Endoscopic ultrasound guided gallbladder drainage—is it time to change practice?

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Comment on: Teoh AYB, Kitano M, Itoi T, *et al.* Endosonography-guided gallbladder drainage versus percutaneous cholecystostomy in very high-risk surgical patients with acute cholecystitis: an international randomised multicentre controlled superiority trial (DRAC 1). Gut 2020;69:1085-91.

Laparoscopic cholecystectomy remains the standard of care for management of acute cholecystitis (AC). Historically, in patients with AC who are deemed high risk for surgery, percutaneous cholecystostomy also known as percutaneous transhepatic gall bladder drainage (PT-GBD) was performed as a bridge to delayed cholecystectomy. In the 2018 Tokyo guidelines for management of AC, PT-GBD was recommended as a standard approach for gallbladder drainage in high risk surgical candidates (Recommendation Grade 1, Level B). It also recommended consideration of endoscopic transhepatic gall bladder drainage (ETGBD) or endoscopic ultrasound guided gall bladder drainage (EUS-GBD) in high-volume institutes with therapeutic EUS expertise (Level B) (1).

In a recent publication in *Gut*, Teoh *et al.* reported results of an international multicenter randomized control trial (RCT) comparing outcomes of EUS-GBD *vs.* PT-GBD in management of AC in high risk surgical patients (2). This study included a total of 80 patients enrolled from August 2014 to February 2018. The study reported that EUS-GBD significantly reduced 1-year adverse events, 30-day adverse events, re-interventions (after 30 days), number of unplanned readmissions and recurrent cholecystitis. Also, the post procedural pain score and analgesic requirement were significantly lower with EUS-GBD. The technical success, clinical success and 30-day mortality were statistically similar between EUS-GBD and PT-GBD. The mean procedural time and median hospital stay were not significantly different. The results are

summarized in *Table 1*.

Based on their results, the authors concluded that EUS-GBD significantly improved outcomes compared to PT-GBD in patients with AC who are high risk for surgery. They propose that EUS-GBD should be the procedure of choice in centers with therapeutic EUS expertise in patients who are not candidates for future cholecystectomy.

In a previous RCT comparing EUS-GBD *vs.* PT-GBD in management of AC in patients who are deemed high risk for surgery, Jang *et al.* reported similar rates of technical (97% *vs.* 97%; 95% one-sided CI lower limit, –7%, P values =0.001 for noninferiority margin of 15%) and clinical success (100% *vs.* 96%; 95% one-sided CI lower limit, –2%, P=0.0001 for noninferiority margin of 15%) (3). As the adverse event rates were similar between the two groups, the study established EUS-GBD as an effective non-inferior alternative to PT-GBD. A recent systematic review and meta-analysis of comparative studies reported that EUS-GBD had similar rates of success but lower morbidity in terms of adverse events, re-interventions and shorter hospital stay compared to PT-GBD (4). The current RCT by Teoh *et al.* reports superiority of EUS-GBD over PT-GBD in management of AC in patients who are high risk surgical candidates.

Compared to pancreatic fluid collections, EUS guided drainage of gallbladder is technically more challenging, as gallbladder is not fixed in relation to stomach or duodenum. Hence, in addition to basic skills in EUS, expertise in therapeutic EUS is necessary for EUS-GBD. Previous

Table 1 Comparison of the clinical outcomes between the EUS-GBD and PT-GBD

Clinical outcomes	EUS-GBD (n=39)	PT-GBD (n=40)	P value
1 year adverse events (%)	10 (25.6)	31 (77.5)	<0.001
Recurrent acute cholecystitis	1 (2.6)	8 (20.0)	0.029
Re-interventions after 30 days	1 (2.6)	12 (30.0)	0.001
Unplanned admissions	6 (15.4)	20 (50.0)	0.002
30-day adverse events	5 (12.8)	19 (47.5)	0.001
30-day mortality	3 (7.7)	4 (10.0)	1
Technical success	38 (97.4)	40 (100.0)	0.494
Clinical success	36 (92.3)	37 (92.5)	1
Procedure time (minutes)	22.7 (13.0)	27.4 (12.0)	0.108
Analgesic requirements [total paracetamol in milligram]	3,345 [5,663]	5,165 [5,068]	0.034
Hospital stay (days) [median]	8 [4–13]	9 [7–14]	0.181

Source: The data in the table is derived from "Endosonography-guided gallbladder drainage versus percutaneous cholecystostomy in very high-risk surgical patients with acute cholecystitis: an international randomised multicentre controlled superiority trial (DRAC 1)" written by Teoh *et al.* and published in *Gut*. 2020 Mar 12 (2). EUS-GBD, endoscopic ultrasound guided gall bladder drainage; PT-GBD, percutaneous transhepatic gall bladder drainage.

studies have assessed the learning curves for performance of EUS-GBD. Tyberg *et al.* suggested a minimum of 19 cases to achieve expertise in EUS-GBD (5). In a larger study by Teoh *et al.* (6), endoscopists' experience of fewer than 25 procedures was a significant predictor of 30-day adverse events. Hence, one should consider structured training program in interventional EUS or perform adequate number of EUS-GBD procedures (20–25 procedures) under expert supervision before performing it in individual practice (7).

