J, Jimenez MA et al. Endoscopic Ultrasound Liver Biopsies Accurately Predict the Presence of Fibrosis in Patients with Fatty liver. *Clin Gastroenterol Hepatol.* 2017 Sep;15(9):1477-1478.
- b) Bazerbachi, F.; Vargas, E.J.; Matar, R.; Storm, A.C.; Mounajjed, T.M.; Topazian, M.D.; Levy, M.J.; Chandrasekhara, V.; Abu Dayyeh, B.K. EUS-guided core liver biopsy sampling using a 22-gauge fork-tip needle: A prospective blinded trial for histologic and lipidomic evaluation in nonalcoholic fatty liver disease. *Gastrointest Endosc.* 2019, 90, 926–932.

Supplementary Table 2 Studies on EUS guided treatment of hepatic cysts

| Study | Design | Patients | EUS guided treatment | Size of cyst pre procedure (median) | Size of cyst post procedure (median) | Reduction of cyst on follow up | Complications | Comments |
|-------------------|---------------|-------------------------------|---|-------------------------------------|--------------------------------------|--|------------------------------------|---|
| Lee et al (71) | Retrospective | 8 (+1 combined with PCD) | Ethanol (pure alcohol) | 368.9 (195.3-795.9) ml | 0 ml (0-2.8) | 100% at 15 months | 2 cases (both mild abdominal pain) | 100 ml (mean) ethanol injected |
| Shi et al (a) | Case report | 1 | 1% lauromacrogol | 75 x 45 mm | - | Significantly reduced on CT post 1 week | None | 30 ml used |
| Lee et al (b) | Retrospective | 14 | Pure ethanol (99%) | - | - | Median time to clinical response 17 (10-36) months: no recurrence on follow up | - | Ethanol retention therapy done (mena 100 ml injected) |
| Taguchi et al (c) | Case report | 1 | Transmural pigtail stent (7F) with NBD (6F) | - | - | No cyst at 3 months post procedure | - | Infected hepatic cyst (<i>Edwardsiella tarda</i>) |
| Gupta et al (d) | Case series | 1 (other case managed by PCD) | 7 F pigtail stent with 7 F NBD | 14.5x9.2x1 3 cm | - | 6 weeks post procedure: complete resolution | none | Intrahepatic pancreatic pseudocyst |

Abbreviations: EUS: endoscopic ultrasound; NBD: nasobiliary drain; CT: computed tomography; PCD: percutaneous catheter drain

- a) Shi G, Sun S, Li H et al. A case of a giant cyst in the left lobe of the liver successfully treated with endoscopic ultrasound-guided fine needle aspiration (with video). Endosc Ultrasound. 2017 Jul 13;6(5):343–6.
- b) Lee DS, Lee SK, Seo DW. Long-term safety and efficacy of ethanol retention therapy via percutaneous approach and/or EUS guidance for symptomatic large hepatic cysts (with video). Endosc Ultrasound. 2020 Jan-Feb;9(1):31-36.
- c) Taguchi H, Tamai T, Numata M et al. Endoscopic ultrasonography-guided transmural drainage of an infected hepatic cyst due to *Edwardsiella tarda*: a case report. Clin J Gastroenterol. 2014 Oct;7(5):422-8.

- d) Gupta D, Pipalia N, Pandav N et al. EUS guided drainage of intrahepatic pancreatic pseudocyst. *Trop Gastroenterol*. 2016 Apr-Jun;37(2):131-3.

