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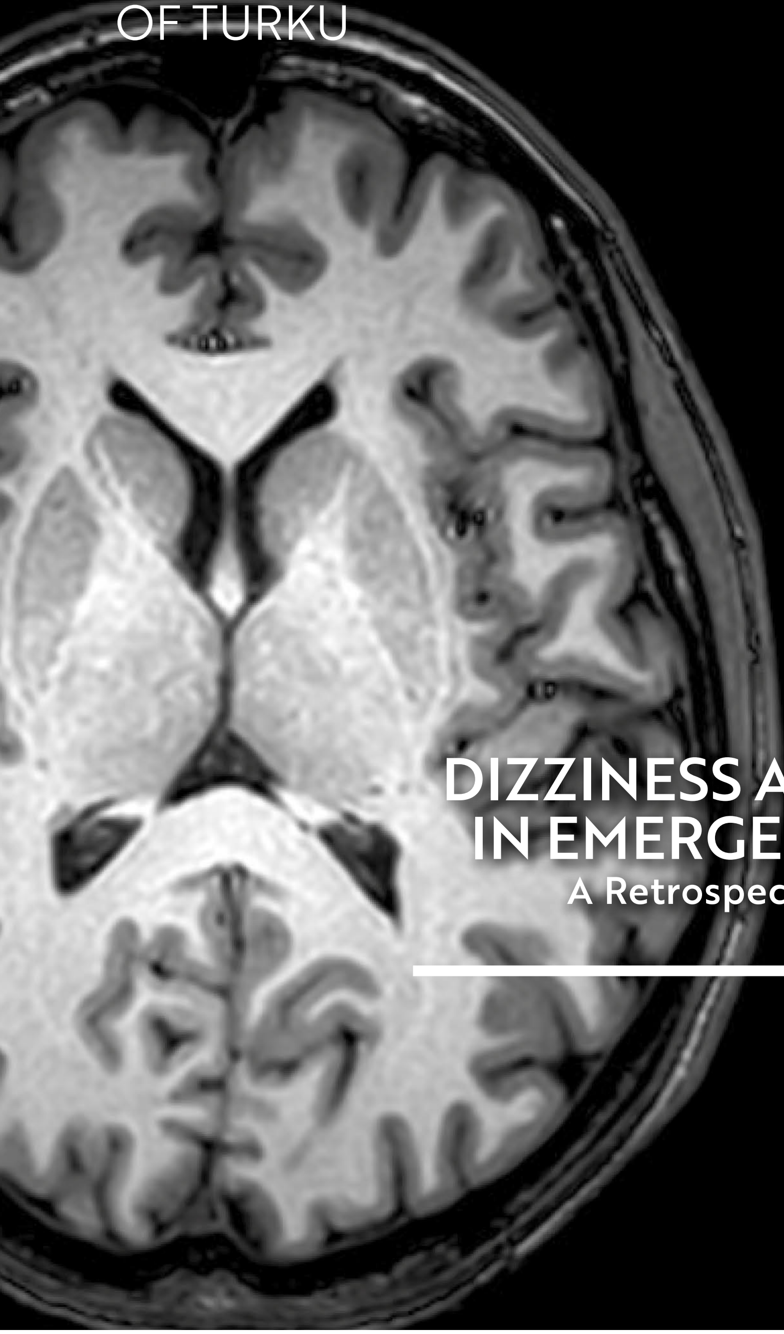

# DIZZINESS AND HEADACHE IN EMERGENCY BRAIN MRI

## A Retrospective Analysis of Imaging Outcomes

Tatu Happonen

TURUN YLIOPISTON JULKAISUJA – ANNALES UNIVERSITATIS TURKUENSIS
SARJA – SER. D OSA – TOM. 1820 | MEDICA – ODONTOLOGICA | TURKU 2024

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## ABSTRACT

Dizziness and headache may pose diagnostic challenges and are common reasons for emergency neuroimaging. While computed tomography has traditionally been the first-line imaging method for emergency neuroimaging, magnetic resonance imaging (MRI) provides an alternative with high accuracy and without ionizing radiation. This thesis aimed to explore the imaging outcomes of emergency brain MRI in patients presenting with these symptoms and to identify clinical factors predictive of acute imaging findings.

This thesis included patients who underwent emergency brain MRI because of acute dizziness, headache, or clinical suspicion of cerebral venous sinus thrombosis (CVST) between April 2014 and January 2019 in Turku University Hospital, an academic tertiary care referral center. Patient characteristics, relevant clinical data, and imaging outcomes were recorded and analyzed.

Among the 1,169 patients imaged for dizziness, acute stroke was found in 17%, and other clinically significant pathology in 8% of patients. Older age, male sex, and a prevalence of cardiovascular risk factors and neurologic signs were predictive of acute stroke. Stroke was observed in 14% of patients presenting with dizziness as their sole symptom. Of the 696 patients with headache, 20% had clinically meaningful findings, and a similar proportion presented incidental findings of little clinical relevance. Older age, smoking, nausea, and signs/symptoms of infection were associated with significant findings, whereas patients with numbness or history of migraine had less significant findings. Among the 327 patients imaged for suspected CVST, a low rate of CVST (1.5%) was observed, with 15% exhibiting other clinically significant pathology.

Predictors of acute pathology may aid in prioritizing patients for emergency MRI. This thesis demonstrates the current diagnostic yields of emergency brain MRI and contributes to optimizing the clinical impact of emergency neuroimaging.

KEYWORDS: Magnetic resonance imaging, Emergency imaging, Dizziness, Headache, Stroke, Diagnostic yield

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## TIIVISTELMÄ

Huimaus ja päänsärky voivat aiheuttaa diagnostisia pulmatilanteita, ja ne ovat yleisiä syitä päivystykselliselle neurokuvantamiselle. Tietokonetomografia on perinteisesti ollut ensisijainen päivystyksellisen neurokuvantamisen menetelmä, jolle magneettikuvaus (MRI) tarjoaa tarkan vaihtoehdon ilman ionisoivaa säteilyä. Tämän väitöskirjatutkimuksen tarkoituksena oli tutkia päivystyksellisen aivojen MRI:n kuvantamislöydöksiä huimaus- ja päänsärkypotilailla, sekä selvittää kliinisiä tekijöitä, jotka ennustavat akuutteja kuvantamislöydöksiä.

Tutkimukseen sisällytettiin akuutin huimauksen, päänsäryn tai kliinisen sinustromboosiepäilyn vuoksi päivystysluonteisesti aivojen MRI:lla kuvatut potilaat, huhtikuun 2014 ja tammikuun 2019 välillä Turun yliopistollisessa keskussairaalassa. Kartoitimme ja analysoimme potilaiden olennaiset kliiniset tiedot, sekä kuvantamislöydökset.

1 169:stä huimauksen vuoksi kuvatusta potilaasta 17 %:lla todettiin akuutti aivoinfarkti ja 8 %:lla jokin muu kliinisesti merkittävä kuvantamislöydös. Korkea ikä, miessukupuoli, sydän- ja verisuonitautien riskitekijät, sekä neurologiset oireet ennustivat akuuttia aivoinfarktia. Potilaista, joilla huimaus oli ainoa oire, 14 %:lla todettiin aivoinfarkti. 696:sta päänsäryn vuoksi kuvatusta potilaasta 20 %:lla oli kliinisesti merkittävä kuvantamislöydös, ja vähämerkityksellisiä sattumalöydöksiä todettiin samassa suhteessa. Korkea ikä, tupakointi, pahoinvointi ja infektio-oireet olivat yhteydessä merkittäviin kuvantamislöydöksiin, kun taas puutumisoireen tai migreenihistorian omaavilla potilailla merkittäviä löydöksiä todettiin vähemmän. 327:n potilaan joukosta, joilla epäiltiin sinustromboosia, vain 1,5 %:lla todettiin sinustromboosi ja 15 %:lla muita kliinisesti merkittäviä löydöksiä.

Akuuttien kuvantamislöydösten ennustetekijät voivat auttaa päivystyksellisten MRI-tutkimusten potilasvalinnassa. Väitöskirjatutkimus osoittaa päivystyksellisen aivojen magneettikuvauksen ajankohtaista diagnostista arvoa ja edistää täten päivystyksellisen neurokuvantamisen kliinisen arvon optimointia.

AVAINSANAT: Magneettikuvaus, Päivystyskuvantaminen, Huimaus, Päänsärky, Aivoinfarkti, Diagnostinen arvo

# Table of Contents

# Abbreviations

| | |
|---|---|
| ADC | Apparent diffusion coefficient |
| AIS | Acute ischemic stroke |
| ALARA | As low as reasonably achievable |
| AUC | Area under the curve |
| AVS | Acute vestibular syndrome |
| BMI | Body mass index |
| CE | Contrast-enhanced |
| CI | Confidence interval |
| CSF | Cerebrospinal fluid |
| CT | Computed tomography |
| CVST | Cerebral venous sinus thrombosis |
| CVT | Cerebral venous thrombosis |
| DWI | Diffusion-weighted imaging |
| ED | Emergency department |
| EMR | Electronic medical records |
| FLAIR | Fluid-attenuated inversion recovery |
| GRACE-3 | Guidelines for reasonable and appropriate care in the emergency department 3 |
| HINTS | Head impulse, nystagmus, test of skew |
| IQR | Interquartile range |
| MIP | Maximum intensity projection |
| MRA | Magnetic resonance angiography |
| MRI | Magnetic resonance imaging |
| MRV | Magnetic resonance venography |
| NMR | Nuclear magnetic resonance |
| NPV | Negative predictive value |
| NS | Non-significant |
| OR | Odds ratio |
| PACS | Picture archiving and communication systems |
| PPV | Positive predictive value |
| RF | Radiofrequency |
| RIS | Radiological information systems |
| ROC | Receiver operating characteristic |

| | |
|---|---|
| S | Significant |
| STANDING | Spontaneous nystagmus, direction, head impulse test, standing |
| SWI | Susceptibility-weighted imaging |
| T1 | T1-weighted imaging |
| T2 | T2-weighted imaging |
| TE | Time to echo |
| TFE | Turbo field echo |
| TI | Inversion time |
| TOF | Time-of-flight |
| TR | Repetition time |

# List of Original Publications

This dissertation is based on the following original publications, which are referred to in the text by their Roman numerals:

I Happonen, T., Nyman, M., Ylikotila, P., Mattila, K., & Hirvonen, J. (2024). Imaging Outcomes of Emergency MR Imaging in Dizziness and Vertigo: A Retrospective Cohort Study. *American Journal of Neuroradiology*, 45(6), 819–825.

II Happonen, T., Nyman, M., Ylikotila, P., Merisaari, H., Mattila, K., & Hirvonen, J. (2022). Diagnostic yield of emergency MRI in non-traumatic headache. *Neuroradiology*, 65(1), 89–96.

III Happonen, T., Nyman, M., Ylikotila, P., Kytö, V., Laukka, D., Mattila, K., & Hirvonen, J. (2023). Imaging Outcomes of Emergency MRI in Patients with Suspected Cerebral Venous Sinus Thrombosis: A Retrospective Cohort Study. *Diagnostics*, 13(12), 2052.

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# 1 Introduction

Magnetic resonance imaging (MRI) could be considered one of the pinnacles of modern science, combining principles from quantum mechanics, superconducting magnets, computer science, and mathematics. The research towards contemporary MRI technology traces back to the early twentieth century. In 1944, American physicist Isidor Isaac Rabi won the Nobel Prize in Physics for his resonance method, which recorded the magnetic properties of individual atomic nuclei in a vacuum chamber. He is often credited for the discovery of nuclear magnetic resonance (NMR) – the foundational principle of MRI. In 1946, independent teams led by Felix Bloch at Stanford University and Edward Purcell at Harvard University simultaneously demonstrated the phenomenon of NMR in condensed matter. Intriguingly, they achieved this using two distinct experimental methods. In recognition for this work, they shared the Nobel Prize in Physics in 1952.

Fast forward a few decades, American chemist Paul C. Lauterbur invented a mechanism to encode spatial information into an NMR signal using magnetic field gradients in 1971. He published his theory in *Nature* in 1973 (Lauterbur, 1973), eventually sharing the Nobel Prize in Physiology or Medicine in 2003 with Peter Mansfield. Thus, MRI has come into existence, prompting rapid advancements in its field of research thereafter.

The first clinical MRI scanners were installed in the early 1980s, followed by widespread use in the medical field in subsequent decades. Today, MRI stands among the most important diagnostic imaging methods across specialties. It offers superior soft tissue characterization and therefore precise images on various organs and structures in the human body, albeit at a relatively high cost. Unlike imaging methods employing X-rays for contrast between different structures, MRI does not utilize ionizing radiation, making it a safer option.

Traditionally, MRI scans have been primarily conducted on a non-emergent, by-appointment practice. However, due to various technical advancements, MRI has become increasingly accessible and feasible, extending its implications to emergency settings. While computed tomography (CT) has remained the go-to imaging modality in emergency neuroimaging, accumulating literature suggests that emergency MRI can offer an accurate and cost-effective alternative, especially in areas where CT may perform poorly, such as diagnosing acute posterior circulation ischemic strokes (Shah et al., 2023a; Tu et al., 2024; Kepka et al., 2022). With the growing demand for medical imaging, there is a pressing need to research the clinical value of advanced imaging techniques. This thesis aimed to explore this topic in the context of dizziness and headache, both common reasons for emergency neuroimaging.

# 2 Review of the Literature

## 2.1 Magnetic resonance imaging

### 2.1.1 Technique

#### 2.1.1.1 Physical basis

MRI is a non-invasive medical imaging technique that uses a strong magnetic field and radio waves to generate detailed cross-sectional images. In a modern MRI machine, a strong magnetic field is produced with a superconductive electromagnet, cooled to a temperature near absolute zero (approximately -270°C) to achieve superconductivity. Unlike CT, MRI does not use ionizing radiation but instead relies on the quantum properties of hydrogen atoms. There are abundant hydrogen atoms in the human body, situated within various chemical environments, including water, carbohydrates, proteins, and fatty acids.

NMR is the core principle of MRI. When in a magnetic field, the magnetic spin (a quantum property of an atom) of the hydrogen atom aligns with the field. Then, targeted radiofrequency (RF) pulses are applied, causing the hydrogen nuclei to absorb energy. Upon returning to their original state, the nuclei emit this energy, which is then detected and used to generate cross-sectional images.

#### 2.1.1.2 T1 and T2 relaxation

Following the RF excitation, the magnetization of the hydrogen nuclei returns to equilibrium. The two main types of this relaxation are longitudinal relaxation (T1 relaxation) and transverse relaxation (T2 relaxation).

During longitudinal relaxation, the magnetization of the hydrogen nuclei gradually realigns with the external magnetic field (**Figure 1**). This realignment occurs as the nuclei transfer energy to their surroundings. The time it takes for the longitudinal magnetization to recover to 63% of its initial value after the RF pulse is known as T1 relaxation time. Different tissues have varying T1 relaxation times, providing contrast between tissues in T1-weighted images. For instance, fat tissue has a faster T1 relaxation time than water.

As a result of a RF pulse, hydrogen nuclei spins start oscillating in the same phase, forming a net magnetization vector in the transverse plane (perpendicular to the magnetic field). Transverse relaxation occurs when the magnetization of the hydrogen nuclei dephase, i.e., loses coherence. This phenomenon takes place as the hydrogen nuclei interact with each other within the tissue. The time it takes for the transverse magnetization vector to decay to 37% of its initial magnitude after the RF pulse is known as T2 relaxation time. T2-weighted images are generated based on different T2 relaxation times between different tissues. For example, fat loses transverse magnetization more rapidly than water.

#### 2.1.1.3 Image acquisition

Adjustable imaging parameters include repetition time (TR), echo time (TE), flip angle, field of view and slice thickness. TR is the time interval between RF pulses and affects T1-weighted contrast. TE denotes the time between the RF pulse and the acquisition of the signal, affecting T2-weighted contrast. The flip angle is the angle at which the RF pulse is applied, also playing a role in contrast enhancement.

After RF pulses are applied, the MRI scanner detects the signals emitted by the hydrogen nuclei using RF coils placed around the body part being imaged. Gradient magnetic fields are applied in three dimensions, introducing slight variations in the strength of the magnetic field across the body. These gradients enable precise encoding of signal locations.

The signals received from the RF coils are then processed by the MRI scanner's computer system. The raw data is subjected to a series of computational and mathematical procedures to form meaningful images. Following preprocessing, the received signals undergo Fourier transformation, decomposing complex signals into constituent frequencies. Coupled with spatial encoding, the MRI scanner can determine the precise locations of the signal sources within the body. Finally, the processed signal data is combined to reconstruct detailed anatomical images.

