

Contents lists available at ScienceDirect

European Journal of Radiology



journal homepage: www.elsevier.com/locate/ejrad

Research article

Real-time MRI for dynamic assessment of gastroesophageal reflux disease: Comparison to pH-metry and impedance



Ali Seif Amir Hosseini^{a,*}, Johannes Uhlig^a, Ulrike Streit^a, Nina Gliem^b, Edris Wedi^b, Volker Ellenrieder^b, Michael Ghadimi^c, Saheeb Ahmed^a, Martin Uecker^{a,e}, Jens Frahm^{d,e}, Joachim Lotz^{a,e}, Lorenz Biggemann^a

^a Department of Diagnostic and Interventional Radiology, University Medical Center, Göttingen, 37075, Germany

^b Department of Gastroenterology and Gastrointestinal Oncology, University Medical Center, Göttingen, Germany

^c Department of General, Visceral, and Paediatric Surgery, University Medical Center, Göttingen, Germany

^d Biomedical NMR, Max-Planck-Institute for Biophysical Chemistry, Göttingen, Germany

^e DZHK (German Centre for Cardiovascular Research), Partner Site, Göttingen, Germany

ARTICLE INFO

Keywords: Gastroesophageal reflux disease GERD Magnetic resonance imaging Esophageal pH recording Impedance

ABSTRACT

Purpose: To evaluate the diagnostic potential of real-time MRI for dynamic assessment of gastroesophageal reflux in patients with GERD (gastroesophageal reflux disease)-like symptoms compared to pH-metry and impedance.

Methods: Patients who underwent real-time MRI and pH-metry between 2015–2018 were included in this retrospective study. Real-time MRI at 3 T was achieved by undersampled radial FLASH acquisitions with iterative image reconstruction by NLINV. Real-time MRI visualized transit of pineapple juice through the gastroesophageal junction and during Valsalva maneuver. MRI results were compared to 24 h pH-metry to assess acidic reflux (following Lyon Consensus guidelines) and to impedance to assess non-acidic reflux. A standard 2×2 table was chosen to calculate diagnostic performance.

Results: 91/93 eligible patients fulfilled inclusion criteria (male n = 49; female n = 42; median age 55 y). All MRI studies were successfully completed without adverse events at a mean examination time of 15 min. On real-time MRI, reflux was evident in 60 patients (66 %). pH-metry revealed reflux in 41 patients (45 %), and impedance in 54 patients (59 %). Compared to pH-metry and impedance, real-time MRI sensitivity was 0.78 (95 % CI: 0.66-0.87), specificity 0.67 (95 % CI: 0.45-0.84) and PPV 0.87 (95 % CI: 0.75-0.94).

Conclusion: Real-time MRI is an imaging method for assessment of gastroesophageal reflux in patients with GERD-like symptoms. Considering its high positive predictive value, real-time MRI can accurately identify patients in which further invasive testing with pH-metry and impedance might be considered.

1. Introduction

The prevalence of gastroesophageal reflux disease (GERD) ranges between 10–28% in Western countries and increased over the last decades [1,2]. Characteristic symptoms include heartburn and regurgitation [3]. Associated high symptom burden not only impairs quality of life, but also decreases work productivity and yields high diseaserelated costs [4]. An accurate diagnosis of GERD is crucial for effective treatment, as well as for prevention of esophageal complications, such as Barret's esophagus and adenocarcinoma [5]. While GERD can be diagnosed and treated empirically, further testing is required in cases with diagnostic uncertainty, persisting symptoms or suspected complications [6,7]. The most common diagnostic modalities for GERD are upper endoscopy (esophago-gastro-duodenoscopy; EGD) and reflux monitoring by 24 h pH-metry or 24 h impedance measurement [8]. Endoscopy is usually performed to rule out complications and to assess alternative diagnosis. Still, less than 50 % of all patients with gastroesophageal reflux symptoms show signs of mucosal injury on endoscopy [9,10]. PH-metry and impedance carry the advantage of direct assessment of reflux exposure to the distal

* Corresponding author.

https://doi.org/10.1016/j.ejrad.2020.108856

0720-048X/ © 2020 Elsevier B.V. All rights reserved.

Abbreviations: AET, acid exposure time; EGD, esophagogastroduodenoscopy; GERD, gastroesophageal reflux disease; NLINV, regularized nonlinear inversion; PPI, proton pump inhibitor; LES, lower esophageal sphincter

E-mail address: ali.seif@med.uni-goettingen.de (A. Seif Amir Hosseini).

