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Endoscopic versus surgical management of biliary complications – Outcome analysis after 1188 orthotopic liver transplantations

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ABSTRACT

Background and aim: After liver transplantation, the endoscopic approach has become the standard treatment modality for biliary complications. Aim of this study was to compare primary endoscopic with primary surgical management.

Patients and methods: A retrospective review on 1188 consecutive liver transplant patients between 1989 and 2009 was performed. Management strategies (endoscopic, surgical or combined approach) were evaluated for treatment success as well as patient survival.

Results: Biliary complications after liver transplantation were diagnosed in 211 (18%) patients.

Initial endoscopic approach ($N = 162$, 77%) was successful in 97 of 162 (60%) patients. In 80% of patients, success was achieved within a median of four ERCPs.

Sixty-one patients (38%) were referred to surgery after non-successful ERCP.

Initial surgical approach was performed in 49/211 patients (23%) with successful management in 38/49 (78%) of patients.

Patients presenting with intraluminal objects needed a significantly higher number of ERCPs to reach treatment success (median 3 versus 2 interventions, $p = 0.001$) but had an equal endoscopic success rate ($p = 0.427$).

Patients with successful endoscopic treatment showed lower mortality compared to patients with primary surgical treatment ($p = 0.029$).

Conclusions: Endoscopic management should be considered as the primary approach for biliary complications after liver transplantation.

1. Introduction

Despite the advancements in organ procurement, immunosuppression and transplantation technique, biliary complications (BC) remain a frequent cause of morbidity after orthotopic liver transplantation (oLT). In previous studies the rate of BC after oLT were reported to be between eight and 30% [1–5].

Biliary complications include leaks, anastomotic strictures (AS) or non-anastomotic (NAS) strictures, complicated by stones, cast or debris. In some cases patients might develop more than one complication [6–9].

Over the last two decades, endoscopic retrograde cholangiopancreatography (ERCP) has emerged to the gold standard for diagnosis and treatment of BC after oLT [7,9–12] despite low grade evidence. Limited data is available comparing a primary endoscopic versus primary surgical treatment approach for BC. With endoscopy biliary leaks can be sealed by bile-duct stenting, anastomotic strictures are treated by dilatation and temporary stent placement, non-anastomotic strictures are treated by stents, stones or debris can be removed in many patients [13]. Nevertheless in some cases ERCP might not result in a definitive treatment for patients presenting with biliary concrements or strictures [14–16] resulting in multiple endoscopic re-interventions. Furthermore, long-term follow-up data on outcomes and complications after ERCP in liver transplant patients is scarce [17].

Surgical therapy of BC after oLT is reported as primary intervention and as secondary approach after endoscopic intervention.

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Surgical treatment consists of simple bile duct revision with or without placement of a T-Tube for leaks, choledochojejunostomy and hepaticojejunostomy [18,19].

The aim of this study is to evaluate the primary endoscopic, primary surgical or combined approach for treatment of biliary complications after oLT in terms of success rate, postoperative/post-interventional complications and survival.

2. Patients and methods

The study population consisted of all patients who underwent liver transplantations at the Medical University of Vienna between 1989 and 2009. Data were prospectively collected in the transplant surgery database of the Medical University Vienna and analyzed retrospectively. Parameters included baseline demographic data, indication for liver transplantation, age at oLT, time from oLT to diagnosis of BC, type of BC, type of intervention, number of interventions required for success, intervention related complications, standard liver function tests including bilirubin, gamma GT and AP before intervention and one month after intervention. Donor related factors included donor age, cold ischemia time (CIT) and type of perfusion. Patients under the age of 18, as well as patients receiving a split liver graft and patients receiving re-transplantation were excluded. This study was approved and registered by the Ethics-Committee of the Medical University of Vienna (research ethics reference 354/2010).

2.1. Classification of biliary complications

Biliary complications were defined as morbidity related to the reconstructed biliary tract requiring endoscopic or surgical intervention.

