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Abstract

BACKGROUND: The aim of this study was to determine the occurrence of extra-enteric findings in a large cohort of patients undergoing magnetic resonance enterography (MR-E) and to classify the clinical significance of these findings. MATERIALS AND METHODS: We retrospectively analyzed 1154 MR-E performed in 1006 patients referred to our radiological department between 1999-2005. The reasons for referral were suspected or proven inflammatory bowel diseases (IBD) (n = 710), further diagnostic work-up for small bowel disease because of non-specific abdominal symptoms (SBD; n = 182) or suspected small bowel malignancies (SBM; n = 114). All extra-enteric findings were reviewed by a radiologist and a gastroenterologist and were classified as having high, moderate, or low significance for further diagnostic or therapeutic procedures. RESULTS: The average age of all patients was 40+/−16 (Mean+/−SD) years (y) (IBD 35+/−13 y; SBD 49+/−16 y; SBM 57+/−15 y). A total of 1113 extra-enteric findings were detected in 600 of 1006 patients (59.6%). Of these findings 180 (16.2%) were judged as having a high, 212 (19.0%) a moderate and 721 (64.8%) a low significance. On a per group basis in patients with IBD 12.0% of the findings were of major clinical significance compared to 13.7% and 33.3% in patients with SBD and SBM, respectively. The most common major findings were abscesses (69.9%) in the IBD group and extraintestinal tumors, metastases or masses in the SBD and SBM groups (41.9% and 74.2%, respectively). CONCLUSIONS: MR-E reveals a substantial number of extra-enteric findings, supporting the role of a cross-sectional imaging method for the evaluation of the small bowel.
Frequency and nature of incidental extraenteric lesions found on magnetic resonance enteroclysis (MR-E) in patients with inflammatory bowel disease

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Abstract

Background: The aim of this study was to determine the occurrence of extraenteric findings in a large cohort of patients undergoing MR-E and to classify their clinical significance.

Methods: 1154 MR-E performed on 1006 patients referred to our radiological department between 1999-2005 were analyzed retrospectively. The reasons for referral were suspected or proven IBD (n=710), further diagnostic work-up for small bowel disease because of non-specific abdominal symptoms (SBD; n=182) or suspected small bowel malignancies (SBM; n=114). All extraenteric findings were reviewed by a radiologist and a gastroenterologist and were classified as having high, moderate, or low significance for further diagnostic or therapeutic procedures.

Results: The average age of all patients was 40±16 (Mean ± SD) years (y) (IBD 35±13y; SBD 49±16y; SBT 57±15y). A total of 1113 extraenteric findings were detected in 600 of 1006 patients (59.6%). Of these findings 180 (16.2%) were judged as having a high, 212 (19.0%) a moderate and 721 (64.8%) a low significance. On a per group basis in patients with IBD 12.0 % of the findings were of major clinical significance compared to 13.7% and 33.3% in patients with SBD and SBM, respectively. The most common major findings were abscesses (69.9%) in the IBD group and extraintestinal tumors, metastases or masses in the SBD and SBT groups (41.9% and 74.2%, respectively).

Conclusions: MR-E reveals a substantial number of extraenteric findings, supporting the role of this cross-sectional imaging method for the evaluation of the small bowel.
Introduction