Received 3 November 2019; Received in revised form 14 January 2020; Accepted 24 January 2020

esophagus [11]. However, pH-metry requires the placement of a transnasal catheter over 24 h, which results in throat discomfort, nose pain or runny nose in more than 50 % and abortion or failure in approximately 6 % of patients [12–14].

In clinical practice, GERD diagnosis is usually based on presence of typical symptoms and response to PPI treatment. However, uncertain diagnosis warrants further diagnostic workup [8]. While fluoroscopic barium swallows have been routinely used by radiologists for the assessment of gastroesophageal reflux, they are no longer recommended for diagnosis of GERD according to updated diagnostic guidelines but has shifted towards esophageal testing by endoscopy and 24 h pH-monitoring [6,8,15].

Modern ultrafast MRI sequences visualize the esophagus and gastroesophageal junction and allows for dynamic assessment of reflux during repetitive Valsalva maneuver with a high tissue contrast of surrounding anatomical structures in real time at a temporal resolution of up to 20 ms. These sequences are optimized for pineapple juice as an oral contrast agent and do not necessitate off-label oral or intravenous application of gadolinium-based MRI contrast agents [16,17]. Previous feasibility studies showed promising results for the evaluation of anatomical and functional parameters as well as detection of fundoplication failure [18,19]. The diagnostic potential of real-time MRI for the detection of gastroesophageal reflux has yet to be evaluated. The aim of this study was to assess the diagnostic potential of real-time MRI for the diagnosis of GERD compared to 24 h pH-metry and impedance.

2. Materials and methods

2.1. Study population

This retrospective cohort study received approval by the local ethics board (NR 14/5/18) and was conducted in accordance with the Declaration of Helsinki in its most recent version. All participants gave written informed consent before each examination. 25 of the 93 patients have been previously reported [18,19]. Inclusion criteria for this study were patients with GERD-like symptoms for at least 6 months, presenting at a surgical outpatient clinic (Department of General, Visceral, and Paediatric Surgery and Department of Gastroenterology and Gastrointestinal Oncology of the University Medical Center Goettingen, Germany). Further, only patients who underwent real-time MRI and pH-metry were included in this study. General exclusion criteria for real-time MRI were patients with pacemakers/ICDs, implanted gastric reflux devices, inability to swallow and known allergy to pineapple. Patients were also excluded if PPI treatment was continued during pHmetry measurement or achalasia was diagnosed on real-time MRI. Previous or ongoing PPI treatment at the timepoint of real-time MRI was no exclusion criterion.

2.2. Combined pH-metry/impedance monitoring

Combined 24 h esophageal pH-metry/impedance monitoring was performed using a multichannel pH-impedance catheter with 6 impedance segments and one pH-measuring electrode (Standard Instruments GmbH, Karlsruhe, Germany). The catheter was positioned transnasally with the pH sensor 5 cm above the lower esophageal sphincter, and connected to a portable recorder for 24 h. The exact position of the lower esophageal sphincter was identified by high resolution esophageal manometry. All data were uploaded and was analyzed with ViMeDat™ Version 5.0.0.3117 (Standard Instruments GmbH, Karlsruhe, Germany) according to the Lyon consensus criteria [8]: a distal esophageal acid exposure time (AET) > 6 % was considered abnormal with conclusive evidence for GERD and an AET between 4 %-6 % was considered inconclusive evidence for the presence of GERD. An increased number of reflux episodes > 40 reflux episodes in 24 h were also considered as supportive evidence. A distal esophageal AET < 4 %and < 40 reflux episodes were considered normal with strong evidence against GERD. The traditional DeMeester score was automatically calculated by the analyzing software ViMeDat[™]. The parameters that are included in the DeMeester-score are: total number of reflux episodes, the total time of esophageal pH < 4 [%], the time of esophageal pH < 4 in upright position [%], the time of esophageal pH < 4 in supine position, the number of reflux episodes ≥ 5 min, and the length of the longest reflux episode [20].

2.3. Real-time MRI

Real-time MRI was performed on a commercial 3 T MRI system (Skyra, Siemens Healthineers, Erlangen, Germany), combining an 18element thorax coil with suitable elements of the spine coil array. Realtime MRI was accomplished by highly undersampled radial gradientecho MRI with nonlinear inverse reconstruction and temporal regularization to the immediately preceding frame [21]. The temporal fidelity of the approach has been experimentally validated using a dedicated motion phantom [22].

