Removable Intraductal Stenting in Duct-to-duct Biliary Reconstruction in Liver Transplantation (BILIDRAIN-T) : study protocol

ClinicalTrials.gov Identifier: NCT02356939

Sponsor:
Assistance Publique - Hôpitaux de Paris

Information provided by (Responsible Party):
Assistance Publique - Hôpitaux de Paris

Study Description

Summary of the trial:
Randomized controlled trial including 7 French transplantation centers. Pre-inclusion of the patients is made when enlisted for LT. Definitive inclusion and randomization is performed during LT, for patients undergoing a duct-to-duct biliary anastomosis with a graft bile duct diameter smaller than 7mm. In the intraductal stent tube group, a custom-made segment of a T-tube is placed into the bile duct, and removed endoscopically four to six months postoperative. The surgical technique is available on a movie during randomization on the website. The primary endpoint is the occurrence of biliary complications, including biliary fistulae and strictures, during six months of follow-up. Secondary evaluation criteria are the incidence of complications related to the stent placement and its extraction by endoscopy.

Scientific justification:
Biliary complications following LT are significant causes of morbidity, retransplantation and eventually mortality. Although controversial, the use of a T-tube has been proven to be useless and even responsible for specific complications in many studies, including several randomized trials. However, several studies have identified a small bile duct diameter as a risk factor for biliary stenosis. A threshold of 7mm was found to be significantly associated to biliary stenosis. Our team published a preliminary study including 20 patients using a new technique of intraductal stenting. Only 4 complications were reported in the overall study population while no biliary complication occurred in the subgroup of patients who received a whole graft LT. Moreover, no technical failure and no procedure-related complications were noted before and during drain removal. Although intraductal stent tube in duct-to duct biliary anastomosis seems feasible and safe, a multicentric randomized controlled study is needed to validate it as a protective tool for biliary complications following LT.

Detailed Description:
Comparative, multicentric, prospective, randomized non-blinded, two-groups study.
The follow-up is set at six months postoperative for a good screening of the majority of biliary complications.
The inclusion period is set at 3.5 years, for total study duration of 4 years. The patients' inclusion will be made in 7 liver transplantation centers in France.
Patients’ inclusion will be performed in consultation at the moment of enlistment for LT, where they will be informed of the content, the benefits and risks of the study, and have to sign a written consent.

Definitive inclusion will be performed in operating room, during LT, and depends on fulfilling of the following "definitive inclusion criteria" (see below).

The randomization will be performed in operating room by the investigator and coordinated by the Clinical Research Unit of promoters’ center (URC-Est, Saint Antoine Hospital, Paris), with a specific software accessible on the Internet (CleanWeb®).

In the IST group, the surgeon will place the IST in the bile duct, which is a custom-made segment (2 cm) of a 8 French T-tube with no side holes. The stent is inserted in the biliary duct without suture fixation.

In order to minimize bias and to homogenize the technique, a short technical explanatory movie will be realized by the promoter’s team, distributed in each center and published on internet: https://youtu.be/BY29ybb-01M.

Each center will perform its habitual postoperative follow up. Clinical, biological, and radiological exhaustive data will be collected at Day 1, Day 7, Day 15, Month 1, Month 3, Month 6.

A Magnetic Resonance Cholangiography (MRC) will be systematically performed at six months post LT.

In the IST group, an endoscopic retrograde cholangio-pancreatography (ERCP) with sphincterotomy will be planned between the 4th and the 6th month post-transplantation, requiring a short stay in hospital, a general anesthesia, clinical and biological tests including plasmatic lipase dosage at Day 1.

Every undesirable event will be immediately reported to the promoter for further investigation within its severity.

Severe undesirable events previously defined:
- Severe cholangitis
- stent migration
- extraction difficulties
- severe acute pancreatitis
- digestive perforation
- hemorrhage

**Study Design**

**Study Type:** Interventional (Clinical Trial)

**Estimated enrollment:** 248 participants

**Allocation:** Randomized

**Intervention Model:** Parallel Assignment
Masking: None (Open Label)

Primary Purpose: Prevention

Official Title: Efficacy Of A Removable Intraductal Stent In Duct-To-Duct Biliary Reconstruction To Prevent Biliary Complications In Liver Transplantation: A Randomized Controlled Trial

Study Start Date: April 3, 2015

Estimated Study Completion Date: May 8, 2019

Arms and Interventions

Experimental: Intraductal stent (IST)
In the IST group, the surgeon will place the IST in the bile duct, which is a custom-made segment (2 cm) of a 8 French T-tube. The stent is inserted in the biliary duct without suture fixation.

In the IST group, an endoscopic retrograde cholangio-pancreatography (ERCP) with sphincterotomy will be planned between the 4th and the 6th month post-transplantation.

Outcome Measures

Primary Outcome Measures:
1. Incidence of biliary strictures and biliary fistulae within six months post-transplantation. [Time Frame: 6 months]

   A biliary leakage is defined by the presence of bile in the abdominal drainage, and/or an intra-abdominal collection with bilious content requiring drainage.

   A biliary stenosis is defined by a size discrepancy between the two sides of the bile duct anastomosis on specific imaging (MR cholangiography, ERCP), associated to an upstream bile tract distention, with a clinical and biological cholestasis, after excluding other cholestasis causes (rejection, viral reactivation).

Secondary Outcome Measures:
1. Incidence of specific complications related to the IST and its extraction by endoscopy [Time Frame: 6 months]

   Secondary endpoints are the incidence of specific complications related to the IST and its extraction by endoscopy: cholangitis, stent migration, extraction difficulties, acute pancreatitis, digestive perforation, hemorrhage.

2. Graft survival [Time Frame: 6 months]
Incidence of graft loss, i.e. retransplantation rate

3. Patient survival [Time Frame: 6 months]

Incidence of patient death

**Eligibility Criteria**

Ages Eligible for Study: 18 Years and older
Sexes Eligible for Study: All
Accepts Healthy Volunteers: No

**Criteria**

Inclusion Criteria:

- Patients eligible for a liver transplantation
- Patients' written informed consent signed

Exclusion criteria:

- Biliary reconstruction decided to be a hepaticojejunostomy for anatomical/biliary disease reason
- Non eligibility for liver transplantation
- Latex Allergy, polymer or rubber

Randomization criteria (« definitive inclusion criteria ») in operative room during liver transplantation:

- Duct-to-duct biliary reconstruction confirmed,
- Graft or recipient biliary duct diameter ≤7mm,
- Graft not from a donor deceased from cardiac arrest.

**Contacts and Locations**

**Sponsors and Collaborators**
Assistance Publique - Hôpitaux de Paris

**Investigators**
Principal Investigator: Olivier SCATTON Assistance Publique - Hôpitaux de Paris
Scientific coordinator: Claire GOUARD Assistance Publique - Hôpitaux de Paris

| Participating center         | Co-investigator       |
|------------------------------|-----------------------|
| CHU Beaujon, Clichy          | SOUBRANE Olivier      |
| CHRU Lille                   | BOLESŁAWSKI Emmanuel  |
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