In patients with suspected or proven inflammatory bowel disease, radiological imaging techniques of the small bowel are employed to either establish or exclude the diagnosis of small bowel Crohn’s disease (CD) or to evaluate the location, extent and the presence of strictures of small bowel in patients with established CD. Until recently, the small bowel follow-through or the classical conventional enteroclysis have been the preferred radiological technique for the visualization of the small bowel. However, MR-enteroclysis (MR-E) or CT-enteroclysis are more and more considered as a standard imaging procedure in patients with suspected or established inflammatory bowel diseases 1-3. Especially the diagnostic value of MR imaging (MRI) of the small bowel in patients with inflammatory bowel disease has been extensively assessed in recent years using various contrast media and different techniques 4-15. Several studies also demonstrated a high correlation of this technique with the conventional radiological methods such as small bowel follow-through or the conventional enteroclysis, surgery and endoscopy 16-23. The advantage of both CT and MRI as compared to conventional radiological methods is the acquiring of additional information of extraluminal pathologies. Studies comparing MRI or and conventional enteroclysis revealed additional pathological extraenteric abnormalities in 25-58% of the cases, which are sometimes clinically relevant and lead to changes in medical or surgical management 18,20,24-27. All these studies have in common, that only small groups of patients were examined. Additionally, the clinical significances of these extraenteric pathologies never have been evaluated. Several studies analyzing the frequency and clinical significance of extra colonic findings in patients undergoing virtual colonoscopy for screening purposes have been recently published. A systematic review of 17 studies including 3448 patients revealed that up to 40% of the patients had extra colonic pathologies 28. In this analysis clinical significant findings necessitating further diagnostic or therapeutic work-up were described in 10.5% in a subgroup of 2787 patients. Since patients with IBD in general present
at a younger age than patients undergoing screening colonoscopy (age >50 years) and therefore most likely suffer from less co-morbidity, we evaluated the prevalence and clinical significance of extraintestinal findings in this patient group. For this purpose we retrospectively analyzed all extraenteric findings in patients referred to our institution between 1999-2005 for MR-E because of suspected or established IBD. We additionally included two other groups of patients undergoing MR-enteroclysis for unexplained abdominal symptoms without clinical suspicion of inflammatory bowel disease and patients with suspected small bowel tumours. The aim of this study was to determine the frequency of extraenteric findings in these three groups and to classify the clinical significance of these findings.
Material and Methods

We retrospectively analyzed the extraenteric findings of 1154 MR-E performed in 1006 patients referred to our radiological department between 1999-2005. Our institutional review board approved the study.

The reasons for referral were suspected or proven inflammatory bowel disease (IBD) (n=710), further diagnostic work-up for a suspected small bowel disease (SBD) because of non-specific abdominal symptoms (n=182) or suspected small bowel malignancies (SBM) (n=114). All extra enteric findings were reviewed by a radiologist and a gastroenterologist and were classified as having minor, moderate, or major significance.

Findings considered to be of no or little clinical importance were classified as minor and unlikely to require further diagnostic procedures or medical therapy. Examples include e.g. small cystic liver lesions, renal cysts, small renal calcifications or degenerative changes of the spine. Findings of moderate clinical importance did not require immediate further diagnostic workup or therapy, but would likely to be verified later on either by chart review or by further clinical or radiologic follow up. Examples include adrenal masses of <2 cm in diameter, indeterminate cysts of various organs, gallstones, splenomegaly. Findings of definite clinical importance requiring immediate further diagnostic or therapeutic intervention (e.g. hydronephrosis, suspected tumors, aortal aneurysms, pleural effusions) were classified as being major clinically important.

MR-E

All MRI examinations were performed using a 1.5T Scanner (Symphony; Siemens Medical Systems, Erlangen, Germany) and a circular polarized 4-element phased array body coil. For the abdominal MR-E performed between 1999 -2001 the patient drank 2 l of pineapple juice (12.7 mg/l manganese-content) mixed with 20 mg methylcellulose within 2 hours for bright lumen MRE. After 2002 the dark lumen technique was utilized. For this technique the
patients drank 2 liters of tap water during 1 hour continuously. To achieve sufficient small bowel distension we added 50 g mannitol and 5 g carob seed (Nestargel, Nestle, Munich, Germany) to 1 liter water. To reduce bowel peristalsis, patients without contraindications received 40 mg N-butyl-scopolamine intravenously (Buscopan; Boehringer, Ingelheim, Germany) in 100 mL 0.9% NaCl continuously during the examination as drip infusion. For the bright lumen as well as the dark lumen MRE the same MRI sequences were applied.

As a fast screener sequence a coronal true fast imaging with steady precession (TRUFI; TR/TE, 4.76/2.38 msec; flip angle, 60 degrees; slice thickness, 5 mm; 256 matrix; FOV, 450 mm) and an axial half-Fourier acquired single-shot turbo spin echo (HASTE; TR/TE, 1070/77 msec; flip angle, 150 degrees; slice thickness, 8 mm; 256 matrix; FOV, 400 mm) as a T2-weighted sequence were acquired. Before injecting contrast media intravenously, a T1-weighted 2D-FLASH sequence with axial orientation was performed, which was used as a baseline sequence for contrast uptake. Afterward, 0.2 mmol/kg body weight Gd-DTPA (Magnevist; Schering, Berlin, Germany) with a flow of 2 mL/sec was given intravenously followed after 70 seconds by a fat-suppressed 3D-FLASH sequence (TR/TE, 4.6/1.8 msec; flip angle, 25 degrees; slab thickness, 140 to 160 mm with 80 partitions; 512 X 210 matrix; FOV, 400 mm). Additionally a fat-suppressed axial and coronal T1-weighted 2D-FLASH was acquired. Scanner time for the whole examination was approximately 25 minutes (range, 21 to 29 min).
Results

539 patients of the 1006 patients included in this study were females (54%). The youngest patient was 11 years and the oldest 90 years. The average age ± SD in the patient group referred for IBD (n=710), SBD (n=182) and SBM (n=114) were 35 ±13, 49±16 and 57±15 years, respectively.