For real-time MRI of the esophagus and esophagogastric junction, mildly T1-weighted images were continuously acquired with the following parameters: radial FLASH with randomized RF spoiling, 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 measurement time of 40 ms, corresponding to a temporal resolution of 25 frames per second (fps). A field of view of $256 \times 256 \text{ mm}^2$ in conjunction with a data matrix of 170×170 yielded an in-plane resolution of $1.5 \times 1.5 \text{ mm}^2$, while the slice thickness was chosen to be 8 mm.

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

All patients performed a test swallow before the start of the examination. During dynamic imaging, commercially available pineapple juice served as an oral contrast agent based on its inherent concentration of paramagnetic manganese ions resulting 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 pineapple juice into the subject's mouth through a conventional flexible infusion tube (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 and at a comfortable rate. The bolus was given once for each real-time MRI recording, which lasted for at least 25 s (i.e., 1000 images). The patient was queried on any swallowing difficulties after the first MRI acquisitions in supine position (might choose this alternative: The operator asked the patients about swallowing difficulties after the first MRI acquisitions in supine position. After complete esophageal clearance of the administered bolus, all patients were asked to perform Valsalva maneuver by exhaling against a closed mouth and contracting the abdominal muscles in order to provoke sliding hernia and reflux.

2.4. MR image evaluation

All functional MRI examinations were assessed by two radiologists via consensus reading (AS, LB). Reader AS was an attending radiologist with 10 years of experience in abdominal radiology and 3 years of experience in real-time MRI of the gastroesophageal junction. Reader LB was a resident radiologist with 5 years of experience in abdominal radiology and 3 years of experience in real-time MRI of the gastroesophageal junction. Analyses were based on the manufacturer's software (Syngo B17, Siemens Healthineers, Erlangen, Germany).

MRI examinations were assessed for the presence or absence of reflux under Valsalva maneuver and the presence of hernias. On MRI films, any visible fluid or signal increase in the esophagus during



Fig. 1. MRI reflux intensity on a five-level Likert scale according to esophageal signal increase during Valsalva maneuver. Patients with low signal intensity during Valsalva maneuver were graded 1/5 (A). Patients with marginal signal increase and flow-void were graded as 2/5 (B). Presence of fluid in a short section of the esophagus (arrow) was graded 3/5 (C). Continuous presence of fluid without distension of the esophagus was graded 4/5 (D). Large amounts of fluid with distension of the esophagus were graded as 5/5 (E).

Valsalva maneuver was rated as reflux. Increase of MRI signal intensity in the esophageal lumen during Valsalva maneuver compared to the completely cleared esophagus was graded using a five-level Likert scale (Fig. 1).

The height of reflux was assessed on a scale from 0 to 3 by dividing the esophagus in 3 sections according to anatomic landmarks (Fig. 2):

- 1) lower esophagus: between the lower esophageal sphincter and the upper atrial margin
- 2) middle esophagus: between the upper atrial margin and the aortic arch
- 3) upper esophagus above the aortic arch.

The size of hiatal hernia was assessed by measurement of the distance of the diaphragm to the lower esophageal sphincter boundary. All



Fig. 2. MRI reflux grading rated according to anatomical reflux height on a scale form 0–3. The esophagus was divided in 3 segments according to surrounding anatomical landmarks: the lower esophagus between the lower esophageal sphincter and the upper atrial margin (1); the middle esophagus between the upper atrial margin and the aortic arch (2); and the upper esophagus above the aortic arch (3). No visible reflux was graded as 0.

MRI assessments were separately performed under resting condition and Valsalva maneuver.

2.5. Statistical analysis

Continuous variables are given as median and interquartile ranges (IQR), and categorical variables as absolute values and percentage. Continuous variables were compared using the non-parametric Wilcoxon rank-sum test, and categorical variables using the chi-square test. A standard 2×2 table approach was utilized to calculate diagnostic performance: sensitivity was defined as true positive / (true positive + false negative); specificity was defined as true negative / (true negative + false positive); the positive predictive value as true positive / (true positive + false positive). All statistical analyses were performed using R version 3.4.3 and RStudio Version 1.1.414. An alpha level of 0.05 was chosen to indicate statistical significance. All provided p-values are two-sided.

3. Results

3.1. Study population

Of 93 eligible patients, 91 patients fulfilled inclusion criteria. One patient was excluded due to pH-metry probe defect and one due to diagnosis of achalasia on real-time MRI, respectively. Median patient age was 55.0 years (IQR 42.5–63.0 years). Gender was well balanced with n = 42 female (46 %) and n = 49 male patients (54 %). A total of 9 patients had previously undergone fundoplication. Six of these patients have been described in a previous manuscript [19]. Patient characteristics of the study population are summarized in Table 1.

