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MAGNETIC RESONANCE

Hiatal hernias in patients with GERD-like symptoms: evaluation of dynamic real-time MRI vs endoscopy

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Abstract

Purpose To assess the diagnostic potential of real-time MRI for assessment of hiatal hernias in patients with GERD-like symptoms compared to endoscopy.

Material and methods One hundred eight patients with GERD-like symptoms were included in this observational cohort study between 2015 and 2017. Real-time MRI was performed at 3.0 Tesla with temporal resolution of 40 ms, dynamically visualizing the esophageal transport of a pineapple juice bolus, its passage through the gastroesophageal junction, and functional responses during Valsalva maneuver. Hernia detection on MRI and endoscopy was calculated using contingency tables with diagnosis of hernia on either modality as reference.

Results Of 108 patients, 107 underwent successful MRI without adverse events; 1 examination was aborted to inability to swallow pineapple juice in supine position. No perforation or acute bleeding occurred during endoscopy. Median examination time was 15 min. Eighty-five patients (79.4%) were diagnosed with hiatal hernia on either real-time MRI or endoscopy. Forty-six hernias were visible on both modalities. Seventeen hernias were evident exclusively on MRI, and 22 exclusively on endoscopy. Sixteen of the 63 MRI-detected hernias (25.4%) were detectable only during Valsalva maneuver, which were smaller compared to hernias at rest (median − 13.5 vs − 33.0 mm, $p < 0.001$). Diagnostic accuracy for hernia detection was comparable for MRI and endoscopy (sensitivity 74% vs 80%, $p = 0.4223$; specificity 100% vs 100%, $p > 0.99$).

Conclusion Real-time MRI is a fast and safe modality for assessment of the gastroesophageal junction, without radiation exposure or administration of gadolinium-based contrast media. Although MRI and endoscopy yield comparable diagnostic accuracy, dynamic MRI sequences are able to visualize hiatal hernias that were occult on static MRI sequences or endoscopy in a relevant number of cases.

Key Points

- *Real-time MRI is a safe and fast imaging modality for examination of the gastroesophageal junction, combining anatomical and functional information for enhanced detection of hiatal hernias.*
- *Real-time MRI and endoscopy yield comparably high diagnostic accuracy: real-time MRI visualizes hiatal hernias that were occult on endoscopy in a relevant number of patients; however, several hiatal hernias detected on endoscopy were occult on real-time MRI.*

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• *There is clinical potential of real-time MR imaging in patients with GERD-like symptoms and equivocal findings on endoscopy or pH-metry, for anatomical visualization in patients planned for surgical intervention, or those with suspected fundoplication failures.*

Keywords Hiatal hernia · Gastroesophageal reflux disease · Magnetic resonance imaging · Endoscopy · EDG

Abbreviations

EGD	Esophagogastroduodenoscopy
GERD	Gastroesophageal reflux disease
LES	Lower esophageal sphincter
PPI	Proton pump inhibitor

Introduction

Hiatal hernia is defined as a cephalad migration of the gastroesophageal junction or other abdominal contents into the mediastinum via the diaphragmatic hiatus [1]. The true prevalence remains unknown, since many individuals remain asymptomatic and, therefore, are never diagnosed. Further, the inherent subjectivity in diagnostic criteria makes the determination of the exact prevalence of hiatal hernia difficult. However, it is generally recognized that the prevalence of hiatal hernias correlates with obesity and its risk increases with age [2]. The clinical significance of hiatal hernias lies in their association with gastroesophageal reflux disease (GERD) [3]. In patients with hernias, the natural antireflux mechanism is disrupted and the competence of the lower esophageal sphincter (LES) is impaired. Therefore, hiatal hernia is considered to be highly relevant in a subset of GERD patients who are refractory to standard medical treatment, as well as patients suffering from GERD due to transient lower esophageal sphincter relaxations [4–7]. While study cohorts from Western countries indicated that over 50 to 94% of patients with GERD that were diagnosed either endoscopically or radiologically had concomitant hiatal hernias, the prevalence of hiatal hernia was as high as 13 to 59% in the control subjects [8–14]. Although the presence of hiatal hernia therefore cannot be considered indispensable for the diagnosis of GERD, hiatal hernia is still considered as supportive evidence for the diagnosis of GERD in the Lyon Consensus guideline [15].

Although barium swallow examination and upper gastrointestinal endoscopy (esophagogastroduodenoscopy [EGD]) are commonly used for diagnosing hiatal hernia, their diagnostic yield is less than perfect due to a lack of objective diagnostic criteria and subjective variations in assessment [6, 16]. Therefore, there is the clinical need for a robust and preferably non-invasive imaging tool without the use of ionizing radiation to accurately detect hernias, especially in symptomatic patients with inconclusive endoscopy or pH-metry.

