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Results of endoscopic management of anastomotic biliary strictures after orthotopic liver transplantation

Karaciğer nakli sonrası ortaya çıkan bilyer anastomoz darlıklarının endoskopik tedavisinin sonuçları

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Background/aims: *Anastomotic biliary strictures are common biliary complications after orthotopic liver transplantation. We assessed the success of endoscopic retrograde cholangio-pancreaticography (ERCP) in the treatment and outcome of post-liver transplantation anastomotic biliary strictures in a university hospital, retrospectively.* ***Methods:*** *Thirty-three ERCPs were performed in 20 of 162 adult liver transplant recipients with duct to duct anastomosis.* ***Results:*** *In five patients, ERCP failed because the stricture could not be passed with guidewire. Four patients were treated with balloon dilatation only; two of them are recurrence-free with a follow-up of 24 and 8 months. Eleven patients had balloon dilatation and plastic stent placement as their primary treatment modality. In six of them, the anastomosis remained patent for the rest of the follow-up (22 ± 13 months). Five patients had stricture recurrence after first stenting which necessitated re-stenting; four of them required a third, and three had a fourth stenting.* ***Conclusions:*** *Endoscopic balloon dilatation and stenting are safe and effective means of treatment of anastomotic biliary strictures following liver transplantation.*

Key words: Liver transplantation, anastomotic biliary strictures, endoscopic retrograde cholangiography, plastic stent, balloon dilatation

Amaç: *Anastomoz bilyer darlıkları karaciğer nakli sonrası sıklıkla ortaya çıkabilen komplikasyonlardır. Karaciğer nakli sonrası ortaya çıkan anastomoz bilyer darlıklarının tedavisinde ERCP'nin başarısını değerlendirdik.* ***Yöntem:*** *İkiyüzonaltı karaciğer nakli hastasının 20'sinde 32 ERCP uygulandı.* ***Bulgular:*** *Hastaların beşinde darlığın kılavuz ile geçilememesi nedeniyle ERCP başarısız olmuştur. Hastaların dördü sadece balon dilatasyonu ile tedavi edilirken bunlardan ikisi 24 ve 8 aydır nükssüz olarak takip edilmektedir. Sekiz hastaya primer tedavi olarak balon dilatasyonu ile beraber plastik stent uygulanması yapılmıştır. Bunların altısında, takibin geri kalanında (22±13 ay) anastomoz açık kalmıştır. Beşinde ilk stentleme sonrası darlık nüks etmiş ve tekrar stentleme gerekirken, dördünde üçüncü stentleme ve üçünde dördüncü stentleme ihtiyacı olmuştur.* ***Sonuç:*** *Endoskopik balon dilatasyonu ve stentleme karaciğer nakli sonrası ortaya çıkan anastomoz bilyer darlıklarının tedavisinde etkili ve güvenli bir yoldur.*

Anahtar kelimeler: Karaciğer nakli, anastomoz bilyer darlıkları, endoskopik retrograd kolanjiyografi, plastik stent, balon dilatasyonu

INTRODUCTION

Biliary complications are a substantial cause of morbidity and mortality in adult liver transplantation (LT) recipients, ranging from 11.5% to 34% (1, 2, 3). Bile leaks and strictures constitute biliary complications with strictures at the anastomosis the most prevalent form.

Duct to duct (D-D) and duct to Roux loop (D-R) are the two standard drainage procedures. When donor and recipient ducts are of sufficient diameter and length, D-D reconstruction is commonly performed. If ducts are too small or of insufficient length, or have discrepancies in caliber, a D-R reconstruction is preferred (4). When the biliary drainage is accomplished with Roux-en-Y anastomosis, endoscopic access may become difficult or impossible. Percutaneous transhepatic techniques are the alternative for endoscopic treatment of anastomotic biliary strictures, and operative intervention is the last resort for the management of biliary complications. Fortunately, the reconstruction of the common bile duct is mostly performed by end-to-end choledochocholedochostomy, which permits endoscopic intervention in biliary complications.

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Most series for the treatment of anastomotic biliary strictures are suggestive of endoscopic therapy as the primary intervention, but percutaneous (5) therapy results are also comparable to those of endoscopic therapy (6). The aim of this retrospective study was to investigate the outcomes of endoscopic therapy in the management of anastomotic biliary strictures following LT.

