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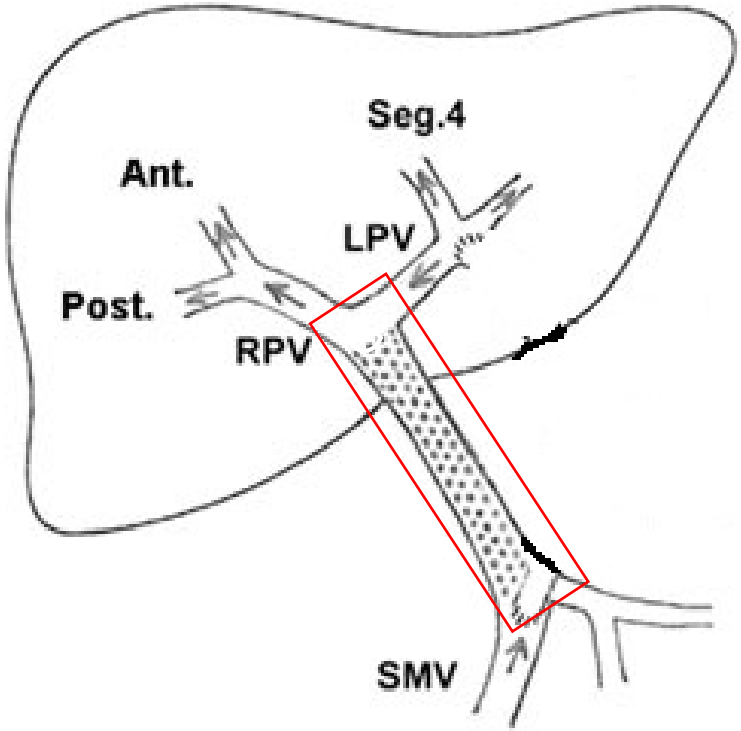
Transplantation of an allogeneic vein bioengineered with autologous stem cells: a proof-of-concept study

Olausson M., Patil P.B., Kuna V.K., Chougule P., Hernandez N., Methe K., Kullberg-Lindh C., Borg H., Ejnell H., Sumitran-Holgersson S. (2012), 380:230-237, *Lancet*

Extrahepatic portal vein obstruction (EPVO)

Impaired hepatopedal blood flow from the superior mesenteric vein, splenic vein, and coronary veins through the portal vein.



SMV…Superior mesenteric vein
RPV…Right portal vein
LPV…Left portal vein

Extrahepatic portal vein obstruction (EPVO)

- Not associated with intrinsic liver disease
- Congenital or acquired
- Predisposition criteria in children
  - Hereditary thrombophilias
  - Neonatal abdominal surgery
  - Sepsis
  - Umbilical vein catheterisation
  - Dehydration

- **Clinical manifestation**
  - Episodes of upper GI bleeding
  - Splenomegaly
- **Complications**
  - Variceal haemorrhage
  - Enlarged spleen
  - Biliopathy
  - Developmental retardation
  - Neurocognitive disability

Diagnosis

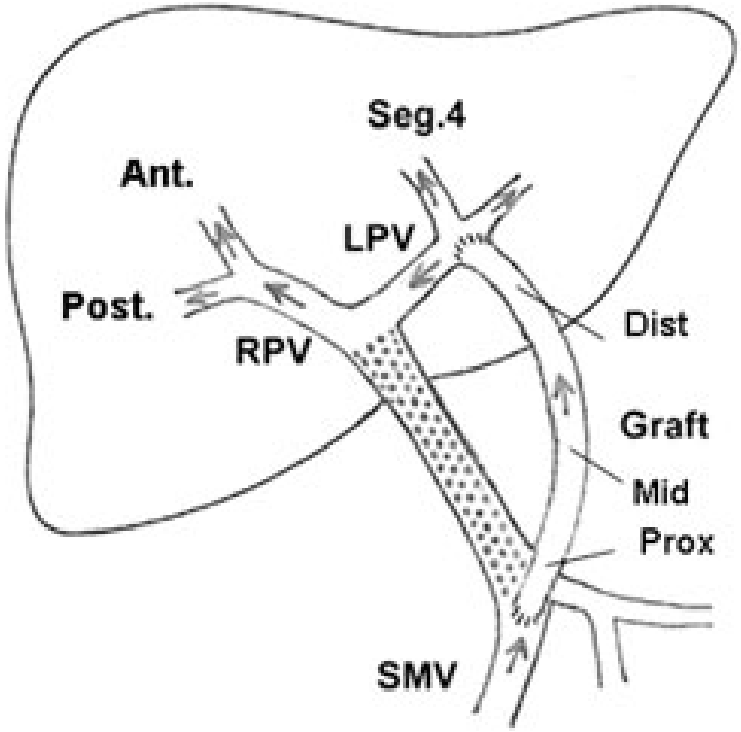
- Abdominal Doppler ultrasonography
- CT angiography

Surgical restoration

- Meso Rex bypass using autologous veins

Umbilical veins, **internal jugular veins**, internal iliac, splenic, inferior mesenteric or saphenous veins

Artificial grafts and cryopreserved veins → shortcomings and little success.

