Quantitative Imaging of Cervical Spinal Structures in Healthy Participants and Patients with Cervical Degenerative Disc Disease - the DISC Pilot Study -

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This study will consist of three parts. Part 1: FeasibilityPrimary objectiveTo evaluate the feasibility and repeatability for the quantitative MRI sequences (i.e. z-DTI, ASL, DSC, DCE, TMRE, and SyMRI) of cervical spinal structures (i.e....

Ethical review	Approved WMO
Status	Pending
Health condition type	Spinal cord and nerve root disorders
Study type	Observational non invasive

Summary

ID

NL-OMON53351

Source
ToetsingOnline

Brief title
Quantitative Imaging of Cervical Spinal Structures - the DISC Pilot Study -

Condition

- Spinal cord and nerve root disorders

Synonym
Cervical Degenerative Disc Disease, Cervical Disc Herniation

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: Ministerie van OC&W,Cock Hadders Subsidie (NF Simoes de Souza). Deze subsidie geldt als aanvulling op de MD/PhD benche fee van het UMCG aan NF Simoes de Souza.

Intervention

Keyword: Cervical spine, MRI, Quantitative, Spine

Outcome measures

Primary outcome

Part 1

- Z-DTI: Fractional anisotropy (FA-metric).

- ASL: *M obtained after transit time (TI) for labelled and unlabelled arterial blood.

- DSC: relative spinal cord blood volume (rSCBV), relative oxygen extraction fraction (rOEF), mean transit time (MTT), capillary-level hemodynamics (CTH), cerebral metabolic rate of oxygen (CMR2) arterial imput function (AIF).

- DCE: transfer constant (k-trans), fractional volume of extravascular-extracellular space (Ve), fractional volume of plasma space (Vp), rate constant.

- TMRE: stiffness and fluidity.

- SyMRI: tissue properties T1, T2 and PD and dynamic contrast weighted images (T1W, T2W, PDW, STIR and FLAIR).

Part 2

In addition to study parameters described in part 1, main study parameters of part 2 are clinical outcome measured with NDI, VAS-arm, VAS-neck, mJOA, Nurick, EQ-5D-5L and WAI-SI.

Part 3

In addition to study parameters described in part 1 and 2, which will be repeated after 1 year of follow-up in part 3 in patients with symptomatic CDDD, also surgical treatment status and characteristics will be documented.

Secondary outcome

Part 1

-To determine a correlation of quantitative MRI sequences of the cervical spinal cord to extent of compression on conventional MRI in healthy participants and patients with symptomatic CDDD (comparison for the spinal cord only as nerve roots are difficult to measure on conventional MRI). Extent of compression on conventional MRI is measured as a ratio between the diameter of the spinal canal and spinal cord.
-Compare quantitative MRI sequences of cervical spinal structures in healthy participants and patients with symptomatic CDDD to available values in literature.
-To do a between-group analysis, comparing quantitative MRI sequences of cervical spinal structures of healthy participants to patients with symptomatic CDDD (as a whole group).
-To do a between-group analysis, comparing quantitative MRI sequences of cervical nerve root and intervertebral disc of healthy participants to patients with cervical radiculopathy (as a subgroup of symptomatic CDDD patients).
-To do a between-group analysis, comparing quantitative MRI sequences of cervical spinal cord and intervertebral disc of healthy participants to

patients with cervical myelopathy (as a subgroup of symptomatic CDDD patients).

Part 2

-To determine a correlation of quantitative MRI sequences of cervical spinal structures to clinical outcome measured with Visual Analogue Scale (VAS)-arm, VAS-neck, Nurick grade, EuroQol 5-Dimension 5-Level (EQ-5D-5L), and Work Ability Single item (WA-SI) in patients with symptomatic CDDD. Evaluating a correlation of quantitative MRI parameters to clinical measurements other than the primary outcomes NDI and mJOA will serve as a test of robustness of the primary outcomes.

Part 3

-To determine correlation of baseline quantitative MRI sequences of cervical spinal structures to clinical outcome measured after 6 months of follow-up (NDI, VAS-arm, VAS-neck, EQ-5D-5L, WA-SI, mJOA or Nurick) in patients with symptomatic CDDD accordingly.

-To compare baseline quantitative MRI sequences to 6-month quantitative MRI sequences in patients with symptomatic CDDD.

