



Radiological criteria for atypical features of femur fractures: what we can learn when applied in a clinical study setting

E.S. LeBlanc¹ · A.G. Rosales¹ · H.K. Genant² · R.M. Dell³ · D.M. Friess⁴ · D.L. Boardman⁵ · A.C. Santora⁶ · D.C. Bauer² · A.E. de Papp⁶ · D.M. Black² · E.S. Orwoll⁴

Received: 20 February 2018 / Accepted: 21 January 2019 / Published online: 26 February 2019
© International Osteoporosis Foundation and National Osteoporosis Foundation 2019

Abstract

Summary The paper focuses on the identification of atypical fractures (AFFs). This paper examines the concordance between objective classification and expert subjective review. We believe the paper adds critical information about how to apply the American Society of Bone and Mineral Research (ASBMR) criteria to diagnose AFFs and is of high interest to the field.

Introduction Assess American Society of Bone and Mineral Research (ASBMR) criteria for identifying atypical femoral fractures (AFFs).

Methods Two orthopedic surgeons independently evaluated radiographs of 372 fractures, applying ASBMR criteria. We assessed ease of applying ASBMR criteria and whether criteria-based assessment matched qualitative expert assessment.

Results There was up to 27% uncertainty about how to classify specific features. 84% of films were classified similarly for the presence of AFF according to ASBMR criteria; agreement increased to 94% after consensus meeting. Of 37 fractures categorized as AFFs based on ASBMR criteria, 23 (62.2%) were considered AFFs according to expert assessment (not relying on criteria). Only one (0.5%) femoral shaft fracture that did not meet ASBMR criteria was considered an AFF per expert assessment. The number of major ASBMR features present (four vs five) and whether there was periosteal or endosteal thickening (“beaking” or “flaring”) played major roles in the discrepancies between ASBMR criteria-based and expert-based determinations.

Conclusions ASBMR AFF criteria were useful for reviewers but several features were difficult to interpret. Expert assessments did not agree with the ASBMR classification in almost one-third of cases, but rarely identified an AFF when a femoral shaft fracture did not meet ASBMR AFF criteria. Experts identified lateral cortical transverse fracture line and associated new-bone formation along with no or minimal comminution as crucial features necessary for the definition of atypical femoral fractures.

Keywords Atypical femur fracture · Bisphosphonate · Fracture · Osteoporosis

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s00198-019-04869-z>) contains supplementary material, which is available to authorized users.

✉ E.S. LeBlanc
Erin.S.LeBlanc@kpchr.org

¹ Kaiser Permanente Center for Health Research NW, 3800 N. Interstate Ave, Portland, OR 97227, USA

² University of California, San Francisco (UCSF), San Francisco, CA, USA

³ Kaiser Permanente Southern California, Cypress, CA, USA

⁴ Oregon Health & Science University (OHSU), Portland, OR, USA

⁵ Kaiser Permanente Northwest, Hillsboro, OR, USA

⁶ Merck & Co., Inc, Kenilworth, NJ, Kenilworth, NJ, USA

Introduction

Atypical femur fractures (AFFs) are rare types of fractures that are associated with long-term bisphosphonate use more often than other femoral fractures [1, 2]. Correct identification is critical for epidemiological study of femoral fractures as well as in clinical practice, where early identification could alter treatment. Unfortunately, there is no gold standard (or “truth”) for assessing whether femoral fractures are atypical. To help in identifying AFFs, the American Society of Bone and Mineral Research (ASBMR) convened a multidisciplinary, international task force in 2009, releasing a case definition of AFF in 2010 [3] and revising it in 2013 [4]. The definition is intended to provide more guidance concerning the radiographic features that distinguish AFFs from other osteoporotic femoral fractures and to facilitate research and clinical care.

The 2013 ASBMR case definition requires AFFs to be in the subtrochanteric or diaphyseal region of the femur above the distal metaphyseal flare and divides characteristics into major features (four of five are required) and minor features (may or may not be present). Major features include transverse configuration at the lateral cortex, no or minimal comminution, complete fracture or incomplete fracture involving only the lateral cortex, periosteal or endosteal thickening at the fracture site, and no or minimal trauma (Supplementary Table 1). Minor features include generalized cortical thickening of the femoral shaft, bilateral fractures, history of prodromal pain, and delayed healing.

Ideally, criteria to identify AFFs should be relatively unequivocal and consistently applied by radiologists, orthopedic surgeons, and other physicians assessing femoral fractures. To evaluate whether 2013 criteria meet these goals, we examined data from our recent study, BEAK2 [5], which applied the criteria to femoral fractures in a community-based sample.

Two experienced orthopedic surgeons independently re-evaluated a set of previously reviewed femoral fractures [6]. In addition to assessing the fractures using 2013 criteria, they rated their degree of uncertainty regarding each feature. They also rated each fracture based on their own assessment (i.e., expert opinion) of whether it was an AFF, independent of the specific ASBMR criteria. Our goal was to assess how easily and consistently the 2013 criteria could be applied in a clinical study setting, the extent to which the ASBMR task force definition matched expert assessment, and whether experts relied on particular features during assessment. We hypothesized that expert assessment of AFF would closely match AFF determination using 2013 AFF ASBMR criteria.