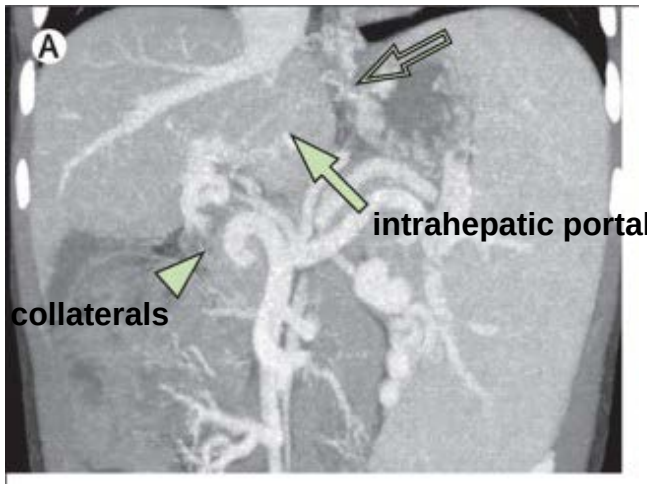


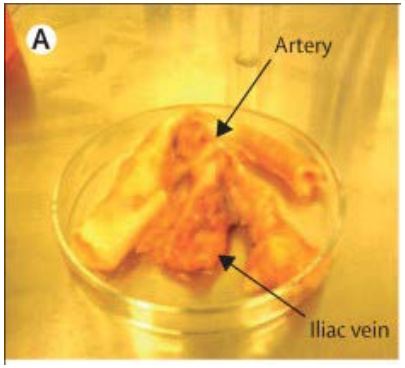
SMV…Superior mesenteric vein
RPV…Right portal vein
LPV…Left portal vein

Patient

- 1-year-old girl
  - Developed thrombocytopenia and splenomegaly
  - Diagnosis: **idiopathic thrombocytopenic purpura**

- At 9 years
  - International normalized ratio (INR): 1,4
  - Protein C & Protein S: normal
  - Activated protein C resistance: none
  - Elastography
  - CT angiography:
    - Portal vein thrombosis
    - Open superior mesenteric vein





72h rinsing of tissue

Vessel decellularization

- 3h incubation with triton X
- 3h incubation tri-*n*-butyl phosphate
- 3h incubation in deoxyribonuclease I

Lumen decelluralization

- Lumen filled with Triton X
- 3h agitation at 37°C
- Washing with PBS
- 3h incubation with tri-*n*-butyl phosphate
- 3h incubation with DNAse
- Washing with distilled water overnight to remove cell debris.