Study description

Background summary

Cervical degenerative disc disease (CDDD) is the consequence of degeneration of intervertebral discs and joints and can result in compression of the cervical

nerve root leading to clinical symptoms of radiculopathy, compression of the spinal cord with symptoms of myelopathy, or a combination of both. The incidence of CDDD is rising with the aging population, and, consequently, a significant increase in surgeries for symptomatic CDDD is predicted in the upcoming years. As such, the decision for- and optimal timing of surgery remain challenging.

Currently, the decision for surgery in patients with symptomatic CDDD is related to symptoms, as well as position and size of disc herniation on conventional Magnetic Resonance Imaging (MRI). However, conventional MRI only enables qualitative morphological evaluation, leaving space for subjective individual interpretation. Also, disc herniations on conventional MRI are frequently found in asymptomatic individuals, while, in symptomatic individuals type and extent of disc herniation does not correlate to severity of symptoms. Altogether, the current standard using conventional MRI cannot optimally predict response to surgery for patients with symptomatic CDDD.

Quantitative imaging is rapidly being recognized as a supplement to conventional MRI and refers to the direct measurement of physical properties of tissue. These novel techniques are promising, as they are noninvasive and could potentially aid in determining objective cut-offs to stage disc herniation. Diffusion tensor imaging (DTI) is one of the most studied quantitative techniques and allows for evaluation of microstructural changes. The DTI fractional anisotropy (FA) metric was demonstrated as valid biomarker for recovery after surgery in cervical myelopathy as well as surgical selection in lumbar radiculopathy. Moreover, recent introduction of zoomed-DTI (z-DTI) could lead to greater imaging accuracy while proven feasible in the cervical spine.

Furthermore, the cervical spinal cord and its nerve roots are highly vascularized and their perfusion could be compromised by disc-herniation related compression. Using the endogenous perfusion technique arterial spin labeling (ASL), as well as contrast-based perfusion techniques such as susceptibility contrast (DSC) and dynamic contrast enhanced (DCE), degree of ischemia, hypoxia as well as signal enhancement can be estimated. ASL has been studied twice for spinal cord perfusion mapping and DSC was demonstrated feasible in the spine of healthy participants as well as patients with cervical myelopathy. Additionally, increased signal enhancement was observed for DCE in degenerative discs of the lumbar spine. To our best knowledge, no studies have been conducted to assess perfusion of the cervical nerve roots, which are compromised in cervical radiculopathy due to CDDD.

Besides microstructure and perfusion, viscoelastic properties of cervical spinal structures may change in relation to disc herniation-related compression. Therefore, it would be interesting to study mechanical properties such as stiffness and viscosity, which can be measured with Tomo-MR-Elastography (TMRE). To our best knowledge, no previous study has assessed cervical intervertebral discs and spinal structures using TMRE, making

this a promising first study.

Finally, imaging is a relatively time-consuming matter, and including additional sequences will only increase its lengthiness. Therefore, several methods are being developed to perform imaging in a more efficient manner. One novel method is Synthetic MRI (SyMRI). Advantages of SyMRI are a reduced acquisition time, possibility of performing automatic tissue segmentation and volume estimation and acquisition of quantitative parameters. SyMRI has been studied once in the spine, and significant differences in quantitative intervertebral disc values were found in relation to hydration-status of the disc.

Since no single measurement has been proven to be the golden standard in previous studies, it is likely that a combination of measurements is needed for clinical application. Therefore, the aim of this pilot study is to explore a multi-parametric quantitative MRI approach including z-DTI, ASL, DSC, DCE, TMRE, and SyMRI to measure cervical intervertebral discs, the spinal cord and its nerve roots.

Study objective

This study will consist of three parts.

Part 1: Feasibility

Primary objective
To evaluate the feasibility and repeatability for the quantitative MRI sequences (i.e. z-DTI, ASL, DSC, DCE, TMRE, and SyMRI) of cervical spinal structures (i.e. intervertebral discs, spinal cord, and nerve roots) in healthy participants and patients with symptomatic CDDD.
Hypothesis:
Quantitative MRI sequences demonstrate repeatability in healthy participants and patients with symptomatic CDDD.

Part 2: Correlation to clinical measurements

Primary objective
To determine a correlation of quantitative MRI sequences of cervical spinal structures to clinical impairment in patients with symptomatic CDDD. Clinical impairment will be measured with the Neck Disability Index (NDI) for cervical radiculopathy, modified Japanese Orthopaedic Association Score (mJOA) for cervical myelopathy, and NDI and mJOA for cervical radiculomyelopathy.
Hypotheses
-In symptomatic CDDD patients with radiculopathy, NDI scores are significantly correlated to quantitative MRI sequence parameters.
-In symptomatic CDDD patients with myelopathy, mJOA scores are significantly correlated to quantitative MRI sequence parameters.