3.2. pH-metry and impedance

On 24 h pH-metry of the distal esophagus, patients had a median number of 24.0 reflux episodes (IQR 11.0–47.5) and a median acid exposure time of 3.5 % (IQR 1.2–9.7 %). According to Lyon Consensus, results of pH-metry were rated as pathological reflux in 30 cases (33 %), as supportive evidence in 10 cases (11 %) and as no evidence for reflux in 51 cases (56 %).

On impedance measurement, the median number of reflux episodes was 51.0 (IQR 27.5–84.5). Pathological impedance measurements were evident in 54 patients, of which 27 cases were pH-metry inconspicuous, probably indicating the presence of non-acidic reflux (Table 2). Further measurements are provided in Table 1.

Table 1

Baseline characteristics of included patients. Continuous variables are provided as median and interquartile ranges (IQR).

	Total No. 91	pH-metry or impedance + No. 67	pH-metry and impedance - No. 24	P-value
age	55.0 (42.5–63.0)	57.0 (44.5–62.5)	51.0 (41.8–65.2)	0.61
gender				0.84
female	42 (46.2%)	30 (44.8 %)	12 (50.0 %)	
male	49 (53.8%)	37 (55.2 %)	12 (50.0 %)	
DeMeester score				0.48
Median (IQR)	9.0	13.1	3.2 (1.7–5.7)	
	(3.7–31.0)	(7.0–39.7)		
Missing	1 (1.1%)	1 (1.5 %)	0 (0 %)	
Acid exposure time (AET) [%]	3.5 (1.2–9.7)	5.2 (2.6–11.9)	1.1 (0.4–1.6)	0.50
reflux episodes on	24.0	34.0	11.0	0.34
pH-metry (n)	(11.0-47.5)	(19.5–56.5)	(4.2–13.2)	
reflux episodes on	51.0	65.0	22.5	0.35
impedance (n)	(27.5-84.5)	(46.0–99.0)	(13.5–29.5)	
Reflux detected on M	IRI			< 0.001
yes	60 (65.9%)	52 (77.6 %)	8 (33.3 %)	
no	31 (34.1 %)	15 (22.4 %)	16 (66.7 %)	
MRI reflux grading	1.0 (0.0-2.0)	1.0 (1.0-2.0)	0.0 (0.0-1.0)	< 0.001
MRI reflux intensity	2.0 (1.0-3.0)	3.0 (2.0-4.0)	1.0 (1.0-2.0)	< 0.001
MRI reflux spontaneo	ously			0.14
ves	9 (9.9 %)	9 (13.4 %)	0 (0.0 %)	
no	82 (90.1 %)	58 (86.6 %)	24 (100.0 %)	
MRI resting hernia				0.47
ves	37 (40.7 %)	29 (43.3 %)	8 (33.3 %)	
no	52 (57.1 %)	36 (53.7 %)	16 (66.7 %)	
Missing	2 (2.2 %)	2 (3.0 %)	0 (0.0 %)	
MRI Valsalva hernia				0.33
ves	47 (51.6 %)	37 (55.2 %)	10 (41.7 %)	
no	43 (47.3 %)	29 (43.3 %)	14 (58.3 %)	
Missing	1 (1.1 %)	1 (1.5 %)	0 (0.0 %)	
0	- (111 /0)	- (1.0 /0)	- (0.0 /0)	

Table 2

Summary of assessment by pH metry and impedance.

	pH-metry pathological	pH-metry normal	Total
impedance pathological	27	27	54
impedance normal	13	24	37
Total	40	51	91

3.3. Real-time MRI

Real time MRI was successfully completed in all 91 patients without adverse events. Mean acquisition time of real-time MRI films was 15 min. A total of 47 patients were diagnosed with hiatal hernia during Valsalva maneuver (52 %). Under resting position, hiatal hernias were detected in 37 cases (42 %). Assessment of real-time MRI revealed presence of reflux in 60 patients (66 %). Spontaneous reflux was detected in 9 patients, all of which showed correlating pathological readings on either pH-metry or impedance. Patients with reflux on pHmetry or impedance showed a significantly higher MRI reflux intensity grading than patients with normal pH-metry and impedance (median 3.0 versus 1.0, p < 0.001). Comparably, MRI reflux grading was significantly higher for patients with versus without reflux on pH-metry or impedance (median 1.0 vs. 0.0, p < 0.001). Four patients were diagnosed with disruption of the fundoplication warp on real-time MRI and recurrent reflux was confirmed on impedance. A telescoping hernia with visible reflux was detected on MRI films in another 3 patients (Figs. 3–5).