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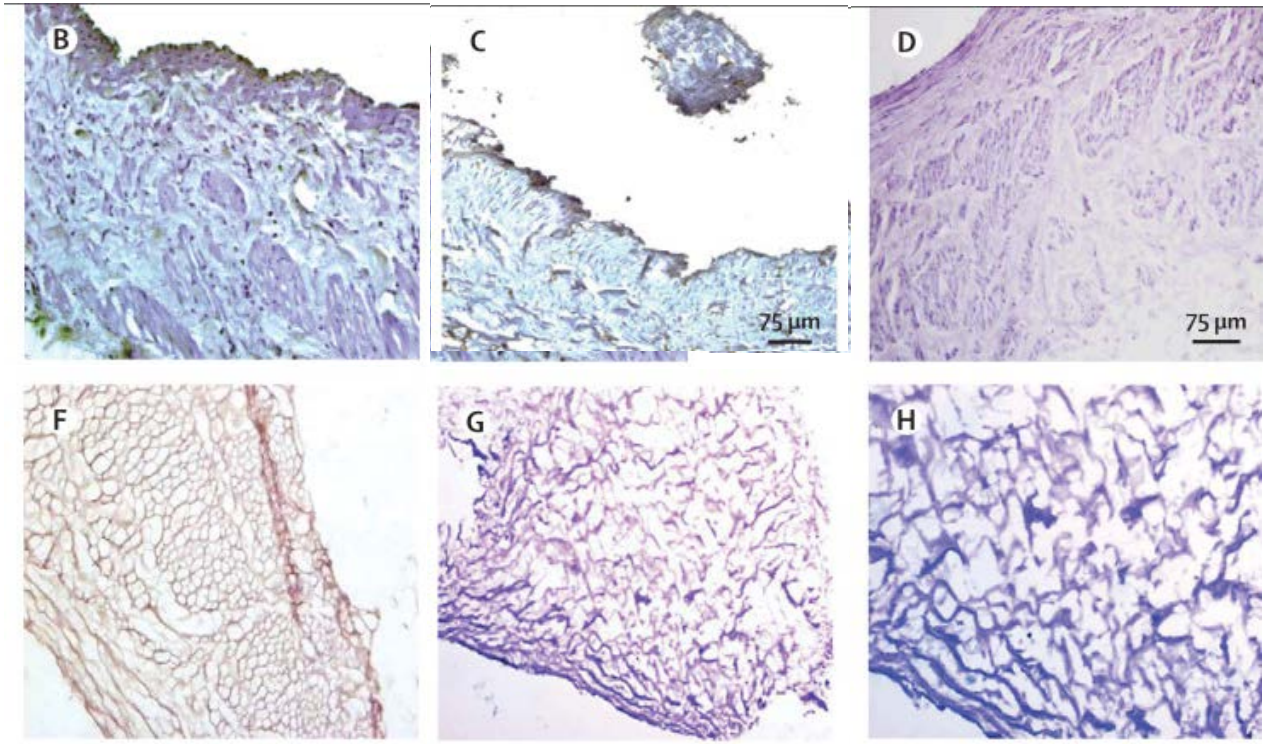
Gross morphology and histology of the iliac vein

Before decellularization

After decellularization



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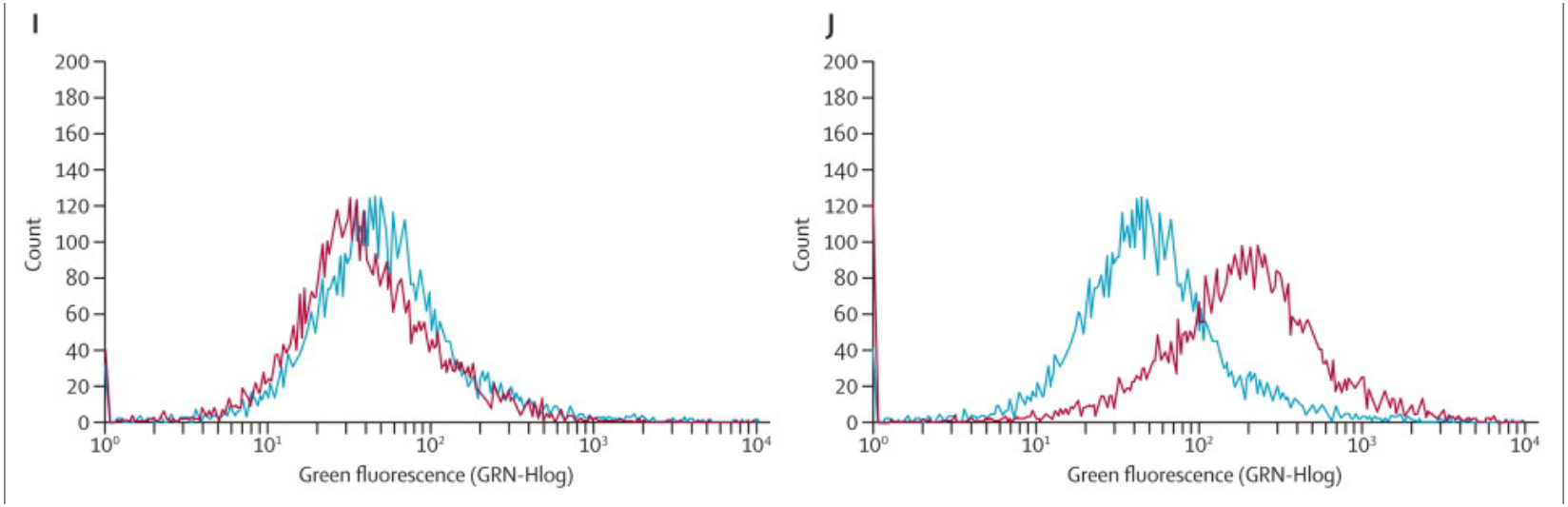
Histogram: absence of binding of anti-endothelial cell antibodies in serum



