Protocol v1 - conduit4olt.org
Outcome Analysis of Arterial Conduits in Liver Transplantation

BACKGROUND

Arterial conduits in liver transplantation are almost as old as the procedure itself. First described by Starzl in 1984, the knowledge remains superficial. Although rarely performed, there is no doubt that thousands of patients' lives were saved because of the use of arterial grafts. However, arterial grafts are known to be associated with a **higher rate of occlusion** and a **lower patient and graft survival** when compared to conventional end-to-end anastomosis. In our recent retrospective study, we showed that retransplantation procedure and aspirin in patients' medication are independent risk factors for the need of an aorto-hepatic conduit. We assume that aspirin could be a surrogate marker for vascular and metabolic status. Furthermore, in our meta-analysis we found a four times higher occlusion rate compared to non-conduits.

Whether the site of conduit placement (Figure 1) or certain types of material have an impact on occlusion and graft survival remains unknown. In addition, several studies discuss that antiaggregation or anticoagulation might be protective for occlusion of arterial conduits. Currently, there is no study that investigated this problem, most probably because of low case numbers.

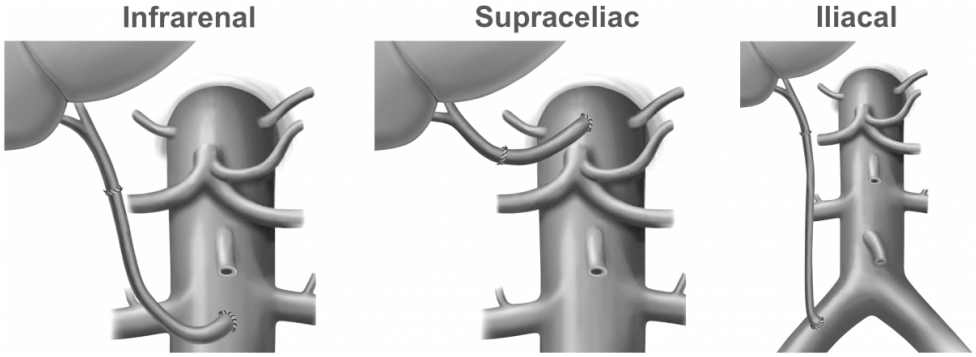

Figure 1

STUDY OBJECTIVES

The primary goal of this study is to conduct a multicenter cohort analysis to define the **outcome of different types of conduits and to investigate whether antiplatelet / anticoagulation has an impact on patency rates.**

Specific aim #1: To identify independent risk factors for early and late occlusion of arterial conduits in liver transplantation.
Specific aim #2: To compare different placement sites (infrarenal, supraceliac, Iliacal, etc) of arterial conduits (Figure 1) in terms of occlusion rates and graft survival.
Specific aim #3: To investigate whether antiagregation therapy is protective in terms of arterial patency.

STUDY DESIGN

This will be a multicenter single cohort study including only cases of deceased donor liver transplantation that required an aorto-hepatic or iliac-hepatic conduit for arterial reconstruction. Primary endpoint is 30-day conduit patency. Secondary endpoints include postoperative complications, death, late conduit occlusion, graft and patient survival.

The study protocol has received approval by the local ethics committee and will be soon registered at ClinicalTrials.gov, as well as published here prior to data collection.

SETTING

This multicenter cohort study will include several high -volume centers worldwide. Each participating center requires a prospective database from that data can be extracted. All consecutive cases of deceased donor liver transplantation requiring an aorto-hepatic conduit *from 1st of January 2007 until 31st of December 2016* are included allowing a minimum follow-up time of 6 months. Data collection at conduit4olt.org will be prospective, structured, anonymized, and encrypted.

PUBLICATION POLICY

For upcoming publications, two authorships of the participating centers will be guaranteed as a group-authorship indexed in PubMed.

INSTITUTIONAL REVWIEW BOARD (IRB) / ETHICAL POLICY

Each participating center is responsible to contact their local ethics committee and receive approval for participation, if applicable. For example, this project is considered as an audit in some countries and thus there is no need for formal approval in the form of a protocol submission.