3.4. Diagnostic accuracy of real-time MRI for detection of reflux

Compared to sole pH-metry as reference, the presence of any

gastroesophageal reflux detected on real-time MRI demonstrated sensitivity 0.82 (95 % CI: 0.67-0.93), specificity 0.47 (95 % CI: 0.33-0.62) and PPV 0.55 (95 % CI: 0.42-0.68, see Table 3). Due to the high number of false positive readings in this setting, a second scenario with assessment of acidic as well as non-acidic reflux was considered. Here, the reference standard was either positive reflux on pH-metry (indicating acidic reflux) or a high number of reflux episodes during impedance (indicating non-acidic reflux). In this scenario, real-time MRI sensitivity was 0.78 (95 % CI: 0.66-0.87), specificity 0.67 (95 % CI: 0.45-0.84) and PPV 0.87 (95 % CI: 0.75-0.94, see Table 4). Compared to pH-metry and impedance, real-time MRI was false positive in 8 patients: the MRI signal intensity increase during Valsalva maneuver was graded as 2/5 in 5 patients, whereas high MRI intensity increases ≥ 3 were detected in another 3 patients. Moreover, 15 patients with reflux on either pH-metry or impedance showed no signs of reflux on real-time MRI films.

4. Discussion

Our study provides a non-invasive real-time MRI protocol to assess gastroesophageal reflux disease. In patients with GERD-like symptoms, real-time MRI demonstrates good diagnostic performance for detection of gastroesophageal reflux compared to invasive pH-metry and impedance. The presence of spontaneous reflux on MRI was associated with pathological reflux on invasive pH-monitoring, although it was reported in only a minority of patients (9.9 %). For the majority of patients, reflux on real-time MRI only manifested during Valsalva maneuver, which underlines the importance of this dynamic imaging component. In subgroup analyses, real-time MRI readings correlated well with combined assessment by pH-metry and impedance, while MRI overcalled reflux compared to sole pH-metry. Still, discrepancies were also evident when comparing pH-metry and impedance measurements, with several patients demonstrating increased number of reflux episodes on impedance but normal acid exposure time. This might indicate the presence of non-acidic reflux in these specific cases. Following this rationale, the visual presence of reflux on real-time MRI seems to indicate either acidic or non-acidic reflux. Further, real-time MRI may identify patients with non-acidic reflux that is not detected by pHmetry. The clinical relevance of increased non-acidic reflux episodes is not yet fully understood and the number of reflux episodes, therefore, only serves as an adjunctive metric for GERD diagnosis [8]. However, recent data demonstrated symptom relief and a reduction in reflux episodes after magnetic sphincter augmentation in patients with moderate to severe regurgitation, highlighting the impact of reflux events on clinical symptoms [23].

The literature on correlation of pH-monitoring with functional radiological imaging for gastroesophageal reflux assessment is scarce: In 1994, Thompson et al. evaluated 117 patients using fluoroscopy and reported a higher sensitivity of up to 70 % using dynamic maneuvers to elicit reflux [24]. In line with our findings, the authors described the presence of reflux on fluoroscopy in pH-metry negative patients, which might indicate non-acidic reflux cases. Curcic and colleagues assessed the gastroesophageal junction and reflux detection by MR-flouroscopy [25,26]. However, the specific MRI protocol employed gadoliniumbased contrast agents and had a lower temporal resolution compared to our technique. More recently, Kulinna-Cosentini and colleagues examined 37 patients with dynamic MRI, reporting a good correlation with pH-monitoring [27]. The study reported a high concordance of MRI results to the pH-metry based DeMeester score (82 %), which is no longer used as a diagnostic criterion in GERD-patients according to updated guidelines [8]. These findings are partially in contrast to our results which indicate that real-time MRI seemed to detect both acidic and non-acidic reflux. This discrepancy might well result from the different pH-metry assessment guidelines, assessment of impedance, patient selection and image acquisition.

Previous feasibility studies using MRI for the evaluation of the



Fig. 3. Real-time MRI of the LES during bolus passage in coronal (A, B) and sagittal planes (C, D). (A and B) As the bolus enters the distal esophagus (arrow), it passes through the gastroesophageal junction (arrow head). (C and D) The same observation can be made on the sagittal planes. Bolus enters the distal esophagus (arrow) and is cleared after several propulsive contractions. Also see supplemental Video 1.

