



Real-time MRI for the dynamic assessment of fundoplication failure in patients with gastroesophageal reflux disease

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Abstract

Purpose To assess the diagnostic potential of dynamic real-time MRI for fundoplication failure in patients with persistent or recurrent GERD-like (gastroesophageal reflux disease) complaints.

Material and methods Twenty-two consecutive patients (male $n = 11$; female $n = 11$; median age 59 years) with recurrent or persistent GERD-like symptom after fundoplication were enrolled between 2015 and 2017. Median duration of GERD-like symptoms was 21 months. Real-time MRI (3 Tesla) was performed at 40 ms temporal resolution using undersampled radial fast low-angle shot acquisitions with nonlinear inverse image reconstruction. MRI movies dynamically visualized bolus transit of pineapple juice through the gastroesophageal junction, position of the fundoplication wrap and recurring hernia or reflux during Valsalva maneuver. MRI results were compared to endoscopic findings.

Results Real-time MRI was successfully completed in all patients without adverse events (average examination time 15 min). Morphological correlates for GERD-like symptoms were evident in 20 patients (90.1%) with gastric reflux in 19 cases. Nine patients (40.1%) had wrap disruption and recurrent gastric hernia. Wrap migration or telescoping hernia was detected in nine patients (40.1%). One patient presented with continued reflux despite intact fundoplication wrap. Esophageal dysmotility with delayed bolus passage was observed in one case. On endoscopy, gastric hernia or wrap disruption was diagnosed in seven cases, and esophagitis or Barret's metaplasia in nine cases.

Conclusion Real-time MRI is a fast and safe modality for dynamic imaging after fundoplication, without radiation exposure or administration of gadolinium-based contrast media. In a relevant number of cases, real-time MRI reveals correlates for GERD-like symptoms.

Key Points

- Real-time MRI reliably visualizes the gastroesophageal junction after fundoplication surgery.
- Patients with recurring GERD-like symptoms have a high rate of morphological failure patterns that can be identified by real-time MRI.
- Dynamic assessment of gastroesophageal junction by real-time MRI is a perspective diagnostic tool for detection of fundoplication failure.

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Keywords Magnetic resonance imaging · Gastroesophageal reflux disease (GERD) · Fundoplication

Abbreviations

GERD Gastroesophageal reflux disease
PPI Proton pump inhibitor

Introduction

Gastroesophageal reflux disease (GERD) is a common condition with a prevalence of 10–20% in Western populations [1]. After its introduction in 1956, fundoplication has become the gold standard surgical treatment of GERD [2, 3]. Because of the advances of minimally invasive surgery, laparoscopic fundoplication has almost completely replaced open antireflux procedures [4].

While studies have reported high patient satisfaction after fundoplication procedures [5, 6], fundoplication failure with recurrent hernia has been reported in up to 30% of cases [7]. These patients commonly present with GERD-like symptoms, including heartburn, regurgitation, and dysphagia [8]. Overall, redo fundoplication is necessary in 2.8–3.5% of all fundoplication cases [8, 9].

Traditionally, the fundoplication wrap in patients with persistent or recurring GERD-like symptoms is assessed by endoscopy. However, concerns have been raised about observer variability and the absence of standardized endoscopic reporting [10].

Moreover, the diagnostic accuracy of endoscopy complications such as esophageal dysmotility or obstruction of the distal esophagus due to a tight fundoplication wrap is limited, and thus further examinations are required for evaluation of the bolus passage [11, 12].

Radiological imaging features of fundoplication wraps have been described for barium examination and computed tomography (CT) [13]. While barium examinations allow morphological and functional evaluation of the gastroesophageal junction, the visualization of the fundoplication wrap and surrounding tissues is limited with this modality. Moreover, computed tomography does not permit dynamic visualization of the bolus passage. However, dynamic assessment of the fundoplication wrap with high soft tissue resolution of the wrap and the surrounding structures is integral for the detection of fundoplication failure.