Supplementary Table 3 Literature on EUS guided drainage of liver abscess

| Study | Design | Patients | Location of abscess | Access | EUS needle used | Stent used | Reduction in collection size | Complications |
|--------------------|--|---|---------------------------------------|----------------|------------------------|--|--|--------------------------------------|
| Seewald et al (72) | Case report | 1 (pyogenic) | Left lobe | TG | 22 G | 7 F DPT with 7 F nasocatheter Teflon drain | Complete resolution in 4 weeks | None |
| Noa et al (73) | prospective case series | 3 (pyogenic) | 2 caudate, 1 gastrohepati c extension | 2 TG/ 1 TD | 19 G FNA | 7 F DPT (I case also has an NCD) | Complete resolution on follow up (2-12 weeks) | None |
| Itoi et al (74) | Case report | 1 (tubercul ar abscess) | Caudate lobe | Both TG and TD | 19 G | TD (7 F straight with 5 F NCD) and TG (7F DPT with 5F NCD) | Complete resolution in 2 weeks | None |
| Ang et al (a) | Case report | 1 (pyogenic) | Left lobe | TG | 19 G | 8F and 10F DPT | Complete resolution in 11 days | None |
| Kumta et al (b) | Case report | 1 (abscess post EUS-HGS) | Left lobe | TG | Electroca utery system | 15 mm LAMS | Resolution in 1 month | None |
| Alcaide et al (76) | Case report | 1 (pyogenic) | Left lobe | TG | 19 G | 10 mm (Hot AXIOS) | Resolution in 6 days | none |
| Koizumi et al (c) | Case report | 1 (ALA) | Intrahepatic subcapsular | TG | 19 G | 7 F NCD | Resolution in 2 weeks | None |
| Carbajo et al (d) | Retrospective comparison study (EUS-AD vs PCD) | 18 EUS vs 62 PCD (9 hepatic abscess drained by EUS) | Left lobe (3), right lobe (4) ? | - | 19 G | LAMS (2), FCSEMS (5) | Clinical success (complete resolution of symptoms and disappearance of lesion) 77.5% | NA for liver abscess (overall 22.2%) |
| Yamamoto et al (e) | Case report | 1 (patient had Chilaiditi | Right lobe | TD | 19G | 5 F NCD | Complete resolution in 6 days | None |

| | | syndrome) | | | | | | |
|---------------------|-------------------------------------|---------------------|----------------------------------|-----------------|------|---|--|------------------------------|
| Molinario et al (f) | Case report | 1 (Fungal abscess) | Left lobe | - | 19 G | LAMS (10 x 20 mm) | Resolution in 1 month | None |
| Ogura et al (77) | Retrospective study (EUS-AD vs PCD) | 8 (EUS) vs 19 (PCD) | Left (6); right lobe (2) | TG (6), TD (2) | 19 G | FCSEMS | Clinical success 100 % (EUS-AD) vs (PCD 89%) | None |
| Tonozuka et al (g) | Retrospective series | 7 | Left (6), right (1) | TG (6), TD (1) | 19 G | FCSEMS with 5/6 F NCD (1 case needed DEN) | Clinical success 71.4% | None |
| Rana et al (h) | Retrospective case series | 14 | Left (11), caudate (3) | TG (10), TE (4) | 19 G | 7 F DPT (2) in all cases | Mean 21.5 days (resolution of abscess) | None |
| Medrado et al (75) | Case report | 1 | Left lobe | TG | 19 G | PCSEMS (60x10 mm) | Resolution in 8 weeks | Transgastric stent migration |
| Chnadra et al (i) | Case series | 3 | Caudate (1), left lobe (2) | TG | 19 G | 8 F DPT with 8F NCD/ 10 F NCD | Clinical resolution in both cases | None |
| Kawaka mi et al (j) | Case report | 1 | Left lobe | TG | 19 G | NAGI stent | NA | None |
| Keohane et al (k) | Case series | 2 | Caudate lobe | TG | 19 G | One case (7F and 10 F DPT); other case (1 7F DPT) | Complete resolution at 5 and 6 weeks | None |
| Ogura et al (l) | Case report | 1 | Right lobe (case of unresectable | TD | 19 G | FCSEMS | Complete resolution (duration NA) | None |

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Abbreviations: EUS: endoscopic ultrasound; TG: trans-gastric; TD: trans-duodenal; G: gauge; DPT: double pigtail; NBD: nasobiliary drain; LAMS: lumen apposing metal stent; FCSEMS: fully covered self-expanding metal stent; NA: not available; PCD: percutaneous catheter drain; ALA: amebic liver abscess; HGS: hepatico-gastrostomy

