Long-term diagnostic value of MRI in detecting recurrent aggressive fibromatosis at two multidisciplinary sarcoma centers

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ABSTRACT

Purpose: To assess the diagnostic accuracy of MRI in detecting recurrent aggressive fibromatosis (AF) during long-term follow-up at two multidisciplinary sarcoma centers.

Methods: Seventy-nine patients from two sarcoma centers were included in this IRB-approved study and were examined postoperatively using 1.5-T MRI. MRI follow-up scans were reviewed for true-positive/-negative and false-positive/-negative results. Available pathological reports and MRI follow-ups were set as reference.

Results: The median age of the patients was 38.1 ± 15.3 years. Of the patients 27.9 % showed recurrent AF lesions. The most common localizations of AF were the axilla/shoulder (n = 15) and the thigh (n = 11). From 498 postoperative MRI follow-ups, 24 true-positive, 16 false-positive, 6 false-negative, and 452 true-negative MRI follow-ups were identified. The overall sensitivity and specificity for detecting recurrent AF was 80 % and 97 %, respectively. There was no significant difference in the diagnostic accuracy at the two sarcoma centers. All false-negative results were found in small lesions. False-positive results mostly mimicked streaky (n = 10) and small ovoid/nodular (n = 5) lesions. The configuration of recurrent AF was significantly most often fascicular (50 %; p = 0.001–0.005).

Conclusion: MRI shows a high long-term diagnostic value in detecting AF recurrences. Nevertheless, radiologists should pay close attention when lesions are small, as they may remain undetected. Although the configuration of recurrent AF is most often fascicular, recurrences may also appear in different shapes.

1. Introduction

Extra-abdominal aggressive fibromatosis (AF), also known as desmoid tumor, is a rare mesenchymal soft-tissue tumor that is locally aggressive and arises from (myo)fibroblasts [1–3]. AF affects 2–4 per million people [4]. The peak incidence of AF is between 25 and 35 years [4–6]. It counts for less than 3 % of all soft-tissue tumors, has no potential to metastasize, and is classified as an intermediate tumor [7,8]. The extremities are the main localization of AF, accounting for approximately 70 % of all AF [9,4]. AF has a high rate of recurrence of up to 77 %, even after wide local excision [3,10,11]. MRI is the imaging modality of choice for postoperative surveillance of patients with soft-tissue tumors [12–14]. On MRI, AF is often reported to show a heterogeneous appearance on T1-weighted and T2-weighted images and enhances avidly after intravenous administration of contrast agent [15]. Additionally, AF is described as having an ovoid or infiltrative appearance [3,16] and is often difficult to distinguish from soft-tissue sarcomas or from postoperative and postradiogenic soft tissue on MRI [3,11]. Nevertheless, studies on the diagnostic accuracy of MRI in the postoperative surveillance of AF do not exist yet. Therefore, we analyzed the diagnostic value of MRI in detecting recurrent AF in the long-term postoperative follow-up at two multidisciplinary sarcoma centers.

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Furthermore, we assessed the configurations of recurrent AF on MRI, as a recent study revealed that primary AF typically shows a fascicular configuration [11].

2. Patients and methods

2.0.1. Patients

All available MRI data on AF from two multidisciplinary sarcoma centers (sarcoma center 1 and 2) were retrospectively collected from 2008 to 2019. Sixty-five patients from sarcoma center 1 and 81 patients from sarcoma center 2 with the diagnosis of “aggressive fibromatosis” were identified.