Methods

Fracture identification

Fractures reviewed were drawn from the BEAK1 study [6], which was conducted in a cohort of women aged 50 and older and men aged 65 and older who were members of Kaiser Permanente Northwest (KPNW), a federally qualified health maintenance organization. In BEAK1 [6], femur fractures that occurred between January 1, 1996, and June 30, 2009, were identified through electronic medical record data and expert medical chart reviews. Two BEAK1-experienced orthopedic surgeons (BEAK1 primary reviewers; DMF, DLB; Supplementary Table 2), blinded to patients' clinical histories except for gender and age and blinded to previous ratings of the fractures, reviewed all available radiographs (pre-, intra-, or post-op) of fractures identified through chart reviews as being in the femoral shaft (subtrochanteric to upper two-third femur, unspecified femoral shaft, proximal femur below the lesser trochanter, mid-shaft) and distal femur (distal one-third femoral

shaft/other above-the-knee femur) and a random sample of fractures in the femoral neck and intertrochanteric region. AFF assessment was based on the 2010 ASBMR AFF criteria [3]. Fractures examined in BEAK2 comprise all of those categorized by BEAK1 reviewers as being in the femoral shaft or distal femur and 15% of those in the intertrochanteric region ($N = 372$; Fig. 1). This research was reviewed and approved by the KPNW Institutional Review Board.

Radiology review of fractures using 2013 ASBMR criteria

An expert panel (ESL, HKG, RMD, DMB, DCB, ESO, DMF, DLB, ACS, AdP) developed radiograph review procedures, a review form, and operational definitions based on 2013 ASBMR criteria (Supplementary Table 3). It was required that fractures be located along the femoral diaphysis from just distal to the lesser trochanter to just proximal to the supracondylar flare in order to be considered as AFFs. If the fracture was considered to be in that location (i.e., considered a femoral shaft fracture (FSF)), the reviewers answered additional “yes” and “no” questions about whether it met the 2013 ASBMR AFF radiological major (transverse configuration at the lateral cortex, no or minimal comminution, complete fracture or incomplete fracture involving only the lateral cortex, periosteal or endosteal thickening at the fracture site) and minor (generalized cortical thickening of the femoral shaft, bilateral fractures) features (Supplementary Table 1).

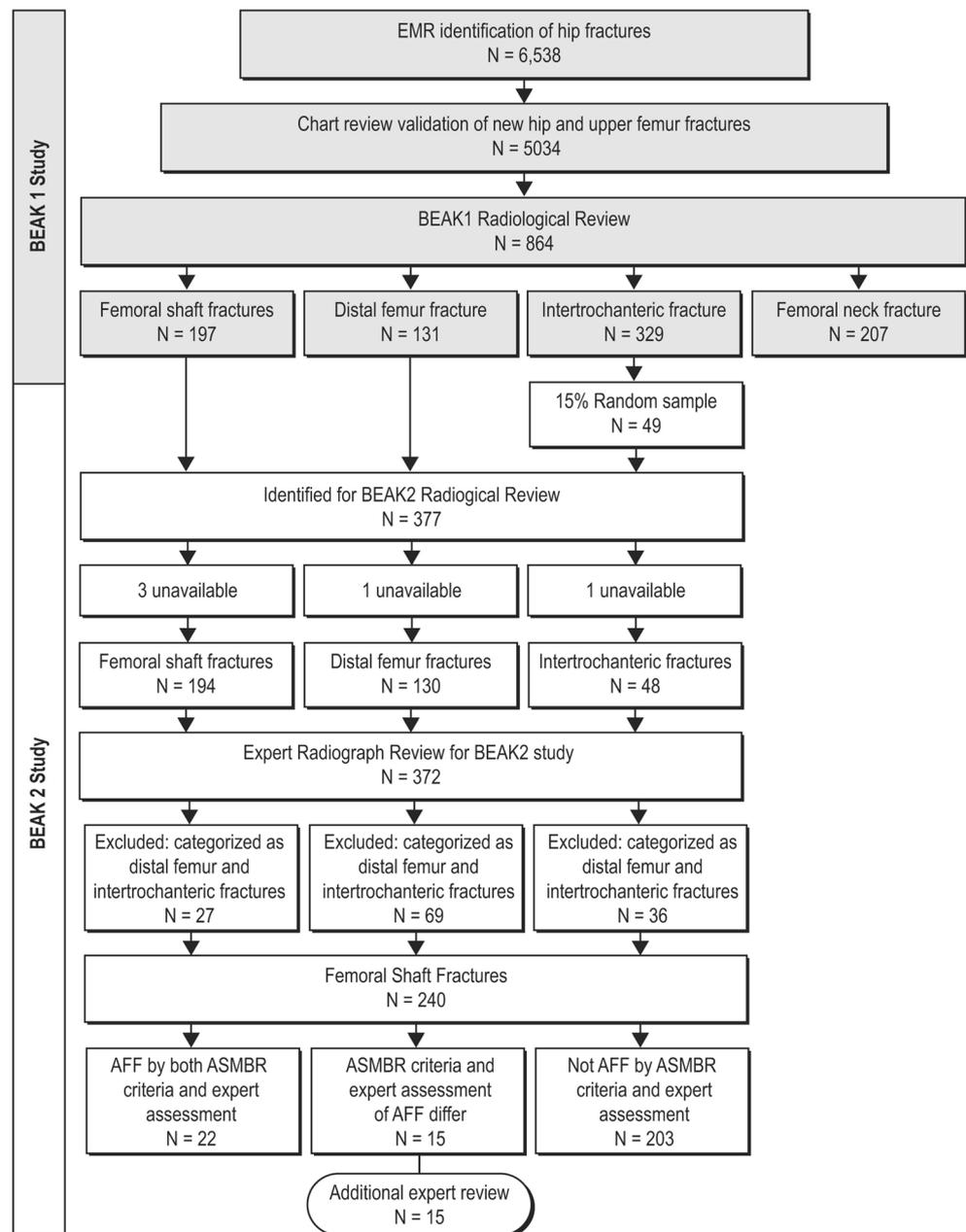
Several features were not re-assessed during BEAK2 as they had been determined via chart review during BEAK1 as follows: whether fractures occurred with no or minimal trauma (major feature) and whether there was prodromal pain (minor feature). BEAK1 assessments were carried forward to BEAK2. Delayed healing (minor feature) was not captured in either study. Only 81 films had bilateral views of the contralateral area.