gastroesophageal junction required the application of gadolinium chelate suspensions or ferric ammonium citrate as oral contrast agents [27,28]. In our study, commercially available pineapple juice serves as a natural contrast agent due to its high manganese content, obviating traditional oral contrast agents and their associated risks [29]. Considering the positive predictive value of 0.87, real-time MRI shows the potential to identify patients that might benefit from further invasive testing. Moreover, real-time MRI provides a non-invasive assessment of the gastroesophageal junction and gastroesophageal reflux in patients that do not tolerate the placement of an esophageal probe for 24 h. The short examination time and physiological, voluntary swallowing might further facilitate patients' acceptance of this modality. Finally, realtime MRI yields diagnostic potential in patients with equivocal or aborted pH-metry: In a previous study, real-time MRI demonstrated high diagnostic potential for detection of recurring hernia and fundoplication failure [19]. The delineation of the gastroesophageal junction and the identification of hiatal hernias by real-time MRI can further provide information for the planning and follow-up of anti-reflux procedures. So far we do not consider real-time MRI as a substitute for current diagnostic methodologies, but rather as an auxiliary diagnostic tool especially in patients that do not tolerate 24 h esophageal and

identification of candidates for anti-reflux surgery.

Still, utilization of real-time MRI for reflux detection is not devoid of limitations. First, the lack of a healthy control group limits the generalizability our results regarding the clinical implementation into diagnostic pathways of GERD. Due to inclusion of patients with typical GERD-symptoms, our study cohort demonstrated a high prevalence of patients with positive pH-metry or impedance (73.6 %). Therefore, the PPV should be reduced in the general population with a lower prevalence of reflux, while MRI sensitivity and specificity should remain unaffected. In addition, 15 out of 67 patients with reflux on either pHmetry or impedance showed no signs of reflux on real-time MRI and real-time MRI was false positive in 8 cases. Insufficient Valsalva maneuvers and intermittent reflux could explain the absence of visible reflux on MRI studies in these cases. Another limitation may be the small volume of the administered pineapple bolus, as it might be insufficient to provoke reflux in all patients. Further, small reflux volumes may remain undetectable by real-time MRI. In this context, quantification of MRI signal level increase between rest and Valsalva maneuver may improve reflux detection in the future. Second, visual assessment of reflux grading and intensity on real-time MRI was performed in an arbitrary matter by consensus reading, which may impose bias. Further



Fig. 4. Real-time MRI of the LES during Valsalva maneuver in sagittal planes. Case 2 depicts a subject with reflux on real-time MRI, pH-metry and impedance. Representative individual images were selected showing instant reflux before and after Valsalva maneuver was performed. Also see supplemental Video 2.



Fig. 5. Real-time MRI of the bolus passage in coronal planes (A–C) and after Valsalva maneuver in sagittal planes (D–F). All real-time MRI images show a large hiatal hernia. The patient had no pathologic reflux on pH-metry, however, reflux was detected on real-time MRI and on impedance. Representative individual images were selected showing bolus passage in coronal planes (A–C). Sagittal planes reveal the extent of the herniation (D, arrow) and spontaneous reflux (E, arrow head). An increased reflux can be observed after performing Valsalva maneuver (F, arrow head). Also see supplemental Video 3.

Table 3

Contingency table for diagnostic accuracy of real-time MRI (index test) for reflux detection compared to pH-metry (reference test).

	pH-metry pathological	pH-metry normal	Total
MRI: Reflux	33	27	64
MRI: no Reflux	7	24	32
Total	40	51	91

Table 4

Contingency table for diagnostic accuracy of real-time MRI (index test) for reflux detection compared to pH-metry and impedance (reference test).

	pH metry or impedance pathological	pH metry and impedance normal	Total
MRI: Reflux	52	8	60
MRI: no Reflux	15	16	31
Total	67	24	91

studies with a healthy control group are required to define exact cutoffvalues. Finally, a short 15 min examination with real-time MRI in supine position and under Valsalva maneuver might not necessarily reflect the conditions given during continuous 24 h pH-monitoring. Still, data by Curcic and colleagues demonstrated high agreement of swallowing events at the EGJ between MRI findings and manometric assessment [26].

5. Conclusion

Real-time MRI is a dynamic imaging technique that visualizes gastroesophageal reflux in patients with GERD-like symptoms. Given its good correlation with pH-metry and impedance measurements, we consider real-time MRI a promising auxiliary diagnostic tool for the diagnosis of GERD.

Transparency document

The Transparency document associated with this article can be found in the online version.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ejrad.2020.108856.

