MR imaging in patients with knee injury

An observational study in general practice

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MR Imaging in Patients with Knee Injury
an Observational Study in General Practice

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een observationele studie in de huisartsenpraktijk

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GENERAL INTRODUCTION

Posttraumatic knee complaints are a frequent reason for consultation in primary or secondary care. The reported incidence in general practice ranges from 1.1 to 1.4%.[1, 2] The incidence of posttraumatic knee complaints in secondary care is more difficult to establish, because clinical research in this area is usually limited to specific patient groups (such as children or sport players).[3-6] Nonetheless, also in the hospital setting knee complaints are common.

Clinical research in the field of posttraumatic knees is usually carried out in a hospital setting and only covers serious or persistent injuries. The obtained information is not representative for patients presenting in primary care. Data on patients with knee complaints in general practice are limited to cross-sectional studies that report on the incidence and prevalence of diagnostic codes and referral rates to medical specialists or physical therapists.[2]

Since the introduction of MR imaging, several studies have reported on the appearance of normal and abnormal cruciate ligaments, collateral ligaments and menisci. Compared to arthroscopy, which is considered the reference standard, the sensitivity and specificity of MR images are high for detecting abnormalities in these structures.[7-10] Therefore, MR imaging is widely used to evaluate knee symptoms, and clinical decision-making is influenced by the results of these scans.[11-13]

There are no data available on the prevalence of internal knee lesions as seen on MR imaging in posttraumatic patients in primary care. Ligamentous, meniscal, and osseous lesions have all been described in posttraumatic knees. However, abnormalities (especially meniscal lesions) are also present in up to one third of asymptomatic knees,[14-17] especially in elderly patients.[14, 15] Therefore, after trauma, it is questionable which visualized lesions are the result of the recent trauma and which lesions might have been pre-existent. In the absence of a recent MRI scan (as is often the case), it is not possible to discriminate between pre-existent and new lesions. There is little knowledge on the natural course and functional outcome of posttraumatic knee lesions, but this kind of information is necessary to make management decisions and to inform patients about their prognosis.

With the advent of MR imaging, a new diagnosis was described: occult bone injury or occult intraosseous fracture.[18-20] These lesions are called occult because no abnormalities are seen on conventional radiographs and in direct observation (arthroscopy) they would be hidden by the overlying cartilage. There is little histological evidence of such lesions, later also referred to as bone bruises. After trauma, they are presumably the result of microfracture of the medullar trabeculae.[19, 20] In the available histological studies, hemorrhage and edema are found in the region of signal abnormalities.[21-23] Mink et al. suggested that bone bruise is a benign disorder,[19] but a later report concluded that, because it is associated with increased disability in patients with anterior cruciate ligament ruptures, it might not be entirely benign.[24] Studies that provide follow-up information on bone bruise describe a natural healing,[25, 26] but also osteochondral sequelae.[27, 28] Because none of these studies used a structured follow-up, the exact natural course is not known. There is no knowledge on determinants of bone bruise. Also, there is virtually no knowledge on the relation between pain and bone bruise. Therefore, it is not possible to provide adequate information to a patient presenting with bone bruise, with respect to prognosis and treatment protocol.

To address the gaps in the available information, we performed two systematic reviews on the natural course of internal knee lesions and bone bruise. We also performed a prospective, observational cohort study of patients with acute posttraumatic knee complaints, presenting in primary care.

STUDY AIMS

The primary objectives of our study were as follows:

1. To summarize available knowledge on the natural course of ligamentous and meniscal knee lesions as seen on MR imaging;
2. To summarize available knowledge on the natural course of bone bruises, as seen on MR imaging;
3. To describe the prevalence of MRI abnormalities in posttraumatic and contralateral knees and to determine whether abnormalities seen on MRI in posttraumatic knees are a result of the recent trauma or might be pre-existent;
4. To evaluate the prevalence and severity of bone bruise in posttraumatic knees in general practice and to describe possible determinants of bone bruise;
5. To evaluate the natural course of posttraumatic bone bruise by using a structured MRI follow-up, and to look for prognostic factors on this course;
6. To evaluate the relationship between the presence (and course) of bone bruise and pain severity.

OUTLINE OF THESIS

The first part of this thesis includes the general introduction and study aims.

In the second part of this thesis, the results of two systematic reviews are presented. In the first review (Chapter 2), the current evidence on follow-up of MRI-detected posttraumatic ligamentous and meniscal knee lesions is summarized. In the second review (Chapter 3), the available knowledge on follow-up of bone bruise is presented.

In the third part of this thesis, the results of our observational cohort study are presented. That is, in Chapter 4 we give complete information on the design of this study. In Chapter 5 we focus on the prevalence of abnormalities in posttraumatic (symptomatic) and contralateral knees. Analyses on the possible pre-existence of knee lesions are given. Chapter 6 focuses on the prevalence and possible determinants of bone bruise. In Chapter 7 our analyses on the follow-up of bone bruise are presented, whereas Chapter 8 focuses on the clinical consequences (especially pain) of bone bruise.

In the final part of this thesis, the findings described in this thesis are discussed (Chapter 9), and summarized (Chapter 10). Chapter 10 also includes the conclusions of this thesis.

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Part Two

Chapter 2

Follow-up of MRI-detected posttraumatic ligamentous and meniscal knee lesions: a systematic review

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ABSTRACT

Purpose To perform a systematic review of the literature regarding the natural course of ligamentous and meniscal knee lesions detected at magnetic resonance (MR) imaging.

Materials and Methods The MEDLINE database was searched from January 1966 to February 2003. Studies were included if all of the following criteria were met: patients had collateral ligament, cruciate ligament, or meniscal lesions; MR imaging was performed in all patients; study included a group and/or subgroup of patients who underwent conservative treatment during follow-up; patients returned to the clinic for follow-up and clinical data or MR imaging outcomes were noted; and article was written in English, Dutch, German, French, Spanish, Italian, Swedish, Danish, or Norwegian. The quality of each study was assessed by using a standardized criteria set, and kappa statistics were used to grade the level of agreement between the two reviewers. Studies with quality scores of eight or more were designated as high quality. Results were compared with regard to study design and quality scores.

Results The literature search identified 649 articles, and 11 studies (five on posterior cruciate ligament [PCL] injuries, five on anterior cruciate ligament [ACL] injuries, and one on meniscal injuries) met the inclusion criteria. No studies on the follow-up of collateral ligament injuries were identified. Four studies were of high quality, and the kappa value for quality items was 0.80. Between 77% and 93% of the partial or complete PCL ruptures regained continuity. In cases of partial or total ACL rupture, repair of continuity was also possible. A possible association between MR imaging continuity and clinical stability was identified.

Conclusion The ACL and PCL can regain continuity after partial or complete rupture. On the basis of this review, no conclusions can be drawn about the natural course of meniscal or collateral ligament injury seen at MR imaging.

INTRODUCTION

Every year, many patients seek medical treatment for a knee injury (incidence 1.1 to 1.4%).[1, 2] Since the introduction of MR imaging, several studies have reported on the appearance of normal and abnormal cruciate ligaments, collateral ligaments and menisci. Compared to arthroscopy, which is considered the reference standard, the sensitivity and specificity of MRI are high for detecting abnormalities in these structures.[3-6] In their recent meta-analyses, Oei et al. described a 79% sensitivity for lateral meniscal tears and 94% sensitivity for posterior cruciate ligament (PCL) tears.[6] Specificity ranged from 88% for medial meniscal tears to 99% for PCL tears.[6]

Treatment of posttraumatic knee lesions remains controversial, especially regarding conservative versus operative treatment of cruciate ligament tears. The decision to reconstruct the injured ligament depends on many factors, such as the severity of rupture, combined or isolated injury, physiologic skeletal maturity, activity level, and type and severity of symptoms.[7-9] Satisfactory functional results have been reported in conservatively treated patients with PCL tears,[10, 11] and natural healing might occur in anterior cruciate ligament (ACL) tears. Proponents of surgical treatment, however, report that fewer degenerative changes are seen following regained joint stability after surgery than are demonstrated with conservative treatment.[12, 13]

Because the functional outcome and healing process of knee lesions remains unclear, treatment remains controversial. MR imaging, however, allows non-invasive diagnosis and gradation of the severity of knee injury. To date, few researchers have reported on the sequential imaging of patients with knee injuries to establish whether changes in appearance occur during the early months of healing, and few have reported on functional outcome (e.g. athletic activity) of patients with knee lesions seen with MR imaging. Therefore, the purpose of this study was to perform a systematic review of the literature regarding the natural course of ligamentous and meniscal knee lesions detected on MR imaging.

MATERIALS AND METHODS

Identification and selection of the literature

A search of relevant publications on the natural history of posttraumatic knee lesions detected at MR imaging was performed by two authors (SSB and SMABZ). The search was conducted by using the Medline database (January 1966 to February 2003). The terms *collateral ligament, cruciate ligament,* and *meniscus* were linked by the Boolean operator OR. The Boolean operator AND was used to link the terms *follow-up*, *knee*, and *MRI*, which were linked to the previous set of terms (i.e., *collateral ligament, cruciate ligament*, and *meniscus*) by using the Boolean operator AND. For each of the keywords, one or more synonyms were used (Appendix 2). The search was extended by screening the reference list (by SSB and SMABZ) of all relevant articles identified. A study was considered eligible for inclusion in this review if it fulfilled all of the following criteria: *(a)* patients had collateral ligament, cruciate ligament or meniscal lesions, *(b)* MR imaging was performed in all patients at baseline, *(c)* the study included a group and/or subgroup of patients who underwent conservative treatment during follow-up (no surgery for ligament reconstruction or meniscal debridement or repair), *(d)* after the initial diagnosis, patients returned to the clinic for follow-up, and clinical data or MR imaging outcomes were noted, *(e)* the article was written in English, Dutch, German, French, Spanish, Italian, Swedish, Danish or Norwegian.

Quality assessment

Because variation in the internal validity of studies may influence the results and conclusions of a systematic review, the quality of each included study was assessed using the following procedure. Two reviewers (SSB and SMABZ) independently scored the quality of the selected studies using a set of criteria, which were previously published in the field of musculoskeletal disorders, and which were modified to cover the topic of our review (Table 2.1).[14] Items were given a binary score of one if a particular criterion was fulfilled, and items were given a binary score of zero if the criterion was not fulfilled or if it was unclear whether the criterion was fulfilled. The final quality score of each study was based on the sum of the individual scores. In case of disagreement, both reviewers discussed the scores to achieve a consensus.

Table 2.1. Criteria used for quality score

1.	consecutive patients enrolled
2.	description of setting
3.	time between trauma and MR imaging described
4.	researchers blinded to clinical and functional outcome during MR image interpretation
5.	description of symptoms
6.	description of inclusion and exclusion criteria for surgery
7.	prospective study design
8.	cohort of 100 or more patient-years
9.	cohort of 50 or more patient-years
10.	cohort of 20 or more patient-years
11.	follow-up period 3 months or greater
12.	drop-out rate of 20% or less
13.	information provided on patients who completed study vs. those that were lost to follow-up[a]
14.	description of conservative treatment

Note - For each item, reviewers assigned a binary score of 1 or 0. [a] For this criterion, a binary score of 1 was assigned when information was provided concerning three or more of the following items: sex, age, severity of lesion, type of lesion, isolated or multiple lesions, and knee load.

A prospective cohort study is judged as the preferred study design. In most systematic reviews, studies receiving a quality score of more than 50% of available quality points are considered 'high quality'. In our study, 14 quality items were scored. Therefore, studies receiving a quality score eight points or more were considered 'high quality'.

Data extraction

Two authors (SSB and SMABZ) extracted the main characteristics of each study - that is, study center, study design (retrospective or prospective), study population (consecutive patients, inclusion criteria, and number of participants), and follow-up period. Results from the different studies were also extracted and included description of the initial lesions at MR imaging, clinical follow-up (patient complaints and physical examination results), MR imaging follow-up, and association between MR imaging and clinical findings at follow-up.

Data analysis

A kappa statistic was used to rate the level of agreement between the two reviewers on each quality item, and studies were ranked according to their quality score. Because the observational studies in this review were considered to be heterogeneous with regard to follow-up, study population, quality, and outcome measures, we refrained from statistical analyzing the pooled data. Owing to the scarcity of data, the main statistic tool that was used was the analysis of counts and proportions. The kappa statistic was estimated by using SPSS (version 11.0.1, SPSS Inc., Chicago, Ill).

We compared the results of the different studies with regard to the quality score (i.e., high score [eight or greater] versus low score [less than eight]), and the study characteristics.

RESULTS

Identified studies and their characteristics

The primary literature search identified 649 references. On the basis of the title and abstract, 31 articles were read completely. Of these, 10 articles met our inclusion criteria. After screening the reference lists, another study (on ACL lesions) was included, resulting in 11 included articles. Of these, there were five studies on PCL injuries, five on ACL, and one on meniscal injuries.[15-25] No studies on the follow-up of collateral ligament injuries were identified. Nine articles were published in English, and two were written in Italian.

One study on ACL lesions included three different follow-up periods.[21] Because each follow-up period had a different quality score, this study was ranked according to the highest score.