Recent development of an ultrafast MRI technique allows monitoring the dynamics of physiological processes in real time at a temporal resolution of up to 20 ms per frame. This novel methodology is already well-established for cardiovascular applications and has shown great promise for characterizing neurological disorders which lead to swallowing disorders [17–19]. It allows real-time imaging of the gastroesophageal junction, combining anatomical information with dynamic sequences for enhanced detection of hiatal hernias. In previous studies, we were able to prove the feasibility of real-time MRI with high spatiotemporal resolution in patients with GERD and identify anatomical and functional parameters with low inter- and intra-observer variability, being the prerequisite of a robust clinical tool [20, 21]. In a recent feasibility study, real-time MRI has demonstrated high diagnostic potential for the detection of fundoplication failure and recurring hernia, while some hiatal hernias were occult on endoscopy [22]. These findings raised the question whether real-time MRI can aid in assessment of hiatal hernias, especially in patients with otherwise normal endoscopy. The purpose of this study is to assess the diagnostic potential of real-time MRI for assessment of hiatal hernias in patients with GERD-like symptoms and compare MRI to endoscopy.

Materials and methods

Study population

This retrospective study was conducted in accordance with the Declaration of Helsinki in its most recent version and received approval by the local ethics board. All participants gave written informed consent before each examination. Inclusion criteria for this study were patients with GERD-like symptoms for at least 6 months. General exclusion criteria for real-time MRI were unknown metallic implants, inability to swallow, known claustrophobia, and known allergy to pineapple. Previous or concurrent medical treatments with PPI or H_2 receptor inhibitors as well as previous hiatal hernia repair were no exclusion criteria. A total of 126 patients with GERD-like symptoms underwent real-time MRI of the gastroesophageal junction between 2015 and 2017. Eighteen patients had not undergone endoscopy and were consequently excluded. One single case was excluded due to the inability to swallow the pineapple juice in supine position.

Overall, 107 consecutive patients (male $n = 53$, female $n = 54$, median age 58 years/IQR 46–66 years) who presented

themselves in our surgical outpatient clinic (Department of Surgery and Department of Gastroenterology and Gastrointestinal Oncology of the University Medical Center, Goettingen, Germany) with GERD-related symptoms were included in this study. GERD-related symptoms were heartburn, regurgitation, and dysphagia. The median duration of GERD-like symptoms was 21 months (IQR 7.5–42 months) at time of presentation. Patient flow is depicted in Fig. 1.

Endoscopy

Endoscopic evaluation of the esophagus, LES, and stomach was performed in all patients by specialized gastroenterologists. Endoscopy was performed under IV sedation with propofol in left lateral supine position. Following standard operating procedure of the Department of Gastroenterology, patients received an initial 20–40 mg bolus of propofol followed by repeated smaller dosages to maintain sedation. Endoscopists assessed the gastroesophageal junction in antegrade and retroflexed view. Hiatal hernia diagnosis was defined as clear separation of the gastroesophageal junction and the crural diaphragm. No minimum length of separation was defined. The esophageal mucosa was assessed by standard white light endoscopy as well as additional narrow band imaging. Biopsies were taken in cases of endoscopically visible changes or clinical implications of histologic mucosal abnormalities, such as suspected eosinophilic esophagitis or for *Helicobacter pylori* detection.

Real-time MRI

MRI examinations were carried out in supine position using a commercial 3 Tesla MRI system (Skyra, Siemens Healthineers) and a combination of an 18-element thorax coil with suitable elements of the spine coil array. As previously described, real-time MRI was accomplished by highly undersampled radial FLASH acquisitions with NLINV image reconstruction [23]. While the former encodes gradient echo MRI signals with a few radial spokes which are equally distributed in data space, NLINV jointly calculates the image and all coil sensitivities in an iterative optimization process solving a nonlinear inverse problem. For dynamic imaging, numerical robustness is ensured by exploiting a priori knowledge about the temporal continuity of body movements. This is accomplished by temporal regularization to the immediately preceding frame, i.e., the image and its coil sensitivities. The temporal fidelity of the approach has been experimentally validated using a dedicated motion phantom [24].