Real-time MRI is a new imaging technique that offers both anatomic and functional visualization of the gastroesophageal junction with high image quality at a temporal resolution of 10 to 40 ms [14, 15]. Initial studies showed promising results for the evaluation of the gastroesophageal junction in GERD patients [16, 17]. Due to the altered anatomy after fundoplication procedure, the diagnostic potential of real-time MRI for the evaluation of fundoplication failure has yet to be analyzed. Therefore, we conducted this study to evaluate the diagnostic

potential of real-time MRI in the assessment of the fundoplication wrap in patients with persisting or recurring GERD-like symptoms after antireflux surgery.

Materials and methods

Study population

Twenty-two consecutive patients 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 persisting or recurring GERD-like symptoms after fundoplication surgery underwent real-time MRI of the lower esophageal sphincter between 2015 and 2017. Inclusion criteria were recurring or persisting GERD-like symptoms such as heartburn, regurgitation, or chest pain in patients after fundoplication surgery. No patients were excluded for contraindications to MRI or inability to swallow. Simultaneous PPI therapy was no exclusion criteria. Exclusion criteria were general MRI contraindications such as internal electrical devices (e.g., cardiac pacemaker or defibrillator, cochlear implant), ocular foreign bodies, pregnancy, and known allergy to pineapple. The study was approved by the local ethics board and consent was obtained from all patients prior to study inclusion. All 22 patients (11 men and 11 women) presented with recurring GERD-like symptoms after fundoplication. No patient presented with persisting symptoms since fundoplication procedure. Typical symptoms were heartburn, dysphagia, and regurgitation. No patient complained about gas bloating, belching, or inability to relieve bloating. Mean age was 56 ± 16 years with a range of 15–76 years. Mean interval between fundoplication procedure and MRI scans was 9 ± 6 years (range 2–25 years). Four patients already had underwent redo fundoplication. Mean duration of recurring or persisting GERD-like symptoms was 25 ± 18 months (range of 6 to 66 months). Eleven patients were under PPI medication and four patients reported no relief of symptoms by medication. Twelve patients underwent redo fundoplication based on imaging findings. In all cases, MRI-based diagnoses were confirmed intraoperatively. Another ten patients were treated conservatively with PPI, including four patients that initially presented with redo fundoplication. The patient characteristics are summarized in Table 1.

Real-time MRI

MRI was carried out in supine position at 3.0 Tesla (Skyra, Siemens Healthcare) combining an 18-element thorax coil

Table 1 Characteristics of patients

Parameter	Total (<i>n</i> = 22)
Age (years)	56 (± 16)
Gender	
Female	11 (50.0%)
Male	11 (50.0%)
Previous redo fundoplication	4 (18.2%)
Interval	
Concurrent PPI treatment	11 (50.0%)
Endoscopy	18 (81.8%)
Recurring hernia/wrap disruption	7 (31.8%)
Esophagitis or Barrett's metaplasia	9 (40.9%)
Subsequent redo fundoplication	12 (54.5%)

with suitable elements of the spine coil array. Real-time MRI was accomplished by highly undersampled radial FLASH acquisitions with nonlinear inverse image reconstruction [15]. The temporal fidelity of the approach has been experimentally validated using a dedicated motion phantom [14]. T1-weighted images of the lower esophageal sphincter and the fundoplication wrap were acquired with the following parameters: RF-spoiled radial FLASH, repetition time TR = 2.12 ms, echo time TE = 1.31 ms, flip angle 8°, in-plane resolution 1.5 mm, slice thickness 8 mm, FOV 256 × 256 mm², 2 × 7 spokes, 128 × 128 Matrix. The measuring time was 40 ms per image corresponding to a rate of 25 frames per second without any data sharing or interpolation.

Online reconstruction of real-time images was achieved with use of a reconstruction computer (sysGen/TYAN Octuple-GPU, Sysgen; 8 GeForce GTX TITAN, Nvidia) fully integrated into the commercial MRI system as a “user-invisible” by-pass system.