Table 2.2. Characteristics and quality assessment of studies on the follow-up of knee lesions detected on MR imaging

Reference	Study centre	Inclusion criteria	N	Follow-up (average)	quality criteria[a] and quality score 1	2	3	4	5	6	7	8	9	10	11	12	13	14	sum
PCL injury																			
Griffin [15]	Orthopedic clinic, Atlanta, GA, USA	Isolated PCL injury (physical examination)	8	6-34 months	+	+	+	+	+	-	?	-	-	-	+	+	-	+	8
Akisue [16]	Orthopedic clinic, Japan	Acute isolated PCL injury noted in patient history and at physical examination	48	≥ 1 year (17 months)	-	+	-	-	+	-	?	-	-	-	+	+	+	+	6
Shelbourne [17]	Sports medicine centre, Indianapolis, IN, USA	Acute PCL injury at MR imaging performed more than 6 months earlier	40	3.2 years	+	+	+	-	-	-	-	-	+	+	+	-	-	-	6
Tewes [18]	Sports medicine centre, Minneapolis, MN, USA	Complete PCL tear at clinical examination, no other ligament abnormalities except grade I and II MCL injury, MR imaging performed within less than 10 weeks of injury, and grade III PCL injury noted at MR imaging	13	5-48 months (20 months)	?	+	+	+	-	-	-	-	-	+	+	+	-	-	6
Bellelli [19]	Radiology dept, Rome, Italy	Acute traumatic PCL injury at MR imaging	10	9-36 months (14.2 months)	+	-	-	-	-	-	+	-	-	-	+	+	-	-	4
ACL injury																			
Kocher [20]	Sports medicine division, tertiary-care children's hospital, Boston, MA, USA	Knee injury and acute hemarthroses, partial or complete ACL tear at MR imaging, Lachman and Pivot shift normal or near normal, and partial ACL tear at arthroscopy	45	2.3-11.6 years (mean 6.1)	+	+	+	-	-	+	+	+	+	+	+	+	+	+	12
Ihara [21]	Orthopedic surgery dept, Japan	Acute complete intraligamentous ACL rupture at MR imaging	50	3, 11, 24 months	+	+	+	+	-	-	+	-	-	-	+	+	+	+	9
Fujimoto [22]	Orthopedic clinic, Japan	Sedentary occupation and low athletic demand, acute ACL injury at physical examination and MR imaging, continuous ACL with area of high signal intensity at MR imaging, and no contralateral knee ligament injury	31	6-36 months (16.1 months)	?	+	-	-	-	+	+	-	-	+	+	+	+	+	8
Zugaro [23]	Radiology dept, Italy	Hyperacute and acute knee trauma; ACL injury at MR imaging	104	3-6 months	-	-	+	-	-	-	?	-	-	+	+	-	-	-	3
Zeiss [24]	Radiology dept, Toledo, OH, USA	ACL tear at clinical examination and MR imaging	71	6 months-2 years	?	?	+	-	-	-	?	-	-	+	+	-	-	-	3
Meniscal injury																			
Deutsch [25]	Radiology dept, Los Angeles, CA, USA	Tears of peripheral one-third of either meniscus, which were successfully treated with conservative treatment	6	3-13 months	+	-	-	-	-	-	-	-	-	-	+	+	+	+	5

Note - Studies are listed according to the highest total quality score for ACL, PCL, and meniscal injuries. ACL = anterior cruciate ligament, PCL = posterior cruciate ligament. [a] Quality criteria are listed according to the numbering system used in Table 2.1. For each criterion, reviewers assigned a binary score of 1 or 0. Question marks indicate an unclear presentation of a particular criterion within the study and were counted as a binary score of 0 for total quality score.

Regarding study characteristics seven studies were retrospective and four were prospective. In these studies the follow-up period ranged from three months to 11.6 years. All studies were hospital-based. The study population was generally small; in eight studies less than 50 patients were included (Table 2.2).

Quality assessment

The two reviewers scored 154 quality items and initially agreed on 139 items (kappa 0.80). The disagreements were resolved in a single consensus meeting; 14 disagreements were caused by inadequate documentation by the authors of the reviewed papers (especially regarding 'consecutive patients' and 'prospective or retrospective' study design).

The quality of the included articles was generally poor. Only four studies scored eight or more for the 14 available quality points (Table 2.2). The shortcomings generally involved a poor description of symptoms or inclusion criteria for surgery, a retrospective study design, a small study size, and insufficient information on loss to follow-up.

PCL injury

For the five studies on the natural course of a PCL tears, the study population ranged from eight to 48 patients and the quality scores ranged from four to eight out of a maximum of 14 points (Table 2.2).

No conflicting results were found (Table 2.3). In total (all study results combined), 81 patients had partial or complete PCL ruptures. Regained continuity was observed on MR imaging and ranged from 77% ($CI_{95\%}$ 46 to 95%) after 20 months of follow-up,[18] to 93% ($CI_{95\%}$ 80 to 98%) after 3.2 years of follow-up.[17] In two studies, all continuous ligaments showed altered morphology (elongation) at follow-up.[15, 17] In another study, two of six PCLs with regained continuity showed focal intraligamentous changes.[19]

In three studies, investigators described positive posterior drawer test results in the majority of patients at the follow-up physical examination. In one study, seven of eight patients had positive posterior drawer test results.[15] In two studies, all cases demonstrated positive posterior drawer test results.[16, 18] Furthermore, researchers emphasized that, although apparent MR imaging continuity does not guarantee normalization at physical examination, a continuous ligament results in a firmer endpoint more often than does a discontinuous ligament when the posterior drawer test is used.

In only three studies was follow-up MR imaging correlated with complaints and/or function.[15, 18, 19] Tewes et al. described no significant correlation between healing and clinical or functional status.[18] In the study by Griffin et al., all eight patients (seven in whom the lesions regained continuity) were without complaints at follow-up.[15] Bellelli reported complaints in only five patients with instability; four of these patients demonstrated an abnormal PCL at follow-up.[19] The five patients without instability showed natural repair of the PCL, but no reference was made to the subjective complaints in this group.[19]

Table 2.3. Follow-up of posterior cruciate ligament (PCL) lesions detected on MR imaging

Reference	Initial MRI lesion	Clinical follow-up	MRI follow-up	Association between MRI and clinical findings
Griffin [15]	5 complete and 3 partial ruptures	Seven patients had positive (1+) posterior drawer test results with a definitive endpoint, one had normal stress test results; all returned to previous occupations and recreational sports, and no complaints were noted	7 regained continuity with elongated appearance, 1 persistent loss of normal signal intensity	not described
Akisue [16]	38 patients did not undergo initial MR imaging and 10 PCLs were diffusely swollen and had increased signal intensity	48 patients had positive posterior instability	36 of 48 patients who underwent follow-up MR imaging demonstrated a slack but continuous low-signal-intensity PCL and eight of 10 patients who underwent initial MR imaging demonstrated a continuous PCL at follow-up MR imaging	MR imaging appearance related to presence of firm endpoint with posterior drawer test and less anteroposterior translation
Shelbourne [17]	four grade I, 14 grade II, 19 grade III, 3 grade IV injuries[a]; 23 isolated PCL ruptures,17 PCL and other ligament injury	not described	All grade I and II, 17 of 19 grade III, and two of three grade IV injuries regained continuity and 16 of 17 patients with combined lesions regained PCL continuity	not described
Tewes [18]	13 complete ruptures (Gross grade III); three additional MCL sprains, and two additional medial meniscal tears[b]	All patients had positive posterior drawer test results and all returned to former occupation	10 ruptures regained continuity and had altered morphologic features and three showed no continuity but abnormal PCL healing, with attachment of the stump to the accessory ligaments	No significant correlation between PCL continuity and clinical findings (pain, posterior sag, and patellofemoral crepitus), HSS radiographic score for degeneration[c], Lysholm functional score, satisfaction ratings, and changes in sport activities; inverted association between PCL continuity and HSS functional score; continuous PCL at MR imaging possibly related to presence of firm endpoint with posterior drawer test
Bellelli [19]	One Gross grade II, and nine Gross grade III ruptures[b]	Five patients had instability and subjective complaints and five had no instability	Six normal PCLs, two focal intraligamentous changes within continuous PCL, and two absent PCLs	Five patients had instability and subjective complaints (two had absent PCLs, two had PCLs with focal signal changes, and one had atrophic quadriceps muscle); five patients showed natural PCL repairs without instability

Note - MCL = medial collateral ligament. [a] Grade I injuries demonstrated edema on T2-weighted MR images and no disruption in the fibers or in the shape of the PCL; grade II injuries consisted of partial disruption of the PCL, with bridging fibers present; grade III injuries had no bridging fibers present; and grade IV injuries had no bridging fibers present and either fluid or fat interposed between the two ends of the torn PCL. [b] Gross grade II ruptures were defined as an alteration in signal intensity in the central or peripheral part of the ligament, and Gross grade III ruptures were defined as a loss in ligament continuity and/or full thickness interruption of normal low-signal-intensity areas by areas of high signal intensity on T2-weighted MR images. [c] HSS = Hospital for Special Surgery scoring scale.

ACL injury

For the five studies on the natural course of ACL tears, the study population ranged from 31 to 104 patients (Table 2.2). The quality score ranged from three to 12, with three studies scoring more than eight points. No conflicting results were found (Table 2.4). We refrained from pooling the results because of differences in rupture definitions and outcome measures.

In one high-quality study concerning 50 complete ACL ruptures, researchers found a normal ACL in 21 (42%) of 50 patients ($CI_{95\%}$: 28 to 57%) and a partial repair in 20 (40%) of 50 patients ($CI_{95\%}$: 26 to 55%) at 3-month follow-up; at 11-month follow-up, results showed that further repair was possible.[21] In another high-quality study on 31 partial ACL ruptures, researchers found a continuous ligament in 21 (68%) of 31 cases ($CI_{95\%}$: 49 to 83%) at an average of 16.1 months follow-up.[22] In low-quality studies, this healing capacity was also shown.

In three studies, investigators reported on the clinical follow-up of ACL injuries detected at MR imaging. In one study on adolescents, researchers found a diminished functional outcome for patients with ACL tears that were larger than 50% or for patients with tears in the posterolateral portion of the ACL.[20] In one study, authors described a diminished clinical outcome in the concurrent presence of bone bruise at baseline.[24] In two other studies, follow-up MR imaging was correlated with complaints and/or function; in both studies, a moderate association between normalization of ACL appearance and normal function was described.[22, 23]

Meniscal injury

In only one retrospective study did investigators report on the short-term follow-up of six meniscal lesions.[25] Because successful conservative treatment was one of the inclusion criteria in that study, no conclusions can be drawn about the natural course of meniscal lesions on MR images.

DISCUSSION

To our knowledge, our study is the first systematic review on the natural course of knee lesions detected at MR imaging. Although only 11 studies on this subject met our inclusion criteria and the quality scores were low, the results were generally consistent. Results of both high-quality and low-quality studies suggest that the PCL and the ACL can regain continuity after partial or total rupture. In cases of partial rupture or total rupture of the PCL, 77% to 93% of the ligaments regained continuity after six months to 4.5 years of follow-up. Ruptured ACLs regained continuity in a slightly lower proportion of cases: 42% of complete ruptures regained continuity after three months and 68% of partial ruptures

Table 2.4. Follow-up of anterior cruciate ligament (ACL) lesions detected on MR imaging

Reference	Initial MRI lesion	Clinical follow-up	MRI follow-up	Association between MRI and clinical findings
Kocher [20]	10 complete and 32 partial tears at MR imaging, three partial tears at arthroscopy, 17 concomitant meniscal tears, and nine MCL grade II sprains	Of the 31 tears without reconstruction, 13 were classified as Lachman grade A, 18 as Lachman grade B, 30 as pivot shift grade A, and one as pivot shift grade B; of the 14 ACL reconstructions, all were for complete ruptures[a]	not described	For patients who had undergone conservative treatment, diminished functional outcome was noted in those who had ACL tears that were larger than 50% and in those with tears in the posterolateral portion of the ACL
Ihara [21]	Complete intraligamentous ACL rupture	At 3 months, five of the 45 initial ruptures still had positive pivot shift; 46 ruptures had full range of motion	grade[b] I II III IV 3 months: 21 16 4 9 11 months: 14 8 3 4 24 months: 5 1 1 0 - Grade evaluation at 3 and 11 months significantly correlated ($r_s = 0.801$, $p < 0.0001$)	not described
Fujimoto [22]	Continuous ACL with area of high signal intensity	At 3 months, 23 patients regained knee stability, all with an endpoint on Lachman test; 16 had negative findings, seven had gliding pivot shift, 21 had no complaints, and two had pain during athletic activities; of the eight patients for whom reconstruction was performed, none regained endpoint on Lachman test at the time of the operation	At 3 months, 21 ACLs were continuous, with normal attachments and gradual reduction in MR imaging signal intensity; one ACL was attached to the PCL, and one was attached at a more anterior location on the lateral femoral condyle	In eight patients with instability who had undergone reconstruction, the ACL was unclear or had disappeared; no reduction in signal intensity was noted
Zugaro [23]	16 complete ruptures, 23 partial ruptures, and 65 enlarged and inhomogeneous ACLs	not described	Of the 16 complete ruptures, seven regained continuity, six regained partial continuity, and three were unchanged; of the 23 partial ruptures, 14 were unchanged and nine became complete ruptures; of the 65 enlarged ligaments, 53 maintained continuity and 12 became complete ruptures; in a subgroup of 60 continuous but inhomogeneous ligaments, 24 remained inhomogeneous (group A) and 34 regained normal morphologic characteristics and signal intensity (group B)[c]	In group A, 24 patients had laxity and two had normal function; in group B, 18 had laxity and 16 had normal function
Zeiss [24]	Five of 42 partial tears were high grade with bone contusion, 37 of 42 partial tears were low grade without bone contusion, and 21 of 29 complete tears had bone contusion (no follow-up)	not described	For partial rupture with bone contusion, four complete ACL ruptures were noted in 6 months; for partial rupture without bone contusion, six complete ACL ruptures were noted after 1–2 years of follow-up	not described

Note - MCL = medial collateral ligament, PCL = posterior cruciate ligament. [a] The Lachman side-to-side difference was 1–2 mm for grade A tears and 3–5 mm for grade B tears. Pivot shift grade A indicated equal, and Pivot shift grade B indicated glide. [b] Grade I ruptures consisted of a well-defined, normal-sized, and straight band of homogeneous low signal intensity. Grade II ruptures consisted of a well-defined straight band of low signal intensity with spotty areas of high signal intensity. Grade III ruptures consisted of a thin band of low signal intensity that contained a high-signal-intensity mass. Grade IV ruptures consisted of a dark band of signal intensity that was not discernable. [c] It was unclear whether additional MR imaging follow-up was performed, and it was unclear how the subgroup was defined.

regained continuity after six to 36 months. There seems to be a weak association, however, between continuity at MR imaging and clinical stability at follow-up.

Oei et al. previously found that MR imaging is highly accurate in facilitating the diagnosis of meniscal and cruciate ligaments tears.[6] In that study, no data on follow-up were used. In contrast, we were particularly interested in the natural course of such lesions. We found only one study on conservatively treated meniscal injuries.[25] However, because only six patients were followed up and because successful conservative treatment was one of the inclusion criteria in that study, we could not draw any conclusions on the natural history of meniscal injuries seen at MR imaging. A previous systematic review reported that there were no studies that described the conservative follow-up of meniscal injuries seen at arthroscopy or that compared conservative treatment with surgical treatment.[26] Because all the retrieved follow-up studies on meniscal injuries in that review concerned surgically treated menisci, the natural history of meniscal injuries remains unclear.[26]

A potential drawback of the present review might be the literature search. Although we used a sensitive set of keywords, we might have missed some relevant studies. Also, because our search was limited to indexed journals, unpublished studies and articles in nonindexed journals might have been missed. Finally, studies published in languages other than the nine we selected would have been missed. The study population for each of the included studies was generally small, and seven studies used a retrospective study design. Moreover, poor data documentation in some studies interfered with the assessment of quality scores. Furthermore, the quality of the studies was generally poor; only four studies scored more than eight quality points. Finally, because of heterogeneity in study design and data presentation, comparing the results was difficult, and quantitatively pooling the data was impossible. These factors hamper generalization of our results.