ELIGIBILITY CRITERIA

Inclusion criteria:

- Liver transplantation requiring aorto-hepatic or iliac-hepatic conduits
- Deceased donor after brain death (DBD) or deceased donor after circulatory death (DCD)
- Whole organ as well as split allografts
- Primary liver transplantation as well as liver retransplantation
- Adult recipient (age ≥18 years)

Exclusion criteria:

- Living donor liver transplantation
- Pediatric liver transplantation (recipient age <18 years)
- Arterial reconstruction other than aorto-hepatic or iliac-hepatic conduits
- Multivisceral transplantations

VARIABLES

The PDF version of the online Case Report Form is available at the Appendix.

ESTIMATED SAMPLE SIZE

Each center should provide at least 30 cases that meet the inclusion criteria to allow adequate event rates for each outcome.

STATISTICAL METHODS

The primary and secondary endpoints will be compared with patient and operation characteristics with univariate analysis. ROC Curve analysis will be performed to dichotomize continuous variables. Multivariable analysis (binary logistic and Cox regression) will be performed to identify independent risk factors. Statistical analysis will be performed using R Studio version 1.0.44 (RStudio, Inc. GNU Affero General Public License v3, Boston, MA, 2016) with the graphical user interface rBiostatistics.com beta version (rBiostatistics.com, Zurich, Switzerland, 2016, GNU License).

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conduit4OLT.org
Collaborative

Data Entry Management System (DEMS)

Case identification

Case ID *

Please assign above a case identification number related to this case submission. Please ensure that you keep this "Case ID" in your records (excel file or any other database) if you would like to access this case in the future and perform changes. For each case there should be a unique ID assigned to it. Please ensure that the "Case ID" does not contain any patient identification information, such as date of birth, hospital number, case number, etc.

Patient characteristics

Recipient gender * Male Female

Recipient age * years

Recipient height * cm

Recipient weight * kg

Height / weight converter

Donor age years

Lab MELD at time of liver transplantation * points

MELD Score Calculator

Account

My account
Log out

Documents

Protocol
Instructions
Case report form in PDF

Case Report Form

Submit cases
My submitted cases
Height/ weight converter
Clavien Dindo Classification
Date duration calculator
Lab unit converter

Life support prior to transplantation *

	Yes	No	Unknown
Dialysis prior to transplantation	○	○	○
Ventilation prior to transplantation	○	○	○
Vasopressors prior to transplantation	○	○	○

Retransplantation * ○ Yes ○ No

Retransplantation indicates prior liver transplantation(s)

Underlying liver disease (multiple options): *

	Yes	No	Unknown
Non-alcoholic steatohepatitis	○	○	○
Hepatitis B virus infection	○	○	○
Hepatitis C virus infection	○	○	○
Alcohol	○	○	○
Autoimmune hepatitis	○	○	○
Wilson's disease	○	○	○
Other	○	○	○

If other underlying liver disease, please indicate

Indication for transplantation (multiple options): *

	Yes	No	Unknown
Acute liver failure	○	○	○
Hepatocellular carcinoma	○	○	○
Cholangiocarcinoma	○	○	○

Other	○	○	○

If other indication for liver transplantation, please indicate

TACE prior to transplantation ○ Yes ○ No

Radiation prior to transplantation ○ Yes ○ No

Direct to the liver, for example for cholangiocarcinoma.