Exclusion criteria were patients in whom fewer than four post-operative MRIs were performed, patients with abdominal AF, and patients in whom examinations other than MRI had been conducted (n = 30). Furthermore, 37 patients (15 from sarcoma center 1 and 22 from sarcoma center 2) were excluded due to insufficient imaging data. Four postoperative MRI follow-ups per patient were regarded as the minimum of follow-up for this study and corresponded to a follow-up period of one year. This minimum period of follow-up was intended because the retrospective evaluation of recurrences and postoperative changes became clearer over this minimum follow-up. Finally, 38 patients from sarcoma center 1 and 41 patients from sarcoma center 2 were included in this study. For statistical purposes, the last examination of each patient and those examinations in which proof of predictive values could not be determined due to incomplete reference follow-ups were excluded (n = 97). Ultimately, 232 and 266 follow-up MRIs from sarcoma center 1 and 2, respectively, were included and systematically reviewed (Fig. 1). All patients with lesions suspected of being recurrences received either core-needle or open biopsy. Both radiologists and surgeons identified the most suspect localizations for biopsy by consensus. In these cases, the pathological results were set as reference for MRI follow-ups. In all other cases, MRI follow-up images were taken as the basis for comparison showing whether lesions had been overlooked in the previous MRIs. MRI follow-ups were performed after 3–6 months. Post-operative MRI follow-up was routinely performed three to four times in the first postoperative year, twice in the second postoperative year and afterwards once a year. The mean MRI follow-up period was 32 months (Min.: 12, Max.: 67) and the mean number of MRI follow-up per patient was 6 examinations (Min.: 4, Max.: 10). The median age of the patients was 38.1 years (Min.: 14, Max.: 78). 51.9 % of the patients were female (n = 41).

Recurrence lesions with a mean diameter of up to 1 cm were defined as small lesions.

Two dedicated musculoskeletal radiologists with a minimum of five years of experience in sarcoma diagnostics reviewed each MRI, with findings reached by consensus.

2.0.2. Magnetic resonance imaging

At both sarcoma centers, all patients were examined by using a 1.5-T MRI system (MAGNETOM Aera or MAGNETOM Symphony, Siemens Healthineers, Erlangen, Germany). The following MRI sequences were used: T2-weighted (T2w) TSE (TE: 64–114 ms, TR: 3010–5840 ms, FOV: 22–44 cm²), T1-weighted (T1w) SE (TE: 10–14 ms, TR: 587–868 ms, FOV: 22–44 cm²), proton density-weighted (PDw) FS (TE: 26–36 ms, TR: 2740–4610 ms, FOV: 22–40 cm²), or Turbo-Inversion Recovery Magnitude (TIRM) (TE: 68–77 ms, TR:4410–6980 ms, FOV: 37–45 cm²) and contrast-enhanced T1w SE FS (10–13 ms, TR: 533–1440 ms, FOV: 22–45 cm²).

2.0.3. Statistical data

Diagnostic accuracy was determined by calculating predictive values (positive and negative), sensitivity, specificity, and accuracy using Fisher’s exact test and 2 × 2 tables. The 95 % confidence interval was determined using Wald’s method. Statistical significance for all tests was set at a level of p < 0.05. Statistical analysis was performed using the IBM-SPSS version 22.0 software package (IBM, Armonk, NY, USA).

2.0.4. Ethics approval

The study was approved by the local institutional review board (IRB).

3. Results

The most common localization of AF was the axilla/shoulder (n = 15), followed by the thigh (n = 11) and the chest wall (n = 9;
Of the patients 27.9 % presented with recurrences (n = 22) and, in total, 30 recurrent lesions were identified. Two patients with recurrences needed unscheduled MRI examination due to clinical symptoms. All other patients showed their recurrences on routine MRI follow-up. From the 498 postoperative MRI follow-ups, 24 true-positive, 16 false-positive, 6 false-negative, and 452 false-positive MRI follow-ups were identified (Table 1). The overall sensitivity and specificity for detecting recurrent AF was 80 % and 97 %, respectively (Table 2). The sensitivity was slightly higher at sarcoma center 2 than at sarcoma center 1 (83 % and 78 %, respectively). The specificity was 97 % at both sarcoma centers. There was no significant difference in the diagnostic values at of the two sarcoma centers. At sarcoma center 1, diagnoses were false positive for 7 lesions and false negative for 4 lesions, while the data from sarcoma center 2 showed 9 false-positive and 2 false-negative results. All false-negative results were found in small lesions, which were difficult to distinguish from the surrounding postoperative and post-radiogenic tissue. 32 % of the patients underwent radiation therapy after primary tumor resection. Post radiation changes were associated with an increased severity for the readers but had no significant impact on the diagnostic accuracy.