References

- J. Dent, Epidemiology of gastro-oesophageal reflux disease: a systematic review, Gut 54 (2005) 710–717.
- [2] H.B. El-Serag, S. Sweet, C.C. Winchester, J. Dent, Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review, Gut 63 (6) (2014) 871–880.
- [3] N. Vakil, S.V. van Zanten, P. Kahrilas, J. Dent, R. Jones, G. Global Consensus, The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus, Am. J. Gastroenterol. 101 (8) (2006) 1900–1920 quiz 1943.
- [4] S. Bruley des Varannes, H.G. Lofman, M. Karlsson, P. Wahlqvist, M. Ruth, M.L. Furstnau, N. Despiegel, N.O. Stalhammar, Cost and burden of gastroesophageal reflux disease among patients with persistent symptoms despite proton pump inhibitor therapy: an observational study in France, BMC Gastroenterol. 13 (2013) 39.
- [5] J. Maret-Ouda, K. Wahlin, M. Artama, et al., Risk of esophageal adenocarcinoma after antireflux surgery in patients with gastroesophageal reflux disease in the nordic countries, JAMA Oncol. (2018).
- [6] P.O. Katz, L.B. Gerson, M.F. Vela, Guidelines for the diagnosis and management of gastroesophageal reflux disease, Am. J. Gastroenterol. 108 (3) (2013) 308–328 quiz 329.
- [7] H. Koop, K.H. Fuchs, J. Labenz, P. Lynen Jansen, H. Messmann, S. Miehlke, W. Schepp, T.G. Wenzl, L. und die Mitarbeiter der, S2k-Leitlinie: gastroösophageale refluxkrankkheit unter Federführung der Deutschen Gesellschaft für

gastroenterologie, verdauungs- und stoffwechselkrankheiten (DGVS), Z. Gastroenterol. 52 (11) (2014) 1299–1346.

- [8] C.P. Gyawali, P.J. Kahrilas, E. Savarino, F. Zerbib, F. Mion, A.J.P.M. Smout, M. Vaezi, D. Sifrim, M.R. Fox, M.F. Vela, R. Tutuian, J. Tack, A.J. Bredenoord, J. Pandolfino, S. Roman, Modern diagnosis of GERD: the lyon consensus, Gut 67 (7) (2018) 1351–1362.
- [9] J. Ronkainen, P. Aro, T. Storskrubb, S.E. Johansson, T. Lind, E. Bolling-Sternevald, H. Graffner, M. Vieth, M. Stolte, L. Engstrand, N.J. Talley, L. Agreus, High prevalence of gastroesophageal reflux symptoms and esophagitis with or without symptoms in the general adult Swedish population: a Kalixanda study report, Scand. J. Gastroenterol. 40 (3) (2005) 275–285.
- [10] C.H. Poh, A. Gasiorowska, T. Navarro-Rodriguez, M.R. Willis, D. Hargadon, N. Noelck, J. Mohler, C.S. Wendel, R. Fass, Upper GI tract findings in patients with heartburn in whom proton pump inhibitor treatment failed versus those not receiving antireflux treatment, Gastrointest. Endosc. 71 (1) (2010) 28–34.
- [11] R. Sweis, M. Fox, A. Anggiansah, T. Wong, Prolonged, wireless pH-studies have a high diagnostic yield in patients with reflux symptoms and negative 24-h catheterbased pH-studies, Neurogastroenterol. Motil. 23 (5) (2011) 419–426.
- [12] R. Sweis, M. Fox, R. Anggiansah, A. Anggiansah, K. Basavaraju, R. Canavan, T. Wong, Patient acceptance and clinical impact of Bravo monitoring in patients with previous failed catheter-based studies, Aliment. Pharmacol. Ther. 29 (6) (2009) 669–676.
- [13] W.M. Wong, J. Bautista, R. Dekel, I.B. Malagon, I. Tuchinsky, C. Green, R. Dickman, R. Esquivel, R. Fass, Feasibility and tolerability of transnasal/per-oral placement of the wireless pH capsule vs. Traditional 24-h oesophageal pH monitoring–a randomized trial, Aliment. Pharmacol. Ther. 21 (2) (2005) 155–163.
- [14] J. Lee, A. Anggiansah, R. Anggiansah, A. Young, T. Wong, M. Fox, Effects of age on the gastroesophageal junction, esophageal motility, and reflux disease, Clin. Gastroenterol. Hepatol. 5 (12) (2007) 1392–1398.
- [15] B.T. Johnston, M.B. Troshinsky, J.A. Castell, D.O. Castell, Comparison of barium radiology with esophageal pH monitoring in the diagnosis of gastroesophageal reflux disease, Am. J. Gastroenterol. 91 (6) (1996) 1181–1185.
- [16] S. Zhang, A.A. Joseph, D. Voit, S. Schaetz, K.D. Merboldt, C. Unterberg-Buchwald, A. Hennemuth, J. Lotz, J. Frahm, Real-time magnetic resonance imaging of cardiac function and flow-recent progress, Quant. Imaging Med. Surg. 4 (5) (2014) 313–329.
- [17] A. Olthoff, S. Zhang, R. Schweizer, J. Frahm, On the physiology of normal swallowing as revealed by magnetic resonance imaging in real time, Gastroenterol. Res. Pract. 2014 (2014).
- [18] A. Seif Amir Hosseini, A. Beham, J. Uhlig, U. Streit, A. Uhlig, V. Ellenrieder, A.A. Joseph, D. Voit, J. Frahm, M. Uecker, J. Lotz, L. Biggemann, Intra- and