Comorbidities *

	Yes	No	Unknown
Coronary artery disease	○	○	○
Stroke prior to transplant	○	○	○
Smoker	○	○	○
Valvular heart disease	○	○	○
Heart arrhythmias	○	○	○
Hypertension	○	○	○
Cerebrovascular disease	○	○	○
Hypercoagulation disease	○	○	○
Dyslipidemia	○	○	○
Diabetes mellitus	○	○	○
Stroke	○	○	○
Smoker	○	○	○
Sepsis / septic shock	○	○	○
Other	○	○	○

If other comorbidities, please indicate

Anticoagulation prior to transplantation (multiple options): *

	Yes	No	Unknown
Antiplatelet agents	○	○	○
Anticoagulant agents	○	○	○

If yes, please indicate which medications:

E.g. Antiplatelet agents: Aspirin, Clopidogrel (Plavix). Anticoagulant agents: Phenprocoumon (Marcoumar), Warfarin (Coumadin), Rivaroxaban (Xarelto), Heparin, Heparin (Liquemin), Dabigatran (Pradaxa), Apixaban (Eliquis), Edoxaban (Savaysa), Enoxaparin (Lovenox), Fondaparinux (Arixtra), etc.

Operation characteristics

Graft type * ○ DBD ○ DCD

DBD indicates donor after brain death. DCD indicates donor after cardiac death

Simultaneous kidney transplantation * ○ Yes ○ No

Cold ischemia time * minutes

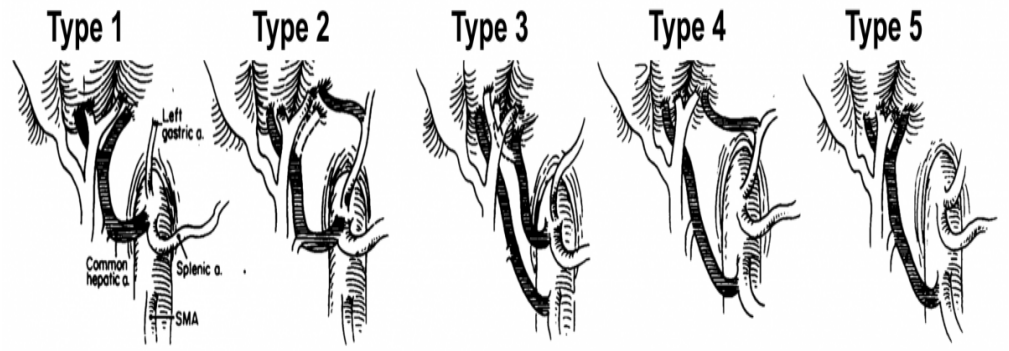
Operation duration * minutes

Use of veno-venous bypass * ○ Yes ○ No

Operation technique * ○ Classic ○ Piggy-bag

Number of arterial anastomoses *

Donor anatomy type * ○ 1 ○ 2 ○ 3 ○ 4 ○ 5



Donor Anatomy according to Hiatt, Gabbay and Busuttil (Ann Surg July 1994): Dotted lines indicate that the variant artery may be accessory (if branch shown by dotted line is present) or replaced (if absent). Type 1: normal. Type 2: replaced (accessory) left hepatic artery from left gastric. Type 3: replaced (accessory right hepatic artery from SMA. Type 4: double replaced system. Type 5: common hepatic artery from SMA.

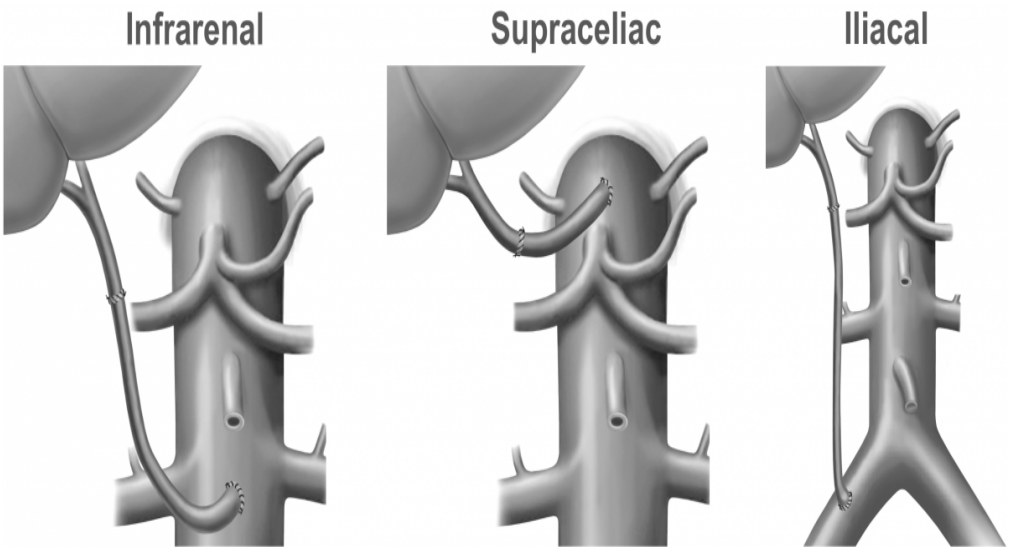
Arterial flow measurement intraoperatively ml/min