The false-positive lesions mimicked streaky (n = 10), small ovoid/nodular (n = 5), or fascicular lesions (n = 1).

The configuration of most of the recurrent AF was fascicular (50 %; p = 0.001–0.005; Fig. 3). Other configurations of recurrent AF were streaky (n = 7), ovoid/nodular (n = 5), and polycyclic/multilobulated (n = 3; Table 3).

4. Discussion

In our study we investigated the long-term MRI performances of two multidisciplinary sarcoma centers in detecting AF recurrences. Furthermore, we investigated how recurrent AF are configured on MRI. AF, also called desmoid-type fibromatosis, is a rare benign (myo) fibroblastic tumor with a locally aggressive but slow growth [4]. The peak incidence is between 25 and 35 years of age [4,17]. AF counts less than 3 % of all soft tissue tumors and occurs in 2–4 per million people [10,18]. As shown in our study, AF has a female predominance [4]. Although mainly presenting as a deep soft tissue mass and infiltrating into the surrounding soft tissue, AF is usually painless [4]. Histologically, AF consists of spindle-shaped cells, which are surrounded by keloid-like collagen and often form fascicles [4,7,19]. This tumor is regarded as a very unpredictable disease with high local recurrence rates and local control remains challenging [17,20]. Our data confirm a high recurrence rate, as previously reported [21–24]. Nevertheless, surgery is still regarded as the primary therapy for AF [20] and radiation therapy is used additionally in some cases, like in our study [23]. Due to the relatively high rate of recurrences and because AF lesions are clinically often silent, the focus of postoperative surveillance is on postoperative imaging. MRI is the imaging modality of choice for both preoperative staging of AF and also for postoperative surveillance of primary AF [9,11,25]. Nowadays, contrast-enhanced MRI is usually performed in patients with soft-tissue tumors, both at primary diagnosis and at MRI follow-up, as distinguishing postoperative soft-tissue changes and recurrent tumor often poses a challenge on conventional MR sequences. The postoperative tissue often presents a heterogeneous signal intensity and diffuse contrast enhancement, which may mimic tumor recurrences. Previous authors stated that the use of contrast agent significantly affects the diagnostic performance of MRI.