Radiological classification of extra enteric pathologies in patients with IBD, SBD and SBT

Overall 1113 extraenteric findings were detected in 600 of 1006 patients (59.6%). 689, 226 and 198 extra enteric findings were detected in 403 of 710 (56.8%), 119 of 182 (65.4%) and 78 of 114 (68.4%) patients with IBD, SBD and SBM, respectively (Table 1).

Extraenteric findings of minor clinical significance

The most common of the 470 minor findings in patients with IBD were ovarian cysts (n=110; 15.5% of all IBD patients), kidney cysts (n=67; 9.4%), liver cysts (n=50; 7.0%) and small amounts of ascites (n=50; 7.0%). 243 of the 470 findings (41.1%) were detected in less than 5% of all IBD patients including e.g. findings of an accessory spleen, liver hemangiomas, sludge in the gallbladder or scoliosis of the backbone.

Most common findings of a total of 156 minor findings in patients with SBD were kidney - (n=40; 22.0 % of all SBD patients), ovarian - (n=19; 10.4%) and liver (n=15, 8.2%) cysts. Small amounts of ascites were found in 7.7% (n=14) of the patients, whereas 43.6 % (n=68) of the remaining findings were identified each in less than 5% of SBD patients.

Of the 95 findings with minor clinical significance in patients with SBM kidney and liver cysts were found in 29 (25.4% of all SBM patients) and 11 (9.6%) patients respectively, small amounts of abdominal ascites was found in 6 patients (5.3%).
51.6% (n=49) of the findings were discovered each in less than 5% of all SBM patients.

**Extraenteric findings of moderate clinical significance**
Findings with moderate significance included most often lymphadenopathy, which was considered as IBD related and not suspicious for lymphoma (n=50; 7.0% of all IBD patients), cholecysto- or choledocholithiasis (n=15; 2.1%), degenerative bone disorders (14; 2.0%), uterus myomas (n=12; 1.7%) and splenomegaly (n=7, 1.0%). The other findings were each detected in a frequency of less than 1% in all IBD patients.

In patients with SBD findings with moderate clinical significance included cholecysto- or choledocholithiasis (n=6; 3.3% of all SBD patients), degenerative bone disorders (5; 2.7%), uterus myomas (n=4; 2.2%), splenomegaly (n=3, 1.6%), complicated kidney cysts (3; 1.6%), slightly dilated collecting tubules in the kidneys (3; 1.6%) and lymphadenopathy (3; 1.6%). The other findings were each detected in a frequency of less than 1% in all SBD patients.

Findings of moderate clinical importance in the group of patients with SBM were cholecyst- or choledocholithiasis (n=6; 5.3% of all SBM patients), degenerative bone disorders (5; 4.4%), uterus myomas (n=4; 3.5%), moderate amounts of ascites (n=4, 3.5%), slightly dilated collecting tubules in the kidneys (n=3, 2.6%), kidney hypoplasia, splenomegaly and abdominal wall herniation (each n=2; 1.7%). The other findings were each detected in a frequency of less than 1% in all SBM patients.

**Extraenteric findings of major clinical significance**
Overall 180 findings were considered being of major clinical significance (table 1). The most common highly significant lesions were extraintestinal tumors, metastases or masses (n=72), abscesses (n=63), pleural effusions (n=13) and hydronephrosis or ureteral obstruction (n=16) (Tables 2-4). 83 major clinical findings occurred in 73 of the 710 patients with IBD (10.3%) (table 2).
In the group of SBD patient’s 31 major clinical findings were detected in 27 of the 182 patients (14.8%) (table 3) and 66 major clinical findings were visualized in 40 of 114 SBM patients (35.1%) (table 4). The most common findings were extraintestinal abscesses in the IBD group (69.9% of all major clinical findings), whereas tumors, metastases or masses were most often described in the SBD and SBM group (41.9% and 74.2%, respectively).