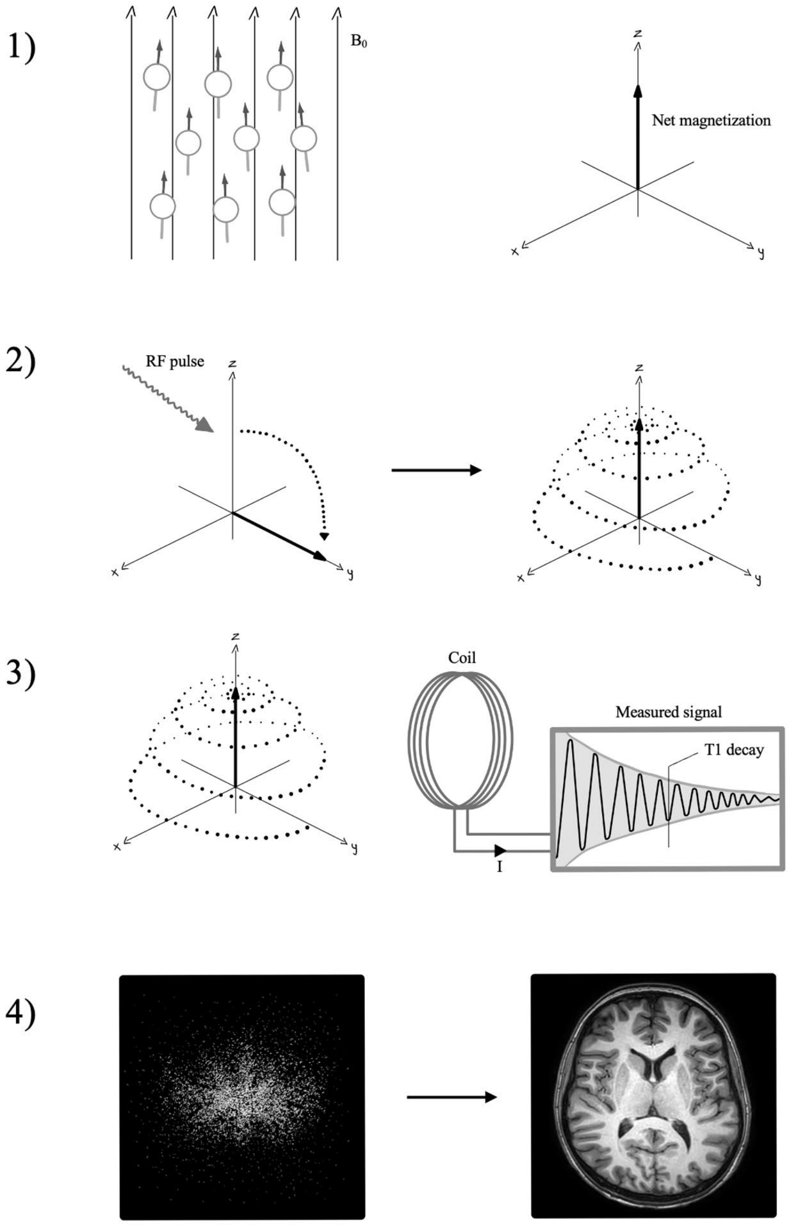


**Figure 1.** A simplified illustration of the MRI technique. **1)** The hydrogen nuclei are aligned with the magnetic field ($B_0$), forming a net magnetization vector. **2)** A targeted RF pulse misaligns the net magnetization vector perpendicular to the MRI machine's magnetic field: from z-direction to xy-plane. The nuclei return to their original state in a spiraling motion, causing a changing magnetic field. **3)** The changing magnetic field induces current (I) in the receiving coil, which can be read as a signal. **4)** The received signals are used to reconstruct detailed images.

### 2.1.2 Common sequences in brain imaging

The sequences most commonly used in the MRI of the brain are T1, T2, fluid-attenuated inversion recovery (FLAIR), diffusion-weighted imaging (DWI), susceptibility-weighted imaging (SWI), and magnetic resonance angiography (MRA) (**Figure 2**).

T1 provides excellent anatomical detail and is broadly used for anatomical definition and tissue characterization. It is useful for identifying structural abnormalities, such as tumors, as well as assessing the morphology of brain structures. Gadolinium-based contrast agents primarily affect T1-weighted images by shortening the T1 relaxation time of the tissues where they accumulate. This results in higher signal intensity in these areas (called enhancement), which can reveal various pathologies affecting the blood-brain barrier (such as infections, tumors, etc.). Contrast-enhanced (CE) T1-weighted images are also often used to ensure the patency of venous structures, such as when cerebral venous sinus thrombosis (CVST) is suspected.

T2-weighted images are sensitive to changes in water content and useful in detecting pathology with increased water concentration, such as edema, demyelination, gliosis, and degeneration.

FLAIR is a modified T2-weighted sequence that suppresses the signal from the cerebrospinal fluid (CSF), making it easier to detect abnormalities adjacent to the CSF spaces. This is useful for identifying lesions in the periventricular regions and pathology caused by conditions such as vascular degeneration or multiple sclerosis. FLAIR can also show pathology in CSF spaces when the suppression fails, for example due to blood or pus in the CSF.

DWI measures the Brownian motion of the hydrogen nuclei in water molecules within tissues. For instance, it is highly useful for detecting acute ischemic stroke (AIS) in brain tissue. In AIS, the areas of restricted diffusion is related to cytotoxic edema due to ischemic injury. Restricted diffusion in the non-enhancing fluid collection denotes purulence and is indicative of an abscess.

SWI is highly sensitive to magnetic susceptibility differences between tissues and is used to detect hemorrhages, microbleeds, and iron deposition in the brain. Paramagnetic degraded blood products present in hemorrhages provide low signal intensity in SWI.

MRA can be achieved using contrast-enhanced angiography or, more typically, using time-of-flight (TOF) angiography. TOF angiography is based on the velocity of arterial blood flow and therefore does not require a contrast agent. MRA is used to detect various vascular pathologies, such as arterial stenosis, aneurysms, malformations, and dissections.

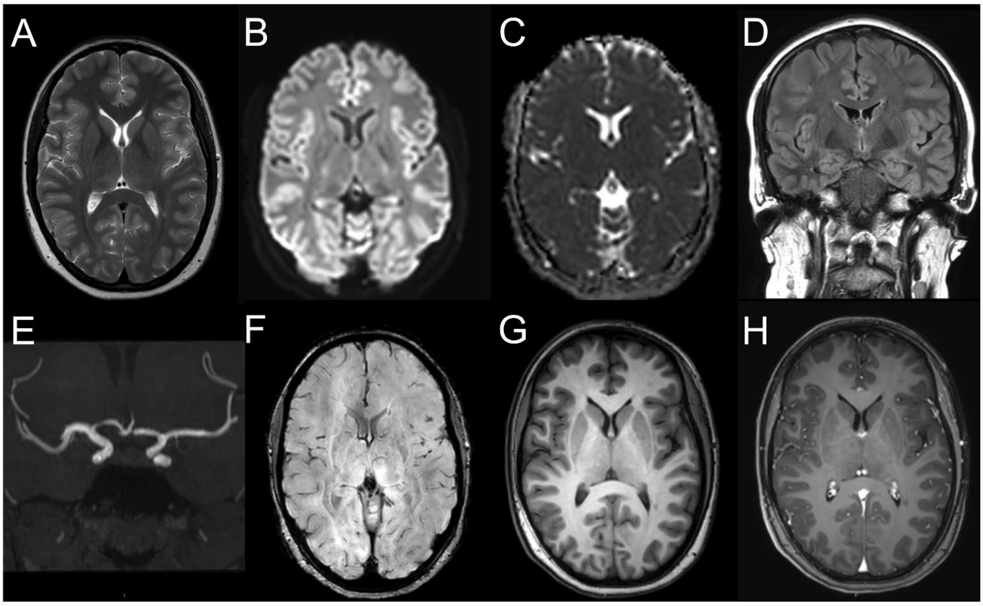


**Figure 2.** Example demonstrations of brain MRI sequences. Sequences are: T2 axial (**A**), DWI trace axial (**B**), DWI ADC (apparent diffusion coefficient) axial (**C**), FLAIR coronal (**D**), TOF-MRA MIP (maximum intensity projection) coronal (**E**), SWI axial (**F**), T1 3D TFE (turbo field echo) axial (precontrast) (**G**), and T1 3D TFE axial (postcontrast) (**H**).

## 2.2 Challenges in emergency radiology

### 2.2.1 Computed tomography

CT is currently the most commonly used method in emergency neuroimaging, primarily due to its fast scan times, widespread availability, and lower cost compared to MRI. Essentially, CT is based on the principles of X-ray imaging, where different tissues and structures are differentiated based on their X-ray attenuation properties. First, X-rays are generated in the X-ray tube by accelerating electrons with high voltage. When the high-speed electrons strike the target anode material, they rapidly lose their kinetic energy, of which a small proportion (~1%) is released as X-rays. The majority of the electrons' kinetic energy transfers to heat. The X-ray beam is altered by filters and collimators. As the X-rays pass through the patient's body, they attenuate based on tissue density, with denser tissues absorbing more X-rays. Prior to reaching the detector, passing X-rays are further refined through a grid for enhanced accuracy. Detectors convert the detected radiation into electrical signals, which are utilized for image reconstruction. The swift rotation of the gantry around the patient allows for the acquisition of projections from multiple angles, which are then reconstructed into cross-sectional images.

A routine non-contrast head CT image acquisition usually takes a few seconds. If a contrast agent is being used, imaging takes a bit longer. At our institution (Turku University Hospital, an academic tertiary care referral center), a cost of head CT outside office hours is ~200€. In emergency neuroimaging, CT is often used as a first-line imaging method due to its high accuracy in the detection of intracranial hemorrhage and other acute abnormalities that influence patient treatment in the emergency setting (Rindler et al., 2020; Potter & Sodickson, 2016; Gibney et al., 2020; Czap & Sheth, 2021; Douglas et al., 2018).

However, CT does have several limitations. In stroke diagnostics, CT performs poorly especially in the posterior cranial fossa, with a low sensitivity of AIS of ~30% in acute dizziness or vertigo (Shah et al., 2023a). Missing an acute stroke can have serious consequences, including an increased risk of future, potentially more severe infarcts. Furthermore, uncertainty in ruling out AIS with CT may result in stroke-mimicking conditions, such as migraine or vestibular pathology, being initially treated as a stroke. In the brain parenchyma, CT has suboptimal sensitivity to detect subtle changes that may be present in cases of very recent or lacunar stroke, infection, demyelination, etc. Moreover, CT utilizes ionizing radiation, which carries inherent risks, particularly with repeated exposure. While the radiation dose from a single CT scan may remain relatively low, cumulative exposure over time adds to the risk of adverse effects, including cancer. This is especially concerning for sensitive populations such as pregnant individuals, children, and adolescents. Non-contrast CT does not have absolute contraindications.

### 2.2.2 Magnetic resonance imaging

Compared to CT, MRI offers superior soft tissue contrast and does not expose patients to ionizing radiation. In emergency neuroimaging, its higher sensitivity to subtle brain pathologies often leads to more accurate and earlier diagnoses. MRI is particularly feasible in cases of infection, demyelination, degeneration, CSF abnormalities, and vascular pathology. MRI is capable of detecting small infarctions, and provides superior visualization of structures within the posterior fossa compared to CT.

Yet, the higher accuracy of MRI comes with trade-offs. Higher cost, longer scan times, and, most importantly, limited accessibility decrease the feasibility of MRI in emergency imaging compared to CT. For instance, currently, a brain MRI scan at our institution costs approximately 2-3 times more than a head CT scan, totaling ~550€ outside office hours. A typical scan time of a brain MRI with routine sequences (T1, T2, FLAIR, DWI, SWI, and TOF MRA) is about 20 minutes. However, the scan process can be expedited by selecting only essential sequences and using acceleration techniques (You et al., 2021). For example, at our institution, the quick "wake-up stroke" protocol has an approximate scan time of 10 minutes.

Absolute contraindications for MRI are "MRI unsafe" implants, devices, or foreign bodies, particularly if these are located close to the eyes or major vessels (e.g., ferromagnetic cerebral aneurysm clips, metallic foreign body in the eye) (Caraiani et al., 2019; Hofman et al., 2024; Kubal, 2008). Through technological advancements, cochlear implants, aneurysm clips, aneurysm coils, and other endovascular devices that are used currently are compatible with MRI (Cass et al., 2023; Todt et al., 2020; Hofman et al., 2024; Tsutsui et al., 2022; Yokota et al., 2023), although they may cause artifacts. Cardiac implantable electronic devices (pacemakers and implantable cardioverter-defibrillators) are considered as relative contraindications – these patients may undergo MRI safely when certain conditions are met (Chow & Nazarian, 2014; Korutz et al., 2017). Morbid obesity and claustrophobia may limit the usability of MRI (Ginde et al., 2008; Hudson et al., 2022; Le et al., 2015; Perry et al., 2018). Children may have a difficult time tolerating MR studies due to long scan times and a frightening environment with loud noises,

and may therefore need sedation/anesthesia. Sedation is often achieved safely, with low adverse event rates (Mallory et al., 2023; Cravero et al., 2006). Various techniques to minimize the need for sedation have been introduced, including fast sequences, earphones and goggles, and prior familiarization (Dong et al., 2019; Sorge et al., 2022). Brain MRI in infants younger than 3 months old, using feed and sleep technique and pillow immobilization, can be done safely and efficaciously without general anesthesia (Antonov et al., 2017; Caro-Domínguez et al., 2022; Mathur et al., 2008).

Currently, dedicated MRI scanners for emergency use are not common on a global scale. Consequently, studies regarding the use of MRI in emergency neuroimaging remain limited.

### 2.2.3 Increasing demands

The utilization of emergency imaging has rapidly increased over the last few decades, particularly with respect to CT scans. This trend of increased CT usage in emergency departments (EDs) has been reported internationally in North America (Selvarajan et al., 2019; Bellolio et al., 2017; Levin et al., 2014; Hess et al., 2014; Berdahl et al., 2013; Larson et al., 2011; Broder & Warshauer, 2006), Australia (Maxwell et al., 2021), Asia (Ahn et al., 2014; Hu et al., 2016; Oh et al., 2012), and Europe (Juliusson et al., 2019). Although the utilization rates varied across different institutions and time periods, the average overall increase in the use of CT in EDs ranged from +50% to +150% from the 2000s to the 2010s. Concurrently, there has been a notable rise in the utilization of MRI in EDs, with increases ranging from +300% to +800% (Selvarajan et al., 2019; Ahn et al., 2014; Levin et al., 2014; Rankey et al., 2008). In the corresponding study periods, changes in ED patient volumes ranged from -9% to +40%. Overall, in the 2010s, CT and MRI were utilized approximately at rates of 100–290 and 4–8 per 1,000 ED presentations, respectively. At our institution, utilization of emergency MRI has shown a steady increase from 2015 to 2018, at least in regard to emergency brain MRI (**Figure 3**). Dedicated emergency MRI has been in use since 2013 at our institution. In addition to optimizing the use of emergency imaging services, the rising utilization of MRI would consequently require increasing funding to ensure sustainability. Unfortunately, hospitals and wellbeing services counties may have difficulties keeping up with the increasing costs of imaging.

In pediatric EDs, CT utilization has decreased over the last decade (Frush et al., 2020; Marin et al., 2020; Ohana et al., 2018), coupled with a rise in MRI usage (Marin et al., 2020; Ohana et al., 2018; Scheinfeld et al., 2017). This shift is likely influenced by the principles of ALARA (As Low As Reasonably Achievable), which emphasize justification and optimization of radiation exposure (Sodhi et al., 2015).

Recent studies have demonstrated significant increases in on-call radiologist workloads, primarily due to the growing utilization of CT. In a large teaching hospital in Israel, the workload of on-call radiologists more than doubled compared to the growth rate of ED visits between 2012 and 2019 (Dan Lantsman et al., 2022). Over a 15-year period from 2006 to 2020, the overall workload during on-call hours, measured in terms of relative value units (i.e., a composite measure of the time, complexity, and resources associated with a study or procedure) (Baadh et al., 2016) quadrupled in one of the largest teaching hospitals in the Netherlands (Bruls & Kwee, 2020). A similar trend of increasing emergency imaging workload has been reported in the United States as well (Poyiadji et al., 2023). As the demand for emergency imaging services continues to grow, there is a need for scientific evidence to support the judicious and effective use of advanced imaging, including emergency MRI. This can be achieved through retrospective analysis of risk factors and imaging outcomes, followed by prospective studies.

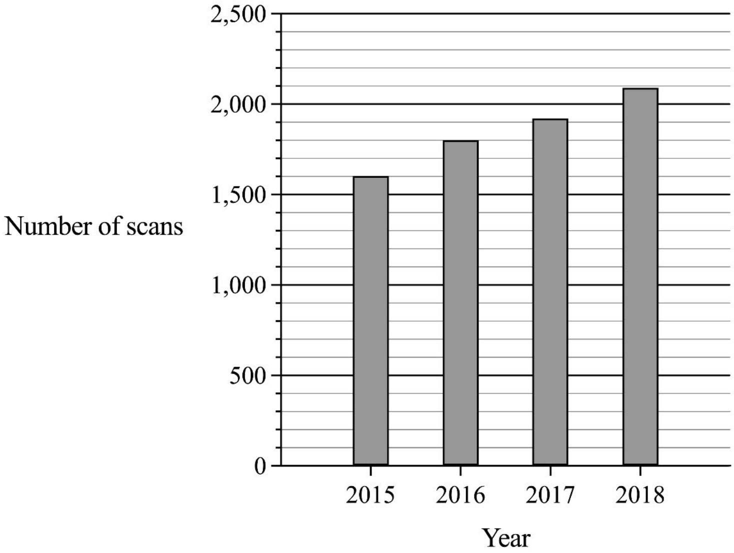


**Figure 3.** Annual emergency brain MRI scans conducted between January 2015 and December 2018 in Turku University Hospital.