During dynamic imaging, commercially available pineapple juice served as an oral contrast agent because of its T1 shortening effect due to a low concentration of paramagnetic manganese ions. After the onset of each real-time MRI recording, an operator injected a bolus of 10 ml juice into the subject's mouth through a conventional flexible infusion tube. 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).

Additional HASTE and TRUFI sequences were obtained for anatomic assessment.

Image evaluation

Anonymized MRI studies were assessed using the manufacturer's software (Syngo B17, Siemens Healthcare) in cine-mode as well as frame by frame. All images were interpreted

in consensus by two abdominal radiologists (L.B., A.S.A.H.) with more than 4 and 8 years abdominal imaging experience and 2 years of experience in dedicated real-time MRI of the gastroesophageal junction. All scans were analyzed regarding the integrity and position of the fundoplication wrap and the presence of herniation during bolus passage of pineapple juice and Valsalva maneuver. Functional parameters were the presence of reflux during Valsalva maneuver and bolus passage through the wrap and lower esophageal sphincter. Results were categorized according to five different failure patterns as described by *Kulinna-Cosentini et al* [18] (Table 2). Morphologic imaging results were compared to intraoperative findings in patients that underwent redo fundoplication and with endoscopic findings.

Statistical analyses

Discrete variables are presented as absolute numbers and percent, continuous variables as mean ± standard deviation and range. Diagnostic accuracy of real-time MRI and endoscopy were assessed as test sensitivity and specificity using a standard 2 × 2 table approach for patients evaluated with both modalities. Fundoplication failure was defined as either direct hernia or wrap disruption visualization, or indirect evidence, including reflux, esophagitis and Barrett's metaplasia. Sensitivity and specificity were compared using the McNemar test.

All statistical analyses were performed using R version 3.4.3 (R Core Development Team) and RStudio version 1.1.414 (RStudio Inc.). An alpha level of 0.05 was considered statistically significant. All *p*-values presented are two sided.

Table 2 MRI findings after fundoplication failure. MRI failure patterns were categorized as previously described by *Kulinna-Cosentini et al* (2014)

Failure pattern	Imaging findings	Total (<i>n</i> = 22)
Normal position	Intact wrap in typical subdiaphragmatic position without herniation	2 (9.1%)
Wrap disruption	Complete or partial disintegration of the fundoplication wrap	9 (40.9%)
Telescoping/*“slipped Nissen”	Herniation of parts of the stomach through the fundoplication wrap	3 (13.6%)
Slipped wrap	Migration of the wrap above the diaphragm or toward the gastric corpus	6 (27.3%)
Too tight or too long wrap	Delayed bolus transit through the wrap region due to segmental stenosis	0 (0.0%)
Motility disorder	Delayed esophageal bolus transit and reduced propulsive peristalsis	1 (4.5%)
Reflux	Fluid present in the esophagus during Valsalva maneuver	19 (86.4%)

Results

Real-time MRI

All 22 real-time MRI studies were accomplished without complications. Mean examination time was 15 min. No complaints were issued during or after the examinations. Real-time MRI was able to visualize critical anatomic landmarks, including the lower esophageal sphincter and lower esophagus, in all patients. A typical swallow as seen by real-time MRI is demonstrated in Fig. 1 by a series of selected images of the gastroesophageal junction during bolus passage. Figure 2 visualizes typical failure patterns after fundoplication procedure. Figure 3 shows a case with a telescoping hernia occurring after Valsalva maneuver. Figure 4 demonstrates esophageal dysmotility with non-propulsive contractions and a considerably delayed incomplete esophageal clearance.

Corresponding real-time MRI movies are shown in Supplementary Video 1, Video 2 and Video 3.

Real-time MRI of the lower esophageal sphincter after fundoplication revealed a morphological correlate for GERD-like symptoms in 20 patients (90.1%) with gastric reflux on real-time MRI in 19 of these cases. A total of nine patients (40.1%) were diagnosed with wrap disruption and recurrent gastric hernia. Wrap migration or telescoping hernia was detected in another nine patients (40.1%). Reflux was

detected in all but three cases. Only one patient presented with continued reflux despite intact wrap.