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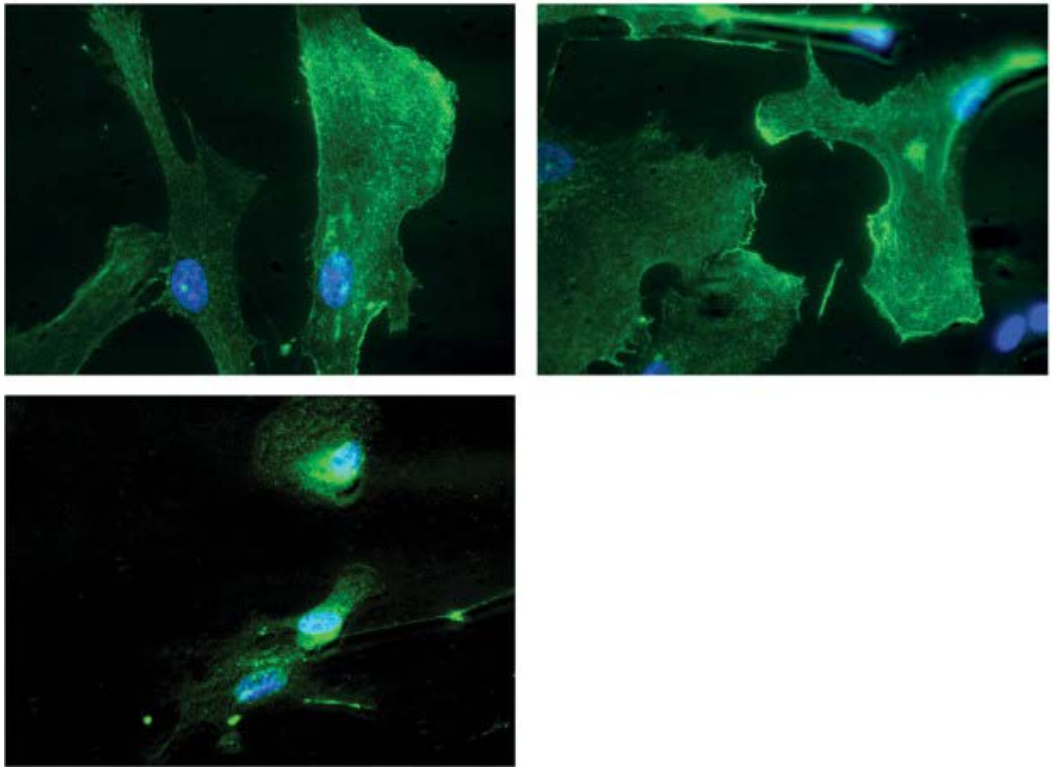
Immunofluorescence staining