## 2.3 Dizziness and vertigo

### 2.3.1 Definition

According to the International Classification of Vestibular Disorders, dizziness is defined as a sensation of disturbed or impaired spatial orientation without a false or distorted sense of motion, whereas vertigo is described as a sensation of self-motion when no self-motion is occurring or the sensation of distorted self-motion during an otherwise normal head movement (Bisdorff et al., 2009). Patients and physicians often use these terms interchangeably, which may lead to imprecision and inconsistency in patient care and research (Newman-Toker et al., 2007; Stanton et al., 2007). In this thesis, vertigo denotes a symptom encompassing false spinning sensations caused by asymmetric involvement of the vestibular system, although the exact definition varies among studies.

### 2.3.2 Epidemiology and clinical characteristics

Dizziness (including vertigo) is a rather common complaint among the general population, affecting 15–35% at some point in their lives (Neuhauser, 2016), and is reported to account for 2.1%–3.6% of all ED visits (Idil et al., 2020; Ljunggren et al., 2018; Newman-Toker et al., 2008; Kerber et al., 2008). Dizziness and vertigo are often recurrent, leading to a higher annual prevalence than incidence. The incidence of dizziness, including vertigo, of moderate or severe intensity was estimated at 3% per year in unselected adults, with a prevalence of 23% (Neuhauser, 2016).

Patients exhibiting acute dizziness or vertigo often represent a diagnostic challenge, as the differential diagnosis is myriad. Despite many patients being diagnosed with benign peripheral vestibular disorders, some patients may need neuroimaging to rule out central causes of dizziness. Stroke, particularly vertebrobasilar acute ischemic stroke, is the primary differential diagnosis among central causes and is diagnosed in approximately 3-5% of all emergency visits for dizziness and vertigo (Kerber et al., 2006; Saber Tehrani et al., 2018).

Children and adults may share common causes of dizziness and vertigo, although epidemiology changes with aging. For instance, the most common causes of pediatric dizziness and vertigo include benign paroxysmal vertigo of childhood and vestibular migraine (Davitt et al., 2020; Fancello et al., 2021; Lee et al., 2017; Pellegrino et al., 2022; Raucci et al., 2016). Although severe causes of pediatric vertigo are rare, the presence of certain red flags (e.g., brutal onset, fever/sepsis, neurologic symptoms) may warrant neuroimaging, preferably with MRI (Beretti & Desnous, 2023).

Several bedside examination patterns, such as HINTS (Head Impulse, Nystagmus and Test of Skew) and STANDING (SponTAneous Nystagmus, Direction, head Impulse test, standiNG) and clinical risk scores (such as TriAGe+ and $ABCD^2$) are developed for early stroke detection (Gerlier et al., 2021; Kuroda et al., 2017; Quimby et al., 2018; Shah et al., 2023b). Despite these attempts to focus on high-risk patients, generally 30% to 50% of acutely dizzy emergency patients undergo neuroimaging (A. S. Kim et al., 2012; Quimby et al., 2018; Saber Tehrani et al., 2018).

A traditional approach to dizziness has relied on defining the type of perceived symptom (e.g., dizziness, vertigo, disequilibrium, presyncope, lightheadedness) when assessing the most likely etiology (Kerber & Newman-Toker, 2015; Stanton et al., 2007). Using the type of dizziness as the primary factor in the diagnostic process presents problems. Literature suggests that this paradigm does not consistently predict underlying causes (Kerber & Newman-Toker, 2015). Moreover, evidence shows that patients often have difficulty distinguishing between different types of dizziness and commonly alter their description when asked even minutes later, and that many simultaneously endorse multiple symptom descriptors (Newman-Toker et al., 2007; Kerber et al., 2017). Although alternative diagnostic strategies exist, accumulating evidence suggests an approach based on symptom timing and triggers that categorize patients into three groups (J. A. Edlow et al., 2018, 2023; Gurley & Edlow, 2019; Kerber & Newman-Toker, 2015; Pelletier et al., 2023). Each vestibular syndrome category has its own differential diagnosis and a targeted bedside approach: 1. Acute vestibular syndrome (AVS), where bedside examination differentiates vestibular neuritis from stroke; 2. Spontaneous episodic vestibular syndrome, where associated symptoms help differentiate vestibular migraine from transient ischemic attack; and 3. triggered (positional) episodic vestibular syndrome, where the Dix-Hallpike test helps differentiate benign paroxysmal positional vertigo from posterior fossa structural lesions.

A subset of patients in the ED with dizziness or vertigo presents with AVS: a clinical syndrome defined by the presence of vertigo, nystagmus, nausea/vomiting, gait instability, and head-motion intolerance, lasting longer than 24 hours. Although the exact prevalence of AVS among patients presenting to the ED with dizziness is unknown, it has been estimated as being between 10% and 20% (Ljunggren et al., 2018; Tarnutzer et al., 2011). The HINTS examination has been validated as a bedside test for frontline clinicians to distinguish a peripheral vestibular disorder (usually vestibular neuritis) from a central one (usually stroke) in those presenting with AVS. However, it should not be used in those with other vestibular syndromes or generalized dizziness. According to GRACE-3 (Guidelines for reasonable and appropriate care in the emergency department 3) from The Society for Academic Emergency Medicine, the HINTS exam is recommended as a first-line bedside test for AVS (J. A. Edlow et al., 2023). If the examination confirms a peripheral disorder, no imaging is required. In several studies (including a meta-analysis of 43 studies), HINTS is demonstrated to yield a high sensitivity of ≥93% for a central cause in AVS when performed by trained clinicians (Shah et al., 2023b; Kattah et al., 2009; Gerlier et al., 2021; Newman-Toker et al., 2013), likely surpassing DWI-MRI within <48 hours of symptom onset (Kattah et al., 2009; Tarnutzer et al., 2023). A meta-analysis of five studies found that both sensitivity and specificity of the HINTS examination were better when it was performed by trained specialists (97% and 95%, respectively) rather than emergency physicians (83% and 44%, respectively) (Ohle et al., 2020). Moreover, Dmitriew et al. claimed that HINTS had a limited diagnostic value in the EDs, reflecting the difficulties in using the exam only in patients who meet the AVS criteria, and in performing and interpreting the test correctly (Dmitriew et al., 2021). Thus, HINTS testing should only be performed by clinicians skilled in its use. Using the HINTS exam on patients who do not meet AVS criteria may have harmful consequences. In particular, the interpretation of the head impulse test depends on whether AVS is present or absent. In patients with AVS, the absence of a corrective saccade is worrying and indicative of stroke, whereas in patients without AVS, the absence of the saccade is the normal presentation. Uncertainty in taking detailed history and using bedside examinations may lead to overuse of neuroimaging. According to the guidelines on dizziness by the American College of Radiology, MRI is usually warranted when dizziness is accompanied by neurologic deficits or HINTS exam is consistent with central vertigo (ACR Appropriateness Criteria® Dizziness and Ataxia, accessed April 16, 2024).

### 2.3.3 Imaging aspects

Imaging options include CT/CTA and MRI. CT scans are the most commonly used method to exclude stroke due to widespread availability and fast scan times, but they have a low pooled sensitivity for stroke of ~30% among patients with acute dizziness and vertigo (Shah et al., 2023a). The pooled specificity for stroke was 99%. CT is especially challenging in the posterior fossa, where vertebrobasilar acute ischemic strokes occur. Combining CT/CTA with CT perfusion might increase the sensitivity of diagnosing acute posterior circulation stroke to as high as 76% (Shen et al., 2017; Sporns et al., 2016). Recent GRACE-3 guidelines deemed CT as very inaccurate in identifying posterior circulation stroke in patients with AVS (J. A. Edlow et al., 2023). If the average pretest probability of stroke at 25% was applied (Tarnutzer et al., 2011), a negative CT would only decrease the posttest probability to 19.4% (J. A. Edlow et al., 2023), which was far above the threshold that emergency clinicians have indicated as acceptable when "ruling out" stroke (<0.5%) among patients presenting with acute dizziness (Kene et al., 2015). In fact, in a study with 8,600 patients discharged with peripheral vertigo and a presumably negative head CT examination were 2.3 times more likely to experience stroke in the next 30 days than matched controls who did not undergo CT, reflecting the false sense of reassurance that a negative CT may provide (Grewal et al., 2015).

Although less frequently used, conventional MRI has a higher pooled sensitivity of 80% and a pooled specificity of 99% for stroke among patients with acute dizziness (Shah et al., 2023a). There are concerns related to the early use of MRI and DWI-MRI among acutely dizzy patients. A meta-analysis showed that small posterior circulation infarcts were five times more likely to be DWI-MRI negative than those in the anterior circulation (B. L. Edlow et al., 2017). The data indicated that DWI-MRI was time dependent for strokes in any arterial distribution (Chalela et al., 2007), and specifically in the posterior circulation (Axer et al., 2007). In summary, MRI scanning, when done within 48 hours of symptom onset, is likely less accurate than the HINTS examination performed by a trained physician. However, by including thin section DWI with a 3 mm slice thickness, an even higher sensitivity of 95% for posterior circulation stroke may be achieved (Entwisle et al., 2016). Recently, MRI was shown to demonstrate a higher rate of critical findings (Tu et al., 2023) and improved cost-effectiveness (Tu et al., 2024) compared to CT with CTA in emergency patients with dizziness.

Only a few studies have been published on the yield of emergency MRI in dizziness and vertigo. In a retrospective study among 188 emergency patients with dizziness or vertigo who underwent MRI, around 20% acute stroke rate and 17% other significant abnormality rate were reported (Kabra et al., 2015). In that study, risk factors for acute stroke were age over 50 years, a high number of cardiovascular risk factors, a short duration of symptoms, and at least one neurological sign. A higher proportion of stroke (33%) has been prospectively recorded among selected emergency patients with acute onset vertigo who did not have a previous diagnosis of peripheral vertigo (Samreen et al., 2021). In another retrospective cohort of consecutive dizzy ED patients from 2007 to 2009, 105 had brain MRI with 9% significant abnormality rate (5% infarction, 2% neoplasm, 2% intracranial hemorrhage) (Navi et al., 2013). The study did not investigate clinical predictors of pathology, but instead predictors leading to neuroimaging (with CT or MRI): in a multivariate analysis, age ≥ 60 years, prior stroke, headache, and focal neurological signs were independently associated with acquisition of neuroimaging, while isolated dizziness was independently associated with not obtaining neuroimaging. Similar to the aforementioned study, a 9% stroke rate (12 of 131 patients) was reported among ED patients with vertigo who underwent MRI (Chase et al., 2012). Furthermore, five of the 12 patients with stroke had a head CT performed before the MRI, and none of the CT scans showed the stroke. A recent congress abstract reported a low emergency MRI yield of AIS (3 patients of 115; 2.6%) among patients presenting to ED with isolated vertigo without neurologic deficits (Officer et al., 2024). Overall, all previous studies on the topic had sample sizes fewer than 200 patients, and none of them specifically explored predictors of acute pathology on MRI.

In the United States, recent annual spending for neuroimaging dizziness was reported as high as 88 million USD, of which MRI accounted for 70%, although a head CT scan was the most frequently used test across settings (Adams et al., 2022). In total, neuroimaging was applied over 376,000 times per year within 6 months of the first presentation with dizziness to an emergency department or an outpatient clinic. For emergency neuroimaging of dizziness, accumulating evidence endorses MRI as a more cost-effective imaging method, compared to CT/CTA (Tu et al., 2024; Kepka et al., 2022). Tu et al. underlined lower long-term costs, and Kepka et al. highlighted reductions in both time to the clinical decision, and costs of hospitalization and readmission, after implicating MRI exclusively dedicated to ED for use in patients with dizziness or diplopia (both possible symptoms of a posterior circulation stroke).

## 2.4 Headache

### 2.4.1 Classification

The third edition of the International Classification of Headache Disorders categorize headaches into three main groups, depending on their etiology: 1. Primary headaches; 2. Secondary headaches; and 3. Painful cranial neuropathies, other facial pains, and other headaches (Headache Classification Committee of the International

Headache Society [IHS] The International Classification of Headache Disorders, 3rd Edition, 2018). Primary headaches represent the most common causes, including migraine, tension-type headache, and trigeminal autonomic cephalgia. Secondary headaches are merely a symptom of an underlying disease, encompassing vascular disorders, infections, malignancies, CSF abnormalities, and disorders of homeostasis (e.g., hypoxia and/or hypercapnia, fasting). Headache can also result from cranial trauma, but this thesis specifically focuses on non-traumatic headache.

### 2.4.2 Epidemiology and clinical characteristics

According to the Global Burden of Disease study, headache disorders rank among the most prevalent and disabling conditions worldwide (Stovner et al., 2018). An estimated global prevalence of 52% (95% conficende interval [CI]: 48.9–55.4) was reported, based on an extensive review of 357 headache prevalence publications, although the majority of these publications were from high-income countries (Stovner et al., 2022). The review reported estimated global prevalences of migraine as 14%, of tension-type headache 26%, and of having headache on ≥15 days/month 4.6%. Moreover, each day, 16% of the world's population was estimated to have headache. The current prevalence marks a notable increase from the previous iteration of the same review conducted in 2007, where the overall prevalence of headaches was reported to be 46% (Stovner et al., 2007).

A meta-analysis found a high pooled prevalence of primary headaches of 62% (95% CI: 53–70) in 8–18 years old children and adolescents, despite a high degree of heterogeneity between studies (Onofri et al., 2023). Although the overall prevalence of headache decreases in the elderly, secondary headaches become more common (Kaniecki & Levin, 2019; Bravo, 2015; Stovner et al., 2022). In those over the age of 65 years, secondary headache disorders can account for up to 15% of new-onset headaches, a significant increase from the estimated 1.6% for those under the age of 65 years (Pascual & Berciano, 1994). Thus, a higher index of suspicion for a secondary headache disorder is warranted in older patients with a new-onset headache.

Non-traumatic headaches are among the most common neurological complaints in the EDs, reported in ~1–4% of all ED visits (Guryildirim et al., 2019; Munoz-Ceron et al., 2019). While most presentations of headache are benign and resolve spontaneously or with minor therapeutic measures, it is crucial to consider the possibility of potentially life-threatening secondary causes that may require further diagnostic workup. The differential diagnosis of secondary headache is vast, and involve conditions such as intracranial hemorrhages, cerebral or cerebellar infarction, carotid or vertebral artery dissection, CVST, idiopathic intracranial hypertension and hypotension, reversible cerebral vasoconstriction syndrome, meningitis, encephalitis, and brain tumors (Raam & Tabatabai, 2021). When history, physical, or neurologic examination elicits "red flags" or critical features of the headache, then further investigation with imaging may be warranted to exclude a secondary cause (Whitehead et al., 2019). Red flags are widely suggested in the literature, and include neurologic deficit (including decreased consciousness), neoplasm history, systemic symptoms including fever, sudden or abrupt onset, pregnancy or puerperium, relation to activity or position, older age (onset after 65 years, or after 50 years in some sources), papilledema, immunocompromised state, and head trauma (Do et al., 2019; Giamberardino et al., 2020; Locker et al., 2006; Munoz-Ceron et al., 2019; Do et al., 2021; Robblee & Grimsrud, 2020). However, further epidemiological and prospective studies are needed to explore the sensitivity and specificity of these clinical features.

In addition to the traditional red flags, a concept of “green flags” has been recently introduced, with a goal to increase diagnostic accuracy and optimize the allocation of diagnostic resources (Do et al., 2021; Pohl et al., 2021; Wijeratne et al., 2023). Green flags refer to information suggesting a primary headache disorder, indicating that further investigations for a secondary cause may not be necessary. The proposed green flags are: 1. The current headache has already been present during childhood; 2. The headache occurs in temporal relationship with the menstrual cycle; 3. The patient has headache-free days; 4. Close family members have the same headache phenotype; and 5. Headache occurred or stopped more than one week ago. As an important notion, the purpose of red flags and green flags differs. The red flags are designed to have high sensitivity for secondary headaches, while green flags are intended to have high specificity for primary headaches. However, these green flags require further studies to evaluate the potential benefit of the concept, as they are based solely on expert opinion.