The BEAK2 primary reviewers (DMF, DLB; Supplementary Table 2) independently analyzed 100 training films (mix of AFF and typical FSF fractures) that had been compiled by an expert panel member (RMD). A BEAK2 adjudicator (HKG) also assessed the radiographs. The entire panel reviewed disagreements to clarify criteria and refine the abstraction process and form.

After training was completed and issues resolved, the BEAK2 primary reviewers independently examined the radiographs ($N = 372$; Fig. 1). They were blinded to previous readings, each other's assessments, and participants' clinical background other than gender and age range (5-year increments).

In addition to marking whether each major and minor feature was present based on 2013 ASBMR Task Force definitions [4], the BEAK2 primary reviewers qualified their answers, if necessary, by marking “uncertain,” meaning they were not sure how to characterize a response but felt the radiographic views were adequate, or “indeterminate due to

Fig. 1 Diagram of study flow



Grey boxes were completed during BEAK1 study and unshaded boxes occurred during BEAK2 study.

insufficient views,” meaning they did not have adequate views to fully assess a specific feature.

Expert assessment of fractures

At the end, we requested BEAK2 primary reviewers’ overall qualitative expert assessments of the fracture’s AFF status by asking: “Based upon radiographic appearance, was this event an AFF (general feeling about radiograph—do not have to rely specifically on the criteria marked)?” Reviewers were encouraged to use their overall assessment of the fracture’s

likelihood of being an atypical fracture, regardless of the number of criteria marked.

Consensus and adjudication

When there was disagreement about whether the fracture was in the femoral shaft, whether major or minor features were present, or whether the fracture was an AFF according to expert assessment, the BEAK2 primary reviewers examined films jointly to attempt to reach consensus. If consensus could not be reached, the BEAK2 adjudicator made the determination about whether the fracture met AFF criteria.

Additional expert review

To further evaluate fractures for which BEAK2 primary reviewers' assessments and ASBMR criteria determination did not match, the adjudicator and the additional panel member—serving as secondary BEAK2 reviewers (RMD, HKG; Supplementary Table 2—re-examined the radiographs ($N = 15$; Fig. 1). Information about whether the fracture had been rated an AFF according to ASBMR criteria or expert assessment was available to the secondary BEAK2 reviewers. They were asked, “Do you agree that the fracture is an AFF?” They were also asked to identify “possible reasons for difference between objective and subjective readings.” Each was blinded to the response of the other reviewer. The following outcomes were tracked as follows: (1) one or both secondary BEAK2 reviewers agreed with the expert assessment of the primary BEAK2 reviewers and (2) neither reviewer agreed with the assessment (i.e., both agreed with ASBMR criteria).

Statistical methods

The fractures on which there was an agreement as to location in the femoral shaft are included in this report ($N = 240$; Fig. 1). Using consensus results, we classified fractures as meeting ASBMR criteria for AFFs if they met four of five major features. Minor features did not need to be present for a fracture to be categorized as an AFF per ASBMR criteria (Supplementary Table 1).

We examined the initial agreement between the primary BEAK2 reviewers on each of the major and minor 2013 criteria, the ASBMR classification of AFF, and their assessment of AFF. For each feature, we also tabulated how often one or both reviewers expressed uncertainty about their response (uncertain) or felt the images (quality or views) were insufficient, resulting in uncertainty (indeterminate).

