ISRCTN10171587 https://doi.org/10.1186/ISRCTN10171587

Autotransplantation of the spleen after distal pancreatectomy and splenectomy for benign lesions of the distal pancreas, will it restore the function of the spleen?

Submission date 18/02/2019	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 18/02/2019	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 10/01/2024	**Condition category** Surgery	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
Patients with benign lesions of the left part of the pancreas often need resection of the left part of the pancreas, a distal pancreatectomy (DP). DP often involves removal of the spleen because the blood supply of the spleen is close or adherent to the pancreas. Patients without a spleen have an increased risk of developing possibly lethal infectious complications, thrombosis, as well as certain cancers. Because of the risk of infectious complications, patients require regular vaccinations and a lifelong course of antibiotics. Because of these risks, spleen-preserving DP is now the preferred approach. However, splenic preservation is not always technically feasible and many patients end up with their spleen resected (splenectomy). In this study the researchers will reimplant pieces of the resected spleen (autogenic splenic implantation) at the same operation and assess the immunological function of these transplanted pieces of spleen.

Who can participate?
Adults who require distal pancreatectomy for a benign or premalignant lesion

What does the study involve?
Undergoing distal pancreatectomy as part of standard of care. Additionally, in case splenectomy is performed, participants are randomly allocated to undergo just splenectomy or to receive splenic transplants (autogenic splenic implantation). Six months after reimplantation, the participants are vaccinated with a Salmonella vaccine to test the immune response of the body to this vaccine by measuring antibodies in the blood. Antibodies are produced by the immune system and help clear the body from infections. The antibody response of participants who underwent autogenic splenic implantation is compared with participants who underwent spleen preserving DP and participants who underwent DP with splenectomy. If the antibody response is adequate, patients may no longer require regular vaccinations and lifelong antibiotics in the future.

What are the possible benefits and risks of participating?
Participants potentially get back their splenic function if the spleen is removed and the new pieces of spleen are transplanted back in the abdomen. This could potentially prevent the increased risk of infectious complications after removal of the spleen. No other treatments exist to restore the function of the spleen after its removal. Participants are at risk of developing the known complications of pancreatic surgery but these are the same in patients who do not participate. Previous research has shown there are very few additional complications in patients who underwent transplantation of pieces of their own spleen. Very rarely one of the pieces does not survive and can get infected and become an abscess. In addition, two cases of bowel obstruction have occurred in the past that could have been related to the transplanted pieces of spleen. A possible risk of the vaccine is local pain after the injection, in most cases this resolves in 24 – 48 hours. Another possible risk is an allergic reaction to the vaccine.

Where is the study run from?
University Hospital Southampton NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
June 2018 to July 2023

Who is funding the study?
NIHR and the Liver & Pancreatic Cancer Charity (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
39052

Study information

Scientific Title
Autogenic splenic implantation in distal pancreatectomy with splenectomy for benign lesions of the distal pancreas

Acronym
RESTORE trial version 1

Study objectives
The hypothesis of this study is that autogenic splenic implantation after distal pancreatectomy and splenectomy for benign lesions is safe and feasible and will restore the immunological function of the spleen.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central – Hampshire B Research Ethics Committee, Level 3 Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, Tel: +44 (0)207 1048055, Email: nrescommittee.southcentral-hampshireb@nhs.net, 16/08/2018, ref: 248540

Primary study design
Interventional

Study design
Randomised; Interventional; Design type: Treatment, Surgery

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Autogenic splenic implantation to prevent hyposplenism following distal pancreatectomy for benign neoplasm of the pancreas

Interventions
All patients are discussed in a multi-disciplinary team (MDT) meeting where the surgical approach will be determined, either distal pancreatectomy with splenectomy (DPS) or spleen-preserving distal pancreatectomy (SPDP). If the determined approach is DPS, patients will be randomised preoperatively to either DPS or DPS with autogenic splenic implantation (ASI). If SPDP is the preferred approach, splenectomy will only be performed if splenic preservation cannot be achieved due to technical or safety reasons during the operation. In case splenectomy is inevitable, intraoperative randomising will be performed to either DPS or DPS with ASI. Three groups will be formed:
1. ASI
2. DPS
3. SPDP
Patients will be randomised between ASI and DPS in a 1:1 ratio. An online randomisation system performing variable block randomisation will be used.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Immunologic splenic function assessed using levels of Salmonella typhi specific antibodies (Ab) prior to and after vaccination with the Typhim Vi™ polysaccharide vaccine. The levels of Salmonella typhi specific of Ab raised in response to the Typhim Vi™ polysaccharide vaccine will be measured by using the Salmonella typhi Vi IgG ELISA Assay. Pre-vaccination levels will be measured at 6 months postoperatively and post-vaccination levels at 7 months postoperatively.

Key secondary outcome(s)
1. 30-day mortality, described as mortality during initial hospitalisation or within 30 days postoperative, measured daily as long as participant is in hospital, thereafter at 2 weeks and 6 weeks after discharge
2. 30-day postoperative complication rate, the occurrence of any postoperative complication, measured daily as long as participant is in hospital, thereafter at 2 weeks and 6 weeks after discharge
3. Hospital stay, described as number of postoperative days in hospital, measured once after discharge
4. Operating time, described as number of minutes from incision to closure of skin, measured once after the operation
5. Estimated blood loss, described as the estimated blood loss during the operation, measured once after the operation
6. Blood transfusion required, described as any blood transfusion given during the operation of after during initial hospitalisation, measured once after discharge

Completion date
31/07/2023

Eligibility

Key inclusion criteria
Current inclusion criteria as of 08/06/2022:
1. Adults
2. Indication for distal pancreatectomy for suspected benign lesion
3. Either spleen-preserving or with splenectomy
4. Either laparoscopic or robotic procedures
5. Fit to undergo distal pancreatectomy (American Society of Anaesthesiologists classification of 3 or below)

Previous inclusion criteria:
1. Adults
2. Indication for distal pancreatectomy for suspected benign lesion
3. Either spleen-preserving or with splenectomy
4. Either open or laparoscopic
5. Fit to undergo distal pancreatectomy (American Society of Anaesthesiologists classification of 3 or below)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Proven or suspected malignant lesion of the pancreatic body or tail
2. Asplenia, either functional, surgical or congenital
3. Any other known immune deficiency disorder
4. Known allergy to any of the Typhim Vi vaccine containing components
5. Pregnancy
6. Unfit to undergo distal pancreatectomy (American Society of Anaesthesiologist classification above 3)
7. Prisoners and adults lacking capacity to consent

Date of first enrolment
01/10/2018

Date of final enrolment
31/12/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospital Southampton NHS Foundation Trust (lead centre)
Tremona Road
Southampton
United Kingdom
SO16 6YD

Sponsor information

Organisation
University Hospital Southampton NHS Foundation Trust

ROR

https://ror.org/0485axj58

Funder(s)

Funder type
Government

Funder Name
NIHR Central Commissioning Facility (CCF); Grant Codes: NF-SI-0515-10059,

Funder Name
University Hospital Southampton NHS Foundation Trust

Alternative Name(s)

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		09/01/2024	10/01/2024	Yes	No