Results of previous studies on conservative treatment of acute ligament tears that were diagnosed with methods other than MR imaging (i.e., with clinical examination or arthroscopy) showed a large variability in findings. Many authors described a satisfactory functional result after conservative treatment of the ACL tears, especially after partial rupture.[27–32] Despite satisfactory to good functional results, there was often a reduction in activity and a change in the athletic performance of patients.[27, 29, 32] Return to sports without functional disabilities in the majority of conservatively treated patients with PCL lesions is also described.[33] Our results agree with those obtained in these studies. It seems that ruptured ligaments can regain continuity after conservative treatment in the majority of cases, which correlates with clinical stability.

We conclude that there is little knowledge on the association between the MR imaging appearance of ruptured cruciate ligaments, functional outcome scores, and complaints. For daily practice, it would be valuable to know whether there is a true association between normalization of MR imaging appearance and functional scores or whether the healing process seen at MR imaging predicts further functional recovery. If this is the case, one could choose to wait for follow-up MR imaging in eligible patients (patients with low functional demands and contraindications for surgery or patients who prefer to undergo conservative treatment) and to perform reconstruction only in cases of persisting abnormal MR imaging findings.

Further study with a longer follow-up period is needed to clarify the relationship between functional outcome, physical examination findings, and MR imaging results in patients with chronically injured knees. Clear data presentation is essential in order to judge the generalizability of the results. These studies should use a prospective study design, a clearly defined study population, a structured follow-up (including at least one physical and MR imaging examination), and an adequate follow-up period.

In conclusion, the ACL and PCL can regain continuity after partial or complete rupture. There is insufficient information on the natural history of collateral ligament and meniscal injuries detected at MR imaging.

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APPENDIX 2

Keywords used for the Medline search

keyword	synonym
collateral ligament	[collat* OR med* OR lat*] AND [ligam* OR band]
cruciate ligament	[cruc* OR oblique] AND [ligam* OR band]
meniscus	menisc*
follow-up	Predict* OR progres* OR heal* OR follow* OR prognos* OR course OR prospect* OR retrospect* OR natural OR long term
knee	knee
MRI	Magnetic resonance imaging OR MRI OR MR imaging OR proton spin tomography OR nuclear magnetic resonance OR NMR OR magnetic resonance tomography OR MR tomography

Chapter 3

Follow-up of MRI-detected occult bone lesions: a systematic review

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ABSTRACT

Purpose To perform a systematic review of the literature regarding the natural course of posttraumatic occult bone lesions (often referred to as bone bruises) detected at magnetic resonance (MR) imaging.

Materials and Methods A systematic review of the literature was performed by searching the MEDLINE database (from January 1966 to February 2003) with the keywords bone bruise, trauma, follow-up, and MRI. Keywords were linked by using the Boolean operator AND. Studies were included if all of the following criteria were fulfilled: patients sustained trauma, MR imaging was used as a diagnostic method, results of clinical or MR imaging follow-up were available, and study was written in English, Dutch, German, French, Spanish, Italian, Swedish, Danish, or Norwegian. The quality of each study was assessed by using a standardized criteria set, and kappa statistics were estimated to rate the level of agreement between the two reviewers. Results were compared with regard to study design and quality scores.

Results The MEDLINE search identified 266 articles, 13 of which met the inclusion criteria. The quality of the included studies was moderate. The two reviewers initially agreed on 179 quality items (kappa 0.84). The study population was generally small, and follow-up periods ranged from one to 73 months. Four different classification systems were used, and in two studies bone bruise was not specified. Study results suggest a generally good clinical prognosis of bone bruises. Normalization of MR imaging appearance is possible and is most often encountered after the occurrence of reticular lesions. Cartilage loss at follow-up is often found in cases of initial cartilage damage (impaction or osteochondral fracture).

Conclusion In general, a healing response was often encountered after sustained posttraumatic occult bone lesions. The initial MR imaging appearance appears to have prognostic value.

INTRODUCTION

Occult bone lesions (often referred to as bone bruises) are seen at magnetic resonance (MR) imaging as signal intensity abnormalities in the subchondral bone and bone marrow and represent a heterogeneous group of injuries. They are called occult because, at direct observation (i.e., at arthroscopy), such lesions would be hidden from view by the overlying cartilage (which may appear normal) and because no abnormalities are seen at conventional radiography. There is little histological evidence of such bone lesions; after trauma, they are presumably the result of microfracture of the medullar trabeculae.[1, 2] In histological studies, researchers have found hemorrhage and edema in the region of the signal intensity abnormalities.[3-5]

In the literature, different classification systems are used. Most authors use either the Mink and Deutsch classification system or the Vellet classification system. Mink and Deutsch defined four categories of occult fractures at the knee: bone bruise, stress fracture, femoral and tibial fracture, and osteochondral fracture.[1] Vellet et al. modified this classification system and defined five categories: reticular fracture, geographic fracture, linear fracture, impaction fracture, and osteochondral fracture.[6] Although bone bruises are often considered to be benign and self-limiting, this opinion seems to be primarily based on results from the earliest studies on this subject.[1, 2, 7] Most of these studies, however, included nonconsecutive patients and had a nonstructural follow-up or concerned only case reports. In more recent studies, researchers have described osteochondral sequelae after a sustained bone bruise.[6, 8-11] Thus, the true natural history of a bone bruise remains unclear. We believed that it is important to gain insight into the natural course of bone bruises detected at MR imaging and their clinical consequences. Thus, the purpose of our study was to perform a systematic review of the literature regarding the natural course of posttraumatic occult bone lesions (often referred to as bone bruises) detected at MR imaging.

MATERIALS AND METHODS

Identification and selection of the literature

Relevant publications on the natural history of posttraumatic occult bone lesions were searched by using the MEDLINE database (from January 1966 to February 2003). The MEDLINE search was performed by two authors (SSB, SMABZ). *Bone bruise*, *trauma*, *follow-up*, and *MRI* were used as keywords and were linked by using the Boolean operator AND. For each of the keywords, one or more synonyms were used (Appendix 3.A). The search was extended by screening the reference list of all relevant articles. A study was determined to be eligible for inclusion if it fulfilled all of the following criteria: *(a)* The study included

Table 3.1. Criteria used for quality score

1.	consecutive patients enrolled
2.	description of setting
3.	time between trauma and MR imaging described
4.	researchers blinded to clinical and functional outcome during MR image interpretation
5.	description of symptoms
6.	description of inclusion and exclusion criteria for surgery
7.	description of associated knee lesions
8.	prospective study design
9.	cohort of 100 or more patient-years
10.	cohort of 50 or more patient-years
11.	cohort of 20 or more patient-years
12.	follow-up period 3 months or greater
13.	drop-out rate of 20% or less
14.	information provided on patients who completed study vs. those that were lost to follow-up[a]
15.	description of conservative treatment

Note - For each item, reviewers assigned a binary score of 1 or 0. [a] For this criterion, a binary score of 1 was assigned when information was provided concerning three or more of the following items: sex, age, severity of lesion, type of lesion, isolated or multiple lesions, and knee load

patients who had sustained trauma, *(b)* MR imaging was used as a diagnostic method, *(c)* after the initial diagnosis, patients returned to the clinic for follow-up, and clinical data or MR imaging outcomes were noted, and *(d)* the article was written in English, Dutch, German, French, Spanish, Italian, Swedish, Danish, or Norwegian.

Methodological quality assessment

Because the variation in the internal validity of the studies may influence the results and conclusions of a systematic review, the quality of each included study was assessed by using the following procedure. Two reviewers (SSB and SMAB) independently scored the quality of the selected studies by using a set of criteria that were previously used in the field of musculoskeletal disorders and were modified to cover the topic of our review (Table 3.1). Items were given a binary score of one if a particular criterion was fulfilled, and items were given a binary score of zero if a particular criterion was not fulfilled or if it was unclear whether the criterion was fulfilled. The final quality score of each study was based on the sum of the individual scores. In cases of disagreement, both reviewers discussed the scores to achieve consensus. A prospective cohort study was judged as the preferred study design.

In most systematic reviews, studies that receive a quality score of more than 50% of the available quality points are considered to be of high quality. In our study, 15 quality items were scored. Therefore, studies receiving a quality score eight points or more were considered high quality.

Data extraction

We extracted the main characteristics of each study - that is, study center, inclusion criteria, study population, study design (i.e., prospective or retrospective), study size, and follow-up period. Study results were also extracted, including the type of bone bruise classification system used, descriptions of MR imaging results at baseline and follow-up, the number of cases of persistent bone lesions and/or cartilage abnormalities at follow-up, descriptions of sustained knee surgery during follow-up period, patient complaints, and physical examination results at follow-up. Data extraction was performed in duplicate by two authors (SSB and SMABZ).

Data Analysis

Study characteristics and quality scores were presented, and studies were ranked according to their quality score. A kappa statistic was used to rate the level of agreement between the two reviewers on each quality item. The percentage of resolution of bone bruise was estimated for each study. The presence of osseous and cartilage abnormalities was compared according to the different bone bruise classification systems that were used in the separate studies.

When data were available, comparisons were made between initial lesions and clinical follow-up results, as well as between lesions seen at MR imaging follow-up and findings observed at clinical follow-up. Because the observational studies in this review were considered to be heterogeneous with regard to follow-up, study population, and quality and outcome measures, we refrained from pooling the data. Because of the scarcity of data, analyses of counts and proportions were used as the main statistic tools. The kappa statistic was estimated by using SPSS (version 11.0.1; SPSS, Chicago, Ill).

RESULTS

Characteristics of identified studies

The primary literature search identified 266 references. On the basis of the title and abstract, 15 articles were read completely and, of these, 11 met our inclusion criteria. After screening the reference list of each article, two more studies were included.[2, 6, 8-18] All included articles were published in English.

Regarding the characteristics and quality scores of the included studies (Table 3.2), six were retrospective and seven were prospective. The follow-up period of these 13 studies ranged from one to 73 months. All studies were hospital-based, and study populations were generally small. In nine studies, less than 30 patients were included. Two studies considered ankle sprains,[16, 18] whereas the other 11 studies considered bone bruise of the knee.

Table 3.2. Characteristics and quality assessment of studies on the follow-up of bone bruise

Reference	Study centre	Inclusion criteria	N	quality criteria[a] and quality score															
				1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	sum
Vellet[6]	University clinic, London, Ontario, Canada	Acute hemarthroses, no intercurrent injury of affected knee before presentation, combined lesions classified as both reticular and geographic, no repeat injury during follow-up, and no cartilaginous injury at arthroscopy	21	+	+	+	-	+	+	+	+	-	-	-	+	+	+	-	10
Miller[12]	Orthopedic surgery dept, San Antonio, TX, USA	Suspected isolated grade 2 or 3 MCL injury at physical examination, with negative findings on conventional radiographs	24	+	+	+	-	+	+	+	+	-	-	-	-	+	+	+	10
Zanetti[16]	Radiology dept, Zurich, Switzerland	Acute lateral ankle sprain	29	+	-	+	+	+	+	-	+	-	-	-	-	+	+	+	9
Bretlau[17]	Casualty ward, Denmark	Trauma, twist, or contusion of the knee in previous 24 hours; no fracture on conventional radiographs; and bone bruise at MR imaging	26	+	+	+	+	+	-	+	+	-	-	+	+	-	-	-	9
Wright[13]	Orthopedic surgery and sports medicine dept, St. Louis, MD, USA	Acute knee injury, normal radiographs, effusion, possible meniscal or cruciate ligament injury at clinical examination, and isolated subcortical trabecular bone injury at MR imaging	23	?	+	+	-	+	+	+	-	-	-	+	+	-	-	+	8
Johnson[14]	Orthopedic surgery dept, Lexington, KY, USA	Acute isolated ACL rupture at MR imaging	40	+	+	+	-	-	-	+	+	-	-	-	-	+	+	+	8
Roemer[15]	Radiology dept, Augsburg, Germany	Posttraumatic bone marrow edema; no previous ligament injury; no ACL reconstruction; no significant knee trauma prior to acute episode; and no obvious degenerative changes	49	+	-	+	-	-	-	+	-	+	+	+	+	-	+	-	8
Faber[8]	Sport medicine clinic, Ontario, Canada	Normal findings at conventional radiography, abnormal bone marrow signal intensity at MR imaging, and normal cartilage at arthroscopy within 12 days of knee injury	23	-	+	+	-	-	-	+	?	+	+	+	+	-	-	+	8
Alanen[18]	Orthopedics and traumatology dept, Helsinki, Finland	Ankle sprain, no fracture on standard radiographs, no history of sprain in either ankle, and no alcoholism or rheumatoid arthritis	95	+	+	-	+	+	-	+	+	-	-	-	+	-	-	-	7
Costa-Paz[9]	Orthopedic dept, Buenos Aires, Argentina	Acute isolated ACL rupture (all reconstructed), bone bruise at MR imaging, no repeat injury of affected knee during follow-up, no cartilage injury at arthroscopy, and no osteochondral abnormalities at conventional radiography and arthroscopy	21	?	+	-	+	-	-	+	?	-	+	+	+	-	-	+	7
Stein[11]	Centre for diagnostic imaging & Sports medicine centre, Minneapolis, MN, USA	Follow-up period of 2 years or more; complete ACL rupture at arthroscopy; preoperative subchondral osseous contusion at MR imaging; and surgical notes, initial radiographs, and preoperative MR images available	20	-	-	+	+	-	-	+	-	-	+	+	+	-	-	+	7
Lahm[10]	Orthopedic surgery dept Freiburg, Germany	Suspected ligament or meniscal tear at clinical examination, persistent complaints lasting 6 weeks or more after knee trauma while undergoing conservative treatment, and osseous or articular lesion at MR imaging	34	?	+	-	-	+	-	+	+	-	-	+	+	-	-	-	6
Yao[2]	Radiology dept, Albany, NY, USA	Evaluation of internal derangement of the knee after injury	8	-	-	+	-	-	-	+	-	-	-	-	+	-	-	-	3

Note - Studies are listed according to the highest total quality score. ACL = anterior cruciate ligament, MCL = medial collateral ligament. [a] Quality criteria are listed according to the numbering system used in Table 3.1. For each criterion, reviewe☐
marks were counted as a binary score of 0 for total quality score.

The two reviewers scored 195 quality items and initially agreed on 179 items (kappa 0.84). The 16 disagreements were resolved in a single consensus meeting; most disagreements were caused by inadequate documentation in the reviewed articles. In cases of remaining uncertainty, four studies scored no points on the poorly documented item (Table 3.2).