The risk of complications with EUS-GBD include perforation, bile leak and stent dislodgement. The availability of lumen apposing metal stents (LAMS) and cautery enhanced stent delivery system has helped improved the safety of EUS-GBD. However, one has to realize that if an adverse event like perforation or stent migration occurred needing surgical intervention, the mortality rates would be high, as these patients were high-risk surgical candidates to begin with. Hence, in addition to availability of expertise in therapeutic EUS, EUS-GBD procedures should be performed in centers where an experienced surgical team, who can manage potential iatrogenic complications is available. Endoscopists should take surgical backup into consideration before performing EUS-GBD in individual practice.

It has to be highlighted that none of the patients in the

current RCT underwent cholecystectomy CCY. There is limited data on feasibility and safety of CCY after EUS GBD. Saumoy *et al.* compared outcomes of CCY after EUS GBD and PT GBD (8). They reported 100% technical success and no differences in the rates of open *vs.* laparoscopic CCY. There was no difference in postoperative adverse events. At current time, EUS-GBD should be offered exclusively to patients who will not be candidates for future CCY, until further studies establish the safety of CCY after EUS-GBD.

In the current RCT, only 4 patients did not undergo 1-month follow up endoscopy after initial EUS-GBD. The other 27 patients underwent follow up per-oral cholecystoscopy with removal of gallstones. It is possible that the results of the current RCT cannot be replicated in clinical practice, if the follow-up endoscopy for removal of gallstones and LAMS is not routinely performed. Currently, there is no consensus on the need for removing the LAMS after the initial EUS-GBD procedure. Limited data is available on long-term outcomes of EUS-GBD. Few retrospective studies have reported that it is safe to leave the LAMS in place indefinitely (9,10). While some experts have recommended exchange of LAMS with double pigtail plastic stents (11), individual patients' risk of anesthesia for follow up endoscopy needs to considered instead of routine removal of LAMS in all patients who have undergone

EUS-GBD.

It is to be noted that the EUS-GBD in the current RCT was performed exclusively using LAMS with a cautery enhanced stent delivery system from a single manufacturer ((AXIOS, Boston Scientific Medical Corporation, Marlborough, USA). The cautery enhanced delivery system removes the need for dilation of puncture track and helps reduce the risk of adverse events (12). The wide caliber of LAMS also enables spontaneous passage of gallstones and direct cholecystoscopy in follow-up procedures for removal of gallstones. The safety profile of EUS-GBD in real life may not be similar to current RCT results if tubular stents or thinner caliber stents are used for EUS-GBD.

As the authors acknowledge, the RCT did not compare cost effectiveness between EUS-GBD and PT-GBD. Despite the higher cost of initial EUS-GBD procedure from dedicated devices and expertise, the authors suspect that it is more cost effective due to significantly lower number of re-interventions and re-admissions. A previous modeling study suggested that endoscopic GBD was more cost effective than PT-GBD because of shorter hospital stay and lower re-admission rates (13). However, further studies on cost effectiveness is needed prior to widespread change in clinical practice.

Given that LAMS are expensive, one could argue that ET-GBD with plastic stents is a cheaper endoscopic alternative to PT-GBD. However, in a recent meta-analysis by Krishnamoorthi and Jayaraj *et al.* (14), EUS-GBD was associated with higher technical, clinical success and lower rates of recurrent cholecystitis when compared to ET-GBD. ET-GBD may have a special role in patients with ascites, those needing ERCP for other reasons and who are potential future candidates for surgery. Another limitation of the current RCT is the lack of assessment of quality of life measurements. The authors state that they were unable to perform it, as the patients were old, fragile and could not comprehend questionnaires. While it might be challenging to obtain this data, it is needed before recommending widespread change in clinical practice.

While the recent RCT by Teoh *et al.* reports EUS-GBD as a superior approach compared to PT-GBD in management of AC in patients who are deemed high risk for surgery, we have not reached a point where EUS-GBD can replace PTGBD as the standard of care. At current time, EUS-GBD could be considered as first line approach for definitive treatment for AC in patients who will never be good surgical candidate for CCY in future and if expertise in therapeutic EUS is available. Further data are needed on long-term efficacy of EUS-GBD, safety of CCY after EUS-GBD and cost-effectiveness of EUS-GBD.

Acknowledgments

Footnote

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