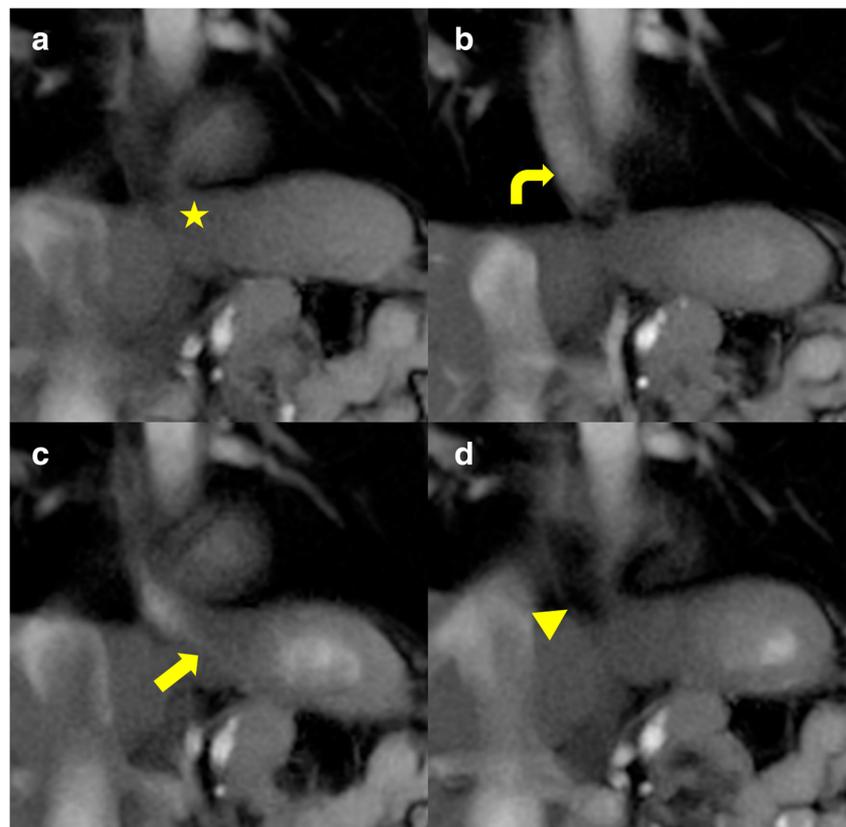
One patient presented with esophageal dysmotility exhibiting reduced propulsive contractions in the middle and lower esophagus and delayed bolus passage during real-time MRI. Anatomic and real-time sequences showed no indication for wrap disruption or migration. Additional high-resolution manometry of this patient confirmed ineffective esophageal motility with reduced contractility.

Only two patients showed no correlate for GERD-like symptoms in real-time MRI with fundoplication wrap in normal subdiaphragmatic position. No reflux was evident after Valsalva maneuver. The DeMeester Score of 1.14 was within normal limits by impedance measurement. However, gastroscopy revealed a small gastric hernia suggesting telescoping that was not detected in MRI.

Endoscopic results

Endoscopic evaluations were available for 18 patients (81.8%), another four patients refused endoscopy. A total of seven patients (38.9%, 11/18) presented with wrap disruption or recurrent hernia on endoscopy. Esophagitis or Barrett's metaplasia was present in nine patients (50%). No patients had evidence for esophageal cancer. Endoscopy was discordant to real-time in only one case: in this patient, telescoping

Fig. 1 Real-time MRI of the gastroesophageal junction after fundoplication during bolus passage. Representative individual images were selected showing bolus passage in coronal oblique planes. **a** and **b** As the bolus enters the distal esophagus (curved arrow), it travels toward the “wrapped” gastroesophageal junction (star). **c** The junction receives the bolus. Since the subject is in a supine position, the liquid bolus may not move into the stomach by gravity alone, as it would do if the subject is standing. **d** The bolus is mainly cleared by peristaltic contraction (propulsive contraction) of the esophagus (arrow head)