### 2.4.3 Imaging aspects

In an emergency setting, various secondary causes of headache can be ruled out by using neuroimaging. Evidence suggests that major neuroimaging findings among outpatients presenting with non-traumatic headache are rare, and concern <10% of these patients (Jang et al., 2019; Clarke et al., 2010). Studies using CT have found secondary causes in 13–15% of emergency patients who had undergone CT for headache, which were mostly intracranial hemorrhages or ischemia (Covino et al., 2019; Lemmens et al., 2021; Wang & You, 2013). When CT is used in the ED in isolated headache (non-traumatic and without specific neurologic findings), it yields a significantly lower rate of significant findings, approximately 1–2%, mainly intracranial hemorrhages, intracranial masses, and CVST (Quon et al., 2015; Jordan et al., 2009). A low rate of clinically significant findings often results in limited cost-effectiveness (Jordan et al., 2009). Among children and adolescents presenting to the ED with headache, “red flag” symptoms are common, but only a small proportion of ~1% has significant neuroimaging findings (Cain et al., 2018; Tsze et al., 2019). A recent retrospective study of 21 EDs between 2015 and 2021 reported a 19% annual increase of CTA use in suspicion of a subarachnoid hemorrhage after non-diagnostic non-contrast head CT (Mark et al., 2024). In that study, the use of lumbar punctures (the currently recommended procedure for the same indication) decreased by 11% simultaneously. This trend indicates a shift towards favoring neuroimaging, at least in regard to the diagnostic strategy for subarachnoid hemorrhages.

MRI is an alternative to CT, with higher sensitivity for various brain pathologies and no ionizing radiation, but only few studies have investigated its yield in an emergency setting (Budweg et al., 2016; Gilbert et al., 2012). Budweg et al. reported that ~22% (18/82) of their walk-in outpatients had at least potentially significant findings that explained acute headache. The most relevant findings included signs of ischemia, intracranial hypertension, and meningitis. Gilbert et al. found that the rate of significant findings related to headaches decreased from 10% to 3.5% between 1998 and 2008, including both CT and MRI. Additionally, they demonstrated that the increased utilization of neuroimaging for headaches actually lowered the prevalence of detected significant pathology, rather than leading to a higher yield. Their results underline the need for support in clinical decision-making regarding the use of neuroimaging, with the aim to make it more judicious.

Clinical risk scores have been proposed for non-traumatic headache to reduce unnecessary imaging (Covino et al., 2019; Bent et al., 2015; Budweg et al., 2016). In these studies, the most frequently presented predictors of intracranial pathology have been age >50 years, a focal neurological deficit, nausea/vomiting and altered mental status. However, most of these prediction models have been developed for head CT. Budweg et al. presented a clinical score for MRI in an outpatient clinic, with variables including syncope, vomiting, ophthalmological symptoms, and female sex (Budweg et al., 2016). Although yielding a high sensitivity of 100% and a specificity of 82% with a ROC AUC (Receiver operating characteristic, area under the curve) of 0.94, the score is limited by a low rate of significant findings and a relatively small sample of 82 patients. It lacks prospective validation, and importantly, the authors note that the findings are not applicable to an emergency setting, due to the low prevalence of patients with “red flag” symptoms compared to those in the EDs.

## 2.5 Cerebral venous sinus thrombosis

### 2.5.1 Epidemiology and clinical characteristics

Cerebral venous sinus thrombosis (CVST) is a potentially life-threatening neurological emergency defined as a blood clot in the major venous outlets of the brain. It is a subtype of cerebral venous thrombosis (CVT), involving a clot specifically in the dural venous sinuses. Previously, the incidence of adult CVST has been reported as 0.3 to 0.5 per 100,000 individuals per year (Stam, 2005; Bousser & Ferro, 2007), but recent studies show higher rates of 1.3 to 1.6 per 100,000 per year (Ruuskanen et al., 2021; Devasagayam et al., 2016). The proportion of women among adult patients with CVST has risen to around 70%, possibly due to increasing use of oral contraceptives (Zuurbier et al., 2016). Despite its relatively low incidence, CVST is frequently suspected in the EDs due to its various and non-specific symptoms and risk factors.

Risk factors of CVST are diverse and include prothrombotic conditions (genetic and acquired, such as pregnancy), malignancies, infections, vasculitis, systemic diseases (e.g., thyroid diseases, sarcoidosis), intracranial defects (e.g. tumors, venous malformations), obesity, dehydration, and cranial trauma (Idiculla et al., 2020). At least one risk factor is implicated in around 65–85% of affected adults (Coutinho et al., 2009; Saadatnia et al., 2009; Ferro et al., 2004). A meta-analysis suggests that traditional risk factors of stroke (smoking, hypertension, diabetes) appear to be of lesser importance as they did not reach statistical significance in the analysis, possibly reflecting the younger age of the population mostly affected by CVT (Green et al., 2018). Headache is the most common presenting symptom, occurring in 80–95% of patients (Spadaro et al., 2021). The headache may be localized or diffuse and is typically persistent. Although often gradually worsening, around 5–10% may experience a ”thunderclap” onset of the headache (Mortimer et al., 2013; Wasay et al., 2010). The headache is frequently accompanied by other symptoms, such as focal neurological deficits, seizures, altered mental status, or symptoms related to raised intracranial pressure, including nausea/vomiting, visual impairment, and papilledema (Idiculla et al., 2020). The differential diagnosis includes diseases such as meningitis, intracranial hemorrhage, carotid/ertebral artery dissection, and idiopathic intracranial hypertension.

The acute mortality rate of CVST is reported to be around 5% (Dentali et al., 2006; Ferro & Canhão, 2014). In a 3-year prospective study of 624 adult CVT/CVST patients, several prognostic factors were identified for poor outcomes: death or dependence (at least moderate disability, requiring some external help but able to walk without the assistance of another individual). These factors were age >37 years, male sex, Glasgow Coma Scale <9 on admission, mental status disorder, thrombosis of the deep venous system, intracranial hemorrhage on admission CT, malignancy, and central nervous system infection (Ferro et al., 2004). Additionally, in a retrospective study of 176 patients, age, abnormal level of consciousness, and focal motor deficits were associated with similar poor outcomes (Ortega-Gutierrez et al., 2020). Treatment for CVST typically includes anticoagulation therapy, symptomatic management and prevention of intracranial hypertension, seizures, and headache.

### 2.5.2 Imaging aspects

CT and MRI are the most commonly used imaging modalities for diagnosing CVST. A meta-analysis comprising 48 studies indicates that both CT and MRI have a high level of diagnostic accuracy in the differential diagnosis of CVT and CVST (Xu et al., 2018). CT had a pooled sensitivity of 0.79 and a pooled specificity of 0.90, while for MRI, the values were 0.82 and 0.92, respectively. Non-enhanced CT and CE-CTV are widely available and cost-effective imaging options in an emergency setting, although they expose the patient to ionizing radiation.

Various MRI techniques, such as CE-MRI and MRV, are alternatives in ruling out CVST. Although CT scans of the mother's head have been shown to expose the fetus to minimal radiation doses, much below the teratogenic threshold (Goldberg-Stein et al., 2012; Proença et al., 2021), evidence suggests that emergency physicians still favor MRI over CT for evaluating headaches during pregnancy (Waldman et al., 2017). The American College of Radiology has stated that any diagnostic examination of the head and neck may be conducted as medically indicated, regardless of pregnancy status (ACR-SPR Practice Parameter for Imaging Pregnant or Potentially Pregnant Adolescents and Women with Ionizing Radiation, accessed in April 20, 2024). However, MRI has its drawbacks, including limited availability in the EDs and higher costs compared to CT. While a previous study by Almqvist et al. reported clinically meaningful CT findings in ~10%, and CVST in <1% of patients with suspected CVST (Almqvist et al., 2020), the additional value of MRI in terms of detecting clinically significant findings in these patients remains unknown.

# 3 Aims

The general aim of this thesis was to explore and analyze the imaging outcomes of emergency brain MRI in patients with dizziness, headache, or suspected CVST, in relation to their clinical presentations. The specific aims were:

1. to evaluate the imaging outcomes of emergency MRI and to demonstrate factors related to these outcomes in patients presenting with acute dizziness or vertigo.
2. to assess the emergency MRI findings regarding non-traumatic headache in outpatients presenting to the ED, to describe these findings in terms of clinical significance, and to demonstrate factors related to significant imaging outcomes.
3. to study the imaging outcomes of emergency MRI in patients presenting with clinically suspected CVST in relation to patient characteristics, and to investigate other intracranial pathology encountered in these patients to identify brain disorders that may clinically mimic CVST.

# 4 Materials and Methods

## 4.1 Study design

This study analyzed consecutive patients who underwent emergency MRI due to acute dizziness, headache, or clinical suspicion of CVST between April 2014 and January 2019. It is a retrospective, single-center cohort study conducted at Turku University Hospital, an academic tertiary care referral center with an approximate patient catchment area of 480,000. The emergency radiology department of Turku University Hospital pioneered MRI as an emergency imaging tool in 2013 and has used it for various indications ever since. During the study period, the emergency radiology department had a Philips Ingenia 3.0 Tesla system dedicated to emergency imaging only with round the clock availability.

## 4.2 Patient data

The study samples consist of patients presenting to the ED and of hospitalized patients who underwent emergency MRI because of acute dizziness, headache, or clinical suspicion of CVST between April 2014 and January 2019 in Turku University Hospital. All patients had emergency MRI as a part of their routine care, and the decision to refer the patient was that of the attending physician on the clinical grounds.

Consecutive emergency brain MRI scans conducted between April 2014 and January 2019 were identified and extracted from picture archiving and communication systems (PACS) and radiological information systems (RIS) using standard MRI codes. Imaging data were cross-referenced with those from electronic medical records (EMR). A total of 17,735 unique emergency MRI scans were conducted during this period, with 8,772 (49%) being emergency brain MRI scans. At our institution, the utilization of emergency brain MRI averaged 1,850 scans annually between 2015 and 2018, showing a steady increase each year (**Figure 3**).

To identify cohorts for each study, the MRI referrals were queried with specific keywords: for Study I “dizziness” and “vertigo”, for Study II “headache” and for Study III “sinus thrombosis” and “(dural) venous sinus/es”. The medical records were not further reviewed for inclusion of patients who had an emergency brain MRI but did not have the aforementioned keywords in their referrals. From the referrals, the patients' demographic characteristics, medical history, symptoms and other relevant clinical features were recorded. Missing information was then retrieved from the EMR. Only completely missing information was sought from the records; the information from the referrals was not cross-checked with the EMR. Imaging findings were documented from the MRI reports.

### 4.2.1 Imaging outcomes of emergency MRI in dizziness and vertigo (I)

The focus of Study I was to analyze the imaging outcomes of emergency MRI and clinical factors related to these outcomes among patients with acute dizziness or vertigo. Patients of all age groups, whether emergency admissions or inpatients, were included as long as the specific keywords were featured in the clinical indication for the emergency MRI request. Postoperative patients, patients with a ventriculoperitoneal shunt, and patients with a recent head injury were excluded, as they almost always undergo neuroimaging if presenting with dizziness, and may have specific complications that are not well generalizable.

### 4.2.2 Diagnostic yield of emergency MRI in non-traumatic headache (II)

The aim of Study II was to assess the emergency MRI findings regarding non-traumatic headache among outpatients presenting to the ED, and to demonstrate factors related to significant imaging outcomes. All patients with non-traumatic headache were included regardless of whether the headache was the main symptom, as the proportional significance of headache among all symptoms would be difficult to evaluate retrospectively. Already hospitalized patients, postoperative patients, patients with a ventriculoperitoneal shunt, and patients with a recent head injury were excluded.

### 4.2.3 Imaging outcomes of emergency MRI in patients with suspected CVST (III)

The purpose of Study III was to assess the imaging outcomes of emergency MRI among patients presenting with clinically suspected CVST in relation to patient characteristics. All patients, whether emergency admissions or inpatients, in whom CVST was suspected as a differential diagnosis were included. Patients referred to MRI with previously diagnosed CVST at an outside institution or with another imaging modality, such as CT, were excluded.

## 4.3 Imaging findings

The emergency MRI findings were classified by their clinical significance. Disagreements between study physicians were resolved using consensus discussions.

In Study I, the MRI reports were evaluated and then classified by two fellowship-trained neuroradiologists (J. Hirvonen & M. Nyman), first separately and then together to achieve consensus. The categories were acute ischemic stroke (AIS), significant but non-ischemic pathology (S), and non-significant findings (NS). Interobserver agreement was not recorded. A clinical neurologist was consulted when necessary. For the patients in the AIS category, results of the preceding CT studies were noted if available.

In Study II, two fellowship-trained neuroradiologists (J. Hirvonen & M. Nyman) and a board-certified neurologist (P. Ylikotila) reviewed all the referrals and reports, and independently classified findings into five categories: likely explaining headache (1), possibly explaining headache (2), incidental findings with clinical significance (3), incidental findings with no clinical significance (4), and normal (no new findings or notable progression in brain diseases) (5). At least two of the three study physicians agreed upon 100% of the likely explaining and 73% of the possibly explaining findings. Similar agreement was reached in 95–99% of incidental and normal findings. Classes 1 & 2, and 3 & 4 were then combined to form a new classification with three categories: findings related to headache, incidental findings and normal scans. Within this classification, at least two of the three study physicians agreed upon all findings.

In Study III, two fellowship-trained neuroradiologists (J. Hirvonen & M. Nyman) independently evaluated all MRI reports and classified the findings into three categories: CVST (1), clinically significant intracranial pathology other than CVST (2), and unremarkable (with no new findings or notable progression in brain diseases) (3). Whether an MRI finding was considered potentially causally related to the symptoms and thus clinically significant was evaluated by a consensus procedure by aforementioned fellowship-trained neuroradiologists and a board-certified neurologist (P. Ylikotila). Interobserver agreement was not recorded.

## 4.4 MRI protocols

The emergency brain MRI examinations were performed using a Philips Ingenia 3.0 Tesla system with a Philips dStream coil system (Philips Healthcare, Best, Netherlands). The MRI protocols varied, but most included routine sequences such as T1, T2, FLAIR, DWI, SWI, and 3D-TOF arterial angiography (**Table 1**). On selected patients, additional sequences included CE-MRV, CE-T1, and high-resolution T2-weighted sequences of the internal acoustic canal and inner ear.

**Table 1.** Detailed MRI protocol.

| Sequence | Orientation | Slice thickness | Parameters |
|---|---|---|---|
| T2 | Axial | 3 mm | TE 80 ms<br>TR 4,300 ms |
| FLAIR | Coronal | 4 mm | TE 125 ms<br>TR 11,000 ms<br>TI 2,800 ms |
| T1 3D TFE | Axial | 1 mm | TE 4 ms<br>TR 8.5 ms |
| DWI | Axial | 4 mm | TE 87 ms<br>TR 4,500 ms<br>b = 1,000 s/mm$^2$ |
| SWI | Axial | 2 mm | TE 28 ms<br>TR 20 ms |
| 3D-TOF arterial angio | Axial | 1.2 mm | TE 3.5 ms<br>TR 23 ms |
| 2D-TOF venous angio | Axial | 3 mm | TE 3.3 ms<br>TR 19 ms |
| DRIVE | Axial | 0.8 mm | TE 186 ms<br>TR 1,500 ms |

## 4.5 Statistical analysis

### 4.5.1 Statistical tests and software

Results are typically expressed as percentages, medians, interquartile ranges (IQR) and odds ratios (OR) with 95% confidence intervals (CIs). The normality assumptions were evaluated both visually and using *Saphiro Wilk's* test. At the univariate level, the *chi-squared* test was used to compare nominal data, and the *Mann–Whitney U* and the *Kruskal–Wallis H* tests were used as nonparametric tests to compare continuous variables that were not normally distributed. Optimal cut-off points for continuous variables were determined using the *Youden's J* statistic. *P*-values less than 0.05 were considered statistically significant.

In Studies I–III, the data were analyzed using JMP for Mac (version 16.1 Pro. SAS Institute Inc., Cary, NC, 1989–2019). Additional analyses in Study II were performed using IBM SPSS Statistics for Mac (version 26, copyright IBM Corporation 2019), R (3.6.3), Elasticnet (glmnet 3.0.2) and Neural Network (4 hidden layers, neuralnet 1.44.2). In Study III, SAS version 9.4 (SAS Institute, Cary, NC, USA) was also used.

### 4.5.2 Risk scores

In Study I, all variables were entered into binary (two outcome classes) and multinomial (three outcome classes) logistic regression models. Variables that were statistically significant predictors at the multivariate level were then included in the risk scores for predicting significant imaging outcomes. Risk score points were derived by rounding the OR (or 1/OR, if OR<1) of the included variables to the nearest integer. The points were summed to form a risk score for each patient. In Study II, a clinical prediction score was derived by multiplying the OR of the predisposing factors and 1/OR of the protective factors by two (to reduce imprecision from rounding), and then rounding to the nearest integer. ROC AUC was used to evaluate the diagnostic ability of the clinical scores in both studies. The optimal cut-off points for the risk scores to optimize sensitivity and specificity were determined by *Youden's J* statistic. In Study I, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were presented for the risk scores.

## 4.6 Ethical considerations

The study was conducted under the institutional permission of the hospital district board (T66/2019). Due to the national legislature of retrospective studies of existing data, no informed consent or ethics committee approval was required.

# 5 Results

The patient samples for Studies I–III were extracted from the pool of 8,772 unique emergency brain MRI scans conducted between April 2014 and January 2019. The study samples had some overlap (*N*=145 in Studies I & II, *N*=56 in Studies I & III, and *N*=222 in Studies II & III). The sample sizes and the patients' demographic characteristics are presented in **Table 2**.