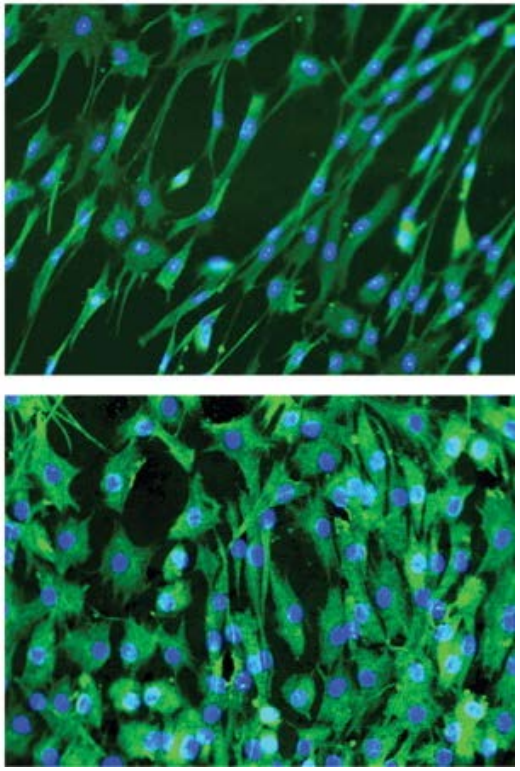
Endothelial cells

Smooth muscle cells

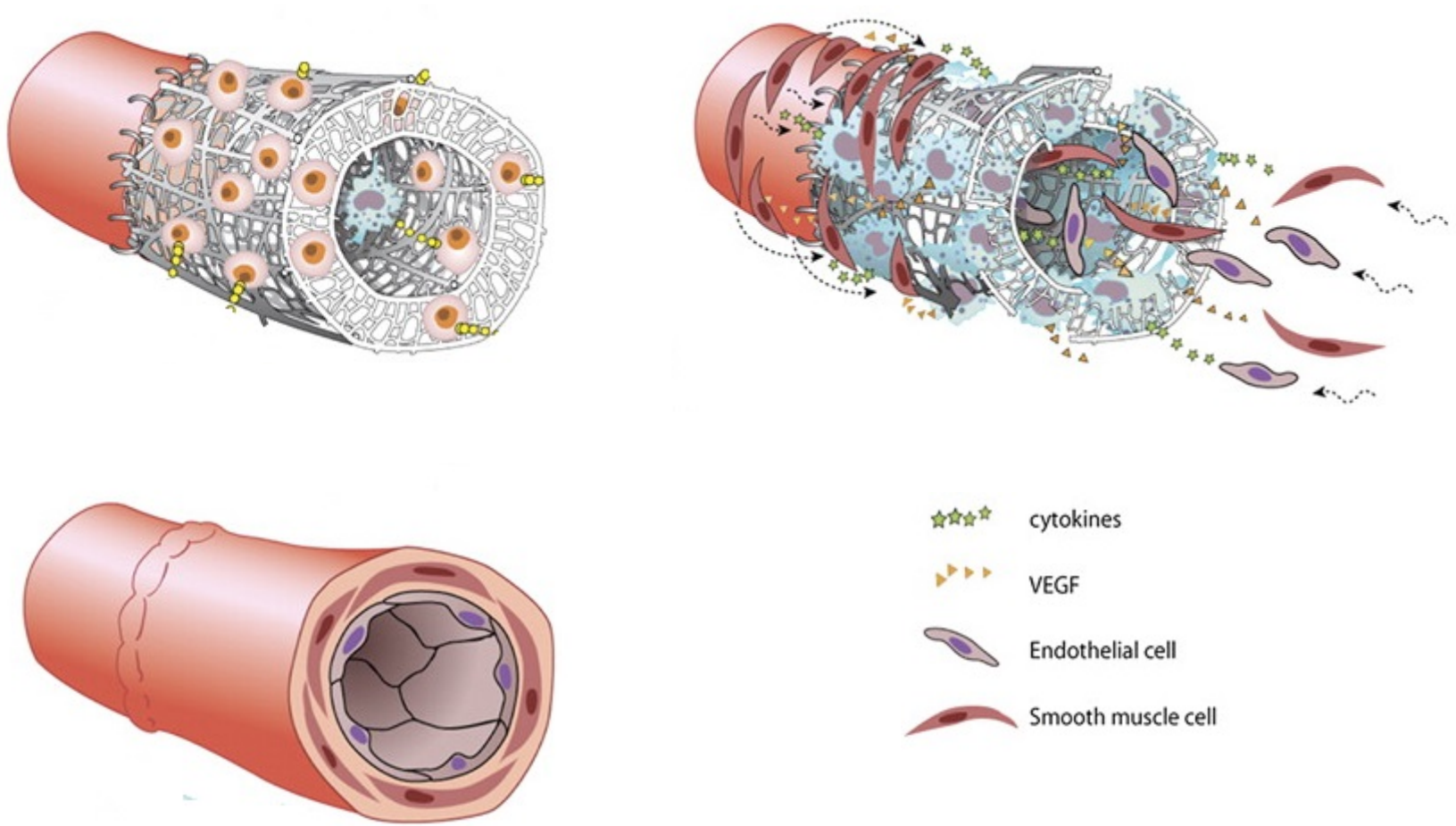
A



B



Seeding of allogeneic vein