We compared fracture categorization as defined by the 2013 ASBMR criteria to the primary reviewers' consensus expert assessment. In the subset of radiographs that the secondary BEAK2 reviewers also reviewed ($N = 15$), we examined whether their assessment agreed with the ASBMR classification or the primary reviewers' assessment. Finally, we examined the number of major and minor features present in the 37 fractures deemed AFFs according to ASBMR criteria, stratified by expert assessment.

Results

Level of uncertainty about specific features

Table 1 displays the uncertainty associated with the assessment of each feature. The most common feature to be marked as uncertain or indeterminate in initial review was periosteal or endosteal thickening (marked by one or both primary

Table 1 Uncertainty during radiological review

All fractures reviewed ($N = 372$)	At least one reviewer marked uncertain* and/or indeterminate** N (%)
Femoral shaft fracture	1 (0.3)
Femoral shaft fractures ($N = 240$)	
Major features	
Transverse configuration	27 (11.3)
Minimal or no comminution	18 (7.5)
Complete fracture (or incomplete only involving lateral cortex)	4 (1.7)
Periosteal or endosteal thickening	64 (26.7)
Minor features	
Generalized cortical thickening	14 (5.8)
Bilateral fracture***	7 (8.6)
Overall	
AFF by expert assessment****	19 (7.9)

*Uncertain meant reviewer was unsure about response but views were adequate to evaluate that feature

**Indeterminate meant reviewer was unsure about response because views were not adequate to evaluate that feature

***Only 81 had bilateral films of contralateral area

****Response to the following question: “Based on radiographic appearance, was this event an AFF (general feeling about radiograph—do not need to rely on criteria marked)”

BEAK2 reviewers in 27% of cases). Transverse configuration was marked by at least one reviewer in 11% of cases, while the other features were marked less than 10% of the time.

Agreement between reviewers

Agreement between the primary BEAK2 reviewers after their first readings ranged from 63 to 100% for specific major and minor 2013 features (Table 2). There was high agreement (> 90%) on the major features of periosteal or endosteal thickening and complete fracture (or incomplete involving lateral cortex) and on both of the minor features. There was less agreement (80%) on the presence of a transverse configuration, with disagreements often occurring when the overall fracture was oblique but the lateral cortex portion was transverse. The lowest level of agreement was reached on comminution (63%), primarily because one reviewer coded films as having minimal comminution when fragment lengths were > 2 cm of length; after reviewing the definition of comminution that had been developed during the training sessions (Supplementary Table 3), it was agreed that fragment lengths of this size should be considered more than minimally comminuted. After the initial review, 84.1% of the films (191) received the same classification regarding the presence or absence of AFF according to the 2013 definition. For the overall expert assessment (not based on ASBMR criteria), the initial agreement was higher (96%).

Table 2 Presence of specific AFF features and level of agreement

Features	Feature determined to be present after consensus <i>N</i> (%)	Agreement after first review <i>N</i> (%)	Consensus after second review <i>N</i> (%)	Adjudicated (unable to reach consensus) <i>N</i> (%)
All fractures reviewed	<i>N</i> = 372	<i>N</i> = 372	<i>N</i> = 372	<i>N</i> = 372
Femoral shaft fracture	240 (64.5)	330 (88.7)	372 (100.0)	0
Femoral shaft fractures reviewed further by both reviewers	<i>N</i> = 240	<i>N</i> = 227	<i>N</i> = 240	<i>N</i> = 240
Major features				
Transverse configuration	64 (26.7)	179 (78.9)	227 (94.6)	13 (5.4)
Minimal or no comminution	143 (59.6)	143 (63.0)	236 (98.3)	4 (1.7)
Complete fracture (or incomplete only involving lateral cortex)*	240 (100.0)	226 (99.6)	240 (100.0)	0
Periosteal or endosteal thickening	22 (9.2)	220 (96.9)	239 (99.6)	1 (0.4)
Minimal or no trauma**	215 (89.6)	n/a	n/a	n/a
Minor features				
Generalized cortical thickening	22 (9.2)	219 (96.5)	240 (100.0)	0
Bilateral fracture***	3 (1.3)	78 (96.3)	79 (97.5)	2 (2.5)
Prodromal pain**	16 (6.7)	n/a	n/a	n/a
Overall				
AFF per ASBMR criteria****	37 (15.4)	191 (84.1)	226 (94.2)	14 (5.8)
AFF per expert assessment*****	24 (10.0)	217 (95.6)	238 (99.2)	2 (0.8)

*All were complete fractures

**Carried forward from previous chart review; not re-reviewed for this study

***Only 81 had bilateral films of contralateral area

****Whether film met 4 of 5 major ASBMR features (not necessarily same features)

*****Response to the following question: “Based on radiographic appearance, was this event an AFF (general feeling about radiograph—do not need to rely on criteria marked)?”

The major feature that required adjudication was transverse configuration (consensus was not reached and adjudication was required in 13 cases [5%]). For the other major criteria, disagreements occurred in fewer than 3% of cases. After consensus review, agreement about the presence or absence of AFF according to the 2013 ASBMR definition rose to 94%, and agreement on the overall expert assessment (not based on ASBMR criteria) was even higher (99%).

