TENSION trial to ExTENSION study: has extension decreased tension? Reply

Onnekink, A.M.; Hooft, J.E. van; Voermans, R.P.

term outcomes, and the gap of long-term effects have been comprehensively addressed by this study. However, there are a few points that need to be addressed for the sake of clarity:

- The article mentions the step-up approach both for surgery and endoscopy, which creates confusion in the mind of the reader. The usual accepted step-up approach is percutaneous drainage (PCD) → endoscopic therapy → surgery.[2] The study did not make a direct comparison of endoscopic vs surgery because individuals in the surgery group were initially treated with PCD and stepped up only if they did not respond to the treatment.
- Total length of hospital stay during overall follow-up did not differ statistically significantly between the endoscopy and surgery groups (median, 52 days [interquartile range, 27–94] vs median, 72 days [IQR, 50–112]; $P = .090$) even though it was longer in the surgery group than in the endoscopic group.
- Clinical and radiologic signs of a disrupted or disconnected pancreatic duct were present in all 8 patients with a new or persistent pancreaticocutaneous fistula after the initial 6-month follow-up. These fistulas resolved after endoscopic transluminal drainage (n = 6), transpapillary drainage with pancreatic duct stenting (n = 6), or percutaneous catheter drainage (n = 1). The trial does not mention a low-output fistula with disrupted pancreatic duct syndrome (DPDS) following acute necrotizing pancreatitis (ANP). The low-output fistula closed spontaneously in the majority of patients within 3 months, with good long-term outcomes.[3]
- After the initial 6-month follow-up, 23 patients (28%) experienced recurrent episodes of acute pancreatitis (8 patients [19%] in the endoscopy group and 15 patients [37%] in the surgery group; relative risk, 0.52; 95% confidence interval, 0.25–1.10). A total of 12 patients (52%) developed recurrent acute pancreatitis in the presence of a disrupted or disconnected pancreatic duct. The study used revised Atlanta criteria for recurrent pancreatitis; however, many of the patients had pancreatic WON and were on drain and thus would not qualify for recurrent pancreatitis as per recent definitions of recurrent pancreatitis.[4,5]
- The endoscopic step-up approach overall resulted in fewer pancreaticocutaneous fistulas, and after the initial 6-month follow-up, fewer reinterventions were needed. However, the percentage of DPDS was more in the surgery group than in the endoscopy group, which could be the reason for fewer reinterventions in the endoscopy group.[6]
- The number of patients with necrosis extending >5 cm down the paracolic gutter were 20 (39%) in the endoscopy group and 22 (47%) in the surgery group. The study does not specify the necrotic content of WON. Extended pancreatic WON and necrotic content of >40% of WON could be one of the reasons for the altered outcome of the endoscopy group.[6,7]
- Time of intervention since onset of symptoms was a median of 39 days for endoscopic group and 41 days for surgery group, reinforcing the findings of advantageous delayed drainage in the recently published POINTER trial.[8] However both the TENSION and POINTER trials could not produce statistically significant results, likely because of their flawed designs.

Finally, congratulations to Onnekink et al[1] for fulfilling a gap in the knowledge of the crucial management of infected pancreatic WON, which always creates tension for the treating physician. We need more multicenter, multinational studies with better designs and increased numbers of patients so that results become statistically significant and recommendations become decisive.

AVINASH TIWARI
Sher-i-Kashmir Institute of Medical Sciences
Soura, Srinagar, Jammu, and Kashmir, India

ALTAF SHAH
Gastroenterology Department
Sher-i-Kashmir Institute of Medical Sciences
Srinagar, Jammu, and Kashmir, India

JASWINDER SINGH
Gastroenterology Department
Sher-i-Kashmir Institute of Medical Sciences
Srinagar, Jammu, and Kashmir, India

References

1. Onnekink AM, et al. Gastroenterology 2022;163:712–722.e14.
2. van Santvoort HC, et al. N Engl J Med 2010;362:1491–1502.
3. Surinder Singh R, et al. Pancreatology 2020;20:177–181.
4. Guda NM, et al. Pancreas 2018;47:653–666.
5. Jagannath S, et al. Curr Treat Options Gastroenterol 2018;16:449–465.
6. Bezmarević M, et al. Visc Med 2019;35:91–96.
7. Rana SS, et al. Endosc Ultrasound 2014;3:118–122.
8. Boxhoorn L, et al. New Engl J Med 2021;385:1372–1381.

Conflicts of interest
The authors disclose no conflicts.

Most current article

https://doi.org/10.1053/j.gastro.2022.06.012

Reply. We thank Tiwari et al[1] for their letter regarding the recently published ExTENSION trial and would like to respond to the addressed points.