**Table 2.** Sample sizes and patients' demographic characteristics in Studies I–III and combined.

| | **Study I** | **Study II** | **Study III** | **Studies I–III combined** |
|---|---|---|---|---|
| MRI scans identified on the initial search, *N* | 1,419 | 1,862 | 332 | |
| Excluded, *N* (%) | 250 (18) | 1,166 (63) | 5 (2) | |
| Included, *N* (%) | 1,169 (82) | 696 (37) | 327 (98) | 1,807 |
| Age [years], median (IQR, range) | 61 (45–71, 6–90) | 31 (23–44, 1–87) | 30 (23–38, 0–81) | 50 (30–67, 0–90) |
| Sex [male], *N* (%) | 523 (45) | 196 (28) | 53 (16) | 700 (39) |
| Sex [female], *N* (%) | 646 (55) | 500 (72) | 274 (84) | 1,107 (61) |

*MRI = magnetic resonance imaging, IQR = interquartile range*

## 5.1 Imaging outcomes of emergency MRI in dizziness and vertigo: a retrospective cohort study (I)

### 5.1.1 Patient characteristics

In Study I, a total of 1,169 patients met the inclusion criteria. A narrow majority were female (*N*=646, 55%) and the median age was 61 years (IQR 45–71) (**Table 3**). Most patients had their MRI study less than 24 hours after the referral (82%), and the rest had a median delay of 1 day (IQR 1–2).

**Table 3.** Clinical characteristics of patients that underwent emergency MRI for dizziness or vertigo by imaging outcome group: acute ischemic stroke (AIS), significant but non-ischemic (S) and non-significant (NS).

| | **AIS**<br>*N*=197 | **S**<br>*N*=97 | **NS**<br>*N*=875 | ***p*-value** |
|---|---|---|---|---|
| Age [years], median (IQR) | 69<br>(58–75.5) | 57<br>(37.5–70) | 59<br>(42–70) | <0.01 |
| Sex [male], *N* (%) | 115 (58) | 36 (37) | 372 (43) | <0.01 |
| Hospitalization status [inpatient], *N* (%) | 148 (75) | 59 (61) | 452 (52) | <0.01 |
| Number of cardiovascular risk factors, median (IQR) | 1 (0–2) | 0 (0–1) | 0 (0–1) | <0.01 |
| **Prevalence of cardiovascular risk factors, *N* (%)** | | | | |
| Smoking | 21 (11) | 8 (8) | 78 (9) | 0.71 |
| Hypertension | 86 (44) | 23 (24) | 286 (33) | <0.01 |
| Hypercholesterolemia | 42 (21) | 7 (7) | 144 (17) | <0.01 |
| Diabetes | 39 (20) | 6 (6) | 89 (10) | <0.01 |
| Coronary artery disease | 14 (7) | 7 (7) | 53 (6) | 0.80 |
| Old cerebral infarction | 29 (15) | 4 (4) | 38 (4) | <0.01 |
| Duration of symptoms [days], median (IQR) | 1 (0–3) | 4 (1–14) | 1 (0–4) | <0.01 |
| Duration of symptoms <2 days, *N* (%) | 116 (59) | 31 (32) | 484 (55) | <0.01 |
| **Prevalence of symptoms, *N* (%)** | | | | |
| Previous episodes | 10 (5) | 6 (6) | 58 (7) | 0.72 |
| Vertigo | 29 (15) | 10 (10) | 225 (26) | <0.01 |
| Positional vertigo | 7 (4) | 3 (3) | 72 (8) | 0.02 |
| Auditory symptoms | 7 (4) | 9 (9) | 32 (4) | 0.03 |
| Nausea/vomiting | 82 (42) | 42 (43) | 357 (41) | 0.88 |
| Headache | 35 (18) | 35 (36) | 203 (23) | <0.01 |
| Pre-syncope | 2 (1) | 2 (2) | 11 (1) | 0.75 |
| Number of neurological signs, median (IQR) | 1 (1–2) | 1 (0–1) | 1 (0–1) | <0.01 |
| **Prevalence of neurological signs, *N* (%)** | | | | |
| Limb weakness | 22 (11) | 10 (10) | 63 (7) | 0.13 |
| Facial weakness | 9 (5) | 3 (3) | 32 (4) | 0.78 |
| Paresthesia | 24 (12) | 10 (10) | 113 (13) | 0.75 |
| Ataxia | 43 (21) | 12 (12) | 85 (10) | <0.01 |
| Aphasia or dysarthria | 47 (23) | 14 (14) | 65 (7) | <0.01 |
| Dysphagia | 8 (4) | 0 (0) | 5 (1) | <0.01 |
| Diplopia | 40 (20) | 12 (12) | 102 (12) | <0.01 |
| Nystagmus | 56 (28) | 11 (11) | 281 (32) | <0.01 |
| No other symptoms or neurological signs than dizziness or vertigo, *N* (%) | 18 (11) | 12 (14) | 96 (11) | 0.40 |

*IQR = interquartile range, AIS = Acute ischemic stroke, S = Significant but non-ischemic, NS = non-significant*

*P*-values are associated with *chi-squared* test for categorical variables and with *Kruskal–Wallis H* test for continuous variables

## 5.1.2 Imaging outcomes

Acute ischemic stroke (AIS) was detected in 197 (17%) of the MRI studies (**Table 3).** Ninety-seven patients (8%) had other significant pathology (S), and for the rest of the patients (*N*=875, 75%), the MRI scans remained non-significant (NS). Of the 197 patients with AIS, 171 (87%) underwent a head CT scan before MRI, usually on the same or the previous day. Acute pathology was suggested in only 62 (36%) of these CT studies.

The cerebellum was the most common infarct location among patients with AIS, involved in 39% of the patients. Other infarcts were found in cerebrum (23%), pons (10%), medulla oblongata (5%), thalamus (5%), basal ganglia (2%), mesencephalon (2%), and in multiple aforementioned locations (15%).

Non-ischemic significant findings included tumors and infections, among other rare findings, such as neurosarcoidosis or central pontine myelinolysis (**Table 4**). The most common incidental findings among the NS group were white matter hyperintensities (**Table 5**).

**Table 4.** Significant, but non-ischemic emergency MRI findings.

| **Finding** | ***N* (%)** |
|---|---|
| Tumor/metastases | 44 (45) |
| Demyelination | 12 (12) |
| Neurosarcoidosis | 1 (1) |
| Normal pressure hydrocephalus | 1 (1) |
| Central pontine myelinolysis | 1 (1) |
| Posterior reversible encephalopathy syndrome | 1 (1) |
| Subdural hygroma | 1 (1) |
| Chiari malformation type 1 | 1 (1) |
| Pineal cyst apoplexy | 1 (1) |
| Leukoencephalopathy | 1 (1) |
| Wernicke encephalopathy | 1 (1) |
| **Vascular diseases** | |
| Intracranial hemorrhage | 6 (6) |
| CADASIL | 1 (1) |
| Carotid artery dissection | 1 (1) |
| Vertebral artery dissection | 1 (1) |
| Giant aneurysm | 1 (1) |
| Subdural hematoma | 1 (1) |
| Septic embolism | 1 (1) |
| Sinus thrombosis | 1 (1) |
| **Infection, inflammation** | |
| Mastoiditis | 7 (7) |
| Encephalitis | 3 (3) |
| Labyrinthitis | 3 (3) |
| Meningitis | 2 (2) |
| Brain abscess | 1 (1) |
| Cerebellitis | 1 (1) |
| Neuritis | 1 (1) |
| Non-specific pachymeningeal enhancement | 1 (1) |
| **Total** | 97 (100) |

## 5.1.3 Predictors of acute pathology and risk scores

In overall univariate analyses between the three finding groups (AIS/S/NS), numerous statistically significant associations were identified (**Table 3**). Patients within the AIS group were more likely older, male, and had a higher prevalence of cardiovascular risk factors and neurological signs. A cut-off point for old age was 55 years. Patients

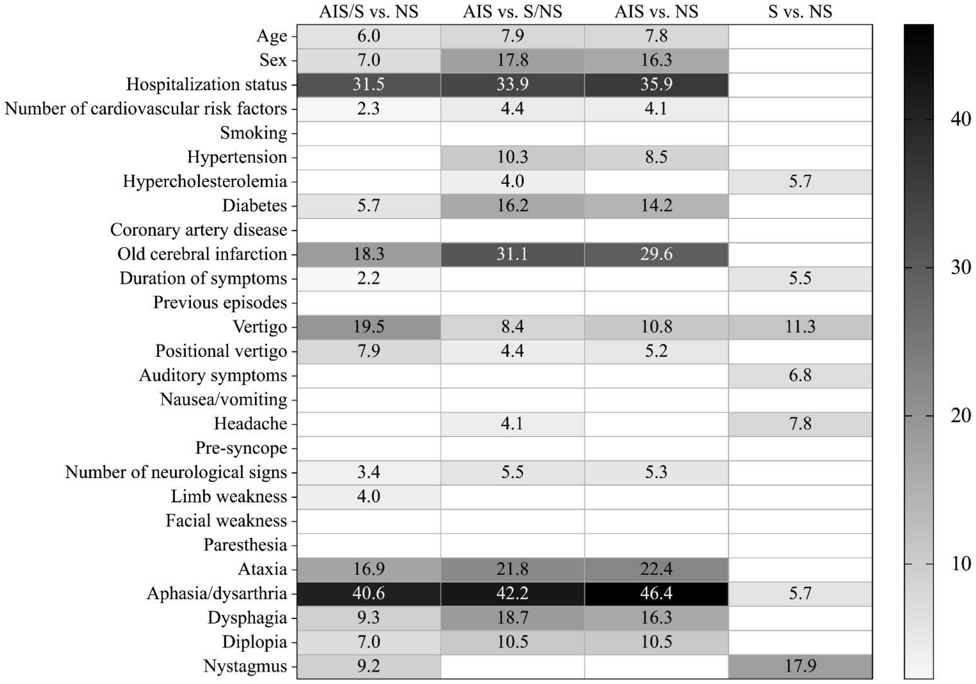
**Table 5.** Non-significant emergency MRI findings.

| **Finding** | ***N* (%)** |
|---|---|
| Unremarkable | 368 (42) |
| White matter hyperintensities | 256 (29) |
| **Known existing pathology** | |
| Old infarcts/bleeds | 105 (12) |
| Traumatic lesions | 1 (1) |
| Infarction and multiple sclerosis | 1 (1) |
| Tumor | 1 (1) |
| Ear pathology | 1 (1) |
| Sinonasal mucosal thickening | 39 (4) |
| Benign cyst | 20 (2) |
| Perivascular abnormalities | 16 (2) |
| Normal variant | 13 (1) |
| Aneurysm | 9 (1) |
| Sinusitis | 9 (1) |
| Vascular stenosis | 8 (1) |
| Meningioma | 8 (1) |
| Chronic demyelination | 6 (1) |
| Cavernoma | 5 (1) |
| Empty sella | 4 (0) |
| Cranial abnormality | 2 (0) |
| Incidental benign tumor | 2 (0) |
| Teleangiectasia | 1 (0) |
| **Total** | 875 (100) |

within the S group had a higher prevalence of headache and a longer duration of symptoms. Patients with vertigo were less likely to present any acute findings on MRI. Pairwise group comparisons further elaborate these differences (**Figure 4**). Among the 126 patients with isolated dizziness, 14% had AIS, 10% other significant findings, and 76% had non-significant findings – in similar proportions to patients with additional signs and symptoms (17% AIS, 8% S, 75% NS; *p*=0.49, *chi-squared* test).

In a multivariate analysis, statistically significant predictors of clinically significant acute pathology (AIS/S) were aphasia/dysarthria, ataxia, old cerebral infarction, auditory symptoms, inpatient hospitalization status, diplopia, nausea/vomiting, age over 55 years, male sex, and absence of vertigo (**Table 6**, **Figure 5**). The ROC AUC of the risk score was 0.70. With a single cut-off of 6 points, the model had a sensitivity of 66% and a specificity of 64%. PPV was 38%, and NPV was 85%. The mean risk score was 7.6 points in the AIS/S group and 5.7 points in the NS group (**Figure 6**).

We also calculated a similar risk score for acute infarcts only (AIS vs. S/NS) and found improved performance, with an ROC AUC of 0.75 (**Table 7**, **Figure 5**). With a single cut-off of 8 points, sensitivity was 51%, specificity was 84%, PPV was 40% and NPV was 90%. The mean risk score was 8.8 points in the AIS group and 5.6 points in the S/NS group (**Figure 6**).



| | AIS/S vs. NS | AIS vs. S/NS | AIS vs. NS | S vs. NS |
|---|---|---|---|---|
| Age | 6.0 | 7.9 | 7.8 | |
| Sex | 7.0 | 17.8 | 16.3 | |
| Hospitalization status | 31.5 | 33.9 | 35.9 | |
| Number of cardiovascular risk factors | 2.3 | 4.4 | 4.1 | |
| Smoking | | | | |
| Hypertension | | 10.3 | 8.5 | |
| Hypercholesterolemia | | 4.0 | | 5.7 |
| Diabetes | 5.7 | 16.2 | 14.2 | |
| Coronary artery disease | | | | |
| Old cerebral infarction | 18.3 | 31.1 | 29.6 | |
| Duration of symptoms | 2.2 | | | 5.5 |
| Previous episodes | | | | |
| Vertigo | 19.5 | 8.4 | 10.8 | 11.3 |
| Positional vertigo | 7.9 | 4.4 | 5.2 | |
| Auditory symptoms | | | | 6.8 |
| Nausea/vomiting | | | | |
| Headache | | 4.1 | | 7.8 |
| Pre-syncope | | | | |
| Number of neurological signs | 3.4 | 5.5 | 5.3 | |
| Limb weakness | 4.0 | | | |
| Facial weakness | | | | |
| Paresthesia | | | | |
| Ataxia | 16.9 | 21.8 | 22.4 | |
| Aphasia/dysarthria | 40.6 | 42.2 | 46.4 | 5.7 |
| Dysphagia | 9.3 | 18.7 | 16.3 | |
| Diplopia | 7.0 | 10.5 | 10.5 | |
| Nystagmus | 9.2 | | | 17.9 |

**Figure 4.** Statistical test values between dichotomic imaging outcome groups. Only values with statistical significance ($p<0.05$) are displayed. *Chi-squared* test was used for categorical variables. *Mann–Whitney U* test was used for continuous variables; "Age", "Number of cardiovascular risk factors", "Duration of symptoms", and "Number of neurological signs".

**Table 6.** Variables predicting significant acute pathology (AIS/S) on emergency MRI with statistical significance ($p<0.05$) in a multivariate analysis.

| **Variable** | **Risk score points** | **OR** | **95% CI (lower–upper)** | ***p*-value** |
|---|---|---|---|---|
| Aphasia/dysarthria | 3 | 3.2 | 2.1–4.9 | <0.01 |
| Ataxia | 2 | 2.3 | 1.5–3.6 | <0.01 |
| Old cerebral infarction | 2 | 2.2 | 1.3–3.8 | <0.01 |
| Auditory symptoms | 2 | 2.1 | 1.1–4.0 | 0.04 |
| Inpatient | 2 | 1.9 | 1.3–2.6 | <0.01 |
| Diplopia | 2 | 1.7 | 1.1–2.5 | 0.02 |
| Nausea/vomiting | 2 | 1.6 | 1.2–2.3 | <0.01 |
| Age over 55 years[1] | 2 | 1.6 | 1.1–2.3 | 0.01 |
| Male | 1 | 1.4 | 1.0–1.9 | 0.03 |
| No vertigo | 2[2] | 0.5 | 0.3–0.8 | <0.01 |

*OR = odds ratio, CI = confidence interval*

*P*-values are associated with *chi-squared* test

1) Age cut-off point determined with *Youden's J* statistic

2) Risk score points are calculated for absence of vertigo: 1/OR rounded

**Table 7.** Variables predicting acute ischemic stroke on emergency MRI with statistical significance ($p<0.05$) in a multivariate analysis.

| **Variable** | **Risk score points** | **OR** | **95% CI (lower–upper)** | ***p*-value** |
|---|---|---|---|---|
| Dysphagia | 5 | 4.7 | 1.4–16.2 | 0.02 |
| Aphasia/dysarthria | 3 | 3.3 | 2.1–5.2 | <0.01 |
| Old cerebral infarction | 3 | 2.9 | 1.7–5.0 | <0.01 |
| Ataxia | 3 | 2.8 | 1.7–4.3 | <0.01 |
| Age over 55 years[1] | 2 | 2.3 | 1.4–3.6 | <0.01 |
| Inpatient | 2 | 2.0 | 1.3–2.9 | <0.01 |
| Diplopia | 2 | 1.9 | 1.2–3.0 | <0.01 |
| Male | 2 | 1.7 | 1.2–2.5 | <0.01 |
| Diabetes | 2 | 1.7 | 1.0–2.8 | 0.04 |
| Symptoms <2 days | 2 | 1.5 | 1.1–2.2 | 0.02 |
| No vertigo | 2[2] | 0.6 | 0.4–1.0 | 0.048 |

