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Injury, inflammatory markers & the exacerbation of confusion: ASCRIBED

Submission date	Recruitment status	[X] Prospectively registered
21/11/2016	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
11/05/2017	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
03/10/2023	Mental and Behavioural Disorders	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Dementia is an umbrella term used to refer to a wide range of symptoms linked to with a reduction in memory and/or other thinking skills which reduce a person's ability to perform everyday activities. Inflammation is generally a beneficial response to tissue damage or infection. However, when inflammation is extensive or prolonged this can damage healthy tissues and disrupt normal cellular function. Research suggests that acute illnesses or injury causing inflammation can accelerate dementia. However there are few studies which examine underlying mechanisms of how this happens in humans. This study aims to address this gap. The study will compare markers of inflammation and injury found in the blood and cerebrospinal fluid (fluid which bathes the spinal cord (CSF)) of people with and without confirmed dementia who fracture their fracture. A hip fracture is a common example of an acute injury causing an inflammatory response. People who fracture their hip will undergo an operation to repair it. A common procedure during this operation is the giving of spinal aesthetic. This involves inserting a needle into the patient's spinal space and injecting anaesthesia into CSF. This means CSF can be collected before operation via the same needle.

Who can participate?
Patients due to have a hip fracture operation via spinal anaesthesia with all levels of pre-operative confusion.

What does the study involve?
Patients are allocated to one of three groups after their operation: those with confirmed dementia (as obtained from patient's GP notes/hospital records and/or carer insight), non-dementia (no evidence of dementia found in patent's GP notes/medical records) groupings; and pre-operatively confused but without confirmed dementia. Consent is gained for the storage of surplus samples in a bio-bank to help future studies. Pre-operative blood and CSF samples, post-operative blood samples and a short cognitive questionnaire is administered to all patients.

What are the possible benefits and risks of participating?
For patients and their families there are no direct benefits taking part. However it is hoped that

the research may help similar patient groups in the future. Postdural-puncture headaches (PDPH) are a common side-effect of spinal anaesthesia. The collection of CSF may slightly increase the chance of PDPH.

Where is the study run from?
This study is being run by University of East Anglia (UK) and takes place in hospitals in the UK.

When is the study starting and how long is it expected to run for?
November 2016 to December 2022

Who is funding the study?
Alzheimer's Research UK (UK)

Who is the main contact?
Dr Simon Hammond
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Contact information

Type(s)
Public

Contact name
Dr Simon Hammond

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
1

Study information

Scientific Title
ASCRIBED: The impact of Acute SystematiC inflammation upon cerebRospinal fluId and blood BiomarkErs of brain inflammation and injury in Dementia: a study in acute hip fracture patients

Acronym
ASCRIBED

Study objectives
The aim of this study is to evaluate whether hip fracture patients with dementia show elevated markers of systemic inflammation and of brain inflammation in comparison to stable patients with dementia and hip fracture patients without dementia, as measured by biomarkers in cerebrospinal fluid (CSF) and blood.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North East - Newcastle & North Tyneside 1, 24/03/2017, ref: ISRCTN43803769

Study design
Observational case-control study

Primary study design
Observational

Secondary study design
Case-control study

Study setting(s)
Hospital

Study type(s)
Other

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

Health condition(s) or problem(s) studied
Dementia patients admitted to acute hospital settings with a hip fracture.

Interventions
Participants due to have a hip fracture operation via spinal anaesthesia with all levels of pre-operative confusion (as assessed by clinical screening procedures, AMTS (England) and 4AT (Scotland)) will be approached and recruited. Capacity will be assessed and consent or consultee agreement gained. During pre-operative procedures a blood sample will be taken and cerebrospinal fluid (CSF) collected.