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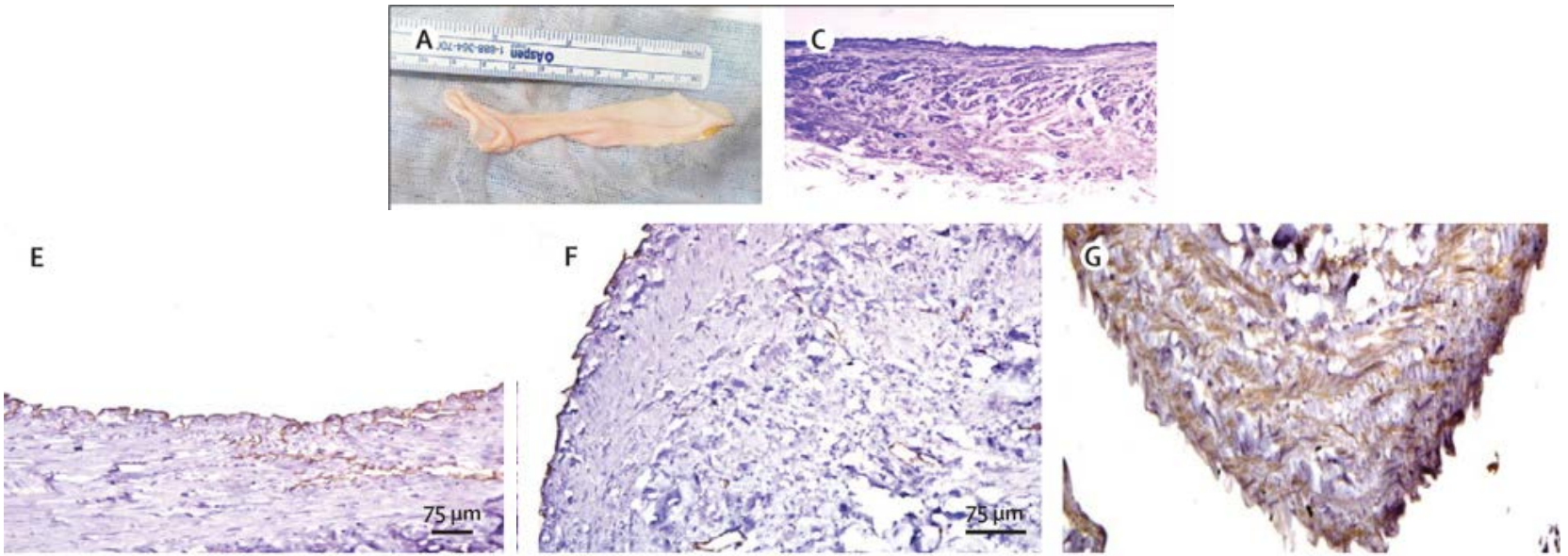
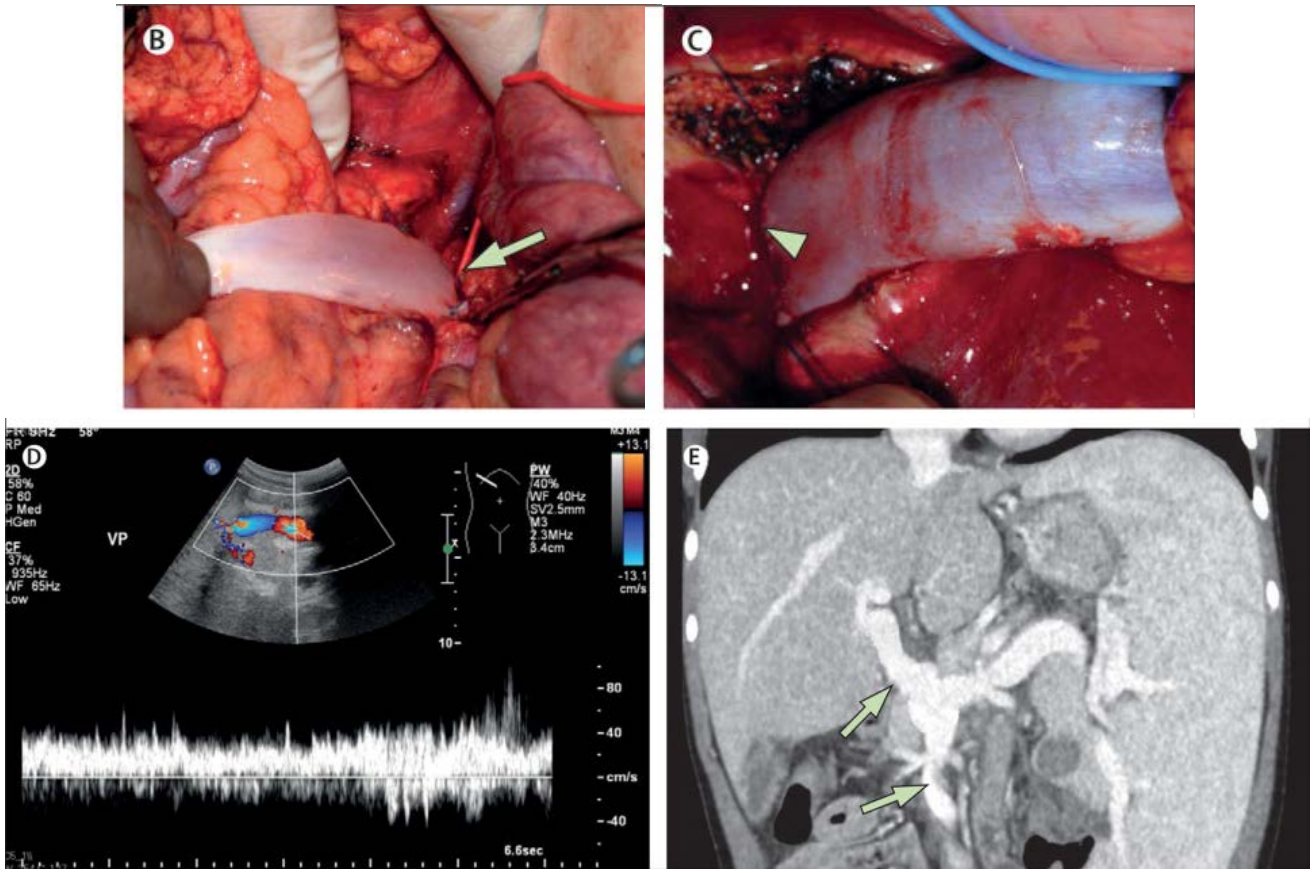
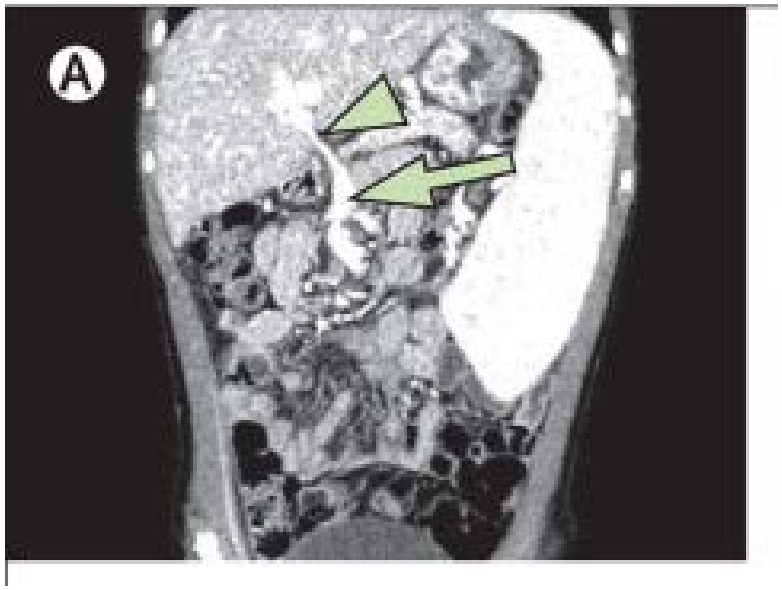
Recellularization of first vein graft