The quality of the included studies was moderate; eight studies scored 8 points or more of the 15 available quality points. The shortcomings generally involved a poor description of inclusion criteria for arthroscopy and/or arthrotomy, a small study size, and a high percentage of patients lost to follow-up (Table 3.2).

Initial and follow-up MR imaging

Four different classification systems were used (Appendix 3.B), and in two studies bone bruise was not specified (Table 3.3). Comparison of the study results was further hindered by differences in outcome measures; at follow-up, researchers considered the persistence of signal intensity abnormalities in the initial osseous lesions,[2, 9, 11, 12, 15–17] osteochondral sequelae,[6, 8, 9, 11] or chondral sequelae only.[10]

The percentage of complete resolution of bone bruises in the knee ranged from 88% after 11 to 16 months of follow-up,[17] to 100% after 2.5 to 12 months of follow-up.[12] In one study of six patients with talar dome bone bruise, complete resolution was seen in two patients after 2.3 to 4.1 months of follow-up.[16] When information on the appearance of persistent bone bruise lesions was given, it appeared that all of the persistent bone bruise lesions were less intense and smaller at follow-up.[15-17] Pooling of these data was hindered because in some studies data were presented on the patient level, whereas in other studies lesions were considered separately.

Researchers who investigated osteochondral sequelae found signal intensity abnormalities in both bone and cartilage in many patients during follow-up periods ranging from six to 73 months (Table 3.3).[6, 8, 9, 11] The authors of these studies described the possibility of fibrosis, sclerosis, or fatty replacement of the bone marrow; cartilage thinning or defect; and cortical depression or osteochondral defect at follow-up imaging. In two studies, investigators used a more or less comparable classification system and found no apparent sequelae in case of initial reticular bone bruise distant from the subchondral bone plate.[6, 9] All cases of disrupted articular surfaces (osteochondral defects or cortical impactions,[6] or type 3 lesions [9]) were associated with cartilage loss at follow-up in both studies.[6, 9] Vellet et al. found osteochondral sequelae in 14 of 18 cases of geographic fractures after six to 12 months.[6] In the study by Costa-Paz et al., only one of 11 geographic lesions was still present after 24 to 64 months.[9] Stein et al. found no correlation between the initial signal intensity type at MR imaging and findings at 24 to 73-month MR imaging follow-up.[11] In the study by Faber et al. it was unclear if the osteochondral lesions at follow-up were preexistent or if they occurred as the result of an initial bone bruise, because

Table 3.3. Classification of initial bone bruise and follow-up on MR imaging

Reference	Classification system	Initial lesion	Other lesions[a]	Follow-up period (mo)	Follow-up operated	Follow-up bone bruise (BB)
Vellet[6]	Vellet	18 geographic occult fractures of the LCF with 18 reticular injuries of the posterior LTP, four occult osteochondral impaction fractures, and four reticular occult MTP fractures; and three reticular LFC and TP fractures were noted	yes	6-12	most	For initial geographic fractures, follow-up of initial lesions was not described; 14 osteochondral sequelae (osteosclerosis, cartilage thinning, loss or defect, osteochondral defect, and cortical impaction) were noted; all osteochondral defects and cortical impactions were associated with cartilage loss or defects; for initial reticular fractures, lesion resolution and no apparent sequelae were noted
Miller[12]	Mink and Deutsch	24 trabecular microfractures, including three occult LTP fractures	yes	2.5-12	none	Complete resolution of all 24 microfractures
Zanetti[16]	Bone bruise not specified	Bone bruise of the talar dome in six patients	no	2.3-41	none	Partial persistence of four bone bruises
Bretlau[17]	Vellet	Isolated bone bruise in two patients, 33 cases of bone bruise with concomitant lesions, osteochondral lesions in 28 patients, and bone bruise in more than one location in 18 patients	yes	2.5-5.5 & 11-16	none	At early follow-up (2.5–5.5 mo), bone bruise resolved in five patients and was more diffuse but of lower signal intensity in 11 patients; at late follow-up (11–16 mo), bone bruise was resolved in 22 patients and was more diffuse but of lower signal intensity in three patients[b]
Wright[13]	Vellet	Seven geographic, seven osteochondral, three linear subcortical, and three reticular fractures; three MR images were not available for retrospective classification of bone bruise	NA[c]	4-54	none	No information was provided on follow-up MR imaging results of initial lesions
Johnson[14]	Vellet	20 geographic bone bruises of the sulcus terminalis and posterolateral TP; 20 patients had no bone bruises	yes	1	none	No information was provided on follow-up MR imaging results of initial lesions
Roemer[15]	Bohndorf	80 edema-like lesions (edema size range, 0.25–175 cm^3; median, 4 cm^3; average, 15.5 cm^3), 35 bone bruises, 19 subchondral impaction fractures (15 geographic, three linear, and one crescent fracture), and 26 chondral and/or osteochondral fractures	yes	25-57	none	Seven of 49 patients had edema-like signal intensity abnormalities (edema size range, 0.3–4.8 cm^3; median, 1.25 cm^3; average, 2.26 cm^3); eight lesions were noted (six persistent but smaller and two new); five lesions were associated with chondral injury

Faber[8]	Defined by author	Bone bruise of the LTP and LFC; no associated cartilage thinning in the LTP, two cases of associated cartilage thinning in the LFC	yes	72	all	In the LTP subchondral bone, 15 cases were normal and five cases of presumed fibrosis, two cases of fat signal intensity, one case of bone bruise (repeat injury), and no cases of significant cartilage thinning were noted; in the LFC subchondral bone, eight cases were normal and six cases of presumed fibrosis, eight cases of fat signal intensity, one case of bone bruise (repeat injury), and 13 cases of cartilage thinning were noted[d]
Alanen[18]	Mink and Deutsch	22 cases of bone bruise in the talus, including one case of subchondral fracture; four cases of bone bruise in the tibia, including three cases of subchondral fracture	yes	3	none	No information was provided on follow-up MR imaging results of initial lesions
Costa-Paz[9]	Costa-Paz	29 bone bruises, including 13 type 1 bruises, 11 type 2 bruises, and five type 3 bruises	no	24-64	all	All type 1 lesions had resolved, 10 type 2 lesions had resolved and one was still present, and all type 3 lesions had persistent abnormalities at MR imaging (cartilage thinning or cortical depression)
Stein[11]	Bone bruise not specified	37 bone bruises, including 20 in the LTP, 13 in the LFC, three in the MTP, and one in the patella	yes	24-73	all	Bone bruise was completely resolved in 24 cases and was sclerotic in 13 cases (LTP lesions were more often sclerotic); five articular cartilage abnormalities were noted, and the natural history of bone bruise and overlying articular cartilage were not related
Lahm[10]	Mink and Deutsch	15 bone bruises, 11 subchondral fractures, six osteochondral fractures, and two stress fractures	no	5.5-41	none	Follow-up of the initial lesions was not described; for cases of bone bruise, no pathologic cartilage sequelae were noted; for subchondral fractures, six cartilage and subchondral bone abnormalities were noted; for osteochondral fractures, three cartilage and subchondral bone abnormalities were noted; and for stress fractures, one case of subchondral sclerosis was noted
Yao[2]	Defined by author	Eight bone bruises, including seven in the epiphysis and one in both the epiphysis and metaphysis [e]	yes	3	none	Essentially complete resolution of abnormal signal intensity was noted; follow-up MR imaging results were available in two patients only

Note - LFC = lateral femur condyle, LTP = lateral tibial plateau, MTP = medial tibial plateau, TP = tibial plateau, NA = not applicable. [a] Refers to concomitant lesions. [b] In this study, it was unclear which patients were recruited for follow-up. [c] Study included isolated bone bruises. [d] Comparison between initial lesion and follow-up results was hampered owing to the different MR imaging sequences used. [e] Location was not specified.

different MR imaging sequences were used at baseline and at follow-up.[8]

We found conflicting results on the prognostic value of the location of a bone bruise; in one study, sequelae were seen more often in lesions of the tibial plateau,[11] whereas in another study no sequelae were found at this site.[8]

By looking at chondral sequelae only, Lahm et al. found no cartilage abnormalities in the case of an initial bone bruise (defined as a geographic nonlinear area of abnormal subchondral signal intensity).[10] Initial subchondral or osteochondral fractures, however, were associated with cartilage abnormalities at follow-up in more than 50% of patients after 5.5 to 41.0 months.[10]

Clinical follow-up

For nine studies, information was presented on the clinical follow-up of bone bruises (Table 3.4).[2, 8-11, 13, 14, 16, 18] In only one high-quality study did the authors report on the clinical outcome of isolated bone bruises in the knee.[13] These authors found a good short-term clinical outcome, all patients showed normal results at physical examination and had returned to their pre-injury activity level within an average of 3.2 months after trauma, and 21 of 23 patients had unchanged activity levels and Lysholm scores of more than 90 points at follow-up.

Four other studies compared the initial lesions detected at MR imaging with the results of clinical follow-up.[2, 10, 14, 18] In one study, researchers described a worse short-term (4-week) prognosis for anterior cruciate ligament rupture in the presence of bone bruise.[14] In another study, investigators described no influence of bone bruise on clinical outcome for ankle sprains after three months.[18] Lahm et al. described a relatively high number of patients with complaints at follow-up (Table 3.4).[10] It is not clear, however, if these symptoms were caused by bone bruise or by other concomitant ligament or meniscal injuries.[10] Also in the study by Lahm et al., bone bruise was found to have a better clinical prognosis than subchondral or osteochondral fractures.

In four other studies, comparisons were made between lesions detected at follow-up MR imaging and the results of clinical follow-up.[8, 9, 11, 16] In two studies, researchers found a generally good clinical outcome after anterior cruciate ligament repair and sustained occult osseous lesions.[9,11] In one study, 19 of 21 patients had normal or near normal findings in the knee after 24 to 64 months of follow-up.[9] In the other study, 19 of 20 patients were subjectively normal or improved, with 15 of 20 patients participating fully in athletics.[11] In three studies, the authors described "no correlation" or "no significant difference" between follow-up MR imaging, follow-up physical examination results, and subjective complaints, without mentioning statistical data.[8, 9, 11]

Table 3.4. Clinical follow-up of bone bruise

Reference	Follow-up period (mo)	Clinical data
	Comparison between initial lesions and clinical follow-up	
Wright[13]	4-54	All patients were normal, with full range of motion at physical examination; patients returned to preinjury activity levels in an average of 3.2 months, and 91% returned to previous activity levels in less than 6 months (not dependant on Vellet classification); IKDC activity levels were unchanged in 21 patients; the performance of the injured knee relative to that of the uninjured knee was 100% in 21 patients before injury and 95%–100% in 15 patients, 90% in three patients, 80%–85% in two patients, and less than 80% in three patients after injury; Lysholm scores were 90 or more in 21 patients
Johnson[14]	1	Patients with ACL lesions and initial bone bruise had larger effusions, a longer period for dissipation of effusion, achievement of nonantalgic gait without external aids, achievement of a symmetric range of motion in the affected knee compared with the uninvolved knee, and higher VAS pain scores compared with patients who had ACL lesions and no bone bruise
Alanen[18]	3	No significant difference in absenteeism from work, walking limitation, or impairment in physical or leisure activities was seen between patients with ankle sprain and initial bone bruise and those with ankle sprain and no initial bone bruise
Lahm[10]	5.5-41	There were two of 15 complaints of initial bone bruise, six of 11 complaints of subchondral fracture (five with pathologic abnormalities at follow-up MR imaging), three of six complaints of osteochondral fracture, and two of two complaints of stress fracture; it was unclear which of the follow-up symptoms was caused by osteochondral lesions and which was caused by ligament or meniscal injury
Yao[2]	3	Six patients showed marked improvement or resolution of symptoms and two showed persistent symptoms
	Comparison between MR lesions during follow-up and clinical follow-up	
Zanetti[16]	2.3-4.1	No differences were seen between patients with persistent bone bruise (four of six patients) and those with no bone bruise (two of six patients)
Faber[8]	72	No statistically significant differences in subjective ACL quality of life knee scores and arthrometric measurements were seen between patients with and those without cartilage or subchondral injuries on follow-up MR images
Costa-Paz[9]	24-64	IKDC standard evaluation according to follow-up MR imaging noted 14 cases of normal or near normal findings in the knee and one case of abnormal findings in the knee for patients with no bone bruise; for patients with persistent bone bruise, five cases of normal or near normal findings in the knee and one case of abnormal findings in the knee were noted; no correlation was found between findings at follow-up MR imaging and those at physical examination or between stability of the knee and IKDC scores
Stein[11]	24-73	A total of 19 of 20 patients were subjectively normal or improved, with 15 fully participating in athletics; no significant correlations were found between follow-up MR imaging and physical examination, age at the time of surgery, time to follow-up, arthrometric measurements, Lysholm scores, follow-up radiographic findings, or initial MR image signal intensity type and size

Note - ACL = anterior cruciate ligament, IKDC = International Knee Documentation Committee, VAS = visual analog scale.

DISCUSSION

To our knowledge, our study is the first systematic review on the follow-up of occult osseous lesions detected at MR imaging. In general, bone bruises have a good outcome at both clinical examination and MR imaging. Various classification systems are used and appear to have prognostic value.

A potential drawback of the present review might be the literature search. Although we used a sensitive set of keywords, we might have missed some relevant studies. Also, because our search was limited to indexed journals, unpublished studies and nonindexed journals might have been missed. Finally, studies published in languages other than the nine we selected would have been missed.

Because the study outcomes described in each of the articles differed, the possible presence of publication bias could not be estimated by using a funnel plot. We believe, however, that in the field of descriptive studies, publication bias might not be strong. In the field of association studies, there might be a publication bias in that nonsignificant relationships may be published less often than are significant relationships. In our review, however, only three studies reported on relationships, and all of these relationships were nonsignificant. Furthermore, there are fewer conflicts of interest (apart from the researchers' own interest) in this field of research than there are in the field of intervention studies. In addition, there are several issues to keep in mind when drawing conclusions from this review. A comparison of the results of individual studies is difficult because the included studies used different time intervals between trauma and initial MR imaging. Moreover, there were differences in follow-up periods, techniques used to detect bone lesions, classification systems, and treatment protocols. All of these factors might influence the presence and identification of bone or cartilage lesions.[19, 20] Most studies contained no information on the initial lesion size and provided no information on the relationship between concomitant lesions and bone bruise; both of these factors might have prognostic value. Despite all these potential problems, the results of the 13 included studies were generally consistent with regard to clinical outcome.