ASBMR criteria compared with reviewer assessment

Of the 37 fractures categorized as AFFs based on ASBMR criteria, 14 (38%) were not considered AFFs based on expert assessments by primary BEAK2 reviewers (not relying on ASBMR criteria; Table 3; example radiograph in Fig. 2). Of the 203 fractures identified as not being AFFs based on ASBMR criteria, one (0.5%) was considered to be an AFF by the primary reviewers.

Secondary assessment

The secondary BEAK2 reviewers examined the 15 fractures that were categorized differently according to the ASBMR

definition and primary reviewer assessment. In 14 (93%) of these cases, at least one secondary reviewer agreed with the primary reviewers' assessment that the fracture was an AFF. In only one case did both secondary reviewers agree with the ASBMR classification of the fracture as an AFF rather than with the primary reviewers' assessment that it was a non-atypical FSF. This fracture was noted as difficult to assess because there was already callus formation.

Table 3 Concordance between ASBMR 2013 criteria and expert assessment of AFF

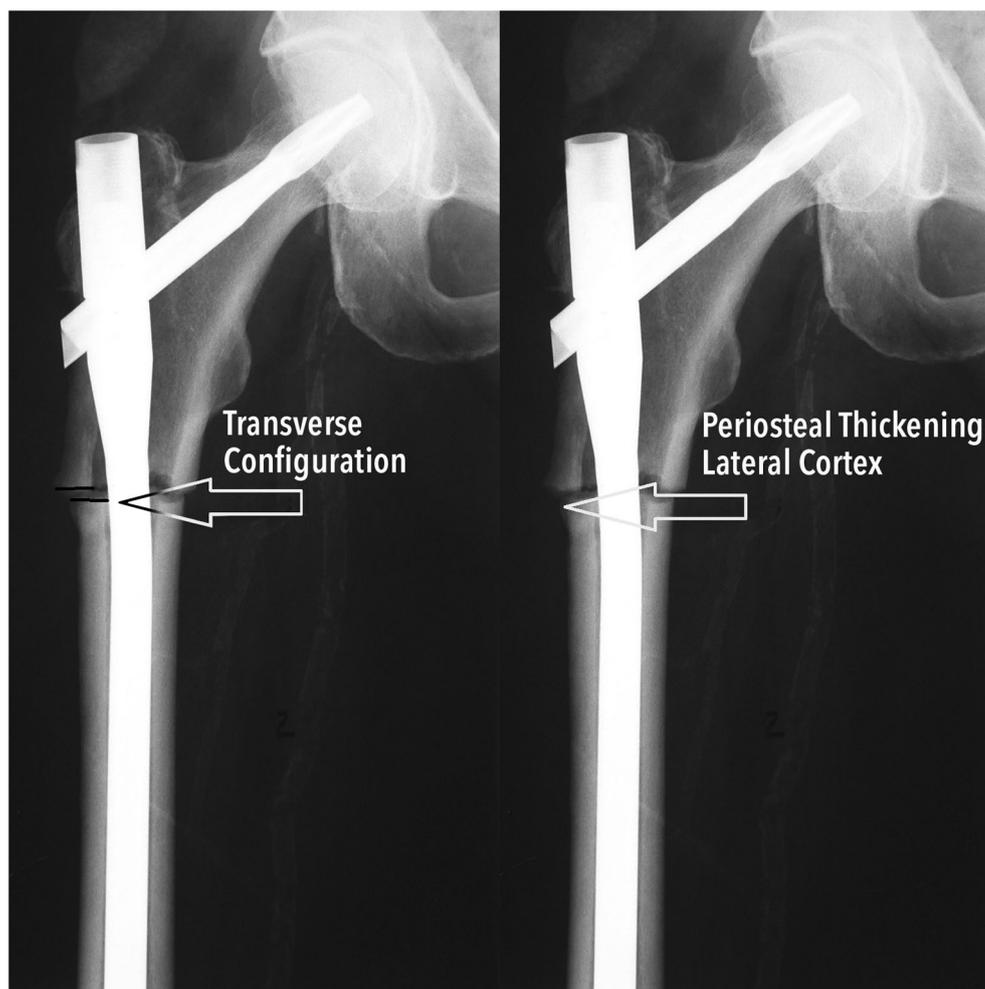
ASBMR 2013 case definition of AFF (4 or 5 major features, regardless of minor features)	Expert assessment*		
	<i>N</i>	Yes	No
Yes <i>N</i> (%)	37	23 (62.2)	14** (37.8)
No <i>N</i> (%)	203	1*** (0.5)	202 (99.5)

*Expert assessment by the two primary reviewers (DMF, DLB)

**Additional review by 2 experts (HKG and RMD) agreed with original expert assessment in 13 of 14 cases

***Additional review of this case by 2 experts (HKG and RMD) agreed with original expert assessment

Fig. 2 a, b Example of fracture determined to be AFF because it met all five major ASBMR features. The black line in panel **a** indicates the transverse configuration of the fracture and the white arrow in panel **b** shows the periosteal/endosteal thickening



Reasons for discrepancy between ASBMR criteria and expert assessment

AFFs with all five major ASBMR features, (Fig. 2) especially those with at least one minor feature, were more often considered AFFs according to primary reviewers' assessment (Table 4). For example, while only 49% of fractures categorized as AFF by ASBMR criteria had five major features, 74% of fractures considered AFFs by expert assessment had all five major features. On the other hand, while 51% of fractures categorized as AFFs by ASBMR criteria had four major features, 26% of AFFs by expert assessment only had four major features, and the presence of minor features did not seem to impact expert assessment when just four features were present.