1st surgical procedure



9 month follow-up: vein lumen decreased



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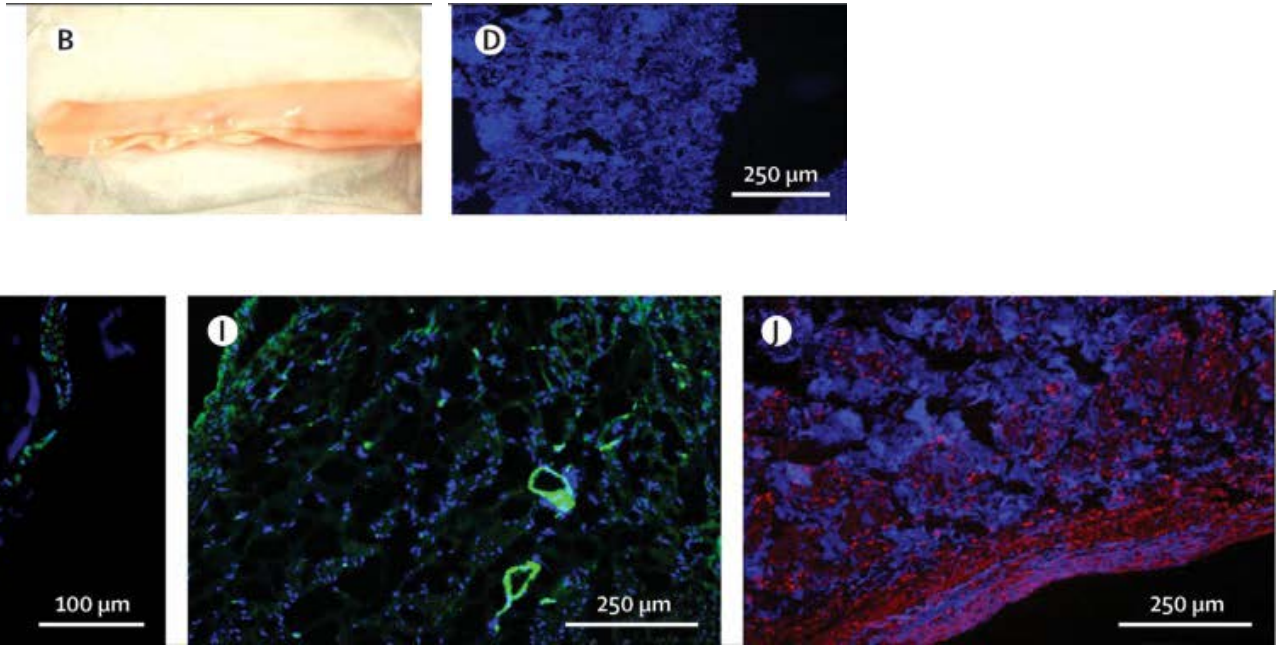
Recellularization of second vein graft