For real-time MRI of the oral cavity, esophagus, and esophageal sphincter, mildly T1-weighted images were continuously acquired with the following parameters: RF-spoiled radial FLASH, repetition time TR = 2.12 ms, echo time TE = 1.31 ms, flip angle 8°. The use of 19 spokes per frame resulted in a measuring time of 40 ms which corresponds to a true temporal resolution of 25 frames per second (fps) without any data sharing or interpolation. A field of view of 256 × 256 mm^2 in conjunction with a data matrix of 170 × 170 yielded an in-plane resolution of 1.5 × 1.5 mm^2, while the slice thickness was chosen to be 8 mm.

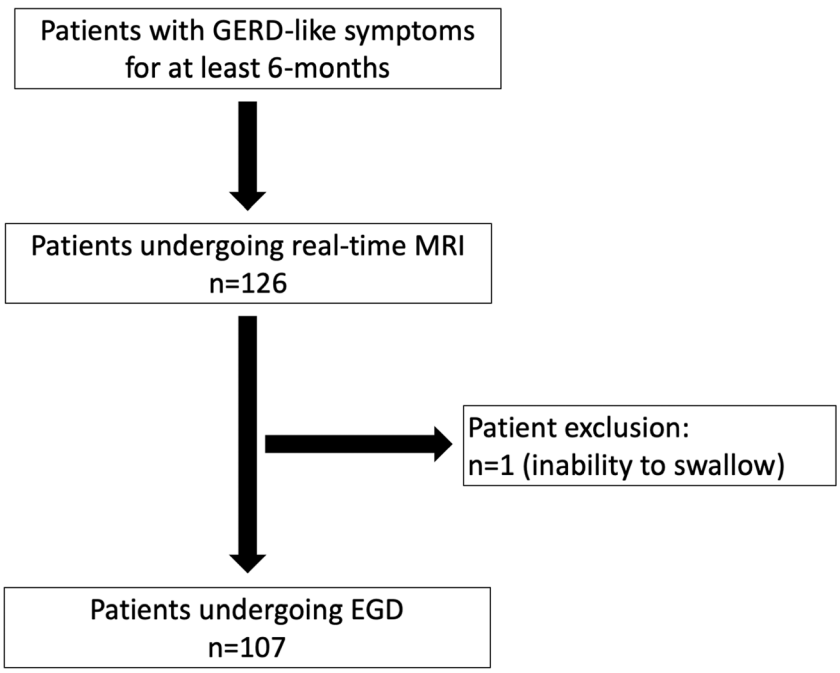

Fig. 1 Patient flowchart

Online reconstruction of real-time images was achieved by a highly parallelized version of the NLINV algorithm and its implementation on a computer (sysGen/TYAN Octuple-GPU, 2 × 123 Intel Westmere E5620 processor, 48GB RAM, Sysgen) with 8 graphical processing units (GPUs, GeForce GTX TITAN, Nvidia).

During dynamic imaging, commercially available pineapple juice served as an oral contrast agent based on its inherent concentration of paramagnetic manganese ions that results in a T1 shortening effect. A few seconds after the onset of each real-time MRI recording, an operator positioned at the front end of the MRI magnet injected a bolus of 10 ml juice into the subject's mouth through a conventional flexible infusion tube infusion (3 mm diameter) connected to a 50-ml syringe. The end of the bolus administration was cued by the operator, after which the patient performed a self-controlled voluntary swallow in a natural manner at a comfortable rate. The bolus was given once for each real-time MRI recording, which lasted for 25 s (i.e., 1000 images). After bolus administration, all patients were asked to perform Valsalva maneuver in order to provoke sliding hernia. All patients were instructed on how to perform Valsalva maneuver prior to real-time MRI. Patients were asked to exhale against a closed mouth and contract their abdominal muscles. During the examination, patients were asked to perform Valsalva maneuver after initiation of real-time MRI sequences. Success of Valsalva maneuver was assessed by movement of the diaphragm and repeated if considered necessary.

MR image evaluation

All functional MRI examinations were analyzed by two radiologists in consensus reading. Reader 1 (AS) was an attending radiologist with 9 years of experience in abdominal radiology. Reader 2 (LB) was a resident radiologist with 4 years of experience in abdominal radiology. Both readers had 2 years of experience in dedicated real-time MRI of the gastroesophageal junction. Analyses were based on the manufacturer's software (Syngo B17, Siemens Healthineers).

Each MRI examination was assessed for the presence or absence of hernias. For size quantification of hernias, the sphincter-to-diaphragm distance was measured from the lower esophageal sphincter boundary. All MRI assessments were separately performed under resting condition and Valsalva maneuver.