1. The minimally invasive surgical stepup approach indeed starts with percutaneous catheter drainage, only followed by video-assisted retroperitoneal

debridement when a patient clinically deteriorates. We, and other previous randomized controlled trials, used this definition as well, so we chose to remain consistent.[2,3]

2. It is correct that although not statistically significant, the median overall length of hospital stay was shorter in the endoscopy group. However, after the initial 6-month follow-up, most hospital admissions were not related to pancreatitis. During the initial 6-month follow-up of the TENSION trial, the hospital stay did differ in favor of the endoscopy group.

3. All pancreaticocutaneous fistulas mentioned in our study occurred or persisted for at least 6 months after infected necrotizing pancreatitis. These fistulas were all considered as complex and were therefore not expected to close spontaneously within 3 months.

4. We provided more details on the etiology and treatment of recurrent acute pancreatitis according to the revised Atlanta criteria in the supplementary apendix.[4] All cases of recurrent acute pancreatitis occurred as separate episodes with resolution of symptoms between episodes.[5] Of note, except for 1 patient, all patients did not have a drain in situ at the time of diagnosis of recurrent acute pancreatitis.

5. Because radiologic imaging was not routinely performed during long-term follow-up, asymptomatic disrupted or disconnected ducts (DPDSs) may have been missed, especially in patients with transluminal plastic stents in situ after endoscopic drainage. Although the consequences of DPDSs differed between the groups, we do not expect that the presence of a DPDS is influenced by either approach.

6. The extent of pancreatic necrosis was assessed by computed tomography (CT) scans and CT severity scores, and described in the original TENSION trial and supplementary appendix.[2] The extent of necrosis did not differ between the endoscopic and surgical stepup approach.

7. The ExTENSION trial focused on the long-term clinical outcomes of the TENSION trial after the endoscopic or surgical stepup approach. The timing of the initial intervention was therefore not the subject of investigation.

ANKE M. ONNEKINK
Department of Gastroenterology and Hepatology
Amsterdam University Medical Center
Amsterdam Gastroenterology, Endocrinology & Metabolism
Amsterdam, the Netherlands, *and*
Department of Gastroenterology and Hepatology
Leiden University Medical Center
Leiden, the Netherlands

JEANIN E. VAN HOOFT
Department of Gastroenterology and Hepatology
Leiden University Medical Center
Leiden, the Netherlands

ROGIER P. VOERMANS
Department of Gastroenterology and Hepatology
Amsterdam University Medical Center
Amsterdam Gastroenterology, Endocrinology & Metabolism
Amsterdam, the Netherlands

References

1. Tiwari, et al. Gastroenterology 2023;164:496–497.
2. van Brunschot S, et al. Lancet 2018;391:51–58.
3. van Santvoort HC, et al. N Engl J Med 2010; 362:1491–1502.
4. Banks PA, et al. Gut 2013;62:102–111.
5. Romagnuolo J, et al. Gastrointest Endosc 2008; 68:966–974.

Conflicts of interest
The authors disclose no conflicts.

Most current article

https://doi.org/10.1053/j.gastro.2022.10.017

Potential Effects of FGFR4 in the *Helicobacter pylori*–Induced Inflammatory Carcinoma Transformation

Dear Editors:

In the pathogenesis of gastric cancer, *Helicobacter pylori* infection was the most important risk factor for noncardia gastric cancer. Recently, the US Department of Health and Human Services had again identified *H pylori* as a human carcinogen in its *15th Report on Carcinogens*,[1] which has sparked global concern. However, the exact mechanism by which *H pylori* induces gastric carcinogenesis remains unclear. In their article in *Gastroenterology*, Zhang et al[2] found a link between *H pylori* infection, inflammation, and fibroblast growth factor (FGF) receptor 4 (FGFR4) activation, where SRC mediated a feed-forward activation loop between FGFR4 and signal transducer and activator of transcription 3 (STAT3) in response to *H pylori* infection. Different from the previous concept of *H pylori* carcinogenicity, a recent study[3] found that the survival time of gastric cancer patients with *H pylori* infection was longer than that for those without *H pylori* infection. Therefore, we want to highlight the possible shifting roles of *H pylori*–host interactions in gastritis cancer transformation.

Cytotoxin-associated antigen A gene product (CagA) is one of the most important virulence factors of *H pylori*.[4] CagA is injected into gastric epithelial cells via a type IV secretion system, triggering the activation of inflammatory signaling pathways.[5] It is well known that both *H pylori* strains (7.13