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Efficacy of fibrin sealant in reducing resection surface crelated complications after partial liver resections

Submission date 18/02/2010	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 28/05/2010	**Overall study status** Completed	
Last Edited 19/09/2012	**Condition category** Surgery	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Robert Porte

Contact details
Chief Department of Hepatobiliary Surgery and Liver Transplantation
University Medical Center Groningen
PO Box 30001
Groningen
Netherlands
9700 RB
r.j.porte@chir.umcg.nl

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Efficacy of fibrin sealant in reducing resection surface crelated complications after partial liver resections (FRESCO trial): A Dutch, multicentre, prospective, randomised, controlled trial

Acronym
FRESCO trial

Study objectives
The application of fibrin sealant to the cut surface of the liver remnant and to the diaphragm after elective hepatic resection will decrease the incidence of resection surface-related complications and diaphragm-related complications.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Medical Ethical Board of University Medical Center Groningen approved on the 12th October 2005 (ref: 2005/183)

Study design
National multicentre prospective randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please contact m.t.de.boer@chir.umcg.nl to request a patient information sheet (Dutch only)

Health condition(s) or problem(s) studied
Partial liver resection complications

Interventions
Randomisation to treatment group will be performed using a sealed envelope and will be performed prior to peritoneal closure after completion of conventional hemostasis and bile stasis. Only the surgeon cannot be blinded to one of two groups. Patients, ward staff and radiologists will be blinded for study medication. Stratification will be done by diagnosis: benign versus malignant.

The fibrin sealant that used in this study is Quixil® Human Surgical Sealant Kit (hereinafter called Quixil®). It consists of a packet containing two components in separate vials of 5 ml. Vial I contains Biological Active Component (BAC): a concentrate of human clottable fibrinogen at a concentration of 40 - 60 mg/ml. A synthetic antifibrinolytic agent, tranexamic acid (85 - 105 mg /ml) is added to the fibrinogen as a stabiliser. Vial II consists of a high concentration of human thrombin (800 - 1200 IU/ml) dissolved in a solution of 5.6 6.2 mg/ml of calcium chloride. Both components undergo double viral-inactivation steps: treatment with solvent detergent followed by pasteurisation (at 60 degrees Celsius for ten hours) for the fibrinogen and nanofiltration for the thrombin. Quixil® is provided by the manufacturer in a 10 ml double-syringe spray-device.

Group 1:
After liver resection and completion of hemostasis the envelope is opened showing treatment arm. Maximum 5 ml of fibrin sealant is sprayed or dripped on the resection surface of the liver. Maximum 5 ml of fibrin sealant is sprayed on the bare diaphragmatic resection surface. Preferably a drain will be placed adjacent to the cut liver surface.

Group 2:
After liver resection and completion of hemostasis the envelope is opened showing control arm. Preferably a drain will be placed adjacent to the cut liver surface.

Duration of treatment: single application during operation when patient is randomised in treatment arm. Total duration of follow-up will be 30 days.

For calculation of the required study-population size, resection surface-related complications such as bleeding, biloma and/or abscess formation are considered the most important target variables. Based on experience and publications of several centres, the overall proportion of these complications is estimated to be 15-20% when no fibrin sealant is applied to the resection surface (control group). A difference of about 50% between the control group and the fibrin sealant group is regarded as clinically significant. This would result in a proportion of 7.5-10% resection surface-related complications in the fibrin sealant group. Based on these assumptions, we calculated that a study size of 220 patients in each group will be needed to achieve 80% power at the 5% significance level. To have some safety margins it was decided to enrol 250 patients in each group.

The primary endpoint of this study, however, will not only be the clinical presentation of a resection surface related complication, but also all CT scan detected complications. Although the exact incidence of CT scan detected complications is not known, this is expected to be higher than that of clinically detected complications. Therefore, an interim analysis will be performed after 180 patients (90 in each group). Main reason to do an interim analysis is to investigate weather the assumed complication rate is indeed 15 to 20%, or much higher. If the complication rate is higher, a smaller number of patients will be required to obtain the same level of statistical power as outlined above.

An interim analysis was performed in November 2009 after we had the completed CRFs of 180 patients enrolled in the FRESCO trial. An independent epidemiologist analysed the complication rate in the control group. This complication rate was higher than expected: 30,4%. Based on the complication percentage of 30.4% and on the assumption that a difference of 50% between the control group and the fibrin sealant group is clinically significant, a study size of 131 patients in each group will be needed to achieve a 80% power at the 5% significance level. To have some safety margins it was decided to enrol 300 patients in total.

Intervention Type

Procedure/Surgery

Phase
Not Applicable

Primary outcome measure
1. Resection surface related complications detected by computed tomography (CT) scan or clinical symptoms: haematoma, biloma or subphrenic abscess
2. Diaphragm related complications detected by CT scan or clinical symptoms: pleural effusion
3. Need for reintervention for bleeding or bile leakage from the cut surface of the liver, or pleural effusion

CT scan after 7 days, further assessment of complications and reinterventions during hospital stay until first out-patient appointment.

Secondary outcome measures
1. Changes in drain bilirubin (micromol/l), drain hemoglobin concentration (mmol/l) and volume of fluid drainage (ml) from the abdominal drains during the first three days post-operatively
2. Decrease in serum haemoglobin concentration (mmol/l) (lab day 1, 3, 5, 7, thereafter weekly)
3. Transfusion requirement (whole admission until first outpatient appointment)
4. Post-operative morbidity (whole admission until outpatient appointment)
5. Post-operative mortality (whole admission until outpatient appointment)
6. Length of hospital stay (whole admission until outpatient appointment)

Overall study start date
23/05/2006

Completion date
01/06/2010

Eligibility

Key inclusion criteria
1. Patients aged greater than or equal to 18 years, either sex
2. Undergo liver resections (at least one segment) for benign or malignant tumours or metastatic tumours, or
3. Undergo liver resection in combination with radiofrequency ablation (RFA)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
600

Key exclusion criteria
1. Aged less than 18 years
2. Undergo liver resections with extrahepatic biliary resection and reconstruction (Klatskin tumours)
3. Cirrhosis
4. Other disorders of haemostasis
5. Polycystic liver disease
6. Any associated operative gastrointestinal procedures (a needle catheter jejunostomy is not excluded)
7. Wedge resections
8. Pregnancy
9. History of hypersensitivity, allergy or anaphylactic reaction to any plasma derived product, including fibrin sealant

Date of first enrolment
23/05/2006

Date of final enrolment
01/06/2010

Locations

Countries of recruitment
Netherlands

Study participating centre
Chief Department of Hepatobiliary Surgery and Liver Transplantation
Groningen
Netherlands
9700 RB

Sponsor information

Organisation
Johnson and Johnson Medical Limited (UK)

Sponsor details
Kirkton Campus
Simpson Parkway
Livingston
United Kingdom
EH54 7AT

Sponsor type
Industry

Website
http://www.jnj.com/connect/

ROR
https://ror.org/03qwpn290

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
University Medical Center Groningen (UMCG) (Netherlands) - local hospital committee performance audit (Doelmatigheidsonderzoek) funding

Funder Name
Johnson and Johnson Medical Limited (UK) - supplying fibrin sealant and funding of CT scans at one week post-operative

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/08/2012		Yes	No