Preoperative endoscopic versus percutaneous biliary drainage in potentially resectable perihilar cholangiocarcinoma: DRAINAGE Trial

Published: 02-09-2013
Last updated: 25-04-2024

This is a Dutch multi-centre study that aims to complete patient accrual through national collaboration. Patients with resectable PHC will be randomized to undergo either EBD or PTBD. The objective of the study is to identify a difference in the…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatic and hepatobiliary disorders
Study type	Interventional

Summary

ID

NL-OMON41627

Source
ToetsingOnline

Brief title
DRAINAGE Trial

Condition

- Hepatic and hepatobiliary disorders

Synonym
Klatskin tumor, perihilar bile duct tumor, Perihilar cholangiocarcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Subsidie KWF datamanagement van klinische studies

Intervention

Keyword: Endoscopic drainage, Percutaneous Transhepatic drainage, Perihilar cholangiocarcinoma, Preoperative biliary drainage

Outcome measures

Primary outcome

The number of drainage related complications between treatment allocation and

explorative laparotomy. Complications in this composite endpoint are consist of:

- Stent dysfunction

- Cholangitis

- Acute cholecystitis

- Acute pancreatitis

- Hemorrhage

- Perforation

- Portal vein thrombosis

- Dehydration

Secondary outcome

- The individual components of the primary endpoint, with special interest to

the incidence of preoperative cholangitis;

- The number of drainage procedures required to achieve technical success;

- The total number of drainage procedures that involved (attempts at) stent

(re-)placement;

- The proportion of patients with therapeutic success at 7 days after technical

success;

- The interval bilirubin decrease at 7 days and 14 days after technical success, relative to the reference level at randomization;

- The bilirubin level at explorative laparotomy;

- The number of days between randomization and explorative laparotomy;

- The number of patients with rescheduled or cancelled laparotomy for clinical reasons;

- Quality of Life (for details about QOL assessment please refer to §9);

- Post-laparotomy mortality, defined as 90-day mortality after explorative laparotomy;

- Post-laparotomy morbidity, defined as any complication from table 3 that occurs within 90 days after explorative laparotomy.

Study description

Background summary

Cholestasis is a significant risk factor in the treatment of patients with suspected perihilar cholangiocarcinoma (PHC) requiring major liver resection. Preoperative biliary drainage (PBD) attenuates the effects of cholestasis caused by the tumor, but there is controversy over the preferred technique of PBD, either via endoscopic biliary drainage (EBD) or using percutaneous transhepatic biliary drainage (PTBD). As PHC is a relatively uncommon disease which complicates patient accrual, no randomised studies have yet been conducted to identify the optimal method of preroperative biliary drainage. Due to the high rate of drainage related complications there is a high need for such a study.

Study objective

This is a Dutch multi-centre study that aims to complete patient accrual through national collaboration. Patients with resectable PHC will be randomized to undergo either EBD or PTBD. The objective of the study is to identify a difference in the rate of drainage related complications between EBD and PTBD

as preoperative biliary drainage in PHC.

Study design

The DRAINAGE Trial is a nationwide multi-centre randomized controlled trial that will be conducted at the Academic Medical Centre (AMC) in Amsterdam, the Erasmus Medical Centre (Erasmus MC) in Rotterdam, the University Medical Centre Groningen (UMCG), the Maastricht University Medical Centre (MUMC) and the University Medical Centre Utrecht (UMC Utrecht).

Patients with obstructive jaundice due to a perihilar cholangiocarcinoma who are scheduled to undergo a curative resection will be allocated to either EBD or PTBD by minimisation. The minimisation will be based on three factors:

- Centre of inclusion (AMC, UMCG, Erasmus MC, AZM or UMC Utrecht)
- Tumor progression into the bilateral segmental bile ducts (BC type 4 tumor, yes/no)
- Drainage naivety (drainage procedure prior to inclusion, yes/no).

The study will be based on the intention-to-treat principle with a superiority design for the primary outcome measure (i.e., the incidence of severe drainage related complications). Crossover treatment will be allowed as specified below.

The study cannot be blinded to the patient or treating physician. A blinded adjudication committee will evaluate all events relevant to the primary outcome measure.

Final follow-up is at 90 days after explorative laparotomy.

Intervention

The index drainage procedure is scheduled at 5 days after treatment allocation. EBD consists of an endoscopic retrograde cholangiography and placement of a plastic endoprosthesis through the stenosis. EBD procedures can be performed in day-care. PTBD consists of ultrasonography-guided cannulation of dilated bile ducts and placement of an internally-externally draining catheter. Patients who undergo a PTBD procedure are admitted to the hospital for 1 or 2 days.

Study burden and risks

Participating subjects are not subject to an additional risk during participation in this study. Preoperative biliary drainage is required for all patients with resectable PHC, so patients would inevitably have been subjected to either drainage modality. There are currently no guidelines for the choice of EBD or PTBD in the preoperative setting, and it is current practice to use both EBD and PTBD in a mixed fashion to accomplish sufficient drainage. In an

attempt to structure the use of EBD and PTBD, this trial aims to identify differences between both treatment modalities.
Participation is associated with a small additional burden. This burden includes a baseline patient history assessment, a single ultrasound 7 days after the initial drainage procedure to assess residual dilatation of the bile ducts, and completing quality-of-life questionnaires.

Biliary drainage has an intrinsic risk of inducing seeding metastasis after resection of the tumor. It is currently unknown which drainage technique has the highest risk of inducing seeding metastases. As participating patients would have been subjected to biliary drainage anyway, participation in this study does not carry an increased risk of inducing seeding metastases.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Diagnosis of perihilar cholangiocarcinoma
• No apparent signs of irresectability on CT-scan and/or MRI, and scheduled to undergo a *curative* liver resection (may need additional lymph node biopsies or a diagnostic laparoscopy to further determine resectability);
• Inadequate preoperative biliary drainage.
For drainage naïve patients this is defined as:
* Serum bilirubin level >= 50 µmol/l;
For drainage non-naïve patients this is defined as:
* Persistent hyperbilirubinemia
* or inadequate drainage of the future remnant liver (stent positioned in contra-lateral side)
• Both the endoscopic and the percutaneous drainage methods are technically feasible.

Exclusion criteria

• Incomplete recovery from side-effects of any prior stenting attempt, including signs of active cholangitis.
• ECOG/WHO score >=3
• Any other contraindication for major liver surgery
• No informed consent

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-09-2013

Enrollment:	106
Type:	Actual

Ethics review

Approved WMO Date:	02-09-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-11-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-11-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-01-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-03-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL42118.018.13