Statistical analyses

For descriptive statistics, continuous variables are given as median with interquartile range (IQR) and categorical variables as absolute number and percent. Test sensitivity and specificity for detection of hiatal hernia were calculated using a standard contingency table approach and compared between modalities via the McNemar test. All statistical analyses were performed using R version 3.3.2 (R Core Development Team) and RStudio version 1.1.383 (RStudio Inc.). An alpha level of 0.05 was considered to indicate statistical significance. All p values provided are two-sided.

Results

Endoscopy and real-time MRI acquisition

Endoscopy was successfully performed in all patients at an average examination time of 20–30 min. No acute adverse events (i.e., acute perforation or bleedings) were reported. The median duration of real-time MRI acquisition was 15 min. Real-time MRI had to be aborted in one patient due to inability to swallow, who was later diagnosed with inclusion body myopathy. No case of pineapple juice aspiration was observed, no claustrophobic incident occurred. Figure 2 demonstrates real-time MRI of the LES during bolus passage and after Valsalva maneuver. Representative individual images were selected showing bolus passage in coronal oblique and sagittal planes. Corresponding real-time MRI movies are shown in Supplementary Video 1, Video 2, and Video 3.

Detection of hernias by real-time MRI and endoscopy

A total of 85 patients (79.4%) were diagnosed with hernias on either MRI or endoscopy; 46 of those were detectable on both modalities. In 17 cases, hernias were evident exclusively on MRI, and in 22 cases exclusively on endoscopy. For 22 patients, neither modality revealed hernias. Quantification of the sphincter-diaphragm distance for all MRI examinations is depicted in Fig. 3, stratified by detectability at rest and during Valsalva maneuver.

Since several hiatal hernias were exclusively detected on one modality, a combined reference test was set for sensitivity and specificity calculation, defined as hernia detection on at least one modality. For real-time MRI, test sensitivity was 74% (95% CI 63–83%) and specificity 100% (95% CI 85–100%) (Table 1). For endoscopy, sensitivity was 80% (95% CI 70–88%) and specificity 100% (95% CI 85–100%) (Table 2). No statistically significant differences were found between real-time MRI and endoscopy sensitivity ($p = 0.423$) and specificity (p value not applicable for unequivocal detection).

Hernias detectable via real-time MRI

Of the 63 MRI-detectable hernias, 16 were seen during Valsalva maneuver only. All hernias visible under resting condition were seen during Valsalva maneuver as well. Considering the 17 hernias visible only by MRI and occult