Type of arterial conduit used * ◯ Allograft ◯ Prosthetic

If allograft conduit used, which vessel?

If prosthetic conduit used, which type?

Placement of conduit * - Select -



If other placement, please indicate

Reason for need of conduit * - Select -

If other reason for need of conduit, please indicate

Additional arterial back-table reconstructions? * Yes No

Biliary reconstruction * - Select -

Intraoperative blood product administration *

	Yes	No	Unknown
Intraoperative fresh-frozen Plasma (FFP)			
Intraoperative red blood cells (RBC)			
Intraoperative platelets (Plt)			

If FFP, how many units? units

If RBC, how many units? units

If Plt, how many units? units

Medications post transplantation

Immunosupression post transplantation

Immunosuppression post transplantation (multiple options) *

- Azathioprine
- Corticosteroids
- Cyclosporine
- Everolimus
- Mycophenolate
- Sirolimus
- Tacrolimus
- Other
- None

If other immunosuppression therapy, please indicate

Anticoagulation post transplantation

Anticoagulation post transplantation (multiple options): *

	Yes	No	Unknown
Antiplatelet agents	○	○	○
Anticoagulant agents	○	○	○

If yes, please indicate which medications:

E.g. Antiplatelet agents: Aspirin, Clopidogrel (Plavix). Anticoagulant agents: Phenprocoumon (Marcoumar), Warfarin (Coumadin), Rivaroxaban (Xarelto), Heparin, Heparin (Liquemin), Dabigatran (Pradaxa), Apixaban (Eliquis), Edoxaban (Savaysa), Enoxaparin (Lovenox), Fondaparinux (Arixtra), etc.

If anticoagulation, please indicate target therapy ○ Prophylactic ○ Therapeutic

Prophylactic therapy means 10000 or 15000 IU heparin per day for example. Therapeutic therapy means according to aPTT or Anti-Xa activity for heparin at therapeutic levels (usually over 20000 heparin)

Posttransplantation outcome

Lab values

Peak AST (up to 7th post-TPL day) * (U/l)

Peak ALT (up to 7th post-TPL day) * (U/l)

Bilirubin at 7th post-TPL day * µmol/l (SI)

Typical normal ranges 3-25 (µmol/l) (SI)

INR at 7th post-TPL day * ratio

Typical normal ranges 3-25 (µmol/l) (SI)

Lab unit converter

Clavien-Dindo Classification of Postoperative Complications within 90 days post-TPL *

	None	1	2	3a	3b	4a	4b	5 (death)
Biliary	○	○	○	○	○	○	○	○
Bleeding	○	○	○	○	○	○	○	○
Graft related	○	○	○	○	○	○	○	○
Hemodynamic	○	○	○	○	○	○	○	○
Infections	○	○	○	○	○	○	○	○
Neurologic	○	○	○	○	○	○	○	○
Renal	○	○	○	○	○	○	○	○
Respiratory	○	○	○	○	○	○	○	○
Vascular	○	○	○	○	○	○	○	○
Other A	○	○	○	○	○	○	○	○
Other B	○	○	○	○	○	○	○	○
Other C	○	○	○	○	○	○	○	○

Please indicate all different types of complications and their grades according to the Clavien-Dindo Classification from transplantation until the 90th posttransplantation day. If the recipient did not encounter any complications from operation until discharge, please indicate "None" for all types and grades of complications.