MR Imaging follow-up

Bone bruises are often regarded as benign and self-limiting lesions, but this opinion is primarily based on findings from the earliest studies on this topic. In the current review, which explores all of the available evidence, we also found a natural healing of bone bruises, and a normalization of bone bruise signal intensity was seen in most cases. In the few patients with persistent bone bruise, lesion size had clearly decreased.[2, 11, 12, 15-17] Other lesions often occurred as a consequence of the initial bone bruise;[6, 8-11] in such cases, the typical bone bruise pattern (i.e. low signal intensity on T1-weighted MR images and high signal intensity on T2-weighted fat-suppressed MR images) had disappeared, but some rest lesions (e.g. fibrosis or fatty replacement of cancellous bone) often remained. The clinical meaning of these findings is, as yet, unclear.

The results of the studies included in our review suggest a good prognosis for reticular lesions but a loss of cartilage in all cases of initially disrupted articular surfaces. The reported prognosis of geographic lesions differed. For instance, Costa-Paz et al. found a better prognosis than Vellet et al., but this difference could be accounted for by the much longer follow-up period used by Costa-Paz et al. during which further healing was possible.[6, 9]

Clinical follow-up

Because bone bruises are presumably the result of a trabecular microfracture,[3-5] one might assume that they cause pain even in the absence of other substantial soft-tissue injuries. For patients, however, it is not possible to discriminate between pain that is caused by bone bruises and pain that is caused by concomitant posttraumatic knee lesions (e.g. meniscal or ligament tear). In only one study in this review did investigators report on the clinical follow-up of isolated bone bruises and describe a good short-term prognosis.[13] Results of other studies also showed a generally good clinical prognosis.

In three studies, researchers described the influence of persistent signal abnormalities on subjective complaints and on physical examination results and found no significant relationship.[8, 9, 11] The study populations, however, were small (20 to 23 patients), and only the total knee symptom scores were reported. An association between the presence of signal intensity abnormalities at follow-up and pain can, therefore, not be excluded. Further studies with a larger study population and clear symptom definition are necessary to clarify the relationship.

Authors of histopathological studies have reported a profound effect of trauma on cartilage metabolism.[8, 10, 14, 21-23] The chondral surface could undergo chondrolysis and death that is proportionate to the impaction force and its distribution.[6] This may lead to premature degeneration even in the absence of other substantial soft-tissue trauma. To prove this assumption, further studies with longer follow-up periods are needed. These studies should use a prospective study design, a clearly defined study population, and a structured follow-up that includes at least one physical and MR imaging examination.

In conclusion, there seems to be a healing response that occurs in most patients with posttraumatic occult bone lesions. The clinical prognosis is generally good. Normalization of MR imaging appearance is possible and is most often encountered after the occurrence of reticular lesions (i.e., a serpiginous region of diminished T1-weighted signal intensity that is distant from the subchondral bone plate). Cartilage loss at follow-up is often found in cases of initial cartilage damage.

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APPENDIX 3.A.

Keywords used for the Medline search

keyword	synonym
Bone bruise	[osseous OR oss* OR bone OR marrow OR osteo* OR trabecular] AND [oedema OR edema OR bruise OR contus* OR microfracture*]
Trauma	Trauma OR trauma* OR injur* OR accident* OR tear* OR rupture
MRI	Magnetic resonance imaging OR magnetic resonance tomography OR MR tomography OR MR imaging OR MRI OR nuclear magnetic resonance OR NMR OR proton spin tomography
Follow-up	Predict* OR progres* OR heal* OR follow* OR course OR prognos* OR retrospect* OR prospect* OR natural OR long term

APPENDIX 3.B.

Description of classification systems or definitions of bone bruise

Vellet classification

- Reticular lesion: serpiginous region of diminished T1W signal distant from subchondral bone plate;
- Geographic lesion: discrete confluent focus of low signal contiguous to the subchondral plate;
- Subcortical fracture: discrete linear zone of diminished T1W signal < 2 mm with sharp zone of transition to adjacent marrow fat;
- Impaction fracture: depression of articular surface in conjunction with a geographic type lesion;
- Osteochondral fracture: geographic lesion with a discrete low signal interface marginating the lesion from the surrounding trabecular bone and communicating with the joint space

Mink and Deutsch classification

- Bone bruise: geographic and nonlinear subchondral area of T1W signal loss and T2W increased signal intensity;
- Subchondral fracture: linear or pronged area of T1W signal decrease and T2W signal increase, frequently extending vertically to reach the cortical bone and articular surface;
- Osteochondral fracture: fracture of cartilage and often a small underlying segment of bone;
- Stress fracture: linear zone of decreased T1W and T2W signal (on T2W surrounded by high signal) or bone bruise signal characteristics with a history of no acute trauma

Bohndorf classification

- Bone bruise: region of reticular stranding of decreased T1W signal and increased STIR signal, distant from subchondral lamella or directly beneath cartilage;
- Subchondral impaction fracture: same signal characteristics as bone bruise, but additionally marked hypo intense area on T1W directly beneath subchondral lamella;
- Chondral lesions: purely chondral fracture, depression of cartilage into bone, osteochondral indentation and partially or totally detached osteochondral flake fracture

Costa-Paz classification

- Type 1 bone bruise: diffuse signal with change of medullar component, often reticular and distant from articular surface;
- Type 2: localized signal with contiguity to articular surface, usually crescent;
- Type 3: disruption or depression of articular surface, often associated with type 2 lesion

Definition used by Faber et al.

Low-intensity signal changes in subchondral bone on T1-weighted imaging

Definition used by Yao and Lee

Irregular medullar high signal intensity (T2W)

Part Three

Chapter 4

Study design

The present study is part of a prospective observational cohort study of patients with new knee complaints in primary care: "The HONEUR Study". Data were collected using questionnaires, physical examination and, in a subgroup of patients, MR imaging. The researchers did not interfere with usual care with respect to advice, diagnostics, or treatment. The HONEUR study was approved by the institutional review board of the Erasmus MC.

The institutional review board of the Medical Centre Rijnmond-Zuid approved the study on MR imaging in the subgroup of patients. Written informed consent was obtained from each participant.

STUDY POPULATION

The general HONEUR cohort comprises patients aged 12 years or older, consulting their general practitioner (GP) with new knee complaints. New complaints were defined as complaints that were presented to the GP for the first time. These patients were divided in traumatic and non-traumatic subgroups, based on the etiology of their symptoms.

A predefined subgroup of the posttraumatic patients underwent a standardized MR imaging protocol, and these patients comprise the study population described in this thesis. Patients were found eligible for the additional MR imaging study if they had sustained an acute trauma of the knee less than 5 weeks before consultation and were 18 to 65 years of age. We excluded patients with contra-indications for MR imaging or with severe trauma for which immediate hospital referral was obligatory, and those showing sustained fracture on conventional radiographs (referred by their GP).

RECRUITMENT

Forty-seven GPs in the southwest region of the Netherlands participated in this prospective cohort study. We started recruitment for the MR imaging study in March 2002 in one municipality and a new municipality was added approximately every 3 months. All GPs recruited patients until October 2003.

Patients were alerted to the existence of the study through posters in the waiting room. During consultation, the GP briefly informed the patient about the existence of the study and handed over written information and a baseline questionnaire. Patients forwarded their contact details to the researchers. The researchers contacted the patients to further inform them about the study and to make an appointment for signing informed consent, performing a standardized physical examination of both knees and, when eligible, to make an appointment for the MR imaging.

Participation of patients was voluntary and patients received no compensation, except for the related travel expenses. Participation did not effect the care given to the patient.

MR IMAGING PROTOCOL

MR images were performed on a GE Signa Horizon LX 1T scanner (GE Medical Systems, Milwaukee, USA). The following MR sequences were acquired in the symptomatic knee: sagittal T1-weighted fast spin-echo sequences (TR/TE 575/min full; section thickness 3 mm; field of view 180 x 135 mm; matrix 384 x 224), sagittal intermediate-weighted (3600/min full) and T2-weighted (3600/102) FSE sequences (section thickness 3 mm; field of view 180 x 135 mm; matrix 512 x 224); coronal gradient-echo T2* (325/min full; flip angle 30; section thickness 3 mm; FOV 180 x 135 mm; matrix 256 x 192) and T2-weighted fat suppressed sequences (12/3700/fatsat, section thickness 3 mm; FOV 180 x 135 mm; matrix 385 x 224); and axial intermediate-weighted FSE sequences (3500/20; section thickness 3 mm; FOV 170 x 127,5 mm; matrix 320 x 256). In the asymptomatic knee, only the sagittal intermediate-weighted and T2-weighted and the coronal GE-weighted sequences were obtained, using the same scanning protocols.

MR IMAGING RESULTS

Participants and GPs were not informed about the presence or absence of detected lesions to prevent influencing the treatment strategy employed by the GP. There were two exceptions to this rule. In case the MR images revealed serious lesions, such as fracture or bone tumor, an orthopedic surgeon and the GP were warned. In case of bone bruise, the patient was informed; the purpose of the additional MR imaging follow-up study was explained and consent was obtained for further follow-up of the bone bruise lesions using MR imaging. In all other cases, no further action was taken.

If participants consulted medical specialists at a later date, the specialists were able to request MR image reports to prevent unnecessary duplication of diagnostic procedures. When the GP thought MR imaging was necessary (based on clinical parameters during follow-up), the GP was also able to request the report.

MR IMAGING FOLLOW-UP

A subgroup of patients, showing bone bruise on the initial MRI scan, participated in the additional MR imaging follow-up study of bone bruise. Initially, we planned only two follow-up MR imaging scans, approximately three weeks and one year after the baseline scan. We saw, however, that bone bruise had not healed after such a short period of follow-up (3 weeks) in most patients. Therefore, we decided to perform two more follow-up scans. This resulted in four follow-up scans, approximately three weeks, 10 weeks, six months and 12 months after the initial scan. Patients underwent follow-up imaging as long as the previous scan showed one or more bone bruise lesions. Follow-up was ceased when bone bruise was no longer discernible or after 12 months of follow-up.

QUESTIONNAIRES

Baseline questionnaires were filled in by the patients before the baseline visit. On the day of the initial and the first follow-up MR imaging, patients filled in a pain score. The three monthly follow-up questionnaires were mailed to the participants, and returned to us by mail. The last questionnaire coincided with the one year follow-up MR imaging and physical examination.

The questionnaires included details on the trauma and medical history, possible prognostic factors, as well as outcome measures. For the MR imaging study, we were particularly interested in the medical history (with special attention paid to the knees) and pain scores. Pain was scored on a numeric rating scale ranging from zero (no pain) to 10 (unbearable pain).

Chapter 5

MR imaging abnormalities in symptomatic and contralateral knees: prevalence and associations with traumatic history in general practice

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ABSTRACT

Background After trauma, internal knee lesions are found in approximately two thirds of patients. However, abnormalities on MR images have also been described in asymptomatic volunteers.

Hypothesis Not all visualized lesions in symptomatic posttraumatic knees are the result of the recent trauma; there are subgroups of lesions that may be pre-existent.

Study Design Cross-sectional study.

Methods Patients visiting their GP after knee trauma were invited for MR imaging of both knees. Prevalence of knee abnormalities was compared between symptomatic and asymptomatic knees. Multivariable analysis was carried out to investigate the association between lesions that were seen in symptomatic and asymptomatic knees (i.e. effusion and meniscal tears) and recent trauma, history of old trauma, age and osteoarthritis.

Results In the 134 participants, ligament lesions were found almost exclusively in symptomatic knees. Meniscal lesions and effusion were almost equally found in symptomatic and asymptomatic knees. Effusion was related to recent trauma (OR 14.0; $CI_{95\%}$ 5.0 to 39.6) and osteoarthritis (4.7; $CI_{95\%}$ 1.4 to 15.5), but not to history of old trauma and age. Meniscal tears were more common in older patients (1.09; $CI_{95\%}$ 1.05 to 1.12), but not related to osteoarthritis. History of old trauma was more strongly related to the group of radial, longitudinal and complex meniscal tears (8.6; $CI_{95\%}$ 3.3 to 22.5) than to horizontal tears (2.3; $CI_{95\%}$ 0.9 to 5.6). Recent trauma was not related to horizontal meniscal tears but strongly related to other types of meniscal tears (3.2; $CI_{95\%}$ 1.4 to 6.9).

Conclusions Ligamentous knee lesions are most probably the result of recent trauma. Radial, longitudinal and complex meniscal tears are strongly related to trauma, whereas horizontal meniscal tears and effusion may be pre-existent in many cases.

INTRODUCTION

MR imaging is widely used to evaluate knee symptoms, and clinical decision-making is influenced by the results of these scans.[1-3] Abnormalities in menisci, ligaments, and bone are found after knee trauma in approximately two thirds of patients.[4] Such abnormalities (especially meniscal lesions) are also present in up to one third of asymptomatic knees,[4-7] especially in those of older age.[6,7] There appears to be a bilateral predisposition of meniscal lesions.[4] Therefore, in the trauma setting it is questionable which visualized lesions are posttraumatic and which lesions might have been pre-existent.

Effusion is frequently seen after knee trauma and a positive correlation with internal derangement has been described.[8] Recently, Kolman et al. concluded that symptomatic patients with no significant effusion in the lateral aspect of the suprapatellar pouch on MR images are free of internal knee derangement in 86% of cases.[9] Their definition of "significant effusion" included a laborious method of measuring fluid in the knee. Moreover, using different cut-off values in their study resulted in important clinical differences. Therefore it remains unclear how to distinguish between physiological and pathological effusion, and which amount of effusion is clinically meaningful.

The purpose of this study was to determine the relationship between abnormalities seen on MR images in posttraumatic knees and trauma, and to look for a subgroup of lesions that may be pre-existent. To this end we evaluated the prevalence and nature of MR abnormalities in posttraumatic (symptomatic) knees and in contralateral (asymptomatic) knees. We used data on patients that were included in a prospective study on traumatic knee injuries presenting in Dutch general practice. Moreover, we evaluated the severity of effusion in relation to internal knee lesions.

SUBJECTS AND METHODS

Patients

The present study is part of a prospective observational cohort study of 1,068 patients with new knee complaints in primary care (HONEUR study). The design of the general cohort is presented in detail elsewhere.[10]

In the present study, we included consecutive patients with posttraumatic knee complaints seeking help from their general practitioner. Patients were found eligible if they had sustained an acute trauma of the knee less than 5 weeks before consultation and were 18 to 65 years of age. Trauma of the knee was defined as a sudden impact or wrong movement of the knee. We excluded patients with contra-indications for MR imaging, or with severe trauma for which immediate hospital referral was necessary, and those referred for conventional radiographs showing sustained fracture. A total of 47 general practitioners participated in this study.

The study was approved by the institutional review board of the Erasmus MC and the Medical Centre Rijnmond-Zuid, and written informed consent was obtained from each patient.