All ERCPs performed were reviewed by an independent gastroenterologist. In all surgical cases operative notes were reviewed.

Biliary complications were classified as follows:

- Strictures involving the donor common bile duct or bifurcation, not related to the anastomosis in presence of a patent hepatic artery – non anastomotic strictures, NAS
- Strictures of the biliary anastomosis – anastomotic strictures, AS
- leakage of the reconstructed biliary system – LEAK

Presence of bile duct stones, cast or sludge was classified as intraluminal obstruction (ILO) – with or without relation to NAS, AS or LEAK.

If more than one complication was present, combinations were recorded as separate entities.

Successful intervention (either endoscopic or surgical) was defined as permanent reduction of bilirubin, gamma glutamyltransferase and alkaline phosphatase within one month after intervention, and not requiring further endoscopic, percutaneous procedures or surgery/re-transplantation. In contrast to previous studies patients receiving even more than four endoscopic interventions were considered successful, if above criteria were met [6].

2.2. Surgical technique for oLT

Orthotopic liver transplantation was performed using hepatectomy with cavo-caval resection. Generally no veno-venous bypass was performed.

Biliary anastomosis was performed as choledocho-choledochostomy using a running PDS 6×0 suture. T-tubes were used in few selected cases based at the surgeons discretion.

2.3. Primary immunosuppression

The primary immunosuppressive regimen consisted of antithymocyte globulin (ATG) induction for three days with delayed introduction of calcineurin inhibitors (CNI) as published before [20].

2.4. ERCP

Endoscopic retrograde cholangiopancreatography in this cohort was performed by experienced (>400 ERCPs performed) endoscopists only. All patients were investigated either under sedation with midazolam, propofol and nalbuphine or were put under general anesthesia for the procedure.

In all cases a therapeutic side view endoscope (Olympus TJF 160, Olympus, Japan) was used.

In case of stones or cast, removal was performed with stone extraction baskets (Flower basket, Olympus, Japan) and extraction balloons (Extraction Retrieval, Boston Scientific, USA), In case of anastomotic or non-anastomotic strictures, dilation with a balloon dilator (Hurricane Rx, Boston Scientific, USA) was performed.

In case of leakage or for treatment of stenosis, plastic stents up to a maximum size of 10 French and a maximum number of five were inserted.

In select cases naso-biliary drainage was applied for up to 10 days.

Complications after ERCP were registered as pancreatitis, bleeding requiring transfusion of packed red blood cells, severe bleeding requiring intervention, and pancreatitis as described in previous studies [21].

2.5. Surgical intervention for BC

2.5.1. Anastomotic strictures/non-anastomotic strictures

For anastomotic strictures and non-anastomotic strictures hepaticojejunostomy was performed in an end-to-end or end-to-side fashion at the surgeons discretion as described before [15].

2.5.2. Leak

Revisions of the choledocho-choledochostomy were performed as re-anastomosis with PDS 6×0 sutures in interrupted manner. T-drains were used in selected cases at the surgeons discretion.

Complications after surgery were defined as need for transfusion of packed red cells as well as surgery within 30 days after revision for biliary complication. Interventional procedures in case of surgical treatment failure were recorded as separate entities.

3. Statistical analysis

Continuous data are given as the median and the interquartile range (IQR, range from the 25th to the 75th percentile) or as mean and standard deviation where applicable. Discrete data are presented as counts and percentages. Chi-square tests or, if appropriate, exact tests were used to compare groups of categorical data. For comparisons of continuous data non-parametric Mann–Whitney *U* test was applied.

Kaplan–Meier survival estimates were used to calculate survival and success rates and Log-rank tests were used to compare between groups. Cox regression analyses were used to assess the influence of potential risk factors. Hazard ratio (HR) and 95% confidence intervals (CI) are reported. A two-sided p-value <0.05 was considered statistically significant.

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