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**Editorial Title: Time to come inside? A novel approach to anastomotic biliary strictures.**

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Liver transplantation is the definitive management for patients with decompensated cirrhosis and/or liver malignancy. Two types of liver transplantation are traditionally performed including deceased donor liver transplantation (DDLT) and living donor liver transplantation (LDLT), the latter of which involves a partial liver from a live donor and is a response to the limited resource of donor livers. In LDLT, the biliary anastomosis can be accomplished by a Roux-en-Y hepaticojejunostomy or a duct-to-duct biliary reconstruction. Biliary strictures, which typically occur at the anastomosis, are known complications of both methods but occur more commonly in LDLT. While the duct-to-duct biliary anastomosis provides normal enteric anatomy and ease of endoscopic access, the anastomosis is more peripheral and angulated, and thus management strategies and outcomes have generally been studied separately from DDLT[1].

Standard treatment of these strictures is performed by endoscopic retrograde cholangiopancreatography (ERCP) and traditionally includes biliary sphincterotomy, dilation, and placement of transpapillary plastic and/or self-expandable metal stents (SEMS) either alone or in combination[1]. Biliary sphincterotomy is implemented for the treatment and palliation of a wide spectrum of biliary and papillary diseases. This intervention also helps facilitate subsequent biliary interventions and potentially decreases the risk of post-ERCP pancreatitis when performed prior to biliary stent placement[2]. However, it does not come without risk. While intra-procedural risks such as bleeding and perforation are well described, the creation of a sphincterotomy also disrupts the inherent sphincter function, potentially leading to increased

duodenobiliary reflux and contributing to both stent occlusion and ascending cholangitis[1,3]. Transpapillary stenting similarly disrupts the sphincter function. In patients with anastomotic biliary strictures, placement of the multiple plastic stents is common practice and leads to high rates of stricture resolution[4]. However, the development of ascending cholangitis with this approach is significant, with a systematic review confirming an incidence of 19% in LDLT[5].

In this issue of *Liver Transplantation*, Nishikawa et al. describe a single center, observational, retrospective study investigating novel inside the bile duct stents ("inside-stents") for anastomotic biliary strictures following LDLT[6]. The inside-stents are plastic stents that are placed above the Sphincter of Oddi (i.e. not transpapillary), obviating the need for sphincterotomy and theoretically decreasing this risk of duodenobiliary reflux[1,3]. While transpapillary stents can be placed without sphincterotomy[7], the technique described in the current manuscript theoretically preserves the function of the sphincter entirely, both while the stent is in place and following removal upon stricture resolution. These stents were predominantly self-made until 2017 when commercially available stents became available[6].

Throughout the study period, inside-stents were successfully placed in 112/136 (82.4%) patients with anastomotic biliary strictures. Nineteen patients were excluded, leaving 93 patients who underwent inside-stenting. Stent exchanges were performed every six months, as needed. 88/93 (94.6%) patients had initial stricture resolution, and 70/93 (79.5%) had persistent resolution after median follow-up of 7.5 years. 17/18 patients with re-stenosis had new inside-stents placed with eventual resolution. Only five (5.3%) patients developed cholangitis during the study period[6].

The work by Nishikawa et al. reports a novel approach to the treatment of anastomotic biliary strictures with placement of inside-stents, and nicely highlights several advantages of this technique. Acceptable rates of stricture resolution were achieved using this strategy, and stent exchanges were only required every six months. Typically, transpapillary plastic biliary stents have a maximum dwell time of only three months given their propensity to become occluded and cause ascending cholangitis. The longer dwell time and low cholangitis rates with inside-stents

further support the possibility that non-transpapillary stenting without biliary sphincterotomy may in fact be mitigating duodenobiliary reflux and reducing stent occlusion and cholangitis. Additionally, this strategy may be cost saving given fewer required ERCPs and fewer interventions during each ERCP. The inside-stents also had a lower migration rate, allowing for safer stenting of smaller intrahepatic bile ducts where SEMS cannot be used routinely[6].

The exciting results presented in this manuscript will certainly guide future work in this area. To demonstrate true superiority of inside-stents in the treatment of anastomotic biliary strictures, this approach should be compared with conventional technique in a prospective randomized controlled trial. A study like this could also control for the presence or absence of sphincterotomy in the development of ascending cholangitis or recurrent biliary obstruction in this patient population. Moreover, the commercialization of an inside-stent has precluded the need for self-made stents which were used during most of the observation period[6]. A commercialized stent would be more generalizable to the majority of practice settings, and should be used in research moving forward.

In conclusion, Nishikawa et al. describe an exciting and emerging approach using inside-stents which obviate the need for a sphincterotomy or a transpapillary stent. These authors demonstrate low rates of ascending cholangitis with acceptable rates of stricture resolution[6]. Prospective studies comparing inside-stents using commercially available products with conventional management will be informative to determine whether this approach should be considered first-line in the management of anastomotic biliary strictures.

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