48 hours post-operatively patients will be approached to undertake a short cognitive test and have a second blood sample collected. A suitable informant will also be sought to complete a

proxy measure about the patient’s memory and thinking. At 1 month post-operatively patient's GP and medical records will be accessed to search for evidence of dementia. Patients also taking part in ASCRIBED’s sister study PERFECTED (ISRCTN99336264) will be asked to give blood samples at 1, 3 and 6 months post-operatively.

Intervention Type
Other

Primary outcome measure
CSF inflammation and injury is measured by TNF-α, IL-1RA, IL-1β, IL-6 and Neurogranin, tTau, Synaptotagmin, SNAP-25 at baseline.

Secondary outcome measures
Magnitude of the brain inflammation is measured by brain injury markers (phospho-Tau, NFL, neurogranin, synaptotagmin, SNAP-25) in CSF at baseline.

Exploratory:
1. Higher levels of inflammatory and brain injury markers in CSF and blood are associated with worsening cognitive and functional decline measured by MMSE at 6 months post-operatively
2. Cytokines ratio CSF:blood pre-op time will show higher ratios in dementia than non-dementia patients measures in blood and CSF at baseline

Overall study start date
01/11/2016

Completion date
31/12/2022

Eligibility

Key inclusion criteria
Group 1: Pre-operative acute hip fracture patients with confusion as defined by the Abbreviated Mental Test (England) or 4AT (Scotland):
Inclusion Criteria:
1. Patient must have had a confirmed proximal hip fracture requiring an operation and be aged 60 or older at the time of operation
2. Patient has a pre-operative Abbreviated Mental Test score of 8 or below or 4AT score of 1 or above
3. Patient must be undergoing spinal anaesthesia

Group 2: Pre-operative acute hip fracture patients without confusion as defined by the Abbreviated Mental Test (England) or 4AT (Scotland):
Inclusion Criteria:
1. Patient must have had a confirmed proximal hip fracture requiring an operation and be aged 60 or older at the time of operation
2. Pre-operative Abbreviated Mental Test score of 9 or above or 4AT score of 0
3. Patient must be undergoing spinal anaesthesia

Participant type(s)
Mixed

Age group
Adult

Sex
Both

Target number of participants
400

Total final enrolment
469

Key exclusion criteria
Group 1 and 2:
1. Decision taken not to have hip surgery
2. Patient has head trauma with bleeding as indicated by a CT scan
3. Patient has confirmed diagnosis of Parkinson's disease
4. Patient not expected to survive beyond 4 weeks

Date of first enrolment
01/06/2017

Date of final enrolment
31/08/2019

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
Royal Infirmary of Edinburgh
51 Little France Crescent
Edinburgh
United Kingdom
EH16 4SA

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Royal Sussex County Hospital
Eastern Road
Brighton
United Kingdom
BN2 5BE

Study participating centre
Princess Royal University Hospital
Farnborough Common
Orpington
United Kingdom
BR6 8ND

Study participating centre
Royal Derby Hospital
Uttoxeter Road
Derby
United Kingdom
DE22 3NE

Study participating centre
Pinderfields Hospital
Mid Yorkshire Hospitals NHS Trust
Wakefield
United Kingdom
WF1 4DG

Study participating centre
York Teaching Hospital NHS Foundation Trust
York
United Kingdom
YO31 8HE

Study participating centre

Princess Royal Hospital
Orpington
United Kingdom
BR6 8ND

Study participating centre
James Paget University Hospital
Great Yarmouth
United Kingdom
NR31 6LA

Study participating centre
Russells Hall Hospital
The Dudley Group NHS Foundation Trust
Dudley
United Kingdom
DY1 2HQ

Study participating centre
Peterborough City Hospital
North West Anglia NHS Foundation Trust
Peterborough
United Kingdom
PE3 9GZ

Study participating centre
Queen's Medical Centre Campus
Nottingham University Hospitals NHS Trust
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Royal Blackburn Hospital
East Lancashire Hospitals NHS Trust
Blackburn
United Kingdom
BB2 3HH

