## **EDITORIAL**



## Comparing the Efficacy and Safety of Transpancreatic Sphincterotomy, Double-Guidewire, and Precut Techniques: Which One Makes the Cut?

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Difficult bile duct cannulation, a commonly encountered and exasperating situation for endoscopists, is often due to obstruction of the bile duct (BD) by an ampullary septum, separating the ducts, which results in repeated entry of the guidewire into the pancreatic duct (PD). Since the risk of post-ERCP pancreatitis (PEP) increases exponentially with repeat guidewire passages into PD [1], this occurrence may be prevented with the use of pancreatic guidewire-assisted methods, including single guidewire methods, the doubleguidewire (DGW) technique, and transpancreatic sphincterotomy (TPS) (Fig. 1), all of which may help facilitate BD cannulation in such situations. The limited literature that exists comparing these advanced cannulation techniques mostly includes underpowered studies. The authors Pecsi et al. [2], from Hungary, have previously performed a metaanalysis comparing the success and complication rates of TPS and needle-knife precut papillotomy (NKPP) in patients with difficult biliary access, suggesting the former to have higher success with cannulation and lower bleeding, PEP rates.

Goff [3] first described 5–7 mm TPS with an overall success rate of up to 97.5%, although subsequent studies described varied success and complication rates, likely reflecting differences in the technique. The key, however, for successful immediate biliary access with TPS appears to be creation of a large TPS during the first attempt. This complete unroofing of the papilla facilitates biliary cannulation with no significant increase in reported perforation rates. Although the incidence of post-TPS bleeding ranges from 3 to 5% [4], much higher rates (close to 15%) were reported from centers with a smaller case volume. Severe post-TPS bleeding, though rare, appears to be through incision of an

aberrant retroduodenal artery but was unrelated to the length of TPS. PEP incidence in the setting of TPS ranges from 5 to 21% in the absence of PD stent prophylaxis but can be reduced to 3.5% with PD stenting [3].

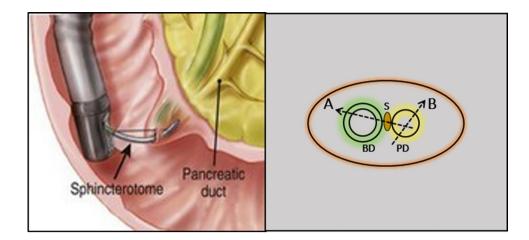
In this issue of Digestive Diseases and Sciences, the authors Pécsi et al. [5] report the results from an expanded meta-analysis now comparing TPS to needle-knife precut papillotomy (NKPP), needle-knife fistulotomy (NKF), and DGW techniques. A total of 14 studies were incorporated into the meta-analysis that were of heterogeneous design including randomized controlled trials (RCTs) and prospective, retrospective cohort studies. Comparison of the cannulation success rates, TPS had higher success when compared to DGW (OR 2.72; 95% CI 1.30-5.69) and NKPP (OR 2.32; 95% CI 1.37), but was not significantly different when compared to NKF (OR 1.38; 95% CI 0.32-5.96). TPS had high overall cannulation success rate of 89.7%, which remained consistent even in the subgroup analysis including only RCTs, at 91.7%. Surprisingly, although there were no significant differences in the PEP rates between TPS and DGW or NKPP, the PEP rate was higher with TPS when compared to NKF (11.5% vs 2.1%, respectively). Moreover, the post-procedural bleeding and perforation rates were not significantly different between the techniques compared.

The authors are to be commended on this exhaustive systematic review with meta-analyses for each of the outcomes of interest as well as the multiple subgroup-based sensitivity analyses. Furthermore, the authors discussed the potential benefits of TPS due to superior control with the depth of cutting compared with the freehand precut techniques and also the ability to place a prophylactic PD stent after sphincterotomy. The results, however, need to be interpreted with caution due to the inherent statistical and design limitations inherent in the literature available for this systematic review and also due to the observation that the choice of suitable technique used to overcome difficult biliary cannulation often varies by anatomy, experience of the endoscopist,

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**Fig. 1** Transpancreatic sphincterotomy (A) from pancreatic duct (PD) into bile duct (BD), passing through the septum (S) and pancreatic sphincterotomy (B). (Reproduced by permission of Division of Gastroenterology and Hepatology, Johns Hopkins Hospital)



and the resources available rather than the "one size fits all" approach.

In this study, the authors have included RCTs, prospective, retrospective cohort studies, and abstracts in the metaanalysis, rather than using RCTs alone, the latter which is considered the "gold standard" in evidence-based medicine, designed to minimize the risk of bias. This may potentially compromise the validity of results as confounding factors such as prophylactic PD stent, difficulty of cannulation, or number of guidewire passes into the PD, e.g., cannot be assessed due to the missing information [6]. This information is especially important for comparative effectiveness research involving TPS, which is an independent risk factor for PEP [7]. That being said, inclusion of "real-world" evidence from non-randomized studies which are more likely to reflect clinical practice in real life, avoiding the strict exclusion criteria of RCTs, may increase precision and generalizability of the results while enhancing the decision-making process. In such situations, where data from observational studies are incorporated to complement RCTs, it is recommended to synthesize the results separately with sensitivity and subgroup analyses, which the authors have performed [8].

One concerning aspect of transpancreatic septotomy, a component of TPS, is the mixing of biliary and pancreatic juices due to fluctuating BD and PD sphincter pressures [9]. The toxic effects of bile acids and changes in pH from biliary influx on the pancreatic ductal lining and acinar cells are well described in the pre-clinical translational literature [10]; indeed, similar toxic effects with the development PD strictures and chronic pancreatitis have been described in human studies [11]. Though the authors attempted analyzing the long-term effects of TPS in this study, the results are limited as it was seldom reported in the source literature. One can suspect that performing pancreatic sphincterotomy (Fig. 1) along with TPS may potentially reduce bile acid toxicity in the PD, facilitating superior flow of pancreatic juices in the long run, although this remains conjectural. We agree with

Kozarek [11] that the type of precut or advanced cannulation technique to be applied may be "institutionally dependent, contingent upon proper performance, relative skill set" and that a percutaneous trans-hepatic biliary or endoscopic ultrasound-facilitated rendezvous procedure may be safer and more effective, especially in the setting of variant anatomy.

TPS may potentially be more effective and safer than other advanced cannulation techniques in the setting of difficult biliary cannulation. Yet, due to the methodological limitations in this meta-analysis owing to the inability to comprehensively assess bias due to the multiple confounding factors and limited follow-up, this conclusion cannot be conclusively recommended as yet. Prospective studies evaluating TPS with long-term follow-up, also including prophylactic PD stent and/or the use of NSAID prophylaxis, are needed.

## **Compliance with Ethical Standards**

**Conflict of interest** The authors declare that they have no conflict of interest.

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