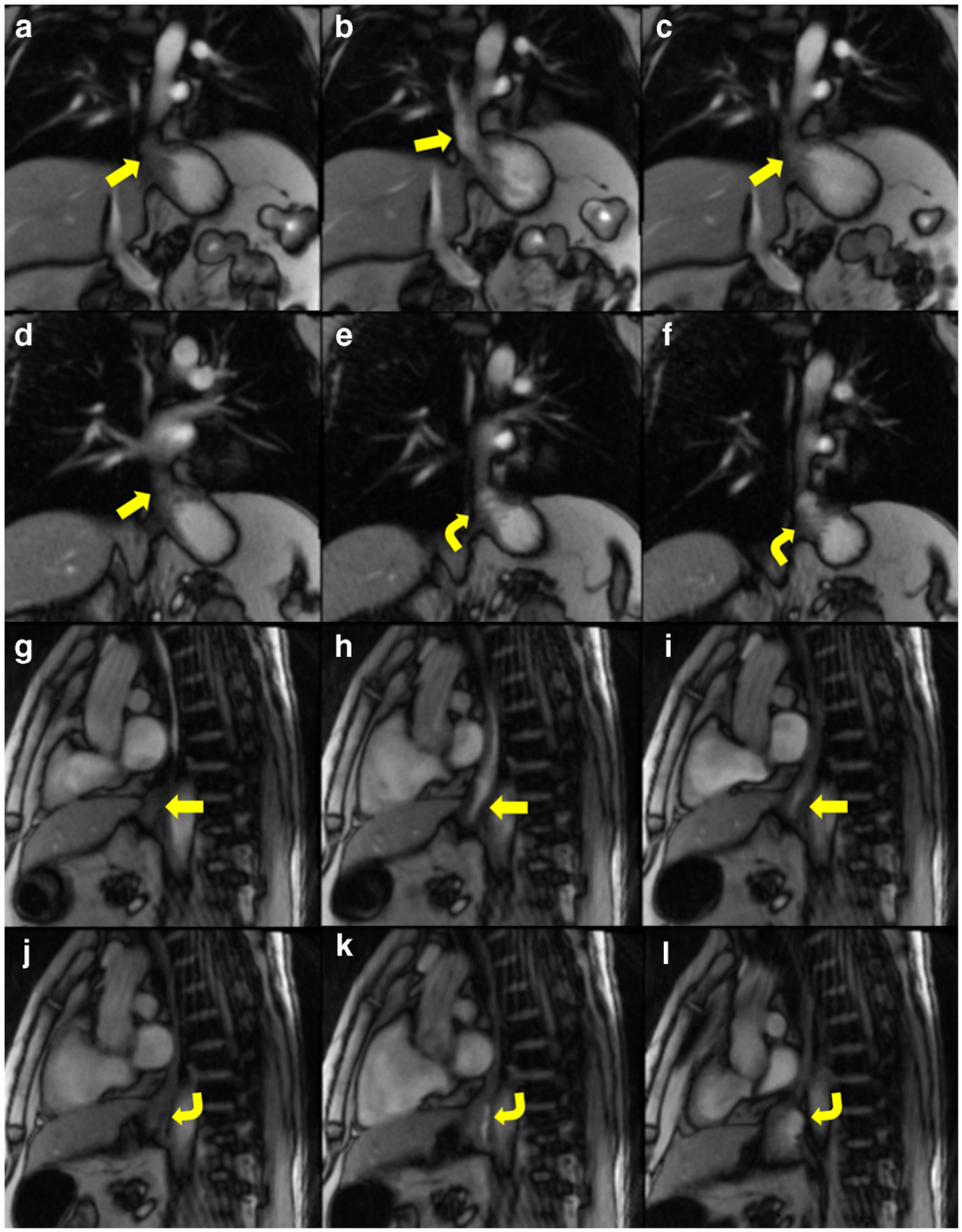

Fig. 2 Real-time MRI of the gastroesophageal junction during bolus passage and after Valsalva maneuver in coronal oblique planes (**a**–**f**) and sagittal planes (**g**–**l**). Representative individual images were selected showing bolus passage (arrow) of 10 ml pineapple juice through the lower esophagus and gastroesophageal junction (arrows) in both planes (**a**–**c** and **g**–**i**). During Valsalva maneuver (**d**–**f** and **j**–**l**), parts of the stomach herniate through the hiatus (curved arrows). Also, see supplemental Video 1

on endoscopy, 10 were visible on resting imaging (58.8%) and 7 were visible during Valsalva maneuver only (41.2%).

Sphincter-diaphragm distance on real-time MRI

Migration of the lower esophageal sphincter above the diaphragm in resting position or during Valsalva maneuver was given with a negative value to indicate the presence and size of a hernia. Median sphincter-diaphragm distances for different scenarios are summarized in Table 3.

The median hernia size was larger for those hernias detected on both MRI and endoscopy compared to those only visible on MRI, but did not reach statistical significance (− 27.5 vs − 21.5 mm, $p = 0.145$). However, hernias detectable only during Valsalva were smaller than those detectable at rest (− 13.5 vs − 33.0 mm, $p < 0.001$). Median sphincter-diaphragm distance of patients with endoscopic hernia occult on MRI was 8.0 mm (IQR 6.0 to 10.0 mm). Patients without hernia in both MRI and endoscopy had a median sphincter-diaphragm distance of 6.5 mm (IQR 5.0 to 8.25) (Fig. 4).

Discussion

Hiatal hernia is a clinically relevant diagnosis in patients with GERD-like symptoms who are refractory to standard