Table 1

<table>
<thead>
<tr>
<th>Detection of aggressive fibromatosis</th>
<th>Combined</th>
<th>Sarcoma Center 1</th>
<th>Sarcoma Center 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
</tr>
<tr>
<td>True positive</td>
<td>24</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>False positive</td>
<td>16</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>False negative</td>
<td>6</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>True negative</td>
<td>452</td>
<td>207</td>
<td>245</td>
</tr>
<tr>
<td>Total</td>
<td>498</td>
<td>232</td>
<td>266</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Detection of aggressive fibromatosis</th>
<th>Combined</th>
<th>Sarcoma Center 1</th>
<th>Sarcoma Center 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>0.8 (95 % CI: 0.61–0.92)</td>
<td>0.78 (95 % CI: 0.52–0.94)</td>
<td>0.83 (95 % CI: 0.52–0.98)</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.97 (95 % CI: 0.95–0.98)</td>
<td>0.97 (95 % CI: 0.93–0.99)</td>
<td>0.97 (95 % CI: 0.93–0.98)</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>0.6 (95 % CI: 0.47–0.72)</td>
<td>0.67 (95 % CI: 0.48–0.81)</td>
<td>0.53 (95 % CI: 0.36–0.69)</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>0.99 (95 % CI: 0.97–0.99)</td>
<td>0.98 (95 % CI: 0.96–0.99)</td>
<td>0.99 (95 % CI: 0.97–1)</td>
</tr>
<tr>
<td>Accuracy</td>
<td>0.96 (95 % CI: 0.93–0.97)</td>
<td>0.95 (95 % CI: 0.92–0.99)</td>
<td>0.96 (95 % CI: 0.93–0.98)</td>
</tr>
</tbody>
</table>
improves the diagnostic accuracy of MRI in detecting tumor recurrences, as the specificity increases up to 97 % [8,13]. The main differential diagnosis of AF by imaging is soft-tissue sarcoma (STS) [25]. While some authors previously investigated the diagnostic accuracy of MRI for detecting STS, studies on the diagnostic accuracy of MRI in identifying recurrent AF do not exist yet. Accordingly, no study has investigated the long-term diagnostic performance of MRI in detecting recurrent AF in a real-world cohort. Del Grande F. et al. described a sensitivity and specificity of 100 % and 97 %, respectively, for contrast-enhanced MRI in detecting STS recurrences [8]. Moulten et al. assessed a sensitivity and specificity of 82 % and 86 %, respectively, for recurrent STS [26]. The specificity and sensitivity reported by Lin Y et al. was 96 % and 88 % for detecting soft-tissue sarcoma recurrences [27]. In a study comparing MRI to PET-MRI, Erfanian et al. calculated a sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of 82 %, 86 %, 92 %, 71 % and 83 %, respectively, for the detection of local tumor recurrences by using MRI [28]. In a recent review, Pennington A. et al. calculated a mean sensitivity and specificity of 88 % and 86 %, respectively, for local recurrences of vertebral primary tumors [29]. The overall sensitivity and specificity in our study was 80 % and 97 %, respectively. In our experience, post-treatment surveillance of AF is more challenging than for STS, as AF is normally located close to the muscle fascia and may infiltrate the muscle tissue, which may render it difficult to distinguish AF recurrences from the surrounding muscle tissue, especially when soft-tissue edema is present [2,11]. The treatment of choice for AF is wide excision, often with additional radiation therapy [9]. Nevertheless, outcome of surgery is often unsatisfactory for AF, as AF is highly variable and unpredictable tumor that may range from spontaneous regressions to rapid progression in the disease course [10]. Owing to their unpredictable behavior, the optimal postoperative management of AF lesions is still not unique [15]. Therefore, active surveillance represents the main approach to postoperative management of AF [17]. Here, an important task is assigned to MRI, as described. Consequently, it is very important to know about the characteristics of AF on MRI. In this study, we did not examine the signal

Table 3
Configuration of recurrent Aggressive Fibromatosis on MRI. Statistical significance was determined with $p < 0.05$ being significant.

<table>
<thead>
<tr>
<th>Configuration of recurrent AF</th>
<th>Combined</th>
<th>Sarcoma Center 1</th>
<th>Sarcoma Center 2</th>
<th>p-value (Sig. &lt; 0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fascicular</td>
<td>15</td>
<td>9</td>
<td>6</td>
<td>$p = 0.001 - 0.005$</td>
</tr>
<tr>
<td>Streaky</td>
<td>7</td>
<td>4</td>
<td>3</td>
<td>–</td>
</tr>
<tr>
<td>Ovoid/nodular</td>
<td>5</td>
<td>3</td>
<td>2</td>
<td>–</td>
</tr>
<tr>
<td>Polycyclic/multilobulated</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>18</td>
<td>12</td>
<td>–</td>
</tr>
</tbody>
</table>
characteristics of recurrent AF, as these findings have already been described in detail in recent studies [3,7,16,25,26]. Accordingly, AF are homogeneously isointense on T1-weighted images, show a high signal on T2-weighted and STIR images, and present a marked and heterogeneous contrast enhancement [2,25]. A simple, new approach involves morphologically characterizing AF by defining the configuration of AF on MRI. The configuration of primary and recurrent AF was described in a recent study. Both primary and recurrent AF most often presented as masses with a fascicular configuration [11]. Nevertheless, that study only included few samples of recurrent AF and did not find any statistical significance for recurrent AF. Therefore, we analyzed the configurations of recurrent AF in a larger cohort with data from two sarcoma centers. Accordingly, our data showed that recurrent AF presents significantly most often with a fascicular configuration. Nevertheless, AF may appear in different shapes, as other authors have previously reported [5,11,25,36]. Other configurations were streaky, ovoid/nodular, or polycyclic/multilobulated.