*OR = odds ratio, CI = confidence interval*

*P*-values are associated with *chi-squared* test

1) Age cut-off point determined with *Youden's J* statistic

2) Risk score points are calculated for absence of vertigo: 1/OR rounded

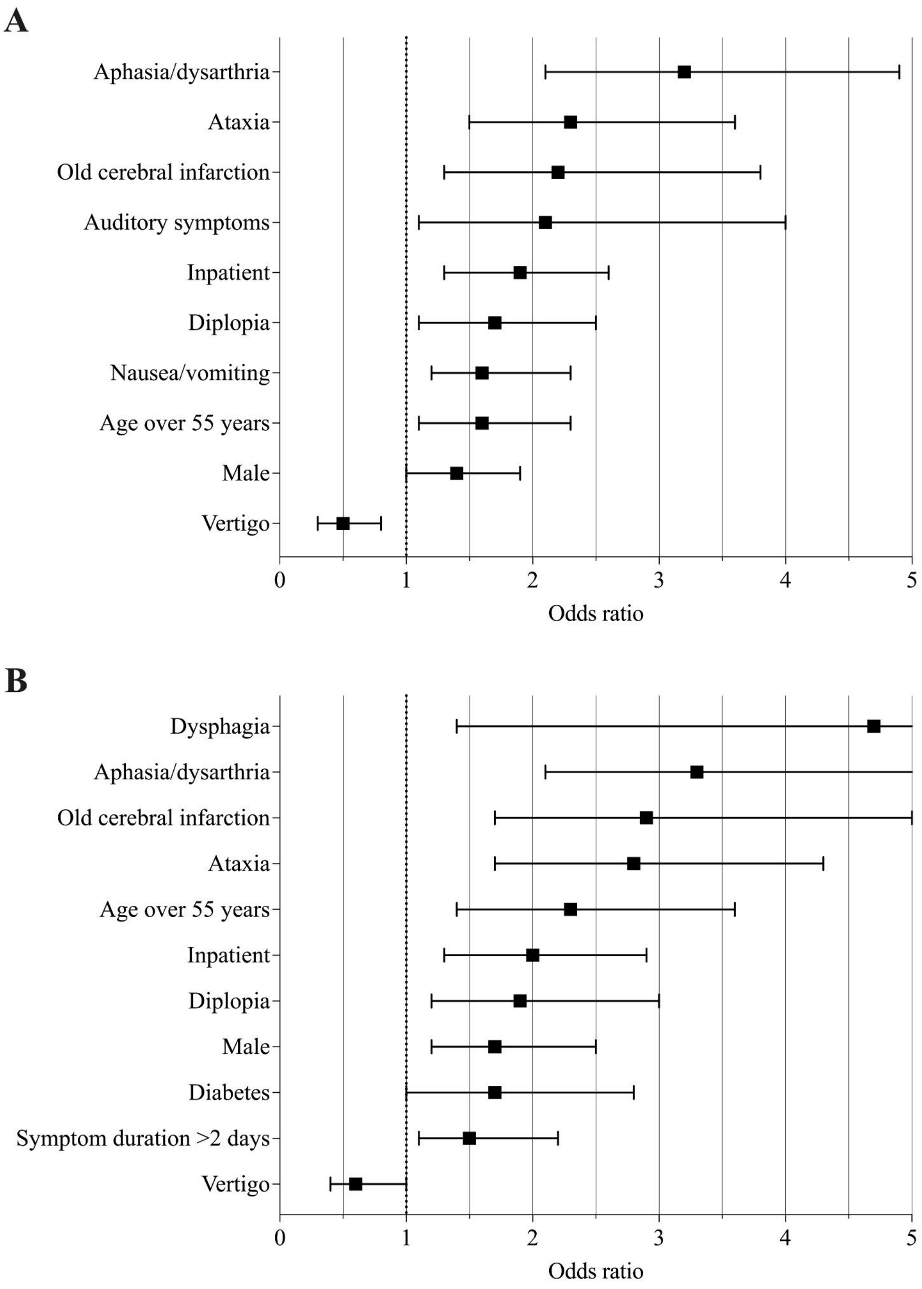


**Figure 5.** **A)** Variables predicting significant acute pathology (AIS/S *vs.* NS) on emergency MRI with statistical significance ($p<0.05$) in a multivariate analysis. **B)** Variables predicting acute ischemic stroke (AIS *vs.* S/NS) on emergency MRI with statistical significance ($p<0.05$) in a multivariate analysis.

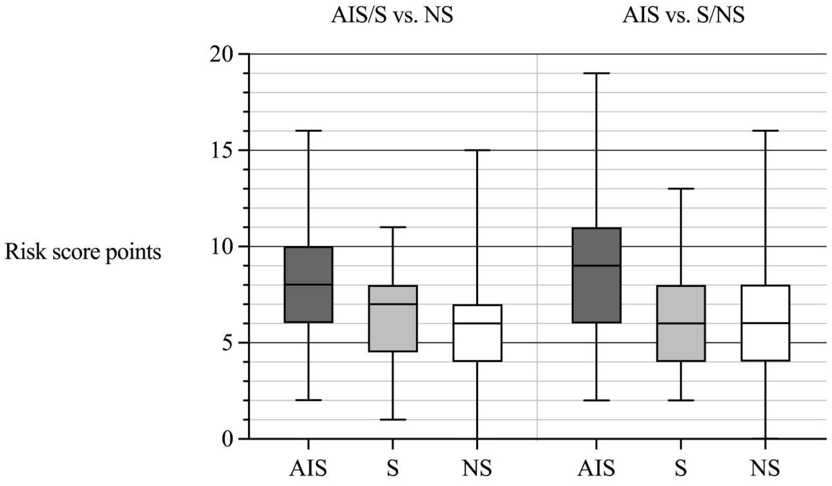


**Figure 6.** Risk score point distributions for both scores within imaging outcome groups.

### 5.1.4 Diagnostic performance of MRI

To ensure that early MRI did not miss infarcts (false negative), we determined if patients with a negative DWI-MRI less than 48 hours after symptom onset had follow-up neuroimaging the following week. Among the 470 patients fulfilling these criteria, only four (0.9%) underwent follow-up CT or MRI. Only one (0.2%) of these patients, scanned because of new neurological symptoms after vertigo had dissipated, had a small new cortical infarction on CT. All patients in the catchment area with a clinically meaningful suspicion of stroke are referred to our tertiary hospital. Therefore, it is likely that acute MRI did not miss any clinically meaningful infarcts in these patients to the extent that such infarcts would warrant repeated neuroimaging.

A total of 145 patients underwent dedicated internal acoustic canal and inner ear imaging with heavily T2-weighted images (3D DRIVE). None of these images revealed any acute findings. One patient was diagnosed with acute labyrinthitis, but this was evident only on post-contrast T1-weighted images and not on T2-weighted images.

## 5.2 Diagnostic yield of emergency MRI in non-traumatic headache (II)

### 5.2.1 Patient characteristics

In the sample of 696 outpatients who presented to the ED with non-traumatic headache and underwent emergency MRI, most were female (*N*=500, 72%) and the median age was 31 years (IQR 23–44) (**Table 8**). Most underwent MRI within 24 hours of presentation to the ED (96%), and others within a week (median 2 days) of presentation. Duration of headache before referring to emergency MRI was recorded from the referrals, which was ≤7 days for 75% and <2 days for 42% of the patients. Other aspects of the headache, such as the intensity of pain and localization were not recorded, as such information was not consistently available in the referrals.

**Table 8.** Clinical characteristics of emergency patients who underwent MRI for non-traumatic headache (Note: potential underestimation of medical risk factors, such as obesity and diabetes, due to possible under-reporting in the MRI referrals).

| | **All patients** *N*=696 | **Headache-related finding on MRI** *N*=136 | **No headache-related MRI finding** *N*=560 | ***p*-value** |
|---|---|---|---|---|
| Age [years], median (IQR) | 31 (23–44) | 38 (24–53) | 30 (23–42) | <0.01 |
| Sex [male], *N* (%) | 196 (28) | 44 (32) | 152 (27) | 0.23 |
| **Medical history, *N* (%)** | | | | |
| Pregnancy at presentation | 32 (4.6) | 3 (2.2) | 29 (5.2) | 0.14 |
| Smoking | 42 (6.0) | 13 (10) | 29 (5.2) | 0.05 |
| Obesity | 22 (3.2) | 8 (5.9) | 14 (2.5) | 0.04 |
| Diabetes | 18 (2.6) | 2 (1.5) | 16 (2.9) | 0.36 |
| Hypertension | 59 (8.5) | 17 (13) | 42 (7.5) | 0.06 |
| Hypercholesterolemia | 14 (2.0) | 3 (2.2) | 11 (2.0) | 0.86 |
| Coagulopathy | 18 (2.6) | 6 (4.4) | 12 (2.1) | 0.14 |
| Cancer | 19 (2.7) | 5 (3.7) | 14 (2.5) | 0.45 |
| Migraine in history | 125 (18) | 13 (10) | 112 (20) | <0.01 |
| Headache duration [days], median (IQR) | 3 (0–7) | 4 (0–8) | 2 (0–7) | 0.23 |
| **Symptoms, *N* (%)** | | | | |
| Nausea | 178 (26) | 49 (36) | 129 (23) | <0.01 |
| Vomiting | 77 (11) | 23 (17) | 54 (10) | 0.02 |
| Vertigo | 153 (22) | 31 (23) | 122 (22) | 0.80 |
| Numbness | 218 (31) | 27 (20) | 191 (34) | <0.01 |
| Photophobia | 37 (5.3) | 7 (5.2) | 30 (5.4) | 0.92 |
| Visual impairment | 211 (30) | 46 (34) | 165 (29) | 0.32 |
| Dysphasia | 96 (14) | 17 (13) | 79 (14) | 0.63 |
| Syncope | 17 (2.4) | 3 (2.2) | 14 (2.5) | 0.84 |
| Seizure | 16 (2.3) | 2 (1.5) | 14 (2.5) | 0.47 |
| Signs/symptoms of infection[1] | 43 (6.2) | 14 (10) | 29 (5.2) | 0.03 |
| No other symptoms than headache | 94 (14) | 13 (10) | 81 (14) | 0.13 |
| **Additional information, *N* (%)** | 24 (12) | 10 (10) | 113 (13) | 0.75 |
| MRI after 24 hours of presentation | 30 (4.3) | 5 (3.7) | 25 (4.5) | 0.69 |
| Contrast-enhanced MRI | 325 (47) | 73 (54) | 252 (45) | 0.07 |
| Recent head CT for same indication | 111 (16) | 35 (26) | 76 (14) | <0.01 |

*IQR = interquartile range, MRI = magnetic resonance imaging, CT = computed tomography*

*P*-values are associated with *chi-squared* test for categorical variables and with *Mann–Whitney U* test for continuous variables

[1] Fever, cough, sore throat, runny or stuffy nose, elevated C-reactive protein levels or neutrophilia

### 5.2.2 Imaging outcomes

In total, 136 (20%) patients had a significant headache-related finding on emergency MRI (**Figure 7**, **Table 9**). Among these, most were due to cerebrovascular disease (*N*=54, 40%), followed by infection/inflammation (*N*=39, 29%). The most common significant findings were infarction, sinusitis, central nervous system infection, and intracranial tumor. Some less common conditions included mastoiditis, intracranial hyper- and hypotension, Chiari 1 malformation, and posterior reversible encephalopathy syndrome. Incidental findings with varying clinical significance were found in 154 (22%) scans; mostly white matter lesions, vascular abnormalities, and sinonasal mucosal thickening. Of all cases, 58% were completely normal with no new findings or progression in chronic brain diseases.

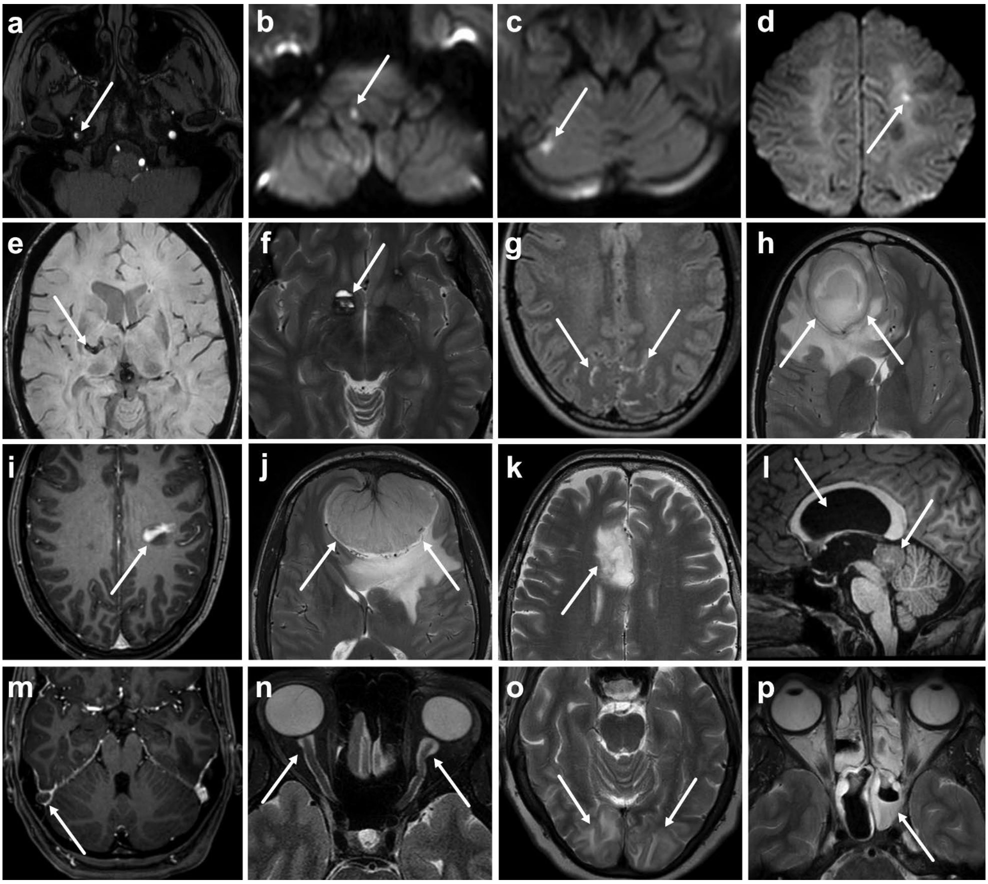


**Figure 7.** Examples of various emergency MRI findings of pathologies considered significantly related to headache. Examples are: internal carotid artery dissection (**a**), small infarcts (**b–d**), intracerebral hemorrhage (**e**), cavernoma (**f**), meningitis (**g**), abscess (**h**), demyelination (**i**), meningioma (**j**), glioma (**k**), central neurocytoma with hydrocephalus (**l**), dural venous sinus thrombosis (**m**), idiopathic intracranial hypertension (**n**), posterior reversible encephalopathy syndrome (**o**), and sphenoid sinusitis (**p**). White arrows denote relevant findings.

Among the 136 patients with significant findings on MRI, 35 patients (26%) had previous CT scans, of which 29% were unremarkable. For example, all previous CT scans of patients with acute infarction on MRI (*N*=10) were normal.

**Table 9.** Emergency MRI findings in patients imaged for non-traumatic headache.

| **Finding** | ***N* (%*)** |
|---|---|
| **Cerebrovascular disease** | **63 (86)** |
| Infarction | 31 (97) |
| Intracranial hemorrhage | 8 (100) |
| Cerebral venous thrombosis | 8 (100) |
| Arterial dissection/occlusion | 7 (100) |
| Aneurysm | 6 (0) |
| Internal carotid artery stenosis | 3 (33) |
| **Infection/inflammation** | **41 (95)** |
| Sinusitis | 26 (92) |
| Central nervous system infection | 13 (100) |
| Mastoiditis | 1 (100) |
| Neuritis | 1 (100) |
| **Other** | **186 (23)** |
| Non-specific white matter hyperintensities | 52 (0) |
| Sinonasal mucosal thickening | 32 (0) |
| Intracerebral/meningeal tumor | 18 (83) |
| Leukoaraiosis | 14 (0) |
| Signs of intracranial hypertension | 12 (100) |
| Developmental venous anomaly | 9 (0) |
| Demyelination | 8 (75) |
| Cavernoma | 6 (17) |
| Arachnoid cyst | 5 (0) |
| Benign cyst | 4 (0) |
| Pineal cyst | 4 (0) |
| Hemosiderosis | 4 (0) |
| Mega cisterna magna | 4 (0) |
| Chiari malformation type 1 | 3 (100) |
| Signs of intracranial hypotension | 3 (100) |
| Posterior reversible encephalopathy syndrome | 2 (100) |
| Tonsillar ectopy | 2 (0) |
| Pineal cyst apoplexy | 1 (100) |
| Lymphadenopathy | 1 (0) |
| Gliosis | 1 (0) |
| Petrous apex effusion | 1 (0) |
| **Total** | **290 (47)** |

*% of findings related to headache and thus considered clinically significant

### 5.2.3 Predictors of acute pathology and risk scores

Among the factors predicting headache-related findings on MRI, age, obesity, history of migraine, nausea, vomiting, numbness, and signs/symptoms of infection reached statistical significance ($p<0.05$) in a univariate analysis (**Table 8**). In a multivariate analysis, age, smoking, signs/symptoms of infection, nausea, numbness, and history of migraine remained statistically significant ($p<0.05$) (**Table 10**). We found that age over 40 years, smoking, signs/symptoms of infection and nausea increased the risk of a headache-related finding on emergency MRI, whereas numbness and history of migraine were perceived as protective factors, reducing the risk of such findings. This multivariate model had 0.696 ROC AUC, and it correctly classified 81% of the patients. However, the classification was correct in 99.8% of patients without headache-related findings, and in only 1.5% of patients with such findings. Neither of the two additionally evaluated models (with Elasticnet and Neural Network) provided statistically significant improvement to the AUC.