All included patients underwent MR imaging of both knees and completed a self-administered questionnaire to evaluate their medical history, with (amongst others) 20 questions on history and treatment of knee problems. For both knees, we defined a previous history of old knee trauma as positive when patients reported to have had one or more of the following items: intra-articular distal femur or proximal tibial fracture, patellar fracture, meniscal, cruciate ligament or collateral ligament lesion, or sustained knee treatment (operation or immobilization).

MR imaging

MR imaging was performed on a GE Signa Horizon LX 1 Tesla scanner (GE Medical Systems, Milwaukee, USA). The following MR sequences were acquired in the symptomatic knee: sagittal T1-weighted fast spin-echo sequences (TR/TE 575/min full; section thickness, 3 mm; field of view 180 x 135 mm; matrix, 384 x 224), sagittal intermediate-weighted (3600/min full) and T2-weighted (3600/102) FSE sequences (section thickness 3 mm; field of view 180 x 135 mm; matrix 512 x 224); coronal gradient- echo T2* (325/min full; flip angle 30; section thickness 3 mm; FOV 180 x 135 mm; matrix 256 x 192) and T2-weighted fat suppressed sequences (12/3700/fatsat, section thickness 3 mm; FOV 180 x 135 mm; matrix 385 x 224); and axial intermediate-weighted FSE sequences (3500/20; section thickness 3 mm; FOV 170 x 127,5 mm; matrix 320 x 256). For feasibility reasons, in the asymptomatic knee, only the sagittal intermediate-weighted and T2-weighted and the coronal GE-weighted sequences were obtained, using the same scanning protocols.

Assessment of MR images and definitions

MR images were evaluated independently by two radiologists (DV and SB). In case of disagreement, the findings were discussed until consensus was reached.

Effusion was classified as small, moderate or large. Menisci were classified as normal, degenerated, or torn. Cruciate ligaments, collateral ligaments, and peri-articular tendons were dichotomized as normal or partial/total rupture. Osteoarthritis of the knee was defined using a modification of the Kellgren and Lawrence scale.[11] This scale was originally made for conventional radiographs. Because no MR imaging-specific scale for osteoarthritis was available, we adapted this scale. Definitions of the abnormalities scored are presented in Appendix 5.

Finally, time between trauma and MR imaging was documented.

Data analyses

For lesions with dichotomous scales, the interobserver agreement was assessed using the kappa statistic. For lesions with more than two categories, the intraclass correlation was used.[12]

The prevalence of lesions is described for the symptomatic and asymptomatic knees. Differences were tested with the Chi-squared test.

In a cross-sectional study it is not possible to define knee lesions as a definite result of the recent trauma or as a pre-existent abnormality, because no earlier MR images are available for comparison. When lesions are seen in symptomatic knees only, it is reasonable to attribute the lesion to the recent trauma. When similar lesions are seen both in symptomatic and asymptomatic knees, however, they may be pre-existent. To unravel this problem, we performed analyses on lesions that were seen in both symptomatic and asymptomatic knees. First we compared these lesions by cross-tabulating the symptomatic and asymptomatic knee to provide 'simple' percentages. Then we looked for possible associations between these lesions and recent trauma, history of old trauma, age, and osteoarthritis of the knee (dichotomized into absent (i.e. grade 0 or 1) and present (i.e. grade 2 to 4)). For this we performed logistic regression analyses with repeated measurements (using Generalized Estimating Equations (GEE)) with the knee lesion (dichotomized) as the dependent variable. The GEE analysis was necessary to take into account the correlation between left and right knees. Univariable analyses were performed, followed by multivariable analyses using all independent variables. Results of the multivariable analyses are presented as odds ratios (OR).

The number of bilateral meniscal ruptures was compared between patients less than 40 years of age and older patients. These age categories were arbitrarily chosen resulting in two equally sized patient groups.

Finally, we tested the hypothesis that patients with no significant effusion are free of internal knee lesions. For this, we compared the prevalence of concomitant meniscal or ligament lesions, and osteoarthritis for effusion severity groups 'none', 'small', and 'moderate to large'.

For all analyses, a p-value < 0.05 was defined as statistically significant. The analyses were performed using SPSS (version 11.0.1, SPSS Inc., Chicago, Ill), except for the repeated measurements analyses that were performed using SAS (version 8.02, SAS Institute Inc., Cary, NC).

RESULTS

One hundred thirty four of the 184 eligible patients (73%) were included in the current study. Reasons for non-participation were distance to study facility or lack of time (n =

Table 5.1. Number of lesions in the symptomatic and contralateral knees of 134 patients with knee trauma

Lesion	Symptomatic n (%)	Contralateral n (%)	p-value	Interobserver agreement[a]
Effusion			< 0.001	ICC 0.92
- none	24 (17.6)	65 (49.2)		(246/268)
- small	68 (50.0)	62 (47.0)		
- moderate	34 (25.0)	5 (3.8)		
- large	10 (7.4)	0 (0)		
Lateral meniscus			0.034	ICC 0.98
- normal	82 (60.3)	99 (75.0)		(260/268)
- degenerative	28 (20.6)	22 (16.7)		
- horizontal tear	16 (11.8)	8 (6.1)		
- radial, longitudinal or complex tear	10 (7.4)	3 (2.3)		
Medial meniscus			0.052	ICC 0.95
- normal	30 (22.1)	36 (27.3)		(260/268)
- degenerative	71 (52.2)	73 (55.3)		
- horizontal tear	19 (14.0)	19 (14.4)		
- radial, longitudinal or complex tear	16 (11.8)	4 (3.0)		
Anterior cruciate ligament			< 0.001	ICC 0.90
- normal	108 (79.4)	131 (99.2)		(263/268)
- partial rupture	9 (6.6)	0 (0)		
- total rupture	14 (10.3)	0 (0)		
- old lesion	5 (3.7)	1 (0.8)		
Posterior cruciate ligament			0.114	ICC 0.98
- normal	130 (95.6)	132 (100)		(267/268)
- partial rupture	3 (2.2)	0 (0)		
- total rupture	2 (1.5)	0 (0)		
- old lesion	1 (0.7)	0 (0)		
Medial collateral ligament			< 0.001	ICC 0.94
- normal	100 (73.5)	131 (99.2)		(264/268)
- partial rupture	35 (25.7)	1 (0.8)		
- total rupture	1 (0.7)	0 (0)		
Lateral collateral ligament			0.003	kappa 0.84
- normal	127 (93.4)	132 (100)		(265/268)
- partial rupture	9 (6.6)	0 (0)		
Osteoarthritis knee			0.947	ICC 0.96
- grade 0	100 (73.5)	96 (72.7)		(257/268)
- grade 1	21 (15.4)	23 (17.4)		
- grade 2	5 (3.7)	4 (3.0)		
- grade 3	6 (4.4)	4 (3.0)		
- grade 4	4 (2.9)	5 (3.8)		
Osteoarthritis patella			0.774	kappa 0.98[b]
- absent	119 (87.5)	119 (90.2)		(267/268)
- present	17 (12.5)	13 (9.8)		

Note - [a] Interobserver agreement estimated on pooled data of symptomatic and asymptomatic knees (absolute number of agreements/total number of observations); ICC: intraclass correlation coefficient; [b] Agreement on non-categorized data: intraclass correlation 0.98.

14), injury too small for participation according to the patient (n = 7), non-compliance with study design (n = 8), and lack of interest or missing appointments (n = 21). Of the 134 patients (60 females), 2 had sustained a bilateral acute knee trauma, resulting in 136 symptomatic and 132 asymptomatic knees. Mean age of the participants was 40.8 years (range 18.8 to 63.8 years). MR images were performed on average 5.4 weeks after the trauma (range 1.3 to 11.6 weeks; 75th percentile 6.7 weeks).

The interobserver agreement ranged from 0.84 to 0.98 (kappa), and 0.90 to 0.98 (intraclass correlation) (Table 5.1).

Regarding cruciate or collateral ligament injuries, the prevalence was less than 1% in contralateral knees, and ranged from 4% to 26% in symptomatic knees (Table 5.1). The prevalence and severity of osteoarthritis was equal in symptomatic and contralateral knees.

Effusion

Effusion was common in both symptomatic and asymptomatic knees, but was more severe in symptomatic knees (Table 5.1, chi-square, $p < 0.001$). Of those with a small effusion in the symptomatic knee (n = 67), 43% showed no effusion in the contralateral knee, 51% showed a small effusion and 6% showed a moderate effusion. Of those with a moderate to large effusion in the symptomatic knee (n = 43), 35% showed no effusion in the contralateral knee, 63% showed a small effusion and 2% showed a moderate effusion.

Because a small effusion was very common in asymptomatic knees, we dichotomized effusion into none to small and moderate to large to be included in the repeated measurement analyses. In the univariable analyses, all independent variables (recent trauma, history of old trauma, age and osteoarthritis) were significantly related to the presence of effusion (all; $p < 0.03$). The multivariable analyses revealed that both recent trauma and the presence of osteoarthritis were related to effusion, whereas a history of old trauma or age were not related (Table 5.2).

In the absence of effusion in symptomatic knees (n = 24), the prevalence of concomitant lesions ranged from 0% (PCL) to 29% (MCL). Patients with a small effusion

Table 5.2. Relation between effusion or meniscal tears and recent trauma, history of old trauma, age, and osteoarthritis in 134 participants with knee trauma

	Effusion[a]		All meniscal tears		Radial, longitudinal or complex meniscal tears[b]		Horizontal meniscal tears[c]	
	OR ($CI_{95\%}$)	p-value	OR ($CI_{95\%}$)	p-value	OR ($CI_{95\%}$)	p-value	OR ($CI_{95\%}$)	p-value
Recent trauma[d]	14.0 (5.0-39.6)	<0.0001	1.7 (1.0-3.0)	0.07	3.2 (1.4-6.9)	0.004	1.2 (0.6-2.3)	0.67
History of old trauma	1.1 (0.5-2.6)	0.78	3.8 (2.0-7.4)	<0.0001	8.6 (3.3-22.5)	<0.0001	2.3 (0.9-5.6)	0.07
Age (years)	1.02 (0.99-1.05)	0.25	1.09 (1.05-1.12)	<0.0001	1.10 (1.05-1.17)	0.0003	1.09 (1.05-1.13)	<0.0001
Osteoarthritis	4.7 (1.4-15.5)	0.01	1.2 (0.4-3.5)	0.71	1.2 (0.3-4.9)	0.76	1.3 (0.4-3.8)	0.63

Note - Results from multivariable logistic regression analyses with repeated measurements with effusion and meniscal tears as dependent variables, and recent trauma, history of old trauma, age, and osteoarthritis as independent variables. [a] effusion: moderate to large effusion compared to none or small effusion; [b] group of radial, longitudinal and complex meniscal tears compared to normal or degenerative menisci (horizontal tears excluded); [c] horizontal meniscal tears compared to normal or degenerative menisci (radial, longitudinal and complex tears excluded); [d] recent trauma indicates symptomatic knee (compared to contralateral - asymptomatic- knee).

(n = 68) showed concomitant internal knee lesions in 6% (PCL and LCL) to 34% (meniscal tears) of the cases.

Meniscal lesions

Degenerative meniscal lesions were more common in the medial meniscus than the lateral meniscus, but equally distributed between both knees (symptomatic knees medial 52% and lateral 21%; contralateral knees medial 55% and lateral 17%; Table 5.1). The prevalence of meniscal tears was high in both symptomatic (medial 26%; lateral 19%) and contralateral knees (medial 17%; lateral 8%). Horizontal tears were more common than radial, longitudinal and complex tears. For statistical purposes, the radial, longitudinal and complex tears were combined into one group. Horizontal meniscal tears were found in 14% (medial) and 12% (lateral) of the menisci in the symptomatic knee, respectively 14% (medial) and 6% (lateral) of the menisci in the contralateral knee. Of the 45 patients with a meniscal tear on the symptomatic side, 19 (42%) also had a meniscal tear on the contralateral side (13 horizontal and six other tears). Of the 87 patients without a meniscal tear on the symptomatic knee, 10 (12%) had a meniscal tear on the contralateral side (nine horizontal and one other tear). Nearly all (18 out of 19) bilateral meniscal tears were seen in patients aged 40 years and older.

Regarding the possible association between meniscal tears and recent trauma, history of old trauma, age and osteoarthritis of the knee, three separate analyses were performed. First we compared all meniscal tears with normal or degenerative menisci. Next, we compared the group of radial, longitudinal and complex meniscal tears with normal or degenerative menisci (horizontal tears excluded). Finally, we excluded the group of radial, longitudinal or complex tears in order to compare horizontal tears with normal or degenerative menisci. In the univariable analyses, all tested associations were statistically significant ($p < 0.02$), except for the association between recent trauma and horizontal meniscal tears ($p = 0.44$). The multivariable analyses yielded that the presence of any meniscal tear had a statistically significant association with recent trauma, a history of old trauma and age, but not with osteoarthritis (Table 5.2). Recent trauma was strongly related to the group of radial, longitudinal and complex tears (OR 2.9, $CI_{95\%}$ 1.3-6.3), but not statistically significant related to horizontal meniscal tears (OR 1.2, $CI_{95\%}$ 0.6-2.3). A history of old trauma was more strongly related to the group of radial, longitudinal and complex tears (OR 8.6, $CI_{95\%}$ 3.3-22.5) than to horizontal meniscal tears (OR 2.3, $CI_{95\%}$ 0.9-5.6).

DISCUSSION

To our knowledge, our study is the first to describe knee lesions detected on MR images in patients visiting their general practitioner (GP) after a knee trauma. All patients underwent

Table 5.3. Prevalence of internal knee derangement according to severity of effusion in 136 symptomatic knees

	Prevalence of derangement, % (n)		
	No effusion (n = 24)	Small effusion (n = 68)	Moderate/large effusion (n = 44)
Medial & lateral meniscus			
- normal/ degenerative	87.5 (21)	66.2 (45)	52.3 (23)
- horizontal tear	4.2 (1)	19.1 (13)	22.7 (10)
- radial, longitudinal or complex tear	8.3 (2)	14.7 (10)	25.0 (11)
Anterior cruciate ligament [a]	4.2 (1)	8.8 (6)	36.4 (16)
Posterior cruciate ligament [a]	0 (0)	5.9 (4)	2.3 (1)
Lateral collateral ligament [a]	4.2 (1)	5.9 (4)	9.1 (4)
Medial collateral ligament [a]	29.2 (7)	23.5 (16)	29.5 (13)
Osteoartritis knee	4.2 (1)	7.4 (5)	20.5 (9)
Osteoartritis patella	8.3 (2)	8.8 (6)	20.5 (9)

Note - [a] Partial or total rupture.