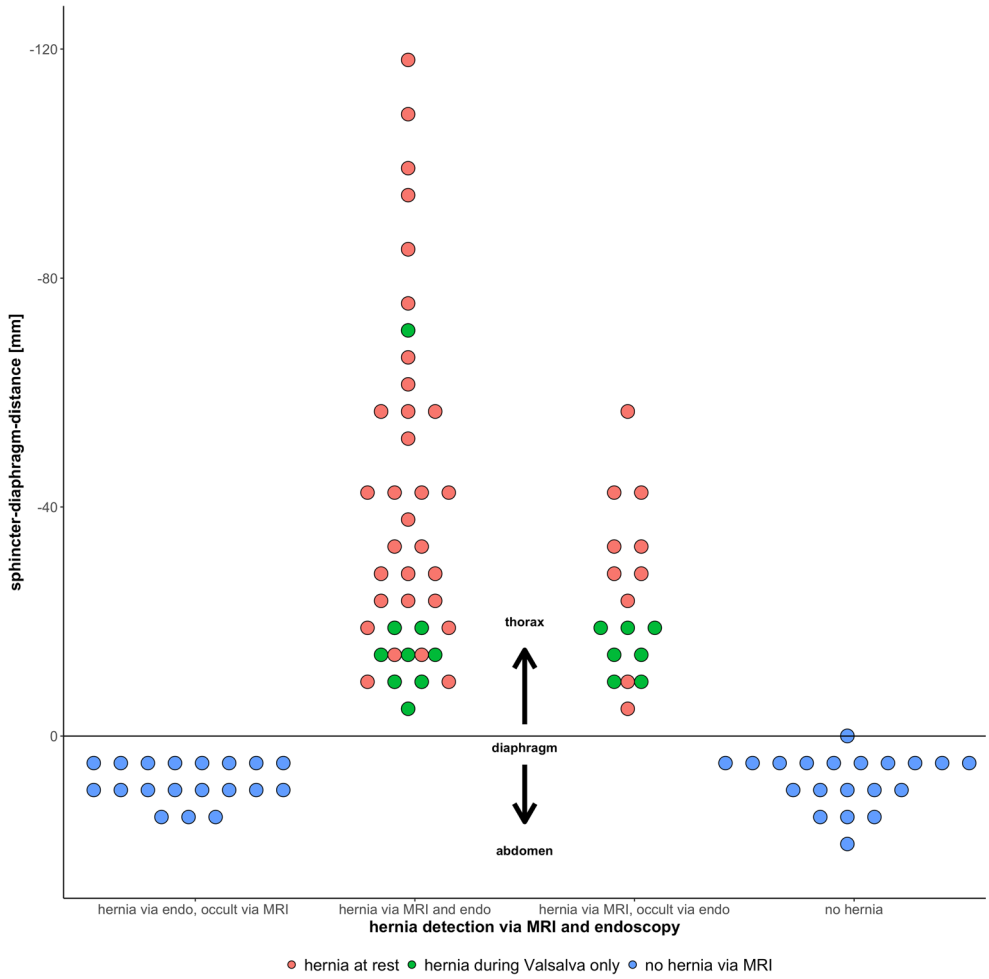

Fig. 3 Visualization of sphincter-diaphragm distances in patients with hiatal hernia detected on (left) both modalities, (middle) either on MRI or endoscopy or (right) no hernia on both modalities. Hernia only detected during Valsalva maneuver are marked with green dots

medical treatment and those suffering from GERD due to transient lower esophageal sphincter relaxations [4–7]. Still, up to date, there is no consensus or gold standard for hiatal hernia diagnosis: while both endoscopy and barium swallow studies have been employed, there are several concerns regarding their diagnostic accuracy as well as associated radiation exposure and contrast media administration. Our study implemented a novel real-time MRI protocol to detect hiatal hernias in patients with GERD-like symptoms and aimed to evaluate its diagnostic accuracy.

In our study, hiatal hernia was diagnosed in 58.9% of all patients with GERD-like symptoms by real-time MRI. While 74.6% of these patients presented with hiatal hernia in resting supine position, sliding hiatal hernia was visualized only during Valsalva maneuver in 25.4% of cases. This underlines the importance and clinical relevance of dynamic imaging as accomplished by real-time MRI: our findings indicate that dynamic visualization of the gastroesophageal junction is necessary for identification of sliding hernia. Moreover, real-time MRI yields a superior temporal resolution of 25 fps compared to fluoroscopy, which allows for evaluation of subtle dynamic

Table 1 Contingency table for diagnostic accuracy of real-time MRI (index test) for hiatal hernia detection compared to combined MRI and endoscopy (reference test)

	MRI or endoscopy: hernia	MRI or endoscopy: no hernia	Total
MRI: hernia	63	0	63
MRI: no hernia	22	22	44
Total	85	22	107

Table 2 Contingency table for diagnostic accuracy of endoscopy (index test) for hiatal hernia detection compared to combined MRI and endoscopy (reference test)

	MRI or endoscopy: hernia	MRI or endoscopy: no hernia	Total
Endoscopy: hernia	68	0	68
Endoscopy: no hernia	17	22	39
Total	85	22	107

Table 3 Median sphincter-diaphragm distances for different patient scenarios with IQR. Negative values indicate the presence and size of gastric hernia. + indicating detectable hernia, − indicating occult hernia in the respective imaging modality

Scenario	Median (IQR) sphincter-diaphragm distance on real-time MRI (mm)
Endoscopy +/MRI −	8.0 (6.0 to 10.0)
Endoscopy +/MRI +	− 27.5 (− 15.0 to − 58.8)
Endoscopy −/MRI +	− 21.0 (− 12.0 to − 33.0)
Endoscopy −/MRI −	6.5 (5.0 to 8.25)
MRI hernia at rest	− 33.0 (− 20.5 to − 57.5)
MRI hernia detected only during Valsalva	− 13.5 (− 10 to − 18)

changes of the gastroesophageal junction. The necessity of minimizing radiation exposure of the patient is the limiting factor in using high framerates during fluoroscopy of the upper abdomen.