The lack of periosteal or endosteal thickening was the key major feature that accounted for the discrepancy between AFF determination per ASBMR criteria vs expert assessment. While 60% of the fractures determined to be AFFs by ASBMR criteria had periosteal thickening, 83% of the fractures determined to be AFFs by expert assessment had

periosteal or endosteal thickening. For example, the fracture shown in Fig. 3 had four major features (transverse configuration, minimal or no comminution, complete fracture, and no trauma) but did not have any periosteal or endosteal reaction. Periosteal or endosteal thickening was determined by expert reviewers to be of such critical importance that they determined it was not an AFF despite having the other four major ASBMR criteria.

Of the fractures determined to have periosteal or endosteal thickening during primary review, only three were not considered AFFs during expert review. In these cases, the periosteal thickening that had been determined to be present when this feature was examined on its own (not considering the other fracture features) was not as clearly evident when the whole fracture was reviewed at once. For example, the fracture shown in Supplemental Fig. 1 was categorized as having localized periosteal reaction of the lateral cortex when just that feature was assessed. However, when the radiograph was reviewed overall and the presence of other AFF features were considered, expert opinion was that the “beak” more likely represented the rotated fracture fragment and the fracture was

Table 4 2013 ASBMR criteria features present in AFFs, according to expert assessment

	AFFs by ASBMR criteria (<i>N</i> = 37)		
		AFFs by expert assessment*	Not AFFs by expert assessment*
Number of major ASBMR features	<i>N</i> = 37 <i>N</i> (%)	<i>N</i> = 23 <i>N</i> (%)	<i>N</i> = 14 <i>N</i> (%)
5 major features, <i>N</i> (%)	18 (48.6)	17 (73.9)	1 (7.1)
4 major features, <i>N</i> (%)	19 (51.4)	6 (26.1)	13 (92.9)
Presence of minor features			
5 major features with at least one minor feature, <i>N</i> (%)	11 (29.7)	11 (47.8)	0
4 major features with at least one minor feature, <i>N</i> (%)	7 (18.9)	3 (13.0)	4 (28.6)
Presence of specific features in ASBMR criteria			
Major features			
Transverse configuration, <i>N</i> (%)	37 (100.0)	23 (100.0)	14 (100.0)
Minimal or no comminution, <i>N</i> (%)	36 (97.3)	23 (100.0)	13 (92.9)
Complete fracture (or incomplete involving lateral cortex), <i>N</i> (%)	37 (100.0)	23 (100.0)	14 (100.0)
Periosteal or endosteal thickness, <i>N</i> (%)	22 (59.5)	19 (82.6)	3 (21.4)
Minor features			
Generalized cortical thickening, <i>N</i> (%)	13 (35.1)	10 (43.5)	3 (21.4)
Bilateral fracture**, <i>N</i> (%)	0	0	0

*Expert assessment by the two primary reviewers (DMF, DLB)

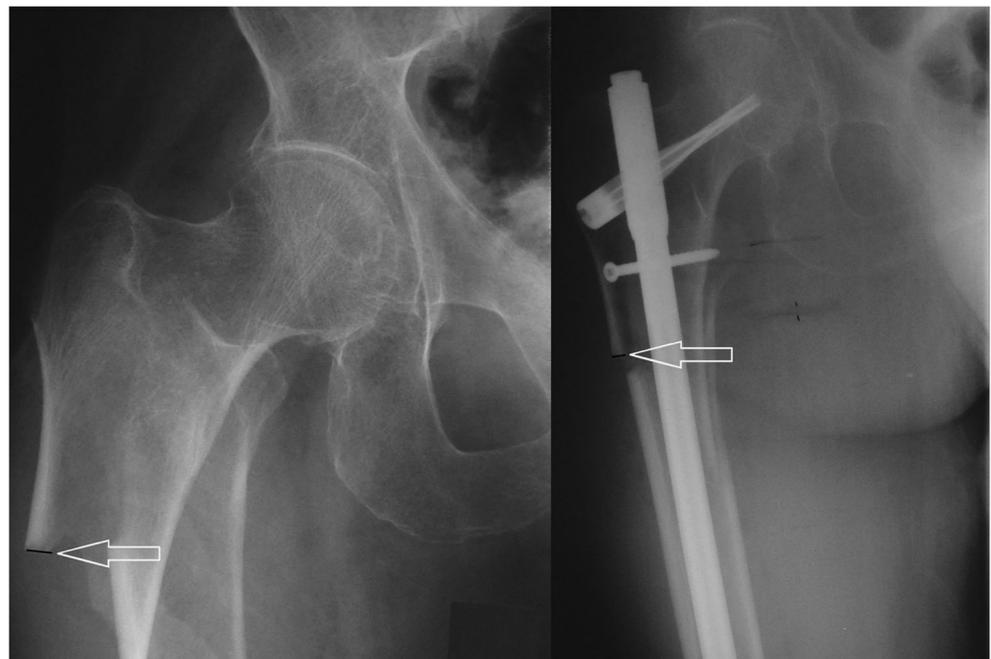
**Only 81 had bilateral films of contralateral area