METHODS

Between July 1998 and April 2004, 216 consecutive adult LTs were performed in our center. One hundred twenty-two were from living donors and 94 were cadaveric transplantations. All but eight of the cadaverics who had sclerosing cholangitis had D-D choledochal anastomosis, while of the 122 living donor transplantations, 76 had D-D anastomosis. Those with D-D anastomosis (86 cadaveric, 76 living donor) were included in the study.

The definition of anastomotic biliary stricture was cholestatic liver enzyme abnormality or suspected cholangitis accompanied by focal narrowing at the anastomosis at endoscopic retrograde cholangiography (ERC) or magnetic resonance cholangiopancreaticography (MRCP), and the same definition was applied after the intervention (balloon or stent). Liver biopsy and Doppler ultrasound (US) were performed to exclude rejection or other parenchymal diseases and arterial thrombosis, respectively, when necessary. The records of cases were investigated for pretransplant diagnosis, recipient age, presence of bile leak or stone, cytomegalovirus infection, laboratory features, time of diagnosis of stricture after LT, use of post-operative T-tube, prior cholecystectomy, its management and complications, and final outcome.

Endoscopic therapy was performed using balloon dilatation (Maxforce, Boston Scientific, Microvasive) with or without biliary stenting. The balloon size was determined by the endoscopist based on the caliber of the non-dilated distal or native duct (min.: 4 mm, max.: 10 mm), and at each treatment two balloon sizes were used after which no bile leaks secondary to dilatation occurred. The balloon was kept inflated for 30 to 45 seconds. The endoscopist also choose the length and number of the10 F Amsterdam type plastic stents. Stents were not allowed to remain more than three months in the biliary tract, and if necessary another stent(s) was inserted for the next three months. For the initial three-month period, one stent was used; however, an increasing number of stents (up to 4) were used for the subsequent interventions. When endoscopic retrograde cholangiopancreaticography (ERCP) failed, percutaneous transhepatic intervention or surgery was used in the management of anastomotic strictures. Success of ERCP for anastomotic biliary strictures was defined as improvement of liver function tests without the need for another treatment. Because the severity of the stricture could not be graded, therapy results could not be related to the severity of the stricture.

A single endoscopist performed all of the procedures. Cholangitis was defined as fever or leukocytosis with an increase in cholestatic liver enzymes. None of the patients had follow-up cholangiographic imaging unless they presented with cholestasis or cholangitis. Primary patency was the period between the initial intervention and second intervention or end of follow-up.

Results are given as mean ± SD, and Mann-Whitney U test was used when appropriate. SPSS statistical package (SPSS software, PC version 10.01; SPSS, Chicago, IL) was used for statistical analyses.

RESULTS

Anastomotic biliary strictures were encountered in 20 (12%) of the 162 adult LT patients who had D-D anastomosis. This complication was more common in cadaverics [15% (13/86)] than from living donor transplantations [9% (7/76)].

The median age was 42 years (range 17 to 60 years). LT indications included cirrhosis due to hepatitis B virus (HBV) (n:10), Wilson (n:4), hepatitis C virus (HCV) (n:4), and alcohol (n:2). Eleven of them had cadaveric LT and nine had received livers from living donors.

Twenty patients underwent 33 ERCPs for post liver transplant anastomotic strictures. Only one of the patients had prior magnetic resonance cholangiography (MRC) which demonstrated the anastomotic stricture. None of the patients had concurrent non-anastomotic stricture. Five patients had accompanying stones, and another two had concomitant bile leak. Fourteen (70%) patients were male and six (30%) female.

Cholestasis and/or cholangitis demonstrated by laboratory and radiologic findings led to ERCP after a mean of 13 ± 17 months after transplantation. Post-procedure follow-up averaged 20±10 months.

In five cases, the stricture could not be passed with the guidewire; one of them underwent surgical intervention, and the other four had percutaneous intervention.

Of the 15 patients in whom ERCP could be performed, all underwent a sphincterotomy during the initial procedure.

Four patients had balloon dilatation only at the beginning. Two of them required no further treatment for the anastomotic stricture with follow-ups of 10 and 22 months. In the other two, one required a stent insertion for a three-month period and no further problem occurred; the second had conversion to Roux-en-Y choledochojejunostomy because of recurrence of the stricture eight months after the dilatation.