- a) Ang TL, Seewald S, Teo EK, Fock KM, Soehendra N. EUS-guided drainage of ruptured liver abscess. *Endoscopy*. 2009;41 Suppl 2:E21-2.
- b) Kumta NA, Torres-Ruiz F, Reinoso PJ, Kahaleh M. Endoscopic management of hepatic abscess after EUS-guided hepaticogastrostomy. *Gastrointest Endosc*. 2016; 84:1054-1055.
- c) Koizumi K, Masuda S, Uojima H, Ichita C, Tokoro S, Sasaki A, Egashira H, Kimbara T, Kako M. Endoscopic ultrasound-guided drainage of an amoebic liver abscess extending into the hepatic subcapsular space. *Clin J Gastroenterol*. 2015; 8:232-5.
- d) Carbajo AY, Brunie Vegas FJ, Garc á-Alonso FJ et al. Retrospective cohort study comparing endoscopic ultrasound-guided and percutaneous drainage of upper abdominal abscesses. *Dig Endosc*. 2019; 31:431-438.
- e) Yamamoto K, Itoi T, Tsuchiya T et al. EUS-guided drainage of hepatic abscess in the right side of the liver of a patient with Chilaiditi syndrome. *VideoGIE*. 2017; 2:299-300.
- f) Molinario F, Rimbaş M, Pirozzi GA et al. Endoscopic ultrasound-guided drainage of a fungal liver abscess using a lumen-apposing metal stent: case report and literature review. *Rom J Intern Med*. 2020. In Press. [DOI: 10.2478/rjim-2020-0035]
- g) Tonozuka R, Itoi T, Tsuchiya T et al. EUS-guided drainage of hepatic abscess and infected biloma using short and long metal stents (with videos). *Gastrointest Endosc*. 2015; 81:1463-9.
- h) Rana SS, Ahmed S, Sharma R et al. Safety and efficacy of EUS-guided drainage of liver abscess: A single-center experience. *Endosc Ultrasound*. 2020; 9:350-351.
- i) Chandra S, Chandra U. Endoscopic ultrasound-guided transgastric drainage of radiologically inaccessible left lobe liver abscess involving segment 4, caudate lobe, and left lateral segments using a modified technique. *Endosc Int Open*. 2021 Jan;9(1): E35-E40.
- j) Kawakami H, Kawakubo K, Kuwatani M et al. Endoscopic ultrasonography-guided liver abscess drainage using a dedicated, wide, fully covered self-expandable metallic stent with flared-ends. *Endoscopy*. 2014;46:E982-3.
- k) Keohane J, Dimaio CJ, Schattner MA et al. EUS-guided transgastric drainage of caudate lobe liver abscesses. *J Interv Gastroenterol*. 2011 Jul;1(3):139-141.
- l) Ogura T, Takagi W, Onda S et al. Endoscopic ultrasound-guided drainage of a right liver abscess with a self-expandable metallic stent. *Endoscopy*. 2015;47:E397-8.

Supplementary Table 4 Studies on endoscopic transluminal drainage of bilomas

| Study | Design | Patients | Access | Size of biloma | Stent used | Reduction in collection size | ERCP findings | Complications |
|------------------------|---------------------------|----------|----------------|---------------------------|--|--|------------------------|---------------|
| Cury et al (a) | Case report | 1 | TG | NA | 9Fx 3cm plastic | No collection at 2 months | No leak | None |
| Baron et al (b) | Case report | 1 | TG | 4.5 x 6 cm | 10Fx5cm DPT | Resolution in 1 month | No leak | None |
| Somani et al (c) | Case report | 1 | TG | NA | 10Fx3 cm DPT | Resolution in 24 hours | No leak; CBD stone 7mm | None |
| Ulla Rocha et al (d) | Case report | 1 | TG | 5.7x6.4x10 cm | 8.5 F plastic | Resolution in 7 days | Not done | None |
| Prachaya kul et al (e) | Case report | 1 | TG | 4.5x 3.5 cm | 7Fx7cm DPT | Resolution in 7 days | Not done | None |
| Shami et al (f) | Retrospective case series | 5 | TG (4), TD (1) | - | 7F/10F single or double plastic stents (DPT) | Resolution in 11 days -2 months | Not done | None |
| Nakamura et al (g) | Case report | 1 | TG | NA | 7F plastic | Resolution occurred immediately | Not done | None |
| Cassis et al (h) | Case report | 1 | TD | 19x15.6x20 cm | LAMS (15x10mm) | No collection at 3 weeks | Not done | None |
| Tonozuka et al (i) | Retrospective case series | 6 | TG (6) | 68.5 (22.0-83.0) (median) | FCSEMS | Clinical success 83.3% (1 DEN); final 100% success | None | None |
| Ogura et al (j) | Case report | 1 | - | NA | 7Fx12 cm DPT | Resolution in 1 week | Not done | None |
| Eso et al (k) | Case report | 1 | TG | NA | 7F DPT | Complete resolution in 4 weeks | Not done | None |

Abbreviations: ERCP: endoscopic retrograde cholangiopancreaticography; TG: trans-gastric; TD: trans-duodenal; NA: not available; DPT: double pigtail; LAMS: lumen apposing metal stent; FCSEMS: fully covered self-expanding metal stent; DEN: direct endoscopic necrosectomy

- a) Cury MS, do Oliveira Conceição RD, Ferrari AP. Gastric drainage of postoperative biloma. Gastrointest Endosc. 2001 Sep;54(3):400-1.