not an AFF. Similarly, during review for specific ASBMR features, the fracture shown in Supplemental Fig. 2 was determined to have cortical thickening about the fracture site. Because this fracture was transverse in configuration, had minimal or no comminution, and was complete, it met four major ASBMR criteria and was labeled as an AFF. However,

when the fracture was reviewed overall (and not for each specific feature), expert opinion was that the thickening at the fracture site was more likely to be healing callus on a postoperative radiograph and was not any atypical process.

In terms of minor features, 44% of the AFFs by expert opinion had generalized cortical thickening compared with

Fig. 3 a, b Radiograph of fracture that met ASBMR AFF criteria but was not felt to be an AFF by expert assessment. Although the fracture had four major features (transverse configuration [marked by dark black line], minimal or no comminution, complete fracture, and no trauma), it did not have any periosteal or endosteal reaction. The lack of periosteal or endosteal thickening was determined by the expert reviewers to be of such critical importance that they determined this fracture was not an AFF (despite having the other four major ASBMR criteria)



21% of those not considered AFFs by expert opinion. No AFFs per ASBMR criteria had bilateral fractures (but only 34% of fractures had sufficient bilateral views to assess for this feature).

Discussion

We found that application of the ASBMR case definition can be challenging. Despite our reviewers' extensive training, uncertainty remained about how to rate specific features, especially periosteal or endosteal thickening and transverse configuration. The primary BEAK2 reviewers agreed on the ASBMR classification of AFFs on 84.1% of the films after initial independent review. After meeting, they agreed on 94.2%, illustrating that the criteria may be open to interpretation. In contrast, there was high agreement as to whether the fracture was an AFF by expert reviewer assessment (i.e., not relying on the number of features marked); there was agreement on 95.6% of the films after the independent reviews, which rose to 99.2% after the consensus meeting.

More than one-third of fractures classified as AFFs when applying the 2013 ASBMR criteria were not considered AFFs according to expert assessment. If fractures had all five major ASBMR features, a high percentage were considered AFFs according to expert assessment, especially if there was at least one minor feature present. If there were four major features present, only about one-third were considered AFFs, and not even half were considered AFFs if even a minor feature was present in addition to the four major features.

A main reason for the discrepancy between ASBMR criteria and expert assessment was that expert reviewers determined that periosteal and endosteal thickening was a critical feature that needed to be present for an AFF to be diagnosed; however, to be an AFF by ASBMR criteria, only four features were required, meaning that 40% of fractures labeled as being AFF by ASBMR criteria did not have periosteal or endosteal thickening. Therefore, future consideration should be given to requiring all major features or particular patterns of features.

Discrepancy between ASBMR criteria and expert assessment also arose because of differences in assessment procedures. During the primary review, reviewers assessed whether each individual ASBMR criteria was present, regardless of the overall characteristics of the fracture or whether other features were present. In contrast, during expert assessments, reviewers assessed the overall fracture, using ASBMR major and minor features as a guide, but not strictly following the guideline that any four major features must be present. Reviewers weighed each factor differently depending on radiographs and participants' age and gender, relying heavily on the presence of a lateral cortical transverse fracture line and associated new-bone formation along with no or minimal comminution. In fact, features that were difficult to assess

during the primary review but determined to be present (such as periosteal thickening) were sometimes no longer determined to be present when the fracture was assessed overall during expert review, which involved taking into consideration all of the fracture's characteristics. This suggests that identification of AFF can be relatively straight forward and consistent when the images are evaluated by a reviewer with expertise in AFF, especially when all of the criteria are considered together. However, when an AFF occurs soon after the stress reaction and there has been little chance for the bone to mount a healing response, identification can be more difficult, especially if the reviewer is less experienced. In these cases, reliance on identifying four of five criteria rather than looking at all of the features together can lead to variable AFF case ascertainment. We suggest that future updates of the guidelines should consider explicitly stating that the pathology of AFF starts in the lateral cortex of the femur. This is the region of high tension forces to which the surrounding bone attempts to react, leading to a progressive thickening of bone endosteal/periosteal either focally or occasionally over a larger region. In particular, we suggest considering changing or adding the phrase "the fracture generally occurs at the level of the femur at the greatest thickness of the lateral cortex for several centimeters proximal or distal to the fracture line." We believe it is often easier to judge local maximal cortex thickening than to judge minimal focal new-bone formation (i.e., the beak/flare).