We then derived the following clinical score to predict headache-related MRI findings based on the corresponding ORs: age >40 years (5 points), smoking (5 p.), signs/symptoms of infection (5 p.), nausea (4 p.), no numbness (3 p.) and no history of migraine (4 p.). The ROC AUC for this model with a single cut-off point of ≥9 points was 0.625, with a sensitivity of 46% and a specificity of 79%. The clinical score points were considerably scattered in both groups (**Figure 8**). Ranges and interquartile ranges were different between groups, but the median scores were identical (7 p.).

We were not able to reliably evaluate whether headache was the primary presenting symptom in all patients because many had several symptoms. However, the 94 (14%) patients with headache as the only (and thereby primary) presenting symptom had similar rates of significant pathology on MRI, although they were more likely to be younger, female, pregnant, and with a history of migraine. In addition, they had a longer duration of headache before imaging than patients with additional symptoms.

**Table 10.** Variables predicting headache-related findings on emergency MRI with statistical significance ($p<0.05$) in a multivariate analysis.

| Variable | Risk score points | OR | 95% CI (lower–upper) | *p*-value |
|---|---|---|---|---|
| Age over 40 years[1] | 5 | 2.6 | 1.7–3.8 | <0.01 |
| Smoking | 5 | 2.4 | 1.1–4.9 | 0.03 |
| Signs/symptoms of infection | 5 | 2.3 | 1.1–4.7 | 0.03 |
| Nausea | 4 | 1.9 | 1.2–2.9 | <0.01 |
| Migraine in history | 4[2] | 0.5 | 0.3–0.9 | 0.02 |
| Numbness | 3[2] | 0.6 | 0.4–1.0 | 0.03 |

*OR = odds ratio, CI = confidence interval*

*P-values are associated with chi-squared test*

1) Age cut-off point determined by *Youden's J* statistic

2) Risk score points are calculated for absence of numbness and migraine in history: (1/OR)*2 rounded

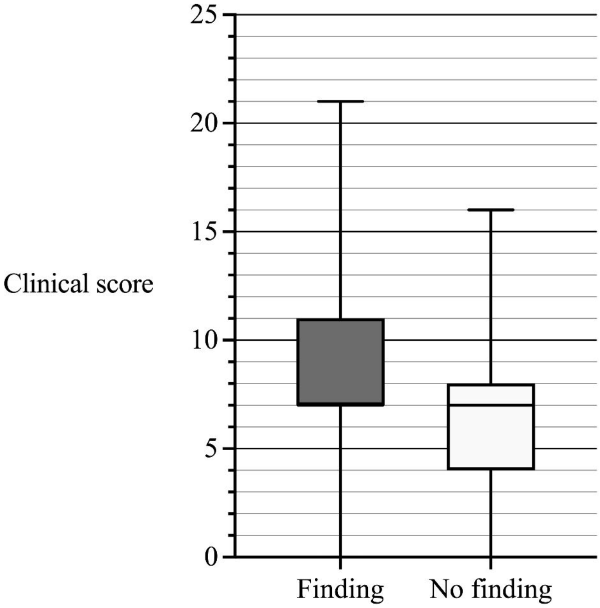


**Figure 8.** Distributions of the clinical score points within groups with and without headache-related findings on emergency MRI. Both groups had a median score of 7 points.

### 5.2.4 Diagnoses and headache etiologies

Regarding the diagnoses of ED discharge and headache etiologies, 25% were diagnosed with a primary headache syndrome, mostly migraine or tension-type headache (**Table 11**). Thirty percent had a confirmed secondary cause of headache (either new or chronic), and the remaining 45% were discharged with a diagnosis of "non-specified headache" due to a lack of further knowledge on the etiology of the headache.

**Table 11.** Diagnoses at emergency department discharge / headache etiologies.

| **Diagnosis / headache etiology** | ***N* (%)** |
|---|---|
| **Primary headache syndromes** | **176 (25)** |
| Migraine | 140 (20) |
| Tension-type headache | 35 (5) |
| Cluster headache syndrome | 1 (0) |
| **Secondary headache syndromes** | **205 (30)** |
| Cerebrovascular disease | 68 (10) |
| Cerebral infarction | 33 (5) |
| Transient ischemic attack | 11 (2) |
| Arterial occlusion/stenosis | 9 (1) |
| Cerebral venous thrombosis | 8 (1) |
| Intracranial hemorrhage | 7 (1) |
| Infectious diseases | 42 (6) |
| Meningitis/encephalitis | 23 (3) |
| Sinusitis | 9 (1) |
| Ocular etiology | 29 (4) |
| Neoplasms | 14 (2) |
| Idiopathic intracranial hypertension | 13 (2) |
| Demyelinating diseases | 7 (1) |
| Intracranial hypotension / Post-lumbar puncture headache | 3 (0) |
| Other: Anemia, asidosis, mental disorders, epilepsy, cerebral aneurysm, Bell's palsy, drug-induced headache, pregnancy-induced headache, hydrocephalus and Arnold-Chiari syndrome | 29 (4) |
| **Unknown etiologies** | **315 (45)** |
| Non-specified headache | 315 (45) |

Note that discharge diagnoses may include chronic diseases, and not only those found on emergency MRI

## 5.3 Imaging outcomes of emergency MRI in patients with suspected cerebral venous sinus thrombosis: a retrospective cohort study (III)

### 5.3.1 Patient characteristics

In total, 327 patients underwent emergency MRI under clinical suspicion of CVST. Of these, 274 (84%) were female and the median age was 30 years (IQR 23–38) (**Table 12**). Medical risk factors of CVST were mentioned in 32% of the referrals, including oral contraception, pregnancy, puerperium, and thrombophilia. The most prevalent clinical symptom at presentation was headache (91%), commonly accompanied by other symptoms such as nausea/vomiting or visual impairment.

Nineteen patients (6%) had a previous diagnosis of a significant brain disease, such as brain tumor, hydrocephalus, Moyamoya disease, or previous cerebral infarction/hemorrhage. A total of 252 (77%) patients received CE-MRV (T1 3D TFE) and 66 patients (20%) received 2D-TOF-MRV.

**Table 12.** Clinical characteristics of patients with clinically suspected CVST who underwent emergency MRI.

| | **Clinically significant MRI finding, including CVST** *N*=53 | **No significant MRI finding** *N*=274 | ***p*-value** |
|---|---|---|---|
| Age [years], median (IQR) | 28 (21–42) | 30 (23–38) | 0.96 |
| Sex [male], *N* (%) | 14 (26) | 39 (14) | 0.03 |
| BMI [kg/m$^2$], data available [*N*]: median (IQR) | 41: 28 (24–36) | 181: 25 (22–30) | 0.02 |
| **Medical risk factors, *N* (%)** | | | |
| Thrombophilia | 1 (2) | 6 (2) | 0.89 |
| Oral contraception | 7 (13) | 44 (16) | 0.60 |
| Pregnancy | 1 (2) | 39 (14) | 0.01 |
| Puerperium | 0 (0) | 11 (4) | 0.14 |
| **Symptoms, *N* (%)** | | | |
| Headache | 47 (89) | 250 (91) | 0.55 |
| Nausea/vomiting | 23 (43) | 122 (45) | 0.88 |
| Visual impairment | 17 (32) | 91 (33) | 0.87 |
| Numbness | 15 (28) | 82 (30) | 0.81 |
| Vertigo | 13 (25) | 72 (26) | 0.79 |
| Photophobia | 17 (32) | 61 (22) | 0.13 |
| Neck muscle tension | 14 (26) | 57 (21) | 0.36 |
| Dysphasia | 7 (13) | 34 (12) | 0.87 |
| Seizure | 2 (4) | 6 (2) | 0.50 |
| No other symptoms than headache | 2 (4) | 24 (9) | 0.22 |
| **Laboratory results, data available [*N*]: median (IQR)** | | | |
| Hemoglobin [g/L] | 53: 135 (125–146) | 259: 133 (125–141) | 0.60 |
| C-reactive protein [mg/L] | 52: 4 (1–19) | 250: 2 (0–5) | <0.01 |
| D-Dimer [mg/L] | 23: 0.3 (0.0–0.7) | 81: 0.2 (0.0–0.8) | 0.90 |
| Contrast-enhanced MRI, *N* (%) | 48 (91) | 204 (75) | 0.01 |
| Duration of headache before MRI [days], median (IQR) | 4 (2–10) | 3 (1–10) | 0.10 |
| Length of hospital stay [days], median (IQR) | 5 (0–9) | 0 (0–0) | <0.01 |

*MRI = magnetic resonance imaging, CVST = cerebral venous sinus thrombosis, IQR = interquartile range, BMI = Body mass index*

*P*-values are associated with *chi-squared* test for categorical variables and with *Mann–Whitney U* test for continuous variables

### 5.3.2 Imaging outcomes

Among the emergency MRI referrals to rule out CVST, we found five positive cases out of 327 (1.5%) (**Figure 9**). That is, 98.5% did not show CVST. All positive CVST findings were detected using CE-MRV (5 out of 252 scans performed), while all 2D-TOF-MRVs were unremarkable. Neither sequence showed any other pathology in the cerebral venous system. Positive cases were confirmed by follow-up MRI six months after the initial diagnosis, which showed partial or complete resolution of the thrombosis. All but one of these patients were young females. All had thrombosis in the transverse sinus and 4/5 had superior sagittal sinus involvement. These thrombi were variably shown by routine MRI sequences: on T2-weighted images in 1/5 patients, on FLAIR images in 2/5 patients, and on T1-weighted images in 4/5 patients (**Table 13**, **Figure 10**). Only one patient had parenchymal changes (edema, no hemorrhage).

Imaging was deemed completely unremarkable for 77%, whereas clinically significant intracranial pathology other than CVST was found in 48 (15%) patients: e.g., intracerebral hemorrhage, cerebral infarction, brain tumor, and sinusitis (**Table 14).** That is, 16% of patients had significant findings on MRI, including CVST. In addition, incidental findings were discovered in 17 (5%) cases, such as developmental venous anomalies and non-specific white matter lesions.

Among patients in this study, only 61 (19%) underwent CT scanning before MRI and 49 (80%) of these scans were considered unremarkable. CT suggested significant pathology in six (10%) patients (intracerebral hemorrhage, infection), and CVST could not be definitively ruled out for the other six. The prevalence of significant findings on MRI was similar in patients with a previous unremarkable CT and in those who did not have CT at all (18% vs. 14%, *p*=0.46, *chi-squared* test).

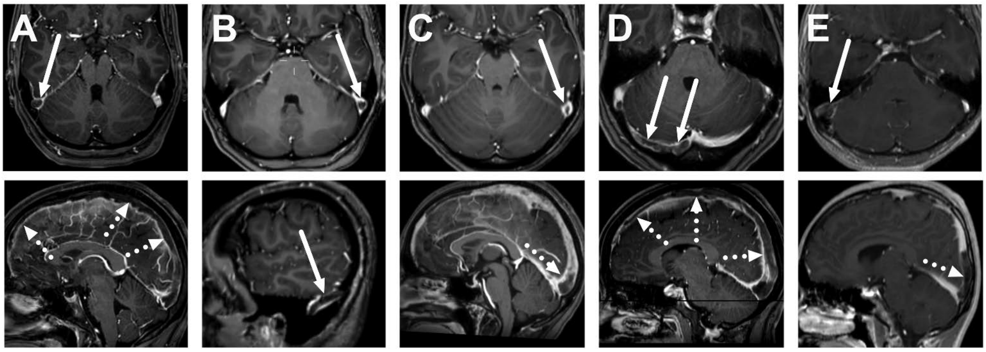


**Figure 9.** True positive cases of cerebral venous sinus thrombosis. Axial (top row) and sagittal (bottom row) images of post-gadolinium T1-weighted 3D MRI images of five patients: a 26-yearold female (**A**), a 33-year-old female (**B**), a 21-year-old female (**C**), a 27-year-old female (**D**), and a 16-year-old male (**E**). Thrombosis is seen as a hypointense filling defect against the high signal from the gadolinium-based contrast agent in the venous sinuses, usually in the transverse sinuses (arrows) and the superior sagittal sinus (dotted arrows).

**Table 13.** MRI findings in different sequences in the venous sinuses of patients with CVST and parenchymal changes (from all sequences). Patient codes correspond to those in **Figure 9**.

| **Patient** | **T2** | **FLAIR** | **SWI** | **T1 pre-contrast** | **T1 post-contrast** | **Parenchymal change** |
|---|---|---|---|---|---|---|
| A | Unremarkable | Loss of normal flow void | Mixed signal intensity | Hyperintense | Filling defect | None |
| B | Unremarkable | Unremarkable | Unremarkable | Unremarkable | Filling defect | None |
| C | Loss of normal flow void | Loss of normal flow void | Mixed signal intensity | Hyperintense | Filling defect | Edema |
| D | Unremarkable | Unremarkable | Unremarkable | Hyperintense | Filling defect | None |
| E | Unremarkable | Unremarkable | Unremarkable | Hyperintense | Filling defect | None |

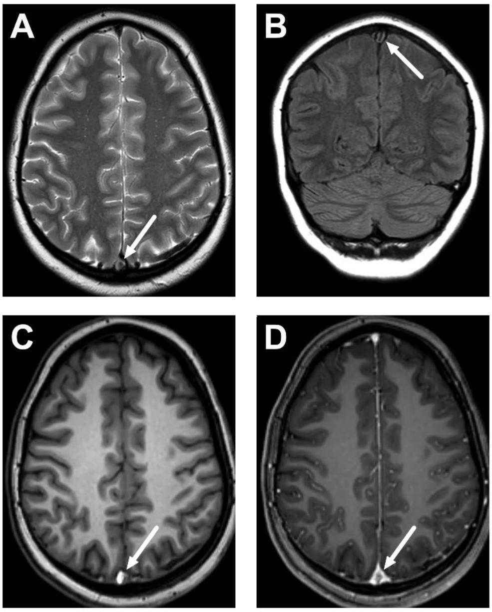


**Figure 10.** An example of cerebral venous sinus thrombosis on routine pre-contrast images. Images show lack of normal flow void on T2-weighted (**A**) and fluid-attenuated inversion recovery (FLAIR) (**B**) images, as well as high signal on the pre-contrast T1-weighted image (**C**), in the superior sagittal sinus (arrows). Post-contrast T1-weighted image is provided for reference (**D**), showing the non-enhancing thrombus (arrow). Most patients did not show thrombosis on all routine sequences, however. The patient is the same as in **Figure 9** (Patient C).

**Table 14.** Clinically significant MRI findings in patients with clinical suspicion of CVST.

| **MRI finding** | ***N* (%)** |
|---|---|
| Sinusitis* | 10 (3) |
| Intracerebral hemorrhage | 8 (2) |
| Cerebral infarction | 7 (2) |
| Intracranial hypertension* | 7 (2) |
| Cerebral venous sinus thrombosis | 5 (2) |
| Blood vessel pathology | 4 (1) |
| Brain tumor | 3 (1) |
| Demyelination | 3 (1) |
| Mastoiditis | 2 (1) |
| Subarachnoid hemorrhage | 1 (0) |
| Subdural hematoma | 1 (0) |
| Brain metastases | 1 (0) |
| Arteriovenous Fistula | 1 (0) |
| Intracranial Hypotension | 1 (0) |
| **Total** | **54* (16)** |

*1 patient presenting with both sinusitis and intracranial hypertension.

### 5.3.3 Predictors of acute pathology

Male sex and high body mass index (BMI) were found to be statistically significantly associated with intracranial pathology on emergency MRI (**Table 12**). Pregnancy was found to decrease the risk of significant findings in our data. Patient age, duration of headache before MRI, and presence of any of the individual symptoms had no statistically significant impact on whether or not significant findings were discovered on MRI.

# 6 Discussion

## 6.1 Dizziness and vertigo (I)

Approximately one in six patients who were imaged for dizziness or vertigo were found to have an acute ischemic stroke. Nearly one in ten patients had other clinically significant findings, whereas in three patients out of four, MRI was unremarkable for acute pathology. Isolated dizziness had no discriminative power concerning imaging outcomes. Dedicated internal acoustic canal and inner ear imaging had no role in the acute setting. CT had a low diagnostic yield among patients who had a stroke on MRI. Acute dizziness and vertigo remain challenging even when emergency MRI is readily available.

Overall, patients who had acute ischemic stroke were characterized by older age (generally >55 years), male sex, and higher prevalences of cardiovascular risk factors and neurological signs; patients with non-ischemic significant pathology by a higher prevalence of headache and longer symptom duration; and patients with no significant pathology by a higher prevalence of vertigo. History-taking and proper clinical examination still play an important role when referring patients for MRI, as the aforementioned factors have a considerable impact on imaging outcomes.