In our cohort, both real-time MRI and endoscopy demonstrated a comparable and high diagnostic accuracy with sensitivity of 74–80% and specificity of 100%. Compared to endoscopy as a routinely applied imaging technique of the gastroesophageal junction, real-time MRI was able to detect hiatal hernias in 17 additional cases that were endoscopically occult. Only a minority of hiatal hernias were occult on real-time MRI. The majority of hiatal hernia in endoscopy was confirmed by real-time MRI in 65.5% of cases.

The median sphincter-diaphragm distance in patients with hernia in both real-time MRI and endoscopy was − 27.5 mm (− 15.0 to − 58.8 mm). Therefore, real-time MRI was able to identify the majority of all hernia detected by endoscopy, while adding diagnostic information via identification of endoscopy-occult hernias in a relevant number of patients. Real-time MRI can therefore be employed in patients with

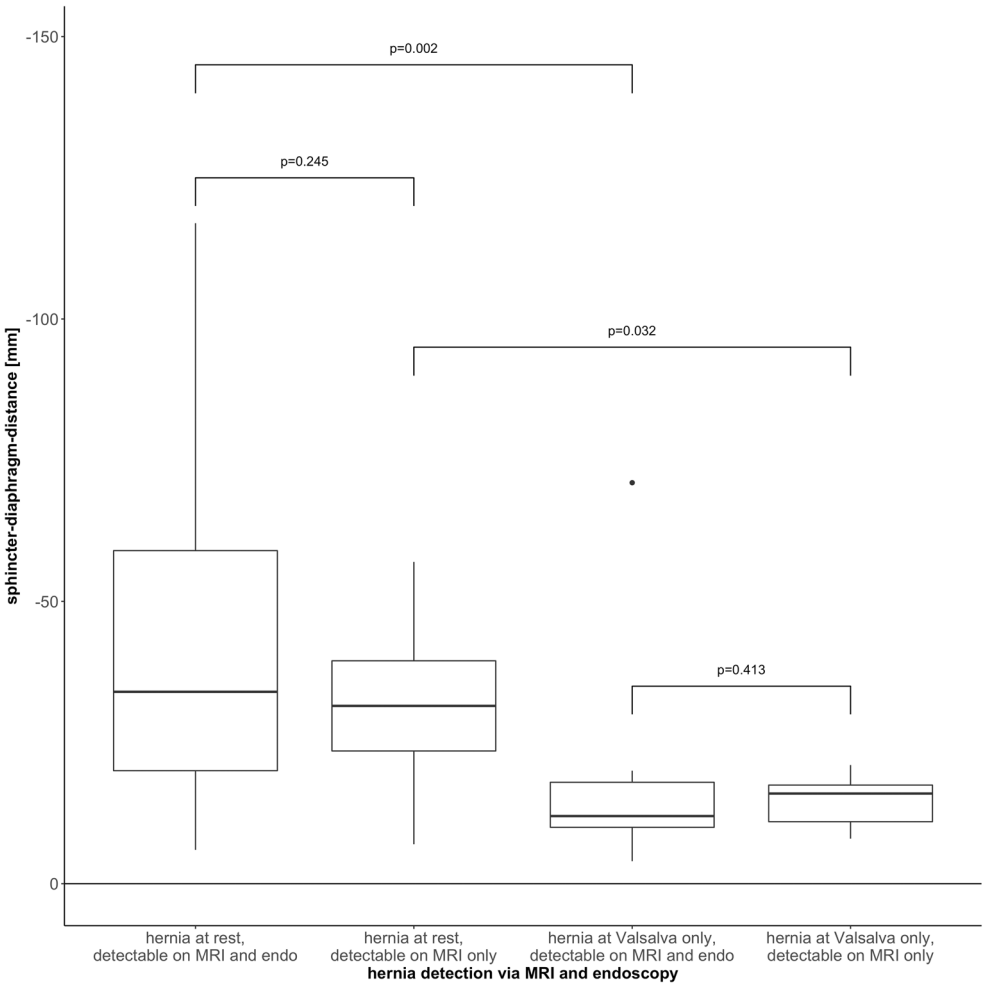

Fig. 4 Box plot of median sphincter-diaphragm distances of hernia detected at rest and during Valsalva maneuver on both MRI and endoscopy or only on MRI. Dot indicating outlier measurement (outside 1.5*IQR whiskers)

inconclusive evidence for the presence of GERD. Endoscopy-occult hernia detected on real-time MRI may be used to shift the final diagnosis towards the presence of GERD in these patients.