Limitations

Reviewers were given only the age range and gender of participants and relied solely on the radiological impression. In clinical practice, decisions about whether a fracture is an AFF are also based on clinical history. Although one major ASBMR feature—whether the fracture is traumatic—is a clinical factor, other factors of importance (including the minor features of prodromal pain) are not required in the definition. However, the reviewers felt that in a clinical setting, such factors could play a key role when assessing whether a fracture was an AFF and that they would not rely solely on radiological interpretation.

The study was also limited by the small number of AFF cases and its retrospective nature, with fractures occurring 10 to 15 years prior to the study. This meant that some fractures had radiographic views that were inadequate for an accurate estimate of the presence or absence of some major features. Few radiographs of subjects' contralateral femurs were available, and comparison to the contralateral femur is an important component of overall clinical assessment. We also had limited pre-fracture films, which can allow examination of bone changes over time, and lacked high-quality intra-operative or early post-operative films, which can be helpful when there is rotation and flexion of the extremity at the fracture site. Reviewers had previously reviewed the films using the earlier

ASBMR criteria although they were unaware of their previous readings of the film. Radiographs were from any time point (i.e., pre- or post-op), which is different than a clinical setting where decisions are made on emergency room films.

Conclusions

Emphasizing the importance of lateral cortex changes and periosteal and endosteal thickening in the ASBMR criteria would likely increase concordance between the ASBMR classification and expert assessment. Our study suggests that more specific definitions of the features in the ASBMR criteria would be useful to others interpreting films for clinical decision-making, epidemiological research, and improving our understanding of the pathophysiology of these fractures.

Acknowledgments We are grateful to Donna Gleason for her assistance with data collection, Katie Essick for editorial assistance, and Cassandra Angus for manuscript preparation.

Source of funding Funded by a research grant from Merck Sharp & Dohme Corp. All final decisions about study design, analysis, and paper content were made by the lead author, who is not employed by the sponsor.

Compliance with ethical standards

Conflicts of interest Erin LeBlanc's and Ana G. Rosales's institutions received a grant from Merck & Co., Inc. to conduct this work. Erin LeBlanc's institution has also received grant funding from Amgen, Astra Zeneca, and Bristol Meyer Squibb for unrelated projects on which she was principal or co-investigator; however, these other projects do not reflect a conflict of interest. Arthur Santora was an employee of Merck during this work but has since retired; he currently has stocks, stock options, and pension from Merck. Anne de Papp is a current employee of Merck & Co., Inc. Harry Genant, Richard Dell, Darin Friess, David

Boardman, Douglas Bauer, Anne de Papp, Dennis Black, and Eric Orwoll declare that they have no conflict of interest.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

1. Adler RA, El-Hajj Fuleihan G, Bauer DC et al (2016) Managing osteoporosis in patients on long-term bisphosphonate treatment: report of a task force of the American Society for Bone and Mineral Research. *J Bone Miner Res* 31:1910
2. Black DM, Rosen CJ (2016) Clinical Practice. Postmenopausal Osteoporosis. *N Engl J Med* 374:254–262
3. Shane E, Burr D, Ebeling PR, Abrahamsen B, Adler RA, Brown TD, Cheung AM, Cosman F, Curtis JR, Dell R, Dempster D, Einhorn TA, Genant HK, Geusens P, Klaushofer K, Koval K, Lane JM, McKiernan F, McKinney R, Ng A, Nieves J, O'Keefe R, Papapoulos S, Sen HT, van der Meulen MCH, Weinstein RS, Whyte M (2010) Atypical subtrochanteric and diaphyseal femoral fractures: report of a task force of the American Society for Bone and Mineral Research. *J Bone Miner Res* 25:2267–2294
4. Shane E, Burr D, Abrahamsen B, Adler RA, Brown TD, Cheung AM, Cosman F, Curtis JR, Dell R, Dempster DW, Ebeling PR, Einhorn TA, Genant HK, Geusens P, Klaushofer K, Lane JM, McKiernan F, McKinney R, Ng A, Nieves J, O'Keefe R, Papapoulos S, Howe TS, van der Meulen MCH, Weinstein RS, Whyte MP (2014) Atypical subtrochanteric and diaphyseal femoral fractures: second report of a task force of the American Society for Bone and Mineral Research. *J Bone Miner Res* 29:1–23
5. LeBlanc ES, Rosales AG, Black DM et al (2017) Evaluating atypical features of femur fractures: how change in radiological criteria influenced incidence and demography of atypical femur fractures in a community setting. *J Bone Miner Res* 32:2304–2314
6. Feldstein AC, Black D, Perrin N, Rosales AG, Friess D, Boardman D, Dell R, Santora A, Chandler JM, Rix MM, Orwoll E (2012) Incidence and demography of femur fractures with and without atypical features. *J Bone Miner Res* 27:977–986