Given the large percentage of patients with tumors, metastases or masses, a systemic medical chart review of these patients was performed. Nine patients in the IBD group presented with 10 extraintestinal findings classified as tumour, metastasis or mass. Five out of these 10 findings (50%) were newly diagnosed in 5 patients, whereas in 4 patients 5 extraintestinal masses were already known before the MR-E examination by either a recently performed abdominal ultrasound examination or a CT-scan. In 12 patients with SBD and 33 patients with SBM 7 of 13 (53.8%) and 11 of 49 (22.4%) of the findings classified as tumour, metastasis or mass were newly detected.
Discussion

MR-E is a newly evolving imaging technology to visualize the small bowel. Aside of the lack of radiation, the advantage of this modality compared to the conventional radiological methods such as a small bowel follow through or conventional enteroclysis is the ability to detect extraintestinal pathology. In our retrospective study in nearly 60% of patients extra enteric findings were detected. Whereas the majority of the findings were of low clinical importance, 35.2% were considered of high and moderate clinical significance. Extraintestinal findings of moderate clinical importance were detected in 19.7%, 17.3% and 18.7% in the IBD, SBD and SBM groups. In the group of IBD and SBD patients 12.1% and 13.7% of all extraintestinal findings were considered of major clinical importance, whereas this was the case in 33.3% in the patients with suspected SBM.

In IBD patients findings of major clinical significance were observed in approximately every tenth patient (73 of 710 patients with IBD). In the majority of the cases these were abscesses (58 of 83 major findings; 69.9%), that had to be drained in almost all cases indicating the value of this cross sectional method for further therapeutic decisions. The high number of patients presenting with abscesses could be due to the fact, that the retrospective analysis was performed in a tertiary care center, which obviously treats more complex IBD patients. In 5 patients new extraintestinal findings were classified as suspicious of a tumor, a metastasis or an abdominal mass. Despite the fact that this comprised less than 1% of the 710 IBD patients, given the generally young age of these patients, these findings had profound implications for the further clinical approach.

Additional extra enteric findings in 20-60% of the IBD patients are described in a number of published studies analyzing the efficacy of MR-E or CT-E in patients with IBD. However, in contrast to the previous studies, we analyzed the clinical significance of the extraintestinal findings in patients with
IBD undergoing MR-E. The results of our investigation indicate, that extra enteric findings of minor or moderate clinical significance are frequent.

The high number of major extraintestinal findings in the SBT group may be explained by the fact, that this patient group underwent the examination already with a high suspicion of an intestinal tumor, lymphoma or tumor metastasis. This is illustrated by the fact that only 11 of the 49 findings were new findings, whereas the others had been previously diagnosed by another imaging technique. Overall the patients in this group were also in average 22 and 6 years older compared to the IBD and SBD group.

Several prospective and retrospective studies report between 20-70% of incidental extracolonic findings in patients undergoing virtual colonography for colorectal cancer screening. In this patient population the frequency of clinically important findings clearly depends on risk stratification. Whereas in average risk cohorts undergoing CT-colonography 4-6% of clinically important extra colonic findings are detected, the percentage of those findings increases to 10-23% in the so called high-risk population for colorectal cancer (defined as: family history of colorectal cancer, personal history of polyps, new onset of anemia)²⁹,³⁶,³⁷. It is difficult to compare those reported findings with our results, since the patient cohorts in our study were clearly different from the patients studied in the colorectal cancer screening studies. All patient underwent the MR-enteroclysis with a clinically based suspicion of small bowel disease, whereas in the colorectal cancer screening studies most of the patients (except the anemia patients) were not symptomatic.

A weakness of the presented study is it´s retrospective character. This may especially affect the comparison of the IBD and SBD patient groups. We classified the patients according to the indication for the examination and not the outcome. Therefore, some patients in the SBD group may have been classified as IBD later. However, since both groups had nearly similar prevalences in the 3
different categories of the extraintestinal findings, the overall results are most likely not affected. It is also difficult determine whether the further diagnostic follow-up was based on the extraintestinal MR-E findings, since often patients underwent several diagnostic procedures. and was not clear whether the other procedures or the MR-E led the further decisions.

