Primary percutaneous placement of metal stents for palliative biliary drainage in patients with a primary malignant perihilar stricture

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Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON22038

Bron
Nationaal Trial Register

Verkorte titel
TESLA

Aandoening

Perihilar cholangiocarcinoma (pCCA), galbladder carcinoma (GBC), intrahepatic cholangiocarcinoma (iCCA)

Ondersteuning

Primaire sponsor: Erasmus MC
Overige ondersteuning: None

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Primary Objectives:
6-months overall survival.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale: Most patients with perihilar cholangiocarcinoma (pCCA) are ineligible for curative-intent resection because of metastatic disease, locally advanced disease, or due to comorbidity. The key to successful palliative treatment is adequate biliary drainage to improve the patient's wellbeing and to allow for palliative systemic therapy. Endoscopic biliary drainage with plastic stents is the most common technique in the Netherlands. The main problem of this approach is that the stents cause bacterial colonization of the previously sterile intrahepatic bile ducts, because the stents cross the ampulla. Cholangitis often develops, especially if undrained segments become colonized. This is reflected by a 35% mortality within 3 months after diagnosis in patients who are ineligible for curative-intent resection. Most of these patients die from biliary obstruction and cholangitis without known metastatic disease. The only method to avoid colonization of the bile ducts is percutaneous placement of uncovered self-expandable metal stents (SEMS) that do not cross the ampulla.

Objective: To proof safety and feasibility of direct percutaneous SEMS placement for palliative treatment of primary malignant perihilar stricture.
Study design: In preparation of the design of a phase-II study, we aim to perform a proof-of-concept pilot study at Erasmus MC, including 10 patients. The expected inclusion period is 1 year.

Study population: Patients with unresectable primary malignant perihilar obstruction on imaging with histopathological confirmation or high clinical suspicion (as determined by the multidisciplinary hepatobiliary team) who did not undergo previous endoscopic or percutaneous drainage procedures and who have no signs of cholangitis.

Intervention: Percutaneous transhepatic biliary drainage, by bridging significant ductal obstruction by self-expandable fenestrated metal stents without cannulation of the ampulla.

Main study parameters/endpoints: Stent-related complications according to Clavien-Dindo grading system within 90 days (see Table 1.), absolute and relative (%) bilirubin decrease after 14 days and number of scheduled and unscheduled reinterventions within 90 days.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: The percutaneous intervention is an alternative approach to the standard of care, which is endoscopic biliary drainage. Complications due to the transhepatic biliary

drainage, i.e. bleeding, infection and bile leakage are uncommon (<5%).
We hypothesize that direct SEMS placement in patients with unresectable primary malignant perihilar obstruction minimizes post-drainage cholangitis and mortality, requires fewer reinterventions, and increases the rate of patients receiving palliative chemotherapy.
In this study, patients will undergo an invasive procedure with hospital discharge on the same day. This corresponds to the standard of care. Follow-up appointments are planned 14 days (T1), one month (T2) and three months (T3) after stent placement. These visits will take 30 minutes. T2 and T3 are extra visits compared to standard of care.

Doel van het onderzoek

We hypothesize that direct SEMS placement in patients with unresectable primary malignant perihilar obstruction minimizes post-drainage cholangitis and mortality, requires fewer reinterventions, and increases the rate of patients receiving palliative chemotherapy.

Onderzoeksopzet

Follow-up appointments are planned as deemed necessary by the treating specialist, but at least 14 days (T1), one month (T2) and three months (T3) after stent placement. Each follow-up will take 30 minutes. During T1, two blood samples (20 ml in total) will be taken. This corresponds to the standard of care. During the other visits blood samples will only be taken by discretion of the treating physician. If patients returned to their referring hospital or if visits are too stressfull, the T2 and T3 visits will be telephone calls. During these calls patients will answer questions about the presence of fever, jaundice and abdominal pain. 1 year after inclusion the treating physician will be contacted about late complications and vital status.

Onderzoeksproduct en/of interventie

Preprocedural intravenous antibiotic prophylaxis is administered (cefuroxime 1500 mg/metronidazole 500 mg; conform institutional ERCP protocol). An interventional radiologist performs the percutaneous transhepatic biliary drainage, by bridging significant ductal strictures by self-expandable fenestrated metal stents without cannulation of the ampulla. Bile cultures are routinely taken. The tract is sealed with glue without leaving an external drain. When histological confirmation is lacking (on estimation about one third of all patients with primarily unresectable pCCA) during the same procedure percutaneous biopsies and brush cytology are taken to confirm the presence of pCCA by frozen section before SEMS-placement, to prevent the placement of non-removable SEMS in patients with non-malignant disease.
The radiologist reports whether stent placement was technically successful, the difficulty of the procedure (scale 1-10) and whether a second drainage procedure is indicated (e.g., in case the stricture cannot be passed in the first attempt). Technical success is defined as successful passage of the stricture. Successful drainage is defined as a bilirubin below 50 mmol/l or a reduction in bilirubin level of at least 50% within 14 days after drainage.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

In order to be eligible to participate in this study, a subject must meet the following criteria:
• Written informed consent must be given according to ICH/GCP, and national/local regulations.
• Unresectable primary malignant perihilar obstruction on imaging with histopathological confirmation or high clinical suspicion (as determined by the multidisciplinary hepatobiliary team)
And
• Symptomatic hyperbilirubinemia (a combination of a total bilirubin level >100 mmol/l, and/or jaundice and/or loss of appetite and/or dark urine and/or steatorrhea)
Or
• Age > 70 years

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

A potential subject who meets any of the following criteria will be excluded from participation in this study:
• Fluctuation or spontaneous decrease of a total bilirubin level before start of any treatment suggesting potential benign origin.

• Patients who underwent previous drainage procedures endoscopically or percutaneously with an internalized biliary catheter.
• Clinical signs of cholangitis. Cholangitis was defined as both fever (i.e. body temperature >38.5°C) and leucocytosis (i.e. ≥10 *109/L) without clinical or radiological evidence of acute cholecystitis (14). Patients who underwent ERCP are eligible, providing no papillotomy was performed or stent was placed and there are no signs of cholangitis.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-10-2020
Aantal proefpersonen:	37
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	23-07-2021
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL9624
Ander register	METC Erasmus MC : METC-2019-0789

Resultaten