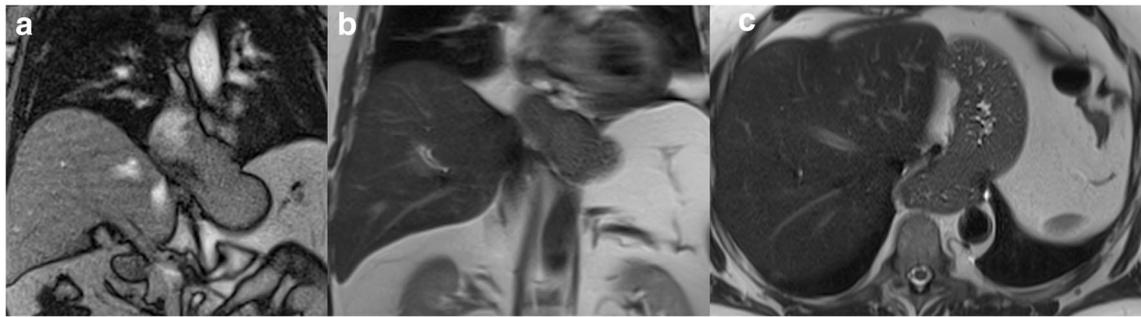


Fig. 2 Hernia after wrap disruption. Comparison of real-time MRI (a) and HASTE in coronary and axial view (b and c). Images show complete disruption of the fundoplication wrap with herniation of a significant portion of the gastric fundus

was seen on endoscopy while real-time MRI detected reflux only.

Diagnostic accuracy

Using endoscopy as the reference test, real-time MRI yielded a sensitivity of 92% (95% CI 62–100%) and specificity of 17% (95% CI 0–64%). The corresponding 2 × 2 table is depicted in Table 3.

The low specificity of real-time MRI might indicate that endoscopy misses a relevant proportion of hernias. A second scenario for diagnostic accuracy assessment was therefore implemented with the reference test of hernia manifestation on either endoscopy or real-time MRI.

Using this combined reference test, real-time MRI showed a sensitivity of 94% (95% CI 71–100%) and specificity of 100% (3–100%). Endoscopy showed a sensitivity of 71% (95% CI 44–90%) and specificity of 100% (95% CI 3–100%). Tables 4 and 5 summarize these findings. Sensitivity and specificity difference for real-time MRI and endoscopy did not reach statistical significance ($p = 0.103$, $p > 0.99$, respectively).

Discussion

Fundoplication wrap failure is one of the major complications after fundoplication surgery, and so far, no diagnostic tool is able to accurately assess potential failure, its patten, and