Besides its diagnostic accuracy, our real-time MRI protocol has several unique advantages: Compared to endoscopy, real-time MRI provides non-invasive visualization of the gastroesophageal junction without the need for sedation. With a median examination time of 15 min, it is comparably fast and can be implemented on routinely used MRI scanners. The utilization of pineapple juice as oral contrast agent supersedes the off-label oral application of gadolinium contrast agents. In our cohort, there was no adverse reaction to pineapple juice or aspiration. Finally, compared to fluoroscopy or computed tomography, real-time MRI does not expose the patient to ionizing radiation.

Considering our findings, we currently see clinical potential of real-time MR imaging of the gastroesophageal junction in patients with GERD-like symptoms and equivocal findings on endoscopy or pH-metry, for anatomical visualization in patients planned for surgical intervention, or those with suspected fundoplication failure [22]. Since hiatal hernia has a high prevalence even in patients without reflux symptoms, we would not advocate real-time MRI as a first-line imaging modality in asymptomatic patients. Further, the current real-time MRI protocol has not been tested for the detection of mucosal injury such as esophagitis or Barrett's metaplasia and therefore cannot substitute traditional examinations in GERD patients.

The comparison of real-time MRI diagnostic accuracy to other imaging modalities has limitations since currently there is no gold standard for hiatal hernia detection. As shown in our study, real-time MRI is able to detect a relevant proportion of additional hernias via Valsalva maneuver compared to endoscopy. Other imaging techniques only play a minor role in primary detection of hiatal hernia. While hiatal hernia is a common finding in computed tomography [25, 26], it is not a standard imaging modality for primary hernia detection [2] but may play a role in emergency situations or for surgical procedure planning [3, 27]. In fluoroscopy, diagnostic accuracy of barium swallow in hiatal hernia is impaired due to limited visualization of the surrounding anatomic structures [9]. While some studies suggested that only a migration of the muscular of at least 1–2 cm above the diaphragm should be rated as hiatal hernia [10], fluoroscopic studies may be inconclusive in more subtle anatomic changes of the gastroesophageal junction. MRI diagnostic of the gastroesophageal junction so far mostly focused on visualization and assessment of gastroesophageal reflux [20, 28, 29]. To the best of our knowledge, this is the first comparative study of the assessment of hiatal hernia by MRI at a high temporal resolution of 40 ms without oral or intravenous administration of gadolinium contrast agents.

Our study is not devoid of limitations: The study was conducted on a Caucasian population with GERD-like symptoms without age restrictions, which may limit the generalizability of our results. Further, since a true gold standard for diagnosis of hiatal hernias is missing, our diagnostic accuracy assessments might be biased. Given the relevant number of occult hernias, the utility of real-time MRI for primary hernia detection is limited. Still, it must be highlighted that real-time MRI is able to detect endoscopically occult hernias in several patients. Clinical applications for real-time MRI might thus be assessment in patients with equivocal endoscopic results, preoperative assessment, and detection of surgical complications after fundoplication.

The real-time MRI technique reported in this study might not be feasible for every institution due to specific technical requirements, such as multi-unit graphical processing. Since we consider the Valsalva maneuver as the most essential component of our protocol, cine MRI sequence might replace our specific real-time MRI protocol in such instances, although their diagnostic performance needs to be evaluated.

Conclusions

Real-time MRI is an innovative non-invasive imaging method to assess the gastroesophageal junction and detect hiatal hernia. In a clinically relevant proportion of cases, real-time MRI visualizes hiatal hernias that were occult on endoscopy, although both modalities yield comparably high diagnostic accuracy. Further considering its safety and short examination time, real-time MRI yields high clinical potential as an adjunct to endoscopy in the diagnostic management of GERD patients, preoperative planning, and imaging of fundoplication failures.

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Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Ali Seif Amir Hosseini.

Conflict of interest Jens Frahm and Martin Uecker are co-inventors of a patent covering the real-time MRI technique used in this study.

Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was obtained from all subjects (patients) in this study.

Ethical approval Institutional Review Board approval was obtained.

Methodology
- descriptive diagnostic study
- performed at one institution

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