All false-negative results in our study were found in small lesions, which were very difficult to distinguish from the surrounding postoperative tissue. In our experience, the combination of small lesions and postoperative edema of the surrounding soft tissue renders postoperative MRI surveillance challenging. Although it is already known that radiation therapy causes an increased rate of soft tissue edema [31], post-radiation changes have no significant influence on the diagnostic accuracy in our study. Nevertheless, our experience shows that post-radiation changes make the detection of recurrences more difficult. Most of the false-positive lesions mimicked streaky and small ovoid/ -nodular tumors, as the postoperative tissue often shows streaky or focal postoperative changes, which are difficult to distinguish from real recurrences and which ultimately may lead to unnecessary biopsies of the postoperative tissue [8,11]. Unfortunately, no imaging technique exists to solve this problem in such cases, as even additional diffusion-weighted images (DWI) have limitations in small lesions. As Del Grande et al. described, small lesions of soft-tissue tumors are even more difficult to detect on DWI than by using conventional MRI sequences [8]. Recurrences with a fascicular or polycyclic/multilobulated configuration are easier to detect and distinguish from the postoperative soft tissue. Accordingly, distinctly post-therapeutic changes and microscopic positive margins are regarded as the main reasons for false-negative and -positive results, respectively [32]. Precise diagnostic accuracy of MRI would be important to reduce misdiagnosis. Therefore, it is very important to know how well MRI performs in the postoperative surveillance of AF patients in a real-world cohort over a long time period and to recognize possible pitfalls. Our data showed that MRI is a highly valuable imaging modality in the long-term postoperative surveillance of AF patients. Nevertheless, we found some false-positive and -negative results. By knowing about the configurations of recurrent AF and the reasons for false-positive and -negative results, diagnostic accuracy could be improved. Furthermore, in uncertain cases, MRI should be repeated after 3 months, as in our experience, recurrent AF most often presents as progressive disease in the subsequent follow-up MRI. A previous study showed that most recurrences of AF occur within the first 9 postoperative months and the first postoperative year is the most critical one for recurrences [11]. From our experience a postoperative surveillance of AF is indicated for 5 years after primary tumor resection with a close MRI follow-up within the first two years. Accordingly, MRI should be performed four times a year in the first year, twice a year in the second year and can be expanded to up to once a year for the following three years. The fact that nearly all of our recurrences were clinically silent shows the importance of routine MRI follow-up in the postoperative control of AF patients.

The main limitation of our study is the retrospective design. Nevertheless, AF is a very rare tumor, making prospective studies on this topic very difficult. Furthermore, not all patients received a biopsy and pathological examination. In many patients in whom biopsy was not performed, MRI follow-ups were set as reference. Although the reviewers’ rate of error is very low due to their exact assessment, smaller errors cannot be excluded here. Another limitation of this study is the lack of diffusion weighted images (DWI), which were only available in a few and mainly recent examinations.

5. Conclusion

MRI shows a high diagnostic value in detecting AF recurrences in a long-term setting. Nevertheless, radiologists should pay attention to small recurrent lesions, which might be misdiagnosed or mistaken as post-therapeutic tissue. Furthermore, post-therapeutic changes might mimic streaky or ovoid/nodular lesions. Although the configuration of recurrent AF is most often fascicular, it may also appear in different shapes.

Transparency document

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

CRediT authorship contribution statement

Sam Sedaghat: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data curation, Writing - original draft, Writing - review & editing, Visualization, Supervision, Project administration. Maya Sedaghat: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Visualization. Sebastian Krohn: Formal analysis, Methodology, Writing - review & editing. Olav Jansen: Conceptualization, Methodology, Validation, Investigation, Writing - review & editing, Visualization, Supervision. Kai Freudenthal: Methodology, Validation, Writing - review & editing, Visualization. Arne Streiburger: Formal analysis, Resources, Writing - review & editing, Visualization. Benjamin Reichardt: Methodology, Validation, Formal analysis, Investigation, Resources, Data curation, Writing - review & editing, Visualization, Supervision, Project administration.

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