EDITORIAL

Management of post-liver-transplant biliary strictures: a work in progress

More than 80,000 liver transplantations have been performed in the United States since 1988, and the overall long-term survival rate has been favorable.[1,2] Unfortunately, biliary complications occur in 11% to 38% of orthotopic liver transplant (OLT) recipients, threatening the viability of the graft.[3-5] Specifically, biliary strictures are the most frequently described complication, occurring in 4% to 13% of patients after OLT surgery.[3-5]

The 2 biliary anastomoses performed during OLT surgery in the United States are choledochocholedochostomy (CC) and Roux-en-Y choledochojejunostomy (CDJ), with CC being the preferred method. However, patients diagnosed with extrahepatic biliary diseases such as primary sclerosing cholangitis or cholangiocarcinoma and children with biliary atresia routinely undergo Roux-en-Y CDJ. Marked size disparity between donor and recipient bile ducts favors Roux-en-Y CDJ as well.[3,6]

Posttransplantation strictures are categorized as either anastomotic or nonanastomotic.[3-5] Hepatic artery thrombosis and prolonged graft cold ischemia time lead to nonanastomotic stricture formation from inadequate perfusion of the donor liver.[7] Blood type incompatability, chronic rejection, recurrent disease, and cytomegalovirus infection are other causes of nonanastomotic strictures.[8-11] Technical problems are the most frequent cause of anastomotic strictures, which comprise up to 85% of biliary strictures diagnosed after liver transplantation.[12-14]

In the early days of OLT, surgical revision of bile duct anastomoses was the preferred approach to treatment of biliary complications,[3] whereas more severe complications would frequently require retransplantation. T-tube insertion during creation of the biliary anastomosis was commonly performed in an attempt to prevent strictures.[3] Randomized studies comparing transplantations performed with a T-tube to those without a T-tube found no difference in stricture development. Higher complication rates, however, were noted within the T-tube groups.[15-17] Construction of biliary anastomoses over an internal stent was a less commonly performed prophylactic measure, but multiple complications, including leaks, obstruction, hemobilia, and death,[3] led to the discontinuation of this practice.

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During the late 1980s, interventions with percutaneous transhepatic cholangiography (PTC) or endoscopic retrograde cholangiography (ERC) became alternatives to surgical treatment of posttransplant biliary complications. Good success rates have been reported with use of PTC-guided balloon dilation of biliary strictures with subsequent placement of a catheter or stent across the stricture.[18-20] Although PTC is a useful intervention and preferred for patients with Roux-en-Y CDJ, the procedure is associated with significant risks. Transhepatic access can result in postprocedural pain, excessive bleeding, and iatrogenic bile leaks.[21] Treatment of a stricture by PTC requires leaving a catheter in place, which may result in infection, catheter displacement, and patient discomfort.[21]

The success rates of ERC support an endoscopic approach as the first-line treatment of posttransplantation anastomotic strictures, although its long-term impact on morbidity and mortality has not been fully established.

The application of ERC is ideal for those patients with CC because of the accessibility of the common bile duct through the duodenum. Although technically challenging, performance of ERC in patients with Roux-en-Y CDJ by experienced endoscopists can also result in successful resolution of biliary complications after liver transplantation.[22]

Results of studies using ERC-guided dilation and stenting vary widely.[5,23-27] Reports of lower success rates have been associated with more conservative forms of endoscopic therapy.[28] Studies comparing ERC with dilation alone with ERC with dilation and stent placement have concluded that serial dilation with stent placement leads to higher success rates (41% vs 75%).[28,29] Complications of ERC including pancreatitis, bleeding, stent migration, bile leaks, and infection have been reportedly low in prior studies (2%-6%).[23-27,30,31] Favorable outcomes have also been reported in a small series using multiple stents for post-OLT anastomotic strictures.[25] The deployment of multiple stents should result in a reduced risk of cholangitis from stent clogging or migration.