- b)** Baron TH. Combined endoscopic transgastric and transpapillary drainage of an infected biloma. *Endoscopy*. 2006 Apr;38(4):436.
- c)** Somani SK, Somani A, Singh V. Endoscopic drainage of a post-cholecystectomy biloma with biloma-gastric stenting. *Endoscopy*. 2013;45:E173-4.
- d)** Ulla-Rocha JL, Lopez-Piñero S, Dominguez-Comesaña E. EUS-Guided Transgastric Drainage of Perihepatic Biloma After Laparoscopic Liver Metastasectomy from Colon Cancer. *J Gastrointest Cancer*. 2016 Dec;47(4):468-469.
- e)** Prachayakul V, Aswakul P. Successful endoscopic treatment of iatrogenic biloma as a complication of endosonography-guided hepaticogastrostomy: The first case report. *J Interv Gastroenterol*. 2012 Oct;2(4):202-204.
- f)** Shami VM, Talreja JP, Mahajan A, Phillips MS, Yeaton P, Kahaleh M. EUS-guided drainage of bilomas: a new alternative? *Gastrointest Endosc*. 2008 Jan;67(1):136-40.
- g)** Nakamura K, Kishikawa H, Ojiro K et al. Stent placement using dual-channel endoscope for biloma after EUS-guided hepaticogastrostomy. *J Hepatobiliary Pancreat Sci*. 2020 Dec 12.
- h)** Cassis P, Shah-Khan SM, Nasr J. EUS-guided drainage of a 20-cm biloma by use of a lumen-apposing metal stent. *VideoGIE*. 2019 Oct 31;5(1):20-21.
- i)** Tonozuka R, Itoi T, Tsuchiya T et al. EUS-guided drainage of hepatic abscess and infected biloma using short and long metal stents (with videos). *Gastrointest Endosc*. 2015;81(6):1463-9.
- j)** Ogura T, Okuda A, Miyano A, Nishioka N, Higuchi K. Successful treatment for infected biloma after endoscopic ultrasound-guided hepaticogastrostomy using double stent placement technique. *Mini-invasive Surgery*. 2018;2.
- k)** Eso Y, Marusawa H, Tsumura T et al. Endoscopic ultrasonography-guided transgastric drainage of infectious biloma following radiofrequency ablation for hepatocellular carcinoma. *Dig Endosc*. 2012; 24:390.

Supplementary Table 5 Technique of PPG measurement (124,126, a)

Technique of the procedure:

1. The measurement of PPG via EUS requires 4 components: 25 G FNA needle, non-compressible tubing, a compact digital manometer, and heparinized saline. The tubing is connected by a luer lock to the distal port and heparinized saline is connected the proximal port of the manometer.
2. With the patient supine, the manometer is placed at the patient's midaxillary line.
3. The HV measurement is conducted first, in which middle HV is targeted most often (larger caliber and better alignment with the needle trajectory). Then PV measurement is taken (umbilical portion of left PV is the target).
4. Doppler flow is used to confirm the typical multiphasic waveform of hepatic venous flow and typical venous hum of the portal venous flow.
5. Trans-gastric trans-hepatic route is taken for HV and PV puncture. Needle is flushed with heparinized saline (1 ml). The steadiest reading at equilibrium is recorded. Three measurements are taken and their mean is calculated (both HV and PV pressures)
6. The FNA needle is slowly withdrawn from the vein into the liver parenchyma and then back into the needle sheath with Doppler flow on to ensure there is no flow within the needle tract.
7. The PPG is calculated by subtracting the mean PVP from the mean HV pressure.
8. Post-procedural antibiotics are usually given for 3 to 5 days after the procedure.

Abbreviations: PPG: portal pressure gradient; EUS: endoscopic ultrasound; FNA: fine needle aspiration; HV: hepatic vein; PV: portal vein

- a) Huang JY, Samarasena JB, Tsujino T, et al. EUS-guided portal pressure gradient measurement with a simple novel device: a human pilot study. *Gastrointest Endosc* 2017; 85:996–1001.

