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Investigating the impact of surgical operations on the human immune system

Submission date 25/09/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 16/10/2024	**Overall study status** Ongoing	
Last Edited 27/05/2025	**Condition category** Surgery	

Plain English summary of protocol

Background and study aims
Following surgery, some patients develop hospital-acquired infections whilst others do not. The development of infections can increase a patient's length of stay in hospital. The immune system, which protects against infections, is made up of cells called white blood cells. Previous studies have demonstrated that following surgery, the white blood cells of patients who develop infections show reduced function when compared to the white blood cells of patients who do not develop infections. However, it is currently unclear as to why this is. To help fight against infections, white blood cells require energy. This study will acquire blood samples from patients before and after their operation to allow an examination of how surgery impacts the ability of white blood cells to make energy and fight against infection. It is thought that white blood cells from patients who develop infections after surgery will generate less energy than white blood cells from patients who do not develop infections and that this lack of energy is associated with the reduced function of the immune system. This study aims to improve the understanding of why infections develop after surgery. By increasing the understanding of this, it may be possible to develop treatments to increase the function of white blood cells after surgery that would reduce the risk of developing infections and improve patient outcomes such as reducing lengths of hospital stay.

Who can participate?
Adult patients aged between 18 and 65 years old who are undergoing elective surgery for abdominal wall reconstruction.

What does the study involve?
Patients undergoing elective surgery will provide two blood samples: one before and one after their surgery. The immune response caused by the operation will be examined by studying the functional activity of immune cells in these samples and recording the numbers and types of immune cells present.

What are the possible benefits and risks of participating?
Participation in this research study will help improve the understanding of how surgical

interventions impact the immune system. Enhancing the knowledge in this area of research could help improve the management and treatment of future surgical patients by reducing their risk of developing infections.

There are no risks to taking part in this study over and above the normal risks associated with this form of elective surgery. When taking the blood sample, there may be slight discomfort of the needle being inserted into a vein and the possibility of bruising developing afterwards around the area where the needle was inserted. This should disappear in a few days.

Where is the study run from?
The University of Birmingham Research Laboratories within the Queen Elizabeth Hospital Birmingham.

When is the study starting and how long is it expected to run for?
July 2024 to March 2028

Who is funding the study?
Medical Research Council

Who is the main contact?
Dr Jon Hazeldine, j.hazeldine@bham.ac.uk)

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
347577

ClinicalTrials.gov number

Nil known

Secondary identifying numbers
IRAS 347577, UKRI MRC Grant ref: MR/X007243/1

Study information

Scientific Title
Investigating the immune response in patients undergoing surgery

Study objectives
Traumatic injuries are known to cause activation and suppression of the immune system. However, owing to the nature of these injuries, it is not possible to analyse the immune system of a trauma patient before their injury occurs. Surgical operations cause tissue damage similar to that experienced during a traumatic injury. By obtaining a blood sample before and after a surgical operation, this study will allow for the effect of trauma to be analysed directly as the blood sample taken prior to surgery will allow for the analysis of the immune system before a trauma occurs. This immune response can then be compared to that measured in the blood sample taken following the operation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/12/2024, East Midlands - Leicester South Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; 02071048193; leicestersouth.rec@hra.nhs.uk), ref: 24/EM/0284

Study design
Observational cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Patients undergoing elective surgery

Interventions
Two blood samples will be taken from elective surgery patients; one before surgery and the second following the completion of the operation. Blood samples will be subjected to laboratory analysis examining the immune and inflammatory response to the surgical intervention. This analysis will involve studying the function of immune cells, their number and the mechanisms that underlie the changes that occur.

Intervention Type
Other

Primary outcome measure
The metabolic activity of neutrophils and monocytes isolated from blood samples obtained from elective surgery patients will be measured by flow cytometry, enzyme-linked immunosorbent assays and metabolic tracing before and after their operation

Secondary outcome measures
The following secondary outcome measures will be assessed in blood samples obtained from elective surgery patients before and after their operations:
1. Anti-microbial activities and surface phenotype of isolated neutrophils, monocytes and/or peripheral blood mononuclear cells (in the absence and/or presence of ex vivo stimulation) will be measured using flow cytometry
2. Circulating markers of inflammation (e.g. pro-inflammatory cytokines, acute phase proteins, cell-free DNA, Damage-associated molecular patterns, whole blood cell counts) will be measured using enzyme-linked immunosorbent assays, whole blood cell haematological analysers and fluorometric-based assays
3. DNA and RNA epigenetic profiles of neutrophils and peripheral blood mononuclear cells RNA sequencing, DNA methylation assays and real-time polymerase chain reaction (RT-PCR) experiments

Overall study start date
26/07/2024

Completion date
01/03/2028

Eligibility

Key inclusion criteria
1. Male or female patients aged 18-65 years
2. Patient able to give informed consent
3. Patient undergoing elective open abdominal wall reconstruction surgery

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex
Both

Target number of participants
40

Key exclusion criteria
1. Under the age of 18 years and over the age of 65 years
2. A known malignancy
3. Pregnancy
4. The operation is contaminated (e.g. there is a bowel resection +/- anastomosis, iatrogenic bowel injury or presence of a stoma)
5. Minimally invasive (laparoscopic or robotic) surgery
6. Significant anaesthetic complication (such as anaphylaxis, malignant hyperthermia, negative pressure pulmonary oedema)

Date of first enrolment
26/05/2025

Date of final enrolment
01/03/2028

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
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Sponsor information

Organisation
University of Birmingham

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Sponsor type
University/education

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The results generated from this study will be shared with the wider scientific community. This will take the form of published articles in peer-reviewed journals and presentations at national and international conferences.

Intention to publish date
01/03/2029

Individual participant data (IPD) sharing plan

1. The datasets generated during and/or analysed during the current study will be available upon request from Dr Jon Hazeldine (j.hazeldine@bham.ac.uk).
2. The datasets generated during and/or analysed during the current study will be stored in a publicly available repository. Specifically, RNA sequencing data will be made available through the public repository Gene Expression Omnibus (GEO) (http://www.ncbi.nlm.nih.gov/geo). Data will be uploaded concurrent to the acceptance of the study associated manuscript that presents data derived from RNA sequencing analysis. Patients who agree to participate in the study will have been provided with a patient information sheet that details how the data derived from the analysis of their samples will be presented as part of scientific literature in an anonymised manner which means it will not be possible to identify them as individuals.

IPD sharing plan summary

Stored in publicly available repository, Available on request