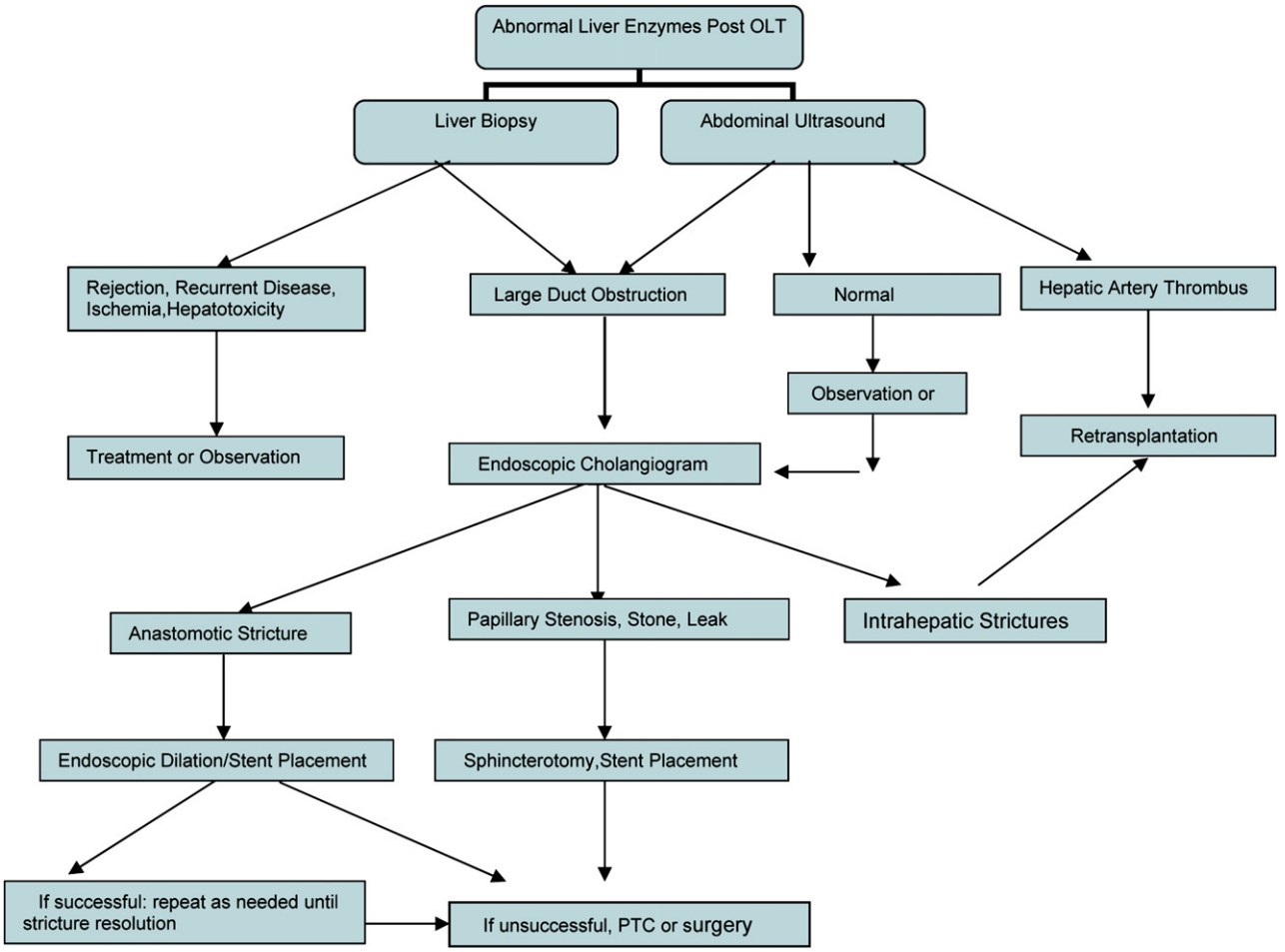

Figure 1. Proposed management of abnormal liver enzyme levels after liver transplantation.

The success rates of ERC support an endoscopic approach as the first-line treatment of post-OLT anastomotic strictures,[5,23-27] although its long-term impact on morbidity and mortality rates has not been fully established. Many of the studies cited have been retrospective; the few published prospective trials are limited by either small sample size or patient heterogeneity.[26,27] To date, no prospective, multicenter, randomized trial designed to determine the optimal management of anastomotic strictures after liver transplantation has been reported.

In this month's issue of *Gastrointestinal Endoscopy*, Morelli et al[32] performed a single-center, prospective study in which OLT patients with anastomotic biliary strictures were treated by ERC. The authors used a rapid sequential stent insertion protocol. Patients with nonanastomotic strictures and intrahepatic biliary strictures were excluded. Initial ERC was performed with dilation of the stricture and subsequent stent placement. The number of plastic stents placed was determined by the size of balloon dilation performed. Balloon dilations to 4 mm were treated with a single 10F plastic stent. Stricture dilations to 6 mm were treated with 2 10F plastic stents. Dilations to 8 mm received 3 10F plastic stents and dilations to 10 mm received either 4 or 5 10F plastic stents. The stents were removed and repeat dilation with stenting was performed 2 weeks after the initial intervention. If a narrowing, or ''waist,'' was no longer appreciated in the stricture at the time of dilation, maximal dilation was considered achieved. At this point, stenting according to protocol was performed. After 3 months, all stents were removed and the stricture was re-evaluated.

Short-term success was defined as stricture resolution after the 3-month period of stenting. Successful dilations were then monitored for evidence of stricture recurrence by monthly laboratory tests and regular transplant clinic visits. Long-term success was achieved if no subsequent interventional procedures were necessary.

The study was performed from January 2003 to December 2005, during which time 236 adult patients received a deceased donor liver transplant. Ninety patients underwent ERC for suspicion of biliary tract conditions and 58 (64%) had demonstrable abnormalities. Of these 58 patients, 38 (66%) were found to have anastomotic strictures and were enrolled in the study. Three had concomitant stones and one had an associated bile leak. Short-term success was 100%, and the mean follow-up time was 1 year. Five (13%) long-term failures occurred, with a mean recurrence