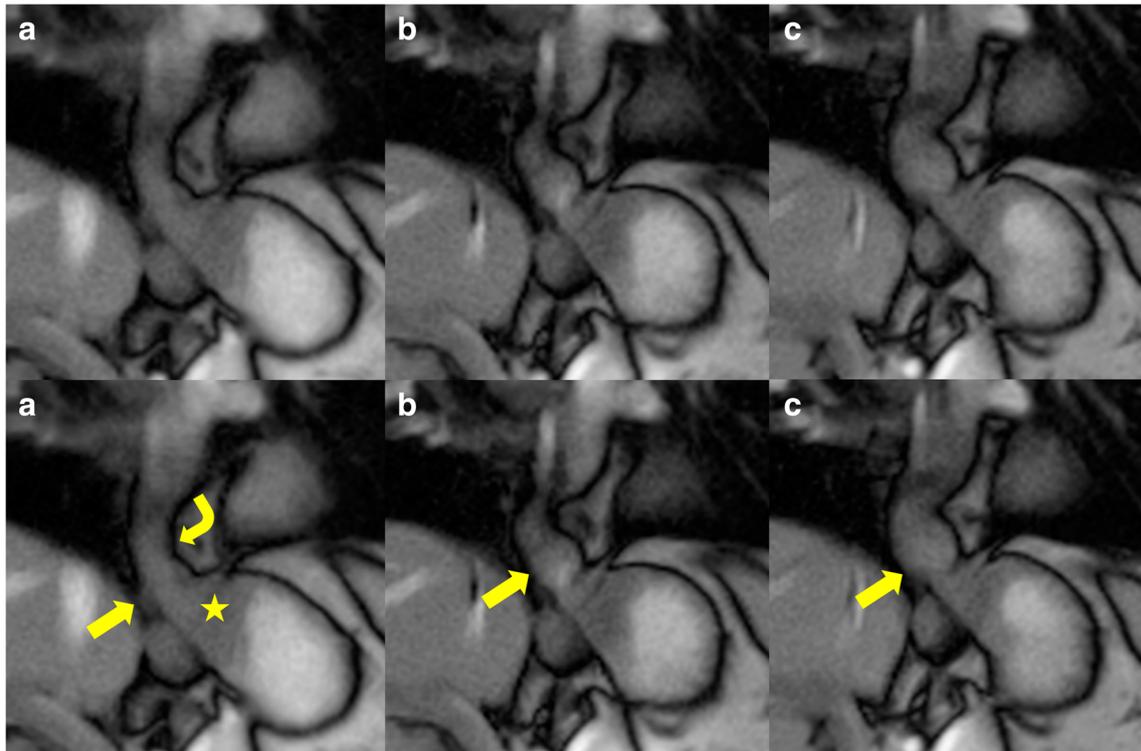


Fig. 3 Telescoping hernia. **a** Normal position before Valsalva maneuver with normal positioning of distal esophagus (curved arrow), gastroesophageal junction (arrow) and the fundoplication wrap (star).

b During Valsalva maneuver of parts of the stomach herniate through the fundoplication wrap. **c** Maximum extend of telescoping during Valsalva maneuver