MR imaging of both knees. Our results show that meniscal lesions and effusion are often found in asymptomatic knees, whereas ligament lesions are found almost exclusively in posttraumatic knees.

A possible limitation of this study is that the group of asymptomatic knees is a heterogeneous group, because patients might have a history of old trauma and/or prior complaints. On the other hand, because participants were asked about previous trauma of either knee, this enabled us to study the influence of trauma in the medical history.

Because the number of images between trauma and non-trauma knee differed, the radiologists were not completely blinded to information on the symptomatic side. This may potentially have caused some under- or overestimation of lesions. We think the highest risk lies in underestimation of lesions in the asymptomatic knee. Our study results of the asymptomatic knee are in line with those of studies in asymptomatic volunteers and we therefore think the influence of 'non-blinding' is small.[5-7, 13]

We realize the fact that the findings, as represented, are tied to our patient group. We included primary care patients with a mean age of 40.8 years (range 18.8 to 63.8 years). Findings might have been different in different patient groups, such as younger patients or exclusively athletes.

The period of time between trauma and MR imaging ranged from 1.3 to 11.6 weeks. In this period natural healing of lesions might have occurred; in our opinion effusion would be the first sign to resolve. It has been emphasized that effusion may resolve within a few days after trauma, especially with cooling and elevation of the knee. Only one patient underwent MR imaging within two weeks after trauma. Still, a considerable number of knees showed moderate to severe effusion. Time between trauma and MR imaging had no influence on the prevalence of effusion, and adjustment for this period did not change significance levels presented in Table 5.1 (data not presented). Therefore, we think that this time interval has no significant impact on the prevalence or severity of the other lesions described in our study.

Distribution of lesions in symptomatic and asymptomatic knees

In the Dutch national health care system referral to secondary care is, in principle, made by the GP. In general, all new (knee) complaints are first seen by the GP. In our study protocol, we planned to include all posttraumatic patients seeking medical help. Nevertheless, the prevalence of lesions in our study might be an underestimation of the true prevalence in general practice, because some patients with more severe knee lesions might have been referred directly to secondary care without being included in the study.

Ligament lesions were found almost exclusively on the symptomatic side, which is in line with a study by Zanetti et al.[4] This suggests that ligament lesions in posttraumatic symptomatic knees are a result of the recent trauma. In contrast, meniscal lesions and effusion were seen in symptomatic as well as asymptomatic knees and may - therefore - be pre-existent.

Effusion

In the current study, a high prevalence of a small effusion was seen in contralateral knees, suggesting that a small effusion in symptomatic knees by itself might not be clinically meaningful. Therefore, we restricted our further analyses to moderate and large effusions. From the multivariable analyses it appeared that effusion occurred more often in patients with osteoarthritis and in posttraumatic knees. Age and a history of old trauma could not predict the presence of a moderate to large effusion.

The hypothesis that a small effusion might not be clinically meaningful, but rather a physiological sign, was also suggested by Kolman et al.[9] They defined a cut-off value of effusion for which the presence of internal knee derangement could be predicted. Using an antero-posterior measurement of 10 mm or more in the lateral aspect of the suprapatellar pouch as a threshold value for a pathologic amount of joint fluid, would give an 80.0% positive predictive value and an 86.1% negative predictive value. There remained a relatively high percentage of cases (14%) that demonstrated internal derangement in the absence of a joint effusion. The use of slightly different threshold values (i.e. 8 and 12 mm) greatly influenced sensitivity, specificity and negative predictive values.[9] Therefore, measurement of the lateral suprapatellar pouch has to be done very accurately. We think that this effusion measurement (as suggested by Kolman et al.) is too laborious for daily practice. Therefore, in our study we chose to use a simplified classification system, based on suprapatellar, medial, and lateral accumulation of intra-articular fluid. Using this classification, however, it seems impossible to define physiological effusion from pathological effusion. Many patients with no or a small effusion show concomitant lesions, especially meniscal lesions and medial collateral ligament tears. Thus, it is not possible to limit further evaluation of the MR images to those with a moderate to large effusion: a significant number of other knee lesions would then be missed.

Meniscal lesions

The high prevalence of meniscal tears in contralateral knees may suggest that similar lesions in the symptomatic knees might have been pre-existent. In a cross-sectional study such as ours, causality of relations cannot be proven. Our analyses indicate, however, that a relation between meniscal tears and the recent trauma is present, but only for the group of radial, longitudinal and complex meniscal tears. The subgroups could not be analyzed separately due to small numbers in each subgroup. For horizontal meniscal tears the multivariable analyses showed that it was clearly not related to recent trauma, but somewhat related to age and a history of old trauma, although the latter variable did not reach statistical significance ($p = 0.07$). The latter could be explained by the relatively low number of lesions found in the present study.

Our results are partly in line with the findings of Zanetti et al., who showed no meniscal abnormalities in the contralateral knee in patients with normal menisci in the symptomatic knee.[4] In those with a meniscal tear, 63% showed meniscal tears on the contralateral side as well, especially horizontal tears.[4] In our study, the percentage of contralateral meniscal abnormalities in patients with meniscal tears in the symptomatic knee (42%) was much smaller than in the study of Zanetti et al. (63%). We would have expected a higher prevalence in our study, because Zanetti et al. included only patients without a history of knee complaints, absenteeism or operation of the asymptomatic knee. We cannot explain this unexpected difference on the basis of the scanning protocols, because these were comparable in both studies. It is possible that more patients with degenerative menisci (which do not necessarily give symptoms) were included in the study of Zanetti et al., or participants may not in fact have been history-free. Our results in contralateral knees are in line with the prevalence described in symptom-free volunteers in other studies.[5-7, 13]

In the univariable logistic regression analyses there was a clear relation between osteoarthritis and meniscal tears (all meniscal tears, vertical meniscal tears or horizontal meniscal tears). In our multivariable analyses however, this association disappeared (see Table 5.2). This might be due to the competing effect of age. There has been some debate about the correlation between meniscal pathology and degenerative changes in the articular cartilage; some authors found no such correlation,[14, 15] whereas others did find a relation between meniscal tears or degeneration and articular cartilage damage.[16-18]

For daily practice it is important to recognize that meniscal lesions seen on MR images might have been pre-existent. Further study is needed to define signs that would help clinicians to decide whether a meniscal lesion seen after trauma is clinically relevant or not. There might be subtle differences between symptomatic and asymptomatic meniscal tears that cannot be detected by current MR imaging analysis but may account for the presence or absence of symptoms. Pending further study, our study results suggest that horizontal meniscal tears should be treated according to symptoms and not just because of their presence on the MR images.

Conclusions

The prevalence of internal knee lesions in patients visiting their general practitioner after knee trauma ranges from <1% in the contralateral knee (PCL and ACL tears) to 32% in symptomatic knees (effusion). Cruciate and collateral ligament lesions appear almost exclusively in symptomatic knees, suggesting that these lesions are a result of the recent trauma. Recent trauma is related to moderate to large effusion, and to the group of radial, longitudinal and complex meniscal tears, but not to horizontal meniscal tears.

A small effusion was seen in a high percentage of symptomatic and contralateral knees, suggesting that a small effusion is not necessarily a result of trauma. A significant number of patients with small effusion appear to have internal knee lesions. Thus, limiting further evaluation to patients with moderate to large effusions would lead to a significant under-diagnosis of possibly clinically relevant lesions.

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APPENDIX 5

Classification of knee abnormalities and MR imaging appearance

Effusion

Accumulation of intra-articular fluid in suprapatellar, medial or lateral compartment.

- small: fluid in one or two compartments
- moderate: fluid in three compartments
- large: fluid in three compartments with bulging of the capsule and pericapsular soft tissues

Menisci

- normal
- degeneration: abnormal high signal centrally, possibly extending to the articular capsule
- tear: abnormal high signal unequivocally reaching the articular surface on at least two adjacent images
    - a horizontal tear lies in the plane of the meniscus and divides it into top and bottom parts
    - a radial tear lies in a plane perpendicular to the meniscal circumference, involving the meniscal free edge
    - a longitudinal (also called vertical) tear parallels the outer surface of the meniscus
    - a complex tear contains a combination of horizontal, radial, or longitudinal cleavage planes

Cruciate ligaments, lateral collateral ligament, patellar ligament and periarticular tendons

- normal
- partial rupture: grade 1 rupture (i.e. thickened ligament with abnormally high signal intensity), or grade 2 rupture (i.e. central or peripheral partial discontinuity
- total rupture: grade 3 rupture (i.e. inability to define fibers with an amorphous area of high signal intensity or focal discrete disruption of all visible fibers)
- possible old lesions: (i.e. abnormal thick ligament with low signal intensity or thin wavy ligament)

Medial collateral ligaments

- normal
- partial ruptured: grade 1 (i.e. periligamentar edema and swelling), or grade 2 (i.e. complete disruption of the superficial layer)

- total rupture: grade 3 rupture (i.e. complete disruption of the deep and superficial layer with periligamentar leakage of intra-articular fluid)
- possible old lesions (i.e. abnormal thick ligament with low signal intensity or thin wavy ligament)

Osteoarthritis

Initially defined for conventional radiographs by Kellgren & Lawrence:
- grade 0: no abnormalities
- grade 1: minimal osteophyte, dubious significance
- grade 2: osteophytes without joint space narrowing
- grade 3: moderate joint space narrowing
- grade 4: severe joint space narrowing with sclerosis of the subchondral bone

Osteoarthritis absent: grade 0 or 1
Osteoarthritis present: grade 2 to 4

Chapter 6

Bone bruise in posttraumatic knees: prevalence and associated knee pathology in general practice

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ABSTRACT

Objectives To study prevalence, severity and determinants of bone bruise in posttraumatic knees in general practice.

Methods Cross-sectional data of patients visiting their general practitioner after sustained knee trauma. All patients underwent MR imaging of the knee. The type of bone bruise was classified according to the Vellet classification. Severity of bone bruise was classified according to the percentage of bone volume involved. Concomitant knee lesions were scored. We tested for possible relations between presence of bone bruise and location or concomitant knee lesions, and between severity of bone bruise and location, bone bruise type or concomitant knee lesions.

Results In 81 of 136 knees (60%), 160 bone bruise lesions were found; 36% concerned reticular lesions, 55% geographic lesions, and 8% impaction, subcortical or osteochondral fractures. In 76% of all lesions less than 25% of the condyle was involved. The lesions were almost equally divided over femur condyles and lateral and medial tibia plateau. Presence of bone bruise was related to medial meniscus lesions, anterior cruciate and medial collateral ligament tears. Bone bruises were significantly more severe in the tibial or lateral location, in case of reticular lesion type, and in the presence of anterior cruciate ligament tears.

Conclusions Bone bruises are frequently encountered after sustained knee trauma in primary care. Presence and severity of bone bruise are related to concomitant knee lesions. Severity is also related to location and lesion type.

INTRODUCTION

Posttraumatic occult bone injuries, also referred to as bone bruises, were first described in the late 1980s,[1-3] and many publications have followed since. There is little histological evidence of such bone lesions; after trauma, they are presumably the result of microfracture of medullar trabeculae.[1, 2] In histological studies, hemorrhage and edema are found in the region of signal abnormalities.[4-6]

Although the occurrence of posttraumatic bone bruise in the knee has been well described, epidemiologic data are scarce. Only a few studies describe the prevalence of bone bruise, ranging from 20% to 72%.[5, 7-11] The interpretation of these data is hampered because limited information is provided in these studies. For example, the severity of bone bruise is not described in most studies,[5, 7-9] the study population is restricted to patients with cruciate ligament tears,[5, 11] or the study population is not clearly described.[8] Only two studies presented additional information on all concomitant knee lesions, but no associations with bone bruise are presented.[8, 9]

Thus, it remains unclear what the prevalence of bone bruise is after knee injury. Moreover, possible determinants of bone bruise are unknown. The purpose of this study was to determine the prevalence and severity of bone bruise in posttraumatic knees and to look for possible determinants of these lesions. To this end, we used MR imaging data on patients that were included in a prospective study on traumatic knee injuries presenting in Dutch general practice.

SUBJECTS AND METHODS

Patients

The present study is part of a prospective observational cohort study of 1,068 patients with new knee complaints in primary care (HONEUR study). The design of the general cohort is presented in detail elsewhere.[12]

In the present cross-sectional study, we included consecutive patients with posttraumatic knee complaints seeking help from their general practitioner. Patients were found eligible if they had sustained an acute trauma of the knee less than 5 weeks before consultation and were 18 to 65 years of age. We excluded patients with contra-indications for MR imaging, or with severe trauma for which immediate hospital referral was necessary, and those referred for conventional radiographs showing sustained fracture. Forty-seven general practitioners participated in this study.

The study was approved by the institutional review board of the Erasmus MC and the Medical Centre Rijnmond-Zuid, and written informed consent was obtained from each patient.

MR imaging

MR imaging was performed on a GE Signa Horizon LX 1 Tesla scanner (GE Medical Systems, Milwaukee, USA). The following MR sequences were acquired in the symptomatic knee: sagittal T1-weighted fast spin-echo sequences (TR/TE 575/min full; section thickness, 3 mm; field of view 180 x 135 mm; matrix, 384 x 224), sagittal intermediate-weighted (3600/min full) and T2-weighted (3600/102) FSE sequences (section thickness 3 mm; field of view 180 x 135 mm; matrix 512 x 224); coronal gradient- echo T2* (325/min full; flip angle 30; section thickness 3 mm; FOV 180 x 135 mm; matrix 256 x 192) and T2-weighted fat suppressed sequences (12/3700/fatsat, section thickness 3 mm; FOV 180 x 135 mm; matrix 385 x 224); and axial intermediate-weighted FSE sequences (3500/20; section thickness 3 mm; FOV 170 x 127,5 mm; matrix 320 x 256). The presence of bone bruise was assessed and classified on the coronal T2-weighted fat suppressed images.

Figure 6.1. (left)
32 year-old female with reticular bone bruise lesions in the medial femur condyle and lateral tibia (i.e. serpiginous region of increased signal distant from subchondral bone plate) on coronal T2-weighted fat suppressed image.

Figure 6.2. (left below)
28 year-old male with geographic bone bruise lesions in the lateral femur condyle and medial tibia (i.e. discrete confluent focus of increased signal contiguous to the subchondral plate) on coronal T2-weighted fat suppressed image.

Figure 6.3.a. (right below)
57 year-old female with a subcortical fracture in the tibia (i.e discrete linear zone of increased (T2-weighted) or decreased (T1-weighted) signal < 2 mm with sharp zone of transition to adjacent marrow fat) on coronal T2-weighted fat suppressed image (a) and on sagittal T1-weighted FSE image (b).