Study participating centre
University Hospital of North Tees
North Tees and Hartlepool NHS Foundation Trust
Stockton-on-Tees
United Kingdom
TS19 8PE

Study participating centre
The Royal Shrewsbury Hospital
The Shrewsbury and Telford Hospital NHS Trust
Shrewsbury
United Kingdom
SY3 8XQ

Study participating centre
Doncaster Royal Infirmary
Doncaster and Bassetlaw Teaching Hospitals NHS Foundation Trust
Doncaster
United Kingdom
DN2 5LT

Study participating centre
Royal United Hospital Bath NHS Foundation Trust
Bath
United Kingdom
BA1 3NG

Study participating centre
University Hospital of North Durham
County Durham and Darlington NHS Foundation Trust
Durham
United Kingdom
DH1 5TW

Study participating centre
Royal Bolton Hospital
Bolton NHS Foundation Trust
Bolton
United Kingdom
BL4 0JR

Study participating centre
Kingston Hospital
Kingston Hospital NHS Foundation Trust
Kingston
United Kingdom
KT2 7QB

Study participating centre
Royal Stoke University Hospital
University Hospitals of North Midlands NHS Trust
Stoke-on-Trent
United Kingdom
ST4 6QG

Study participating centre
Countess of Chester Hospital NHS Foundation Trust
Chester
United Kingdom
CH2 1UL

Study participating centre
Western Sussex Hospitals NHS Foundation Trust
-
United Kingdom
-

Study participating centre
Medway Maritime Hospital
Medway NHS Foundation Trust
Gillingham
United Kingdom
ME7 5NY

Study participating centre
Whiston Hospital
St Helens & Knowsley Teaching Hospitals NHS Trust
Rainhill
United Kingdom
L35 5DR

Study participating centre
Southampton General Hospital
University Hospital Southampton NHS Foundation Trust
Southampton
United Kingdom
SO16 6YD

Study participating centre
Royal Devon & Exeter Hospital
Royal Devon and Exeter NHS Foundation Trust
Wonford
United Kingdom
EX2 5DW

Study participating centre
Basildon University Hospital
Basildon and Thurrock University Hospitals NHS Foundation Trust
Basildon
United Kingdom
SS16 5NL

Study participating centre
Musgrove Park Hospital
Taunton and Somerset NHS Foundation Trust
Taunton
United Kingdom
TA1 5DA

Study participating centre
Scunthorpe General Hospital
Northern Lincolnshire and Goole NHS Foundation Trust
Scunthorpe
United Kingdom
DN15 7BH

Study participating centre
Royal Lancaster Infirmary
University Hospitals of Morecambe Bay NHS Trust

Lancaster
United Kingdom
LA1 4RP

Study participating centre
Yeovil District Hospital
Yeovil District Hospital NHS Foundation Trust
Yeovil
United Kingdom
BA21 4AT

Study participating centre
Watford General Hospital
West Hertfordshire Hospitals NHS Trust
Watford
United Kingdom
WD18 0HB

Study participating centre
Sandwell General Hospital
Sandwell and West Birmingham Hospitals NHS Trust
West Bromwich
United Kingdom
B71 4HJ

Sponsor information

Organisation
University of East Anglia

Sponsor details
University of East Anglia
Norwich Research Park
Norwich.
England
United Kingdom
NR4 7TJ
+44 1603 591460
t.moulton@uea.ac.uk

Sponsor type

University/education

ROR
https://ror.org/026k5mg93

Funder(s)

Funder type
Charity

Funder Name
Alzheimer’s Research UK

Alternative Name(s)
Alzheimer's Research Trust, AlzheimersResearch UK, AlzResearchUK, ARUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal.

Intention to publish date
30/04/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Prof Chris Fox, Norwich Medical School, University of East Anglia, Norwich Research Park, Norwich, NR4 7TJ, United Kingdom.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	07/09/2019	09/12/2020	Yes	No