Eleven patients had balloon dilatation plus biliary stenting as the initial intervention. Six of them did not require any further treatment with a median follow-up of 22 months (range 3 to 34 months), after removal of their stents in three months. Five patients needed re-stenting(s) within a mean time of three months because of either cholangitis or cholestasis. One had 2, one had 3, and three patients had 4 stentings. All but one were recurrence-free with a median follow-up of 11 (range 3 to 24 months) months. Number of stents used per intervention was 1.93. Figures 1, 2 and 3 depict the anastomotic stricture, balloon dilatation of the same anastomotic stricture, and a solitary stent at the same stricture, respectively.

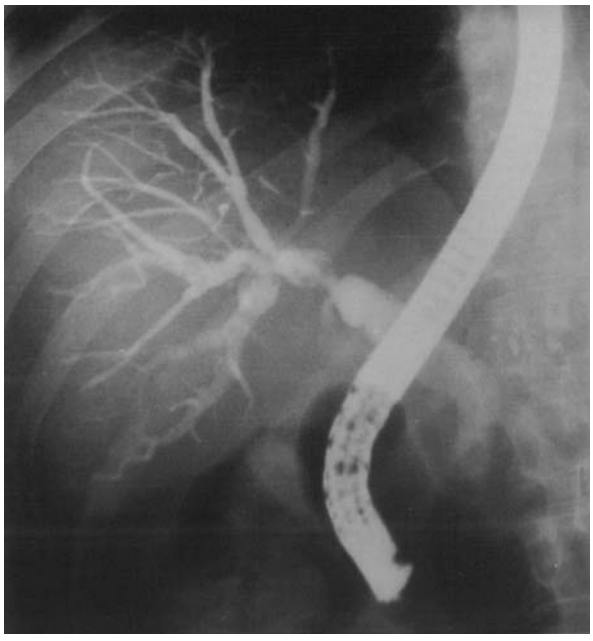

Figure 1. Endoscopic retrograde cholangiographic view of an anastomotic stricture

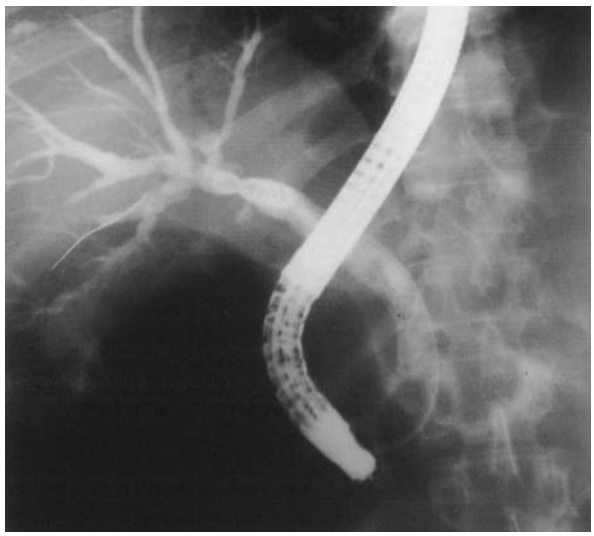

Figure 2. Endoscopic retrograde cholangiographic view of balloon dilatation of an anastomotic stricture

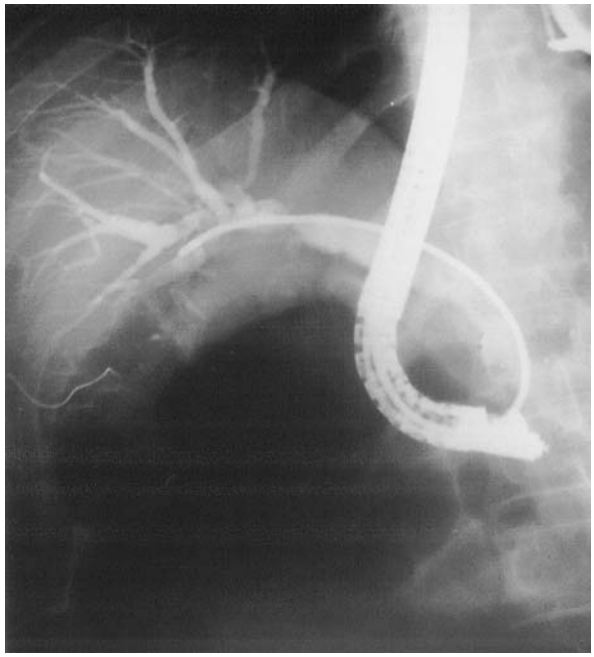

Figure 3. Endoscopic retrograde cholangiographic view of a solitary stent at an anastomotic stricture