If biliary complication, indicate type - None -

If vascular complication, indicate type - None -

If graft related complication, indicate type - None -

If there were any other types of complications encountered, please describe them

below:

Clavien-Dindo Classification

Length of ICU stay * days

In case of readmission(s) to the Intensive Care Unit (ICU), please indicate the total number of ICU stay in days above.

Length of hospital stay * days

Readmission within 90 days from transplantation * Yes No

If yes, what was the reason for readmission?

Arterial patency from transplantation until last follow up or death

Occlusion indicates total occlusion while stenosis indicates partial occlusion.

Arterial occlusion / stenosis - First occasion

Occlusion indicates total occlusion while stenosis indicates partial occlusion.

Arterial occlusion / stenosis * - Select -

If yes, days from transplantation to arterial occlusion / stenosis

days

If stenosis (partial occlusion), please indicate the reason

- None -

First Intervention type (multiple options):

- Percutaneous transluminal angioplasty (PTA)
- Stent
- Thrombolytic therapy
- Redo of the anastomosis
- Redo of the conduit
- Other

If yes, patency rescue by this intervention ◯ Yes ◯ No

Yes indicates that after the intervention, the artery remained opened, thus rescued by the intervention. No means that the intervention was unsuccessful.

Second occasion - Arterial reocclusion / restenosis

Occlusion indicates total occlusion while stenosis indicates partial occlusion.

Arterial reocclusion / restenosis * - Select -

If yes, days from first occlusion to reocclusion

days

Occlusion contains also clinically relevant stenosis (i.e. partial occlusion)

If restenosis (partial occlusion), please indicate the reason

- None -

Reintervention type (multiple options):

- ☐ Percutaneous transluminal angioplasty (PTA)
- ☐ Stent
- ☐ Thrombolytic therapy
- ☐ Redo of the anastomosis
- ☐ Redo of the conduit
- ☐ Other

If yes, patency rescue by reintervention ◯ Yes ◯ No

Yes indicates that after the intervention, the artery remained opened, thus rescued by the intervention. No means that the intervention was unsuccessful.

Third occasion - Arterial re-reocclusion / re-restenosis

Occlusion indicates total occlusion while stenosis indicates partial occlusion.

Arterial re-reocclusion / re-restenosis * - Select -

If yes, days from reocclusion to re-reocclusion

days

Occlusion contains also clinically relevant stenosis (i.e. partial occlusion). This duration in days indicates the time from second to third occlusion.

If re-restenosis (partial occlusion), please indicate the reason

- None -

Re-reintervention type (multiple options):

- [ ] Percutaneous transluminal angioplasty (PTA)
- [ ] Stent
- [ ] Thrombolytic therapy
- [ ] Redo of the anastomosis
- [ ] Redo of the conduit
- [ ] Other

If yes, patency rescue by re-reintervention ◯ Yes ◯ No

Yes indicates that after the intervention, the artery remained opened, thus rescued by the intervention. No means that the intervention was unsuccessful.

Survival

Patient status * ◯ Alive ◯ Dead

The patient status indicates whether the patient was last seen alive or dead at the hospital, followed up at the outpatient clinic, family doctor, or confirmed after being contacted by phone. Below you are requested to indicate the number of days from transplantation until last follow up or death.

Days from transplantation to last follow up or death *

_____ days

i.e. days from transplantation to death or last follow up recording. This value (number of days) may indicate the time form transplantation to the last follow up recording for alive patients or the time from transplantation to death for those that died.

Graft status * ◯ Graft functioning ◯ Graft failure

Graft failure indicates retransplantation or patient death.

Days from transplantation to last follow up or graft failure *

_____ days

The graft status should be calculated from the date of transplantation to the date of retransplantation or death. If the graft was functioning at the last follow up, please indicate the days from transplantation until last follow up.

Comments (optional)

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