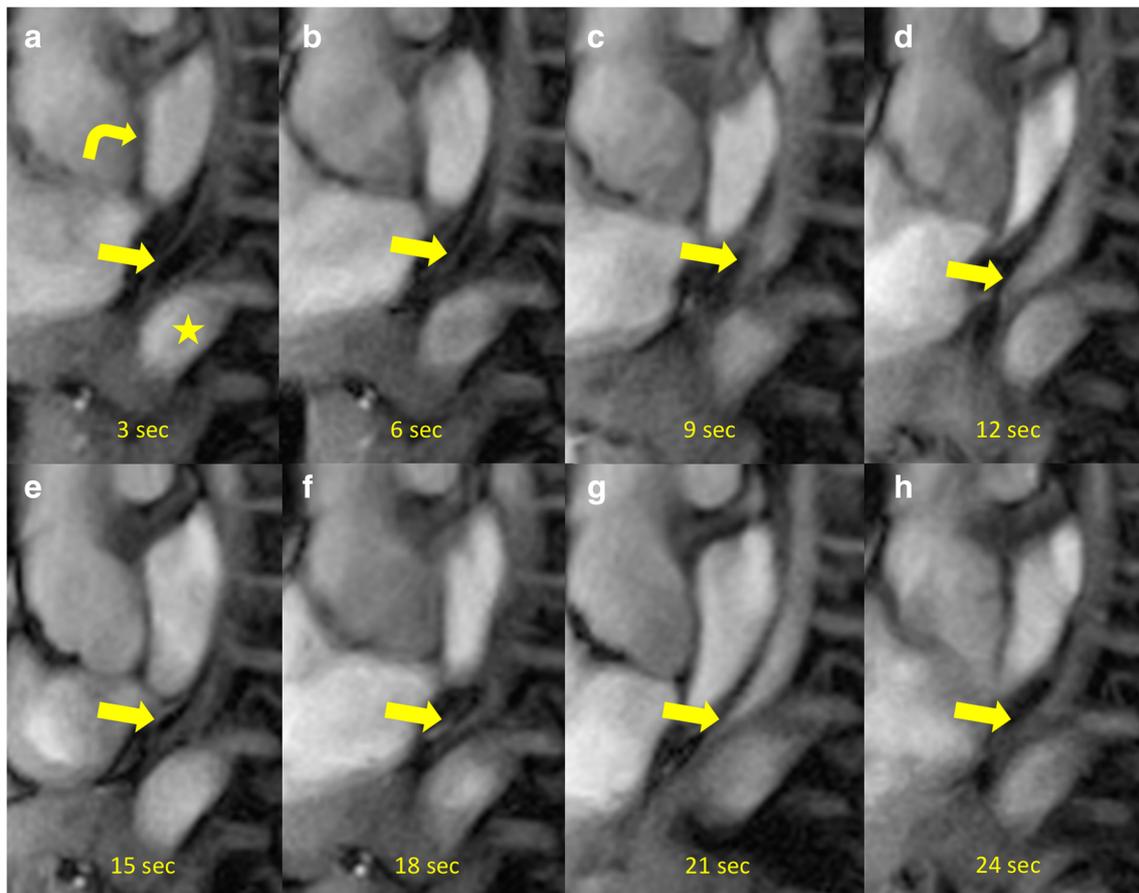


Fig. 4 Real-time MRI of the gastroesophageal junction after fundoplication during bolus passage. Scan was performed at 25 fps. Representative individual images were selected showing bolus passage in sagittal planes. Delayed esophageal bolus transit and reduced propulsive peristalsis. Image **a** shows normal anatomy of the distal

esophagus (arrow) at 3 s after swallowing the bolus (abdominal aorta (star) and the left cardiac atrium (curved arrow)). **b–h** Selected consecutive images reveal esophageal dysmotility with non-propulsive contractions and a considerably delayed incomplete esophageal clearance after 24 s. Also see supplemental Video 3

surrounding anatomic structures, which are crucial for further treatment planning. We aimed to evaluate the diagnostic potential of real-time MRI as an imaging technique for morphologic and functional features of the gastroesophageal junction after fundoplication surgery.

Our study demonstrated that real-time MRI was able to identify morphologic correlates for recurrent or persistent GERD-like symptoms in 90.1% of patients after fundoplication surgery. Moreover, real-time MRI visualized surrounding anatomical structures and thus allowed for

differentiation of fundoplication failure patterns [18]. Real-time was able to visualize fundoplication failure in four patients that would have been missed using endoscopy alone. Based on these findings, diagnostic accuracy was assessed using a combined reference standard of endoscopy and real-time MRI. In this setting, the sensitivity of real-time MRI for detection of hernia after fundoplication was numerically higher than endoscopy (94% vs. 71%), while specificity was equivalent (100%). These results need further validation in a prospective manner, especially given the small number of

Table 3 Sensitivity and specificity of real-time MRI for fundoplication failure using endoscopy for reference

	Reference test: endoscopy hernia +	Reference test: endoscopy hernia –	
Index test: MRI hernia +	11	5	16
Index test: MRI hernia –	1	1	2
	12	11	18

Table 4 Sensitivity and specificity of real-time MRI for fundoplication failure using both MRI and endoscopy for reference

	Reference test: MRI or endoscopy hernia +	Reference test: endoscopy hernia –	
Index test: MRI hernia +	16	0	16
Index test: MRI hernia –	1	1	2
	17	1	18

Table 5 Sensitivity and specificity of endoscopy for fundoplication failure using both MRI and endoscopy for reference