In patients with balloon dilatation and plastic stent, the primary patency rates (for the initial intervention) at 3, 6 and 12 months of treatment were 93%, 80%, and 60%, respectively. Overall, four

cases of post-ERCP cholangitis were observed; three of them resolved with parenteral antibiotics. One of the patients died from recurrence of frequent cholangitis and biliary sepsis episodes (he was one of those who underwent 4 restentings). None of our patients had hepatic artery thrombosis, ABO incompatibility, or cytomegalovirus (CMV) infection, which are accepted as independent risk factors for occurrence of biliary strictures. The number of patients with and without T-tube after the early transplant period was equal in patients with anastomotic strictures, and none of our patients had prior cholecystectomy. The mean cold ischemia time of the cadaveric transplant patients having anastomotic biliary strictures was 9.5±2.7 hours, which was not significantly different from our whole cadaveric transplant population's cold ischemia time (8.5±3.4).

DISCUSSION

Biliary strictures are classified into two groups. One is anastomotic and the other is non-anastomotic. The morbidity, mortality, and outcome of the non-anastomotic strictures are worse than in anastomotic strictures (7). For clarity, we included only the patients with anastomotic strictures in this article.

In the recently published studies, anastomotic biliary strictures were reported to range from 7% to14% in patients with orthotopic LT (8, 9). The incidence of anastomotic biliary strictures in living donor LT is reported to be higher, with an incidence of 27% (10). In our series this complication occurred in 20 of 162 adult orthotopic liver transplant patients (12%) with D-D biliary anastomosis. Anastomotic biliary stricture incidence was similar in both groups of recipients, with their grafts from cadaveric [15% (13/86)] and living donor [9% (7/76)].

For the initial treatment of biliary complications, percutaneous transhepatic and endoscopic retrograde interventions are popular means of management; surgery is generally employed as the last resort because of its morbidity.

In our series, balloon dilatation alone was successful in 50% of the patients (2 of 4). This is well-matched with the results of Schwartz et al. (11), who reported failure of balloon dilatation in 53% of the patients with anastomotic strictures. However, Mahajani et al. (7) reported 79% (23 of 29) success rate of one or more balloon dilatations for anastomotic strictures.

In endoscopic therapies of anastomotic biliary strictures, there is no controlled study comparing the efficacy of the balloon dilatation alone with dilatation and stent treatment, but it is suggested that balloon dilatation alone is not as satisfactory as biliary stenting (15).

Ninty-one percent of the patients (10 of 11) in whom the stricture could be passed with guidewire were successfully treated with balloon dilatation plus stent placement in our series. After one year of biliary stenting in anastomotic strictures, Rossi et al. (8) reported 83% success for an additional one year patency rate. Three other studies reported 90% one year patency rate in patients treated with dilatation and stenting together for anastomotic biliary strictures (12-14). We propose the employment of biliary stenting instead of balloon dilatation only.

An alternative for endoscopic management of biliary strictures is percutaneous transhepatic intervention, and it is the only non-surgical procedure for biliary access after Roux-en-Y anastomosis. Roumilhac et al. (5) reported 57% recurrence-free follow-up of a mean period of 61 months after percutaneous balloon dilatation for anastomotic biliary stricture. The same group reported 58% primary patency rate (without any additional intervention) with metallic expandable stent placement for anastomotic biliary strictures. In the study of Kuo et al. (16) comparable results were reported for percutaneous and endoscopic approaches. However, a substantial number of infectious and procedure-related complications (such as subcapsular hematoma, bleeding, or hemobilia, and acute pancreatitis) and recurrent bile duct obstruction related to mucosal proliferation between metal wires were encountered in this study (17). In comparison with the results of those percutaneous studies, in our series, primary patency rate for biliary stenting (plastic) of anastomotic strictures was similar (54%); however, we experienced almost no other complication.

In conclusion, endoscopic management of anastomotic biliary strictures after orthotopic LT (both cadaveric and living donor) is a safe approach which avoids surgery. In our opinion, balloon dilatation as a sole treatment is not sufficient; biliary stent must be used as an initial treatment.

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