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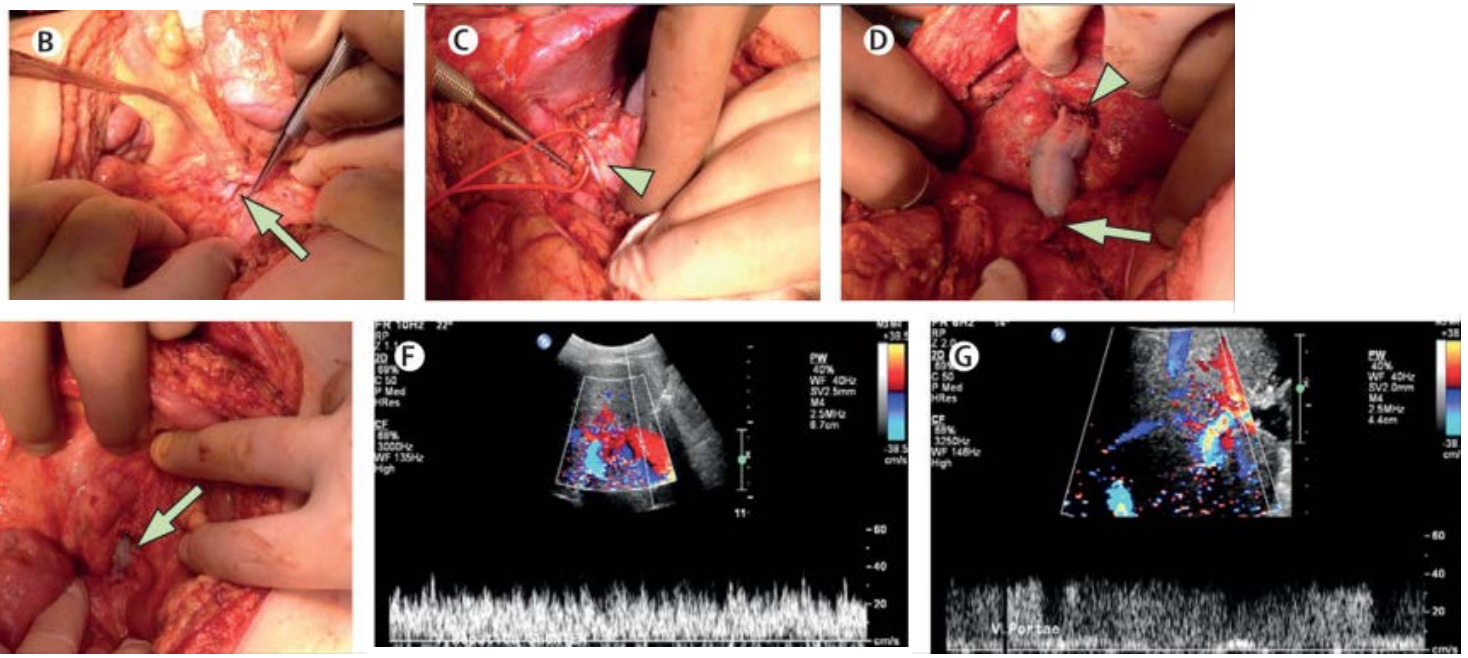
2nd surgical procedure



Follow-up – 1 year

- Patient's height and weight increased .
- No neurocognitive tests done
- Physical activity enhanced
- Articulated speech improved
- Concentration power in school activities developed

- **Risk of postoperative thrombosis**
  - Monitoring the graft → ultrasounds daily postoperatively & heparin

- Change in graft:
  - Lumen was adjusted to the lumen on the portal side of the anastomosis.
  - The flow velocity did not change during this period.
  - Initial circulation to the right lobe was improved after about 2 weeks

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Thank you for your attention!