	Reference test: MRI or endoscopy hernia +	Reference test: endoscopy hernia –	
Index test: Endoscopy hernia +	12	0	12
Index test: Endoscopy hernia –	5	1	6
	17	1	18

patients without fundoplication failure. At this point, one might only speculate that real-time MRI could be used as a screening tool for fundoplication failure given its higher sensitivity than endoscopy. The most common MRI-based diagnoses were wrap disruption, slipped wrap, and telescoping. Further, endoscopy supported MRI-based diagnoses in the majority of cases, although real-time MRI missed one case of telescoping that was only detectable via endoscopy. In this patient, real-time MRI revealed esophageal reflux only. One might speculate that MRI-detected reflux during Valsalva maneuver indicates a loose or disrupted fundoplication wrap even without morphological signs of wrap disruption, although larger case series are necessary to confirm this hypothesis. In addition, we found that real-time MRI allows for assessment of esophageal dysmotility after fundoplication surgery: although only one patient presented with esophageal dysmotility following fundoplication surgery, real-time MRI clearly visualized reduced propulsive contractions and delayed bolus passage.

Anatomical and functional information obtained by real-time MRI are crucial for treatment in patients with persistent or recurrent GERD-like disease after fundoplication surgery: For example, large recurrent hernias might necessitate redo surgery, while tight fundoplication wraps might be endoscopically dilated. Further, distinction of secondary esophageal motility disorders and wrap failure is of critical importance for individualized treatment strategies, including conservative management, endoscopic dilatation, or redo fundoplication with a looser wrap as well as Heller myotomy [19]. Correlating our findings to clinical follow-up, in all patients that underwent redo fundoplication, real-time MRI diagnoses were confirmed intraoperatively.

At the moment, diagnostic tools in used for assessment of patients with GERD-like symptoms after fundoplication surgery include manometry, pH-metry, barium swallows, and endoscopy, although they only allow for limited visualization of surrounding anatomic structures [11, 12, 20]. So far, MRI of the gastroesophageal junction has only been implemented in small case series by Kulinna-Cosentini and colleagues [18]. While they found that wrap disruption and stenosis can be correctly identified using dynamic gradient echo

sequences, the detection rate for esophageal reflux was lower at 56% compared to 86% in our study using real-time MRI. One explanation might be the significantly higher temporal resolution of real-time MRI with 25 fps. Still, discrepant patient populations might contribute to different reflux detection rates as well. Our implemented real-time MRI technique has several additional advantages, including a short examination time of approximately 15 min compared to 30 min in protocols with dynamic gradient echo sequences [18]. Further, the use of pineapple juice as contrast media has to be highlighted, as it allows for a protocol without off-label use of gadolinium-based contrast media. Based on our initial findings on assessment of esophageal dysmotility, real-time MRI might not only play a role after fundoplication surgery but shows promising potential for imaging in neuromuscular disorders of the esophagus.

Our study is not devoid of limitations: the major limitation is its small sample size of 22 patients and descriptive nature of this study. Moreover, no patient presented with a too tight fundoplication wrap, thus limiting the generalizability of the results for all failure patterns. The absence of tight fundoplication wrap can be explained by the fact that all included patients reported recurrence of GERD-like symptoms after initial symptom improvement and the relatively long time interval between the fundoplication procedure and real-time MRI. A tight fundoplication wrap usually manifests with persisting symptoms in the weeks following the procedure [13]. Therefore, patients with persisting or new symptoms following fundoplication surgery should be included in further studies. Furthermore, endoscopic examinations were not available for all patients as some withdrew consent after MRI was successfully completed.

Still, considering the high rate of morphological findings for persisting or recurring GERD-like symptoms, real-time MRI is a promising new imaging technique for evaluation of complications after fundoplication. Real-time MRI not only allows assessing the integrity of the wrap, but also provides valuable function the anatomy of the gastroesophageal junction. With an average examination time of 15 min, real-time MRI can easily be performed in a routine setting and even integrated in thoracic or abdominal MRI protocols.

Conclusion

In conclusion, real-time MRI is an innovative and safe imaging method to evaluate anatomic and functional features of the gastroesophageal junction after fundoplication surgery. Real-time MRI has a high clinical potential for evaluation of different failure patterns of the fundoplication wrap.

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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 Statistical analyses were performed by a co-author with MPH degree.

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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