-In symptomatic CDDD patients with radiculomyelopathy, NDI and mJOA scores are significantly correlated to quantitative MRI sequence parameters.

Part 3: 6 months follow-up

Primary objective
To determine a correlation between baseline quantitative MRI sequences of cervical spinal structures to surgical treatment after 6 months of follow-up in patients with symptomatic CDDD.
Hypothesis
Being surgically treated after 6 months of follow-up in patients with symptomatic CDDD is significantly correlated to baseline quantitative MRI sequences of cervical spinal structures (e.g. patients who were not surgically treated because of improvement of symptoms also had better baseline quantitative MRI sequence values of cervical spinal structures).

Study design

A prospective pilot study.

All participants will be subjected to several MRI sequences, using a state of the art 3T Siemens MRI Scanner available in the UMCG. First, all participants (healthy participants and patients with symptomatic CDDD) undergo baseline neurologic examination. Additionally, the healthy participants fill out the following questionnaires: Neck Disability Index (NDI), Visual Analogue Scale (VAS) for arm and neck pain, modified Japanese Orthopedic Association (mJOA), Nurick grade, EuroQol 5-Dimension 5-Level (EQ-5D-5L), and Work Ability Single Item (WAI-SI). Regarding patients with symptomatic CDDD, the abovementioned questionnaires will be filled out before their visit to the outpatient clinic as part of clinical routine. The data of these questionnaires will be extracted from the EPD for this study. If patients did not fill out questionnaires before their outpatient clinic visit, they will fill out the questionnaires during the study visit.

Finally, during the same baseline visit, all participants undergo MRI scanning: localizer & T2-weighted anatomical (conventional MRI), z-DTI, ASL, DSC, DCE, TMRE, and SyMR. The total scanning time will be approximately 40 minutes. For assessment of reproducibility, 10 healthy participants and 10 patients will be scanned 2 times on different days/times. The patients with symptomatic CDDD will have another study visit after 6 months of follow-up to assess their treatment status (having had surgery yes/no; in case of yes also the surgery characteristics), to fill out the abovementioned questionnaires and have an MRI with additional sequences.

This is a pilot hypothesis-generating study, exploring the feasibility of quantitative MRI sequences z-DTI, ASL, DSC, DCE, TMRE, and SyMRI and assess a correlation to clinical impairment and treatment status after 6 months of

follow-up. There is not sufficient data available for a sample size calculation. Recent TMRE in brain imaging used a cohort of 12-18 subjects, therefore a pragmatic sample size of 20 healthy volunteers and 20 patients with symptomatic CDDD is chosen. An interim-analysis will be performed after 10 participants are included for power and sample size calculations. This will be incorporated in an amendment to inform the METc.

Study burden and risks

All participants (healthy and patients) will need a conventional MRI scan with quantitative MRI sequences, which will take approximately 40 minutes. Most MRI sequences used in this study are non-invasive and do not involve any ionizing radiation. However, DSC and DCE require administration of a bolus contrast. The contrast agent that will be used is Dotarem. Without any contra-indications for an MRI scan or contrast agent, health is not at risk. Scans will be planned outside of clinical workhours, except for patients with symptomatic CDDD who did not undergo a conventional MRI before their visit at the outpatient clinic. Those patients will undergo MRI scanning as part of clinical routine.
Before scanning, all participants undergo neurologic examination. Furthermore, questionnaires are filled out during the study visits, which will take no longer than 20 minutes. The patients with symptomatic CDDD already filled out the same questionnaires before their visit to the outpatient clinic as part of clinical routine.
There is an overall negligible risk for participants, as based on the Risk Classification Checklist of the NFU. Therefore, we can conclude that this study is a low-risk study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Healthy participants and patients with Cervical Degenerative Disc Disease:
-Patients with cervical degenerative disc disease aged >18 years and age-matched healthy participants.
-Sufficient understanding of spoken and written Dutch language
-Agrees to participate in the obligatory measurements of this study and signed informed consent prior to any study-related procedures.
-No contraindication for an MRI scan (e.g. non-MRI compatible heart pacemaker, metallic foreign body in the eye, aneurysm clip in the brain, severe claustrophobia or known pregnancy).

Exclusion criteria

-Patient refusal
-Uncapable to read/understand written and spoken Dutch language
-Contraindications for performing MRI

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2023
Enrollment:	40
Type:	Anticipated

Ethics review

Approved WMO Date:	21-06-2023
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-12-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL83742.042.23