We found several statistically significant associations between clinical variables and imaging outcomes that are consisent with those previously demonstrated in the literature. Kabra et al. reported an acute pathology rate of around 38% on early MRI and several stroke predictors (age over 50 years, a high number of cardiovascular risk factors, a short duration of symptoms, and at least one neurological sign) (Kabra et al., 2015). Machner and colleagues reported a 24% acute pathology rate (varied between 0–50% among clinically defined subgroups) among dizzy emergency patients who underwent adequate neuroimaging (early CT or delayed MRI) (Machner et al., 2020). They documented hypertension, high ABCD$^2$ score, and any central oculomotor sign or focal abnormality to increase the risk for acute lesions. Similar to our analysis, they noted that among patients with vertigo (spinning sensations) acute lesions were less likely. Our findings further corroborate the use of MRI among patients with high age, cardiovascular risk factors or neurological signs.

Our risk scores reached moderate performances. The predictive model for acute strokes had an ROC AUC of 0.75 with an NPV of 90%, while the model for all significant pathology was slightly less accurate. We found no previously published risk scores for emergency MRI. In a retrospective study with 188 patients, Kabra *et al.* demonstrated similar individual predictors of stroke (age, symptom duration, neurological signs and cardiovascular risk factors), each having NPVs of around 88–90% (Kabra et al., 2015).

The most common infarct location was the cerebellum. Notably 25% of infarcts were located elsewhere than in the cerebellum or the brain stem. According to a recent connectivity-based analysis, supratentorial brain regions involved in the brain vertigo network include bilateral insula, somatosensory cortex, higher-level visual areas, cingulate sulcus, and thalamus (Li et al., 2023). Only 36% of prior CTs were positive for AIS, corroborating the role of acute MRI in detecting AIS in patients with dizziness or vertigo. Missing an acute stroke can have serious adverse effects, such as predisposing the patient to a high risk of future, potentially more severe infarcts that could otherwise have been prevented, or potentially fatal secondary complications of the current stroke, such as brainstem compression and obstructive hydrocephalus (J. A. Edlow et al., 2008; Kabra et al., 2015).

While its accuracy is considered superior to CT, even MRI does not have a perfect sensitivity in the early detection of an acute ischemic stroke (Chalela et al., 2007). In fact, diffusion-weighted MRI has been previously reported to be false negative within the first 48 hours in up to 50% of small ischemic strokes in the posterior fossa (Saber Tehrani et al., 2014). In our follow-up analysis of NS-patients, we concluded that acute MRI likely did not miss any clinically meaningful infarcts in our cohort. Modern MRI technology likely has a substantial sensitivity in detecting small infarcts in the posterior fossa and elsewhere in the brain, as was shown in the current study.

These results provide novel information on the diagnostic yield in this patient group when emergency MRI is readily available and commonly used in the emergency radiology department. Regarding the clinical value of emergency MRI findings, MRI likely altered the clinical management of patients with newly discovered neurological disorders such as cerebrovascular (including acute infarction), demyelinating, and infectious diseases. Although the rate of scans with no acute pathology may seem too high (75%), ruling out infarctions with a high sensitivity is likely valuable for these patients and their physicians. As an important notion, isolated dizziness lacked discriminative power on imaging outcomes, as 14% of these patients had AIS on MRI.

## 6.2 Headache (II)

The majority of patients who underwent emergency MRI for non-traumatic headache had normal scans, while around 20% had significant findings that potentially explained the headache. Thus, about five patients needed to be scanned to diagnose one patient with significant intracranial pathology. Although we found significant predisposing and protective factors, the performance of the predictive model was only moderate, and the model could not accurately detect patients with headache-related findings. Judicious use of emergency neuroimaging to rule out secondary causes of non-traumatic headache remains a challenge, even when using MRI.

Regarding MRI findings in patients with headache in general, a fairly recent meta-analysis by Jang et al. found potentially significant abnormalities assessed by MRI in 5.7% (95% CI: 1.6–20%) of all patients suspected of primary headache (Jang et al., 2019). Budweg *et al.* found that ~22% (18/82) of their walk-in patients had findings that could at least potentially explain their acute headache, of whom 10% (8 patients) had findings that were considered clinically significant (Budweg et al., 2016). In both studies, only patients with a provisional diagnosis of a primary headache were included. Our data showed that the yield of MRI was higher among emergency patients (20% with significant findings), most likely due to the higher prevalence of severe intracranial acute-onset pathology (e.g., intracranial hemorrhage, infarctions and central nervous system infections). We also decided to cover all emergency outpatients who had non-traumatic headache, including patients with abnormal neurological findings and suspicion of high-risk pathology, which probably contributed in increasing the imaging yield. Our patients were imaged with significantly shorter latency (96% within 24 hours) compared to those in the previous study by Budweg et al.: 72% of their patients had MRI within three days of presentation, and 54% were imaged on the same day.

Our most common headache-related findings were similar to those reported by Budweg et al. In both studies, findings such as signs of intracranial hypertension, meningitis, and cerebral infarction were prevalent. Moreover, our data showed various, less common causes that were not met in the previous smaller sample, including Chiari 1 malformation, arterial dissection and occlusion, PRES, and signs of intracranial hypotension. When compared to the previous studies using CT for acute headaches, they reported similar prevalences of cerebrovascular conditions (intracranial hemorrhages and ischemia) and newly detected neoplasms, but a lower prevalence of conditions that are more identifiable by MRI (such as infectious diseases and intracranial hypertension) (Covino et al., 2019; Lemmens et al., 2021; Wang & You, 2013). We found recent infarcts (identified with DWI) in 30 patients (4% of all, 22% of those with significant findings). Most of these infarcts were small and often punctate. None of the patients had motor loss, and the prevalence of numbness was not higher than among other patients with significant findings. These small infarcts thus were unlikely to cause major neurological deficits, which are usually primarily imaged with CT. In fact, a third of these patients had previous CT scans, all with unremarkable findings.

The proportion of incidental findings discovered was similar to that of the significant findings, and also to that reported for patients with a new primary headache (B.-S. Kim et al., 2020). Kim et al. reported incidental abnormalities in 25% of new primary headache patients scanned with MRI, of which white matter hyperintensities and sinonasal abnormalities not related to headache were the most common. Our observations were similar, confirming the high prevalence of incidental findings and similarities between emergency and non-emergency settings in regard to these findings. Importantly, clinically insignificant incidental findings may cause unnecessary worry in patients and healthcare providers.

We found that age >40 years, smoking, signs/symptoms of infection, and nausea significantly increased the risk of abnormal headache-related findings on MRI, whereas numbness and history of migraine decreased the likelihood of such findings. Of these factors, high age and nausea were the only ones reported in the previous CT and MRI scores (Bent et al., 2015; Budweg et al., 2016; Covino et al., 2019; Lemmens et al., 2021). A focal neurological deficit was reported as a major risk factor in every CT score, but this was not the case in our data. One explanation is that such patients may have undergone a CT instead of MRI. None of the previous studies reported factors that would reduce the risk of significant findings. The reason why known migraine was a protective factor may be that even a new type of headache in a migraine patient could more likely be migraine, rather than due to a secondary cause. Among the patients with a history of migraine, only 10% had meaningful findings on MRI.

Our model predicting significant imaging outcomes among emergency patients provided limited value with low sensitivity and moderate specificity. The clinical score by Budweg et al. had a considerably higher sensitivity (100% vs. 46%), similar specificity (82% vs. 79%), and a superior ROC AUC (0.94 vs. 0.63). One reason for these differences may be that their model was developed for patients in an outpatient walk-in clinic setting, which usually presents a narrower spectrum of imaging outcomes and symptoms than patients in emergency departments.

According to our model, a typical patient who is the least likely to show abnormal findings is a young non-smoking patient with a history of migraine. Our multivariate model could not accurately detect patients with headache-related findings. The moderate performance of our model reflects how difficult it is to create accurate, universal risk scores for clinical use in such a heterogeneous patient population with various symptoms, risk factors and imaging findings.

These results provide novel information on the diagnostic yield in this patient group when emergency MRI is readily available and commonly used in the ED.

Regarding the clinical value of emergency MRI findings, MRI likely altered the clinical management of patients with newly discovered neurological disorders such as cerebrovascular disease (including acute infarction), demyelinating and infectious disease, and idiopathic intracranial hypertension. In addition, even patients with worrisome symptoms who had a normal emergency MRI scan may have been safely discharged.

## 6.3 Suspected CVST (III)

Diagnosing CVST is challenging, considering that the diagnostic yield of imaging for suspected CVST is relatively low in terms of how often it is suspected on clinical grounds. We found that emergency MRI showed signs of CVST in only 1.5% of all cases and other clinically significant intracranial pathology in 15% of patients. The most prevalent findings among these patients included sinusitis, intracerebral hemorrhage, cerebral infarction, and signs of intracranial hypertension. These novel results add to previous knowledge by showing that the rate of significant imaging outcomes of MRI does not significantly differ from that of CT in these patients.

Across all imaging modalities, a total of 27 patients were diagnosed with CVST in the study period: 15 with MRI, 11 with CT, and one patient with digital subtraction angiography. Notably, CVST was not specifically suspected in the imaging referrals of 10 of the patients diagnosed with MRI. This further highlights the vague nature of the disease.

Our findings regarding patient demographics, history, and specific signs and symptoms that have induced clinical suspicion for CVST are similar to those previously reported in the literature (Capecchi et al., 2018; Behrouzi & Punter, 2018; Kalita et al., 2019; Ropper & Klein, 2021). In our data, a typical patient was a young woman with a headache accompanied by nausea and focal neurological deficits, such as numbness or visual impairment.

We found that the yield of imaging suspected CVST using emergency MRI was higher among patients that were male or had a higher BMI. Females, especially those who were pregnant, underwent MRI more often with no detected intracranial pathology, which further underlines the high alert for clinical suspicion of CVST in these patients. Patient age, duration of headache before referring to MRI, or presence of individual symptoms had no significant impact on whether or not clinically significant findings were discovered on emergency MRI. From the clinical perspective, this indicates that medical imaging plays a considerable role in ruling out CVST regardless of these factors.

The prevalence of other significant findings on emergency MRI (15%) was only slightly higher than that previously reported for nonenhanced CT (11%) (Almqvist et al., 2020). These relatively small differences in results might well be attributed to differences in patient management, demographical characteristics, or referral patterns between institutions. In retrospect, many of our significant findings could likely have been visible on CT (e.g., intracerebral hemorrhage, infarction), which in most circumstances might be sufficient in the emergency environment with regard to its faster scan times and lower costs. On the other hand, MRI could show more subtle but potentially significant findings among these patients (e.g., small infarcts, signs of intracranial hypertension), but for now, this ability of MRI did not translate into a considerably higher overall yield of significant pathology when compared to CT.

Dedicated emergency MRI is a feasible first-line imaging method for various acute pathology (Nurminen et al., 2021). At our institution, this has become a routine modality, especially among young patients, because of its excellent soft tissue contrast and lack of ionizing radiation. Therefore, we sought to characterize MRI findings in suspected CVST in these patients in particular and not include patients who might have undergone only CT for similar clinical suspicion. Some sampling bias toward MRI cannot be excluded. Our patients were slightly younger than those previously reported as having undergone CT based on suspected CVST (Almqvist et al., 2020). In addition, the availability of emergency MRI in our institution might lower the threshold to ask for imaging for young, mildly symptomatic patients compared to when only CT is available. Too liberal patient selection and possible overuse of MRI might partly explain the low diagnostic yield, in addition to inherent difficulties in recognizing CVST because of non-specific symptoms and common risk factors.

MRI with MRV is a highly reliable method for diagnosing CVST, but it is likely that conventional CT will remain the first imaging modality for most acute situations, simply due to wide-spread availability, fast scanning times, and ability to suggest most acute conditions, such as tumors, hemorrhages, and abscesses, although many of these conditions will eventually require MRI for an accurate diagnosis. Added value for MRI over CT as a primary screening tool stems mainly from its superior soft tissue discrimination and lack of ionizing radiation.

## 6.4 Strengths

This study has two major strengths. First, we emphasized large sample sizes due to the routine use of MRI in the emergency radiology department. Large sample sizes afford adequate statistical power to discern clinically meaningful effect sizes. Second, we used a data-driven approach by querying the referrals for specific symptoms instead of relying on diagnosis codes. This approach mitigates against sampling bias because all patients with the queried imaging indication will be included irrespective of the final diagnosis. This imaging phenotypical approach is likely more proximal to the underlying biology than diagnosis codes. This study represents a true clinical situation and offers a real-world overview of patients with dizziness or headache in need for an early MRI.

## 6.5 Limitations

The study has several limitations due to its retrospective, single-center design. Regarding clinical notekeeping, some referrals and mecidal records may have been incomplete or imprecise. This issue is particularly significant, as it is fairly common for imaging referrals in emergency departments to be brief. If a presence of a certain clinical feature was not mentioned in the referral or in the medical records, the feature was assigned a value of "0" or "absent" instead of "not available". Therefore the true prevalence of the relevant comorbidities and symptoms may have been underestimated. The quality of the clinical note-keeping for each patient (reflecting real-world practice) determined the quality of the clinical data included in this study.

The lack of relevant data may have contributed to the performance of the risk scores. In addition, the risk scores require prospective validation before claims of clinical utility can be made.

The findings in the MRI reports may vary, as the reports were written by multiple radiologists with different levels of clinical experience, and not all were subsequently reviewed by a neuroradiologist. We estimate that at our institution, roughly 75% of the reports written by non-neuroradiologists are subsequently evaluated by a neuroradiologist. We only reviewed the additional reports by neuroradiologists if it was recommended in the primary report. However, we believe this had little to no effect on the results. In addition, the neuroradiologists who reviewed the referrals and reports in this study did not routinely examine all of the MR images.

Most importantly, emergency MRI is not readily available in all institutions, limiting the generalizability of our findings. Regarding generalizability, the study is also limited by the fact that we were not able to include patients not scheduled for emergency MRI. Therefore, the factors that contributed to the need for emergency MRI perceived by the referring physician remain obscure. We are not able to estimate the proportion of patients who underwent firstline MRI among all emergency patients. Our results on the diagnostic yield are only generalizable to patients deemed to require emergency brain MRI.

In Study I, classifying findings into NS and S groups was based on expert opinion and may, therefore, have been biased. In the classification, we used a consensus method between neuroradiologists and did not record interobserver agreement. The inclusion of patients with symptoms highly indicative of stroke (aphasia, ataxia, dysphagia) may have contributed to the relatively high diagnostic yield, as these patients may be more likely to undergo neuroimaging regardless of having dizziness. The combination of axial and coronal DWI, which has been shown to have improved diagnostic accuracy for brain stem infarcts, was not used (Steffen et al., 2021).

## 6.6 Future prospects

Currently, the utilization of emergency MRI is limited, yet advancements in technology may improve its accessibility and feasibility in the future. Potential developments encompass optimized image quality and faster acquisition using acceleration techniques (Ye, 2019; De Zwart et al., 2024), solutions based on artificial intelligence (Johnson et al., 2020; Sandino et al., 2021), and synthetic MRI sequences (Ji et al., 2022; Tanenbaum et al., 2017). Hardware improvements include developments in low-field MRI (Bhat et al., 2021; Campbell-Washburn et al., 2019; Marques et al., 2019), alternative MRI scanner designs (Iwan et al., 2021), and portable applications (Wald et al., 2020). The synergy of innovations in both hardware and software is likely to yield results greater than the sum of the individual advancements.

As the demand of emergency imaging, and medical imaging in general, continues to rise, there is a growing need for studies examining the judicious utilization and clinical value of advanced emergency imaging. Investigation of the clinical value is not a simple task. However, it can be broken down into different sub-sections such as diagnostic accuracy, diagnostic yield, cost-effectiveness, and impact on patient management. The currently presented risk scores, clinical variables, and imaging yields are not all-encompassing, but they may serve as a solid starting point for future studies.

# 7 Conclusions

This thesis sought to explore and analyze the imaging outcomes of emergency MRI among patients with dizziness, headache, or a suspicion of CVST. The main findings of the thesis are:

1. Acute dizziness and vertigo remain challenging even when emergency MRI is readily available. One in four patients had acute pathology on MRI. Predictors of acute pathology (older age, male sex, cardiovascular risk factors and neurological signs) may aid patient selection for MRI, optimizing the yield and clinical impact of emergency neuroimaging. Low diagnostic yields of CT and internal acoustic canal MRI may offer opportunities to reduce healthcare expenditures in the future.
2. The majority of emergency patients with non-traumatic headache did not present significant abnormalities on MRI. Predictive modeling to promote using neuroimaging judiciously remains a challenge, even with significant predictors of abnormal findings (older age, smoking, nausea, and signs/symptoms of infection).
3. The diagnostic yield of emergency imaging for suspected CVST using MRI was low and similar to that reported for CT. Significant findings were most likely found in patients that were male or had a higher BMI. Although imaging outcomes were close to similar to that reported for CT, the lack of ionizing radiation might favor the use of MRI as an alternative screening tool for intracranial pathology in emergency patients suspected of having CVST.

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