In conclusion, in more than half of the patients undergoing MR-E additional extra enteric findings were detected. Whereas the majority of extra enteric MR-E findings were of low clinical importance, approximately one third of the patients were diagnosed with findings of moderate or major clinical significance. Especially in the group of IBD patients, in whom the majority of the described major clinical findings were abscesses, cross sectional imaging by MR-E provides important additional clinical information compared to the conventional small bowel techniques such as SBFT or SB-enteroclysis.
| Dx (patients with findings*; n) | Total findings (n) | Clinical significance |
|---------------------------------|-------------------|-----------------------|
|                                 |                   | Major n (%)           |
| IBD (403)                       | 689               | 83 (12.1)             |
|                                 |                   | 136 (19.7)            |
|                                 |                   | 470 (68.2)            |
| SBD (119)                       | 226               | 31 (13.7)             |
|                                 |                   | 39 (17.3)             |
|                                 |                   | 156 (69.0)            |
| SBM (78)                        | 198               | 66 (33.3)             |
|                                 |                   | 37 (18.7)             |
|                                 |                   | 95 (48.0)             |

Table 1: Clinical significance of extraenteric findings in patients with IBD, SBD and SBT. *several findings per patient possible
| Findings                                          | n  | %    |
|--------------------------------------------------|----|------|
| Total                                            | 83 |      |
| Abscess                                          | 58 |      |
| Urethral obstruction                             | 5  |      |
| Pleural effusion                                 | 4  |      |
| Extraintestinal mass*                            | 2  |      |
| Hydronephrosis                                   | 2  |      |
| Lymphadenopathy, suspicion of lymphoma*           | 2  |      |
| Bone metastasis*                                 | 2  |      |
| Pericardial effusion                             | 1  |      |
| Pleural empyema                                  | 1  |      |
| Tumor adrenal gland*                             | 1  |      |
| Solid pancreatic mass*                           | 1  |      |
| Solid ovary mass*                                | 1  |      |
| Bone tumor*                                      | 1  |      |
| Bone necrosis                                    | 1  |      |
| Bone fracture                                    | 1  |      |

Table 2: Major clinical extraenteric findings in 73 patients with suspected or proven IBD undergoing MR-enteroclysis (n=710). *Grouped as tumor, metastasis or mass; n=10.
| Findings                                      | n   |
|----------------------------------------------|-----|
| Total                                        | 31  |
| Abscess                                      | 6   |
| Pleural effusion                             | 5   |
| Tumor adrenal gland*                         | 4   |
| Extraintestinal mass*                        | 3   |
| Urethral obstruction                         | 2   |
| Bone metastasis*                             | 2   |
| Hydrops of gallbladder                       | 1   |
| Aortal aneurysm                              | 1   |
| Celiac artery stenosis                       | 1   |
| Venous thrombosis                            | 1   |
| Pulmonary mass*                              | 1   |
| Renal mass*                                  | 1   |
| Hydronephrosis                               | 1   |
| Pancreatic mass*                             | 1   |
| Bone tumor*                                  | 1   |

Table 3: Major clinical extraenteric findings in 27 patients with suspected SBD undergoing MR-enteroclysis (n=182). *Grouped as tumor, metastasis or mass; n=13.
| Findings                                      | n  |
|----------------------------------------------|----|
| Total                                        | 66 |
| Extraintestinal mass*                        | 16 |
| Lymphadenopathy, suspicion of lymphoma*      | 16 |
| Liver metastases*                            | 8  |
| Adnexal mass*                                | 4  |
| Pleural effusion                             | 4  |
| Aortal aneurysm                              | 4  |
| Urethral obstruction                         | 4  |
| Bone metastases*                             | 2  |
| Hydronephrosis                               | 2  |
| Abscess                                      | 1  |
| Prostate cancer*                             | 1  |
| Mass rectus abdominis muscle*                | 1  |
| Bone tumor*                                  | 1  |
| Bone necrosis                                | 1  |
| Bone fracture                                | 1  |

Table 4: Major clinical extraenteric findings in 40 patients with suspected SBM undergoing MR-enteroclysis (n=114). *Grouped as tumor, metastasis or mass; n= 49.
Figures

Figures 1 demonstrates a pancreatic mass, which turned out to be pancreatic cancer in a 59-year old patient with IBD.

Figure 2: Pericardial effusion in a 47-year-old patient with active Crohn’s disease.
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Figure 2