interobserver variability in the diagnosis of GERD by real-time MRI, Eur. J. Radiol. 104 (2018) 14–19.

- [19] A. Seif Amir Hosseini, J. Uhlig, U. Streit, D. Voit, A. Uhlig, V. Ellenrieder, M. Ghadimi, T. Sprenger, A. Beham, M. Uecker, J. Frahm, J. Lotz, L. Biggemann, Real-time MRI for the dynamic assessment of fundoplication failure in patients with gastroesophageal reflux disease, Eur. Radiol. (2019).
- [20] T.R. DeMeester, C.I. Wang, J.A. Wernly, C.A. Pellegrini, A.G. Little, P. Klementschitsch, G. Bermudez, L.F. Johnson, D.B. Skinner, Technique, indications, and clinical use of 24 hour esophageal pH monitoring, J. Thorac. Cardiovasc. Surg. 79 (5) (1980) 656–670.
- [21] M. Uecker, S. Zhang, D. Voit, A. Karaus, K.D. Merboldt, J. Frahm, Real-time MRI at a resolution of 20 ms, NMR Biomed. 23 (8) (2010) 986–994.
- [22] S. Schätz, J. Frahm, M. Untenberger, S. Zhang, D. Voit, K.D. Merboldt, J.M. Sohns, J. Lotz, M. Uecker, On the temporal fidelity of nonlinear inverse reconstructions for real-time MRI – the motion challenge, Open Med. Imaging J. (8) (2014) 1–7.
- [23] R. Bell, J. Lipham, B. Louie, V. Williams, J. Luketich, M. Hill, et al., Laparoscopic magnetic sphincter augmentation versus double-dose proton pump inhibitors for management of moderate-to-severe regurgitation in GERD: a randomized controlled trial, Gastrointest. Endosc. 89 (1) (2019) 14–22 e1.
- [24] J.K. Thompson, R.E. Koehler, J.E. Richter, Detection of gastroesophageal reflux: value of barium studies compared with 24-hr pH monitoring, AJR Am. J. Roentgenol. 162 (3) (1994) 621–626.
- [25] J. Curcic, M. Fox, E. Kaufman, Z. Forras-Kaufman, G.S. Hebbard, S. Roy, A. Pal, W. Schwizer, M. Fried, R. Treier, P. Boesiger, Gastroesophageal junction: structure and function as assessed by using MR imaging, Radiology 257 (1) (2010) 115–124.
- [26] J. Curcic, S. Roy, A. Schwizer, E. Kaufman, Z. Forras-Kaufman, D. Menne, G.S. Hebbard, R. Treier, P. Boesiger, A. Steingoetter, M. Fried, W. Schwizer, A. Pal, M. Fox, Abnormal structure and function of the esophagogastric junction and proximal stomach in gastroesophageal reflux disease, Am. J. Gastroenterol. 109 (5) (2014) 658–667.
- [27] C. Kulinna-Cosentini, W. Schima, J. Lenglinger, M. Riegler, C. Kolblinger, A. Ba-Ssalamah, G. Bischof, M. Weber, P. Kleinhansl, E.P. Cosentini, Is there a role for dynamic swallowing MRI in the assessment of gastroesophageal reflux disease and oesophageal motility disorders? Eur. Radiol. 22 (2) (2012) 364–370.
- [28] T. Manabe, H. Kawamitsu, T. Higashino, D. Shirasaka, N. Aoyama, K. Sugimura, Observation of gastro-esophageal reflux by MRI: a feasibility study, Abdom. Imaging 34 (4) (2009) 419–423.
- [29] O.J. Arthurs, M.J. Graves, A.D. Edwards, I. Joubert, P.A. Set, D.J. Lomas, Interactive neonatal gastrointestinal magnetic resonance imaging using fruit juice as an oral contrast media, BMC Med. Imaging 14 (2014) 33.