Supplementary Table 6 Studies on EUS-PPG measurement in animal models and humans.

| Study | Year | Animal models | Approach | EUS FNA needle | Technical success | Complications | Correlation between EUS and trans-hepatic PVP measurement |
|----------------------|------|---|---------------|--------------------------------------|-------------------|--|---|
| ANIMAL MODELS | | | | | | | |
| Lai et al (124) | 2004 | 21 pigs (14 PH model with PVA; 7 coagulopathy with heparin) | Transduodenal | 22 G | 18/21 cases | Small subserosal hematomas in all 21 cases | r=0.91 |
| Giday et al (123) | 2007 | 5 pigs | Trans-gastric | 19 G (with a modified ERCP catheter) | 5/5 cases | None | NA |
| Buscaglia et al (a) | 2008 | 5 pigs | Trans-gastric | 19 G | 5/5 cases | None | NA |
| Schulman et al (b) | 2016 | 5 pigs | NA | 22 G | 5/5 cases | None | HVPG within \pm 1 mmHg of PVP |
| Schulman et al (c) | 2017 | 5 pigs | NA | 22 G | 5/5 cases | None | NA |
| Huang et al (d) | 2016 | 3 pigs | Trans-gastric | 25 G | 3/3 cases | None | R=0.985-0.99 |
| HUMAN STUDIES | | | | | | | |
| Fujii-Lau et al (e) | 2014 | 1 | Trans-gastric | 22 G | 1 | None | PPG 1 mmHg (excellent correlation with HVPG) |
| Huang et al (f) | 2017 | 28 | - | 25 G | 25/25 cases | None | Excellent correlation with varices (P = .0002), PH gastropathy (P = .007), and thrombocytopenia (P = .036); few of them also underwent liver biopsy in same setting |
| Samarasena et al (g) | 2018 | 51 | - | - | 51/51 cases | 3 cases had mild abdominal discomfort | Correlated with varices, PHG, low platelets, cirrhosis |
| Zhang et al (h) | 2020 | 12 | - | 22 G | 11/12 cases | None | R=0.923 |

| | | | | | | | |
|-------------------|------|---|---------------|------|---------|------|---|
| | | | | | (91.7%) | | |
| Shah et al (i) | 2021 | 1 | Trans-gastric | 25 G | 1 | None | NA (same session EUS-liver biopsy was done) |

Abbreviations: EUS: endoscopic ultrasound; FNA: fine needle aspiration; PVP: portal vein pressure; PVA: polyvinyl alcohol; HVPG: hepatic vein pressure gradient; G: gauge; ERCP: endoscopic retrograde cholangio-pancreaticography; PHG: portal hypertensive gastropathy

- a) Buscaglia JM, Shin EJ, Clarke JO, et al. Endoscopic retrograde cholangiopancreatography, but not esophagogastroduodenoscopy or colonoscopy, significantly increases portal venous pressure: direct portal pressure measurements through endoscopic ultrasound-guided cannulation. *Endoscopy* 2008;40: 670–4.
- b) Schulman AR, Thompson CC, Ryou M. EUS-guided portal pressure measurement using a digital pressure wire with real-time remote display: a novel, minimally invasive technique for direct measurement in an animal model. *Gastrointest Endosc* 2016; 83:817–20.
- c) Schulman AR, Thompson CC, Ryou M. endoscopic ultrasound-guided direct portal pressure measurement using a digital pressure wire with real-time remote display: a survival study. *J Laparoendosc Adv Surg Tech A* 2017; 27:1051–4.
- d) Huang JY, Samarasena JB, Tsujino T, Chang KJ. EUS-guided portal pressure gradient measurement with a novel 25-gauge needle device versus standard transjugular approach: a comparison animal study. *Gastrointest Endosc.* 2016; 84:358-62.
- e) Fujii-Lau LL, Leise MD, Kamath PS, et al. Endoscopic ultrasound-guided portalsystemic pressure gradient measurement. *Endoscopy* 2014;46: E654–6.
- f) Huang JY, Samarasena JB, Tsujino T, et al. EUS-guided portal pressure gradient measurement with a simple novel device: a human pilot study. *Gastrointest Endosc* 2017; 85:996–1001.
- g) Samarasena JB, Han J, Patel A, et al. EUS-guided portal pressure gradient measurement: a single center experience. *Gastrointest Endosc* 2018;87: AB107.
- h) Zhang W, Peng C, Zhang S et al. EUS-guided portal pressure gradient measurement in patients with acute or subacute portal hypertension. *Gastrointest Endosc.* 2020; S0016-5107:34531-4.
- i) Shah SL, Dawod Q, Kumar S et al. "One stop" liver-focused endoscopy: EUS-guided portal pressure gradient measurement technique. *VideoGIE.* 2020; 5:658-659.