Assessment of MR imaging and definitions

MR images were evaluated independently by two radiologists (DV and SB). In case of disagreement, findings were discussed until consensus was reached.

Bone bruise was categorized in two different ways. First, severity of bone bruise was classified according to the percentage of bone volume involved: none, minimal, <25%, 25-50%, 50-75%, and >75%. This was done for each possible site of bone bruise (i.e. lateral or medial femur, lateral or medial tibia, fibula). We estimated the total volume of femoral and tibial marrow edema for each patient by averaging the sum of four sites (femur and tibia). For this, the severity categories were revalued as follows: zero (primary category "none"), 1% (minimal), 12.5% (<25%), 37.5% (25-50%), 62.5% (50-75%), and 87.5 (>75%). Next, the type of bone bruise was categorized according to the Vellet classification into reticular lesion, geographic lesion, and "other" lesions (i.e. subcortical fracture, osteochondral fracture, and impaction fracture).[7] Examples of the different bone bruise types are given in the Figures.

Figure 6.3.b. (left below)
See explanation figure 6.3.a.

Figure 6.4. (right)
54 year-old female with an impaction fracture in the medial femur condyle (i.e.depression of articular surface in conjunction with a geographic type lesion) on coronal T2-weighted fat suppressed image.

Figure 6.5. (right below)
22 year-old female with a small defect in the lateral femur condyle after a displaced osteochondral fracture (i.e. geographic lesion with a discrete interface marginating the lesion from the surrounding trabecular bone and communicating with the joint space) on coronal T2-weighted fat suppressed image.

Menisci were classified as normal, degenerated, or torn. Cruciate ligaments and collateral ligaments were dichotomized as normal or partial/total rupture (tear). Osteoarthritis of the knee was defined as absent (i.e. no abnormalities or minimal osteophytes of dubious significance) or present (i.e. osteophytes and/or joint space narrowing, possibly associated with sclerosis of the subchondral bone).

Data analyses

The interobserver agreement for the bone bruise volume classification (none, minimal, <25%, 25-50%, 50-75%, and >75%) was assessed for each site using the intraclass correlation coefficient (ICC).[13]

We describe the prevalence of bone bruise in posttraumatic knees. The number of lesions was calculated for each patient and the median number was estimated. We compared the number of tibial and femoral lesions as well as the number of medial and lateral lesions.

The time between trauma and MR imaging was estimated. The relation between the presence of bone bruise (dependent variable) and time between trauma and MR imaging was tested with logistic regression analyses.

The distribution of the different types of bone bruise is presented. The site of origin (femur-tibia, lateral-medial) was compared with types of bone bruise. Differences were tested using the chi-square test.

Multivariable logistic regression analyses were performed on the presence of bone bruise (dependent variable), using concomitant knee lesions as independent variables. Variables were included when the univariate p-value was less than 0.25. Nagelkerke's R^2 was estimated to value the total variance explained by these factors.[14]

Bone bruise severity categories were compared between the different sites of origin (femur-tibia, lateral-medial), and types of bone bruise. Differences were tested using the chi-square test for linear trend.

To test whether concomitant knee lesions were related to the severity of bone bruise, all cases of bone bruise were selected. In this group, the relation between severity of bone bruise and time between trauma and MR imaging was tested using ANOVA. Next, the relation between the total volume-percentage of edema (dependent variable) and other knee lesions (independent variables) was analyzed, using linear regression analyses. For variables with three or more categories, dummy variables were created. Multivariable analyses were performed using variables with a p-value < 0.25. The total variance explained by the multivariable model was estimated.

Finally, we compared bone bruise severity categories between patients with isolated bone bruise (i.e. no other concomitant knee lesions) and patients with meniscus or ligament injury or osteoarthritis, using the chi-square test for linear trend.

Statistical significance was defined as a p-value < 0.05 for all analyses. All analyses were performed using SPSS (version 11.0.1, SPSS, Chicago, Ill).

RESULTS

Of 184 eligible patients, 134 (73%) were included in the current study. Reasons for non-participation were lack of time for participation or travel distance to the research facility (n = 14), injury too small for participation according to the patient (7), non-compliance with the study design (8), and lack of interest or missing appointments (21).

Table 6.1 presents the characteristics of the 134 participants. Two of the 134 patients had sustained a bilateral acute knee trauma, resulting in 136 symptomatic knees.

Table 6.2 shows that the interobserver agreement ranged from an ICC of 0.95 (medial femur) to 1.00 (fibula lesions).

Table 6.1. Characteristics of the 134 study participants.

Characteristic		
Age (years)	40.8 (mean)	18.8-63.8 (range)
Gender		
- females	60	
- males	74	
Time between trauma and MRI (weeks)	5.4 (mean)	1.3-11.6 (range)
Knee lesions[a]	**number**	**percentage**
Medial meniscus		
- degenerative	71	52.2
- tear	35	25.7
Lateral meniscus		
- degenerative	28	20.6
- tear	26	19.1
Medial collateral ligament tear	35	26.4
Lateral collateral ligament tear	9	6.6
Anterior cruciate ligament tear	23	16.9
Posterior cruciate ligament tear	5	3.7
Osteoarthritis of the knee	15	11.0

Note - [a] number of lesions in 136 symptomatic knees.

Table 6.2. Prevalence of bone bruise lesions according to the site of origin.

Site	n	%	Interobserver variability of severity of bone bruise (ICC)[a]
Lateral femur	34	25.0	0.97
Medial femur	41	30.1	0.95
Lateral tibia	38	27.9	0.98
Medial tibia	44	32.0	0.97
Fibula	3	2.2	1.00

Note - [a] ICC: intraclass correlation, estimated on the severity of bone bruise (6 categories) per site of origin.

Prevalence of bone bruise

In 81 of the 136 knees (60%), 160 bone bruise lesions were found (range zero to five lesions per patient; median two). Table 6.2 shows the prevalence of bone bruise according to the site of origin. Only three lesions were seen in the fibula (one with <25%, two with >75% severity; all geographic lesions; two with concomitant edema at another site). Because the surface area of the proximal fibula is not comparable to the surface area of the femur condyles or the medial or lateral tibia plateau, these three lesions are excluded from all further analyses on the site of origin. Thus there were 80 patients with one or more lesions in the femur or tibia. Slightly more lesions were seen in the tibia (n = 82) than in the femur (75), whereas lateral lesions (72) were somewhat less common than medial lesions (85).

There were slightly less bone bruise lesions in patients with a longer time period between trauma and MR imaging, but the difference was not statistically significant (OR per week interval 0.9, $CI_{95\%}$ 0.8 to 1.1).

Of all 160 bone bruises, 36.3% were reticular lesions, 55.4% were geographic lesions, and the remaining 8.3% consisted of 10 impaction, two subcortical and one osteochondral fractures. Bone bruise type did not differ between sites of origin (femur compared with tibia, chi-square p = 0.117; lateral compared to medial p = 0.080).

Table 6.3. Prevalence of bone bruise and total edema volume according to the presence of other knee lesions.

	Prevalence of bone bruise (n=136)				Total volume % of edema in patients with bone bruise (n=80)	
		Univariable[a]		Multivariable[a]	Univariable	
	%	OR	p-value	OR ($CI_{95\%}$)	Mean	p-value[b]
Medial meniscus			0.001			0.88
- normal	33.3	1.0		1.0	8.6	
- degenerative	60.6	3.1		3.0 (1.1-8.0)	10.0	
- tear	80.0	8.0		5.6 (1.6-19.7)	9.1	
Lateral meniscus			0.06			0.24
- normal	52.4	1.0		1.0	8.6	
- degenerative	64.3	1.6		1.3 (0.5-3.6)	8.4	
- tear	76.9	3.0		1.8 (0.7-5.7)	12.6	
Anterior cruciate ligament			0.02			0.015
- normal	54.9	1.0		1.0	8.1	
- tear	82.6	3.9		3.6 (1.1-12.0)	14.1	
Posterior cruciate ligament			0.38			0.62
- normal	60.3	1.0		not included	9.6	
- tear	40.0	0.4			6.3	
Medial collateral ligament			0.01			0.96
- normal	53.0	1.0		1.0	9.6	
- tear	77.8	3.1		3.5 (1.3-9.1)	9.5	
Lateral collateral ligament			0.26			0.53
- normal	58.3	1.0		not included	9.3	
- tear	77.8	2.5			11.7	
Osteoarthritis knee			0.10			0.75
- absent	57.0	1.0		1.0	9.4	
- present	80.0	3.0		3.3 (0.8-14.1)	10.3	

Note - [a] Logistic regression analyses; [b] ANOVA.

Logistic regression analyses showed that the presence of bone bruise was not related to posterior cruciate ligament or to lateral collateral ligament tears (Table 6.3). Multivariable analyses showed an association between the presence of bone bruise and medial meniscal lesions, anterior cruciate ligament and medial collateral ligament tears, but not with osteoarthritis of the knee or lateral meniscal lesions. R^2 (i.e. the total variance explained by these factors) of the multivariable model was 0.27.

Severity of bone bruise

Table 6.4 presents data on the severity categories of bone bruise, according to the site of origin and the type of bone bruise. Reticular lesions were more severe than geographic lesions (chi-square for linear trend, p = 0.024). Tibial bone bruise was more severe than femur lesions (p = 0.019), whereas lateral lesions were more severe than medial lesions (p < 0.001).

Among patients with one or more bone bruise lesions (n = 80), the total volume of bone bruise was on average 12.2% and 0.6% lower with each week that had passed between the trauma and the MR imaging (ANOVA p-value 0.25). The total volume percentage of edema was higher in those with anterior cruciate ligament tears and lateral meniscal lesions (Table 6.3). None of the other concomitant lesions were related (all p-values > 0.25). Multivariable analyses yielded a positive association with anterior cruciate ligament tears (volume 5.8% higher, p = 0.015) and lateral meniscal tears (volume 4.0% higher, p = 0.09). The total variance explained by these factors was 0.11.

Eighteen patients had isolated bone bruises, i.e. bone bruise without other concomitant knee lesions (26 lesions). The severity of these bruises did not differ from the severity of lesions in patients with concomitant lesions (chi-square test for linear trend, p = 0.77).

Table 6.4. Severity of bone bruises according to the type of bone bruise and the site of origin

	Type of bone bruise			Site of origin			
	Reticular (n=57)	Geographic (n=87)	Other (n=13)	Femur (n=75)	Tibia (n=82)	Lateral (n=72)	Medial (n=85)
Minimal	10.5	24.4	7.7	18.7	18.3	9.7	25.9
<25%	59.6	62.2	15.4	68.0	48.8	56.9	58.8
25-50%	21.1	6.7	23.1	9.3	17.1	18.1	9.4
50-75%	7.0	1.1	53.8	2.7	12.2	11.1	4.7
>75%	1.8	5.6	0	1.3	3.7	4.2	1.2
Difference	0.024[a]			0.019[b]		0.001[c]	

Note - Figures represent percentages. Difference: chi-square for linear trend; [a] reticular vs. geographic lesions; [b] femur vs. tibia (fibular lesions excluded); [c] lateral vs. medial lesions.

DISCUSSION

To our knowledge, this is the first study on posttraumatic bone bruise in general practice. We found bone bruise in 60% of the patients, but the lesions were generally small: in 76% of all lesions less than 25% of the bone volume was involved. The vast majority (92%) of lesions concerned reticular or geographic lesions. The presence of bone bruise was related to medial meniscus lesions, anterior cruciate ligament tears, and medial collateral ligament tears. The severity of bone bruise was related to bone bruise type (reticular lesions were more severe), bone bruise location (tibial and lateral lesions were more severe) and concomitant knee lesions (patients with anterior cruciate ligament generally showed more severe bone bruises). Our study provides background epidemiologic data for a diagnosis often encountered in daily practice.

A potential drawback of our study might be the period of time between trauma and MR imaging. Within this period (ranging from 1.3 to 11.6 weeks), natural healing of lesions might have occurred. However, because we found that this period appeared to have no influence on the prevalence and severity of bone bruise, we believe that this relatively broad time interval did not significantly influence our study results. Additional analyses proved this assumption: adjustment for time between trauma and MR imaging did not change the significance levels presented in Tables 6.3 and 6.4 (data not presented).

In addition, the prevalence and severity of bone bruise found in this study may be underestimates of the true prevalence and severity in general practice, because patients with more severe knee lesions might have been referred directly to a hospital without being included in the study.

The prevalence of occult bone lesions in patients with sustained knee trauma, described in earlier studies, ranged from 20 to 72%;[7-10] these studies concern hospital-based study populations,[7, 9] or an unclearly described study population.[8, 10] Only one study presented an estimation of bone bruise severity;[9] in that study, bone bruise volume was calculated by multiplying the maximum diameters of the zone of hyper intensity on STIR images in three orthogonal planes. We believe that this method of volumetry has some drawbacks. First it provides only an approximation of the true volume as the hyperintense zones are not rectangular but more often show irregular borders. Second, this method is rather time consuming for daily practice. Others have described a computer-assisted method for quantification of bone marrow edema.[15] Although this is a much more exact quantification technique with a very low intraobserver variation, this method also proved to be too time-consuming for clinical use. In the present study, we classified severity of bone bruise according to the percentage of bone volume involved. We acknowledge that this method also gives only an approximation of true bone bruise volume, but it proved a quick method with good reproducibility (kappa 0.95 to 1.00). Therefore, we believe that it is a useful classification system for daily practice. Future studies will reveal whether or not there is an association between severity of bone bruise and prognosis.

In the present study 92% of bone bruises concerned reticular or geographic lesions. A recently performed systematic review on the natural history of posttraumatic bone bruise showed that lesion type appears to have prognostic value.[16] However, many different classification systems were used and some studies do not classify bone bruise at all. Two descriptive studies did use a comparable bone bruise classification system: Vellet et al. identified reticular lesions in 70% of the occult fractures and geographic lesions in 22%; impaction, linear and osteochondral fractures accounted for only 6% of occult fractures.[7] Roemer et al., however, identified impaction and osteochondral fractures in 56% of occult fractures.[10] Our study results are more in line with those of Vellet et al. The reason that we found more geographic fractures might be because we classified all lesions with a geographic component as geographic fractures, whether or not there was also a reticular component, because in our earlier review study on the follow-up of bone bruises, geographic fractures proved to be the more severe lesions.[16]

The presence of bone bruise is related to medial meniscal lesions, anterior cruciate ligament tears and medial collateral ligament tears. No relation with lateral collateral ligament (LCL) tears was found, but this might be caused by the relatively small patient group with LCL tears (broad confidence interval: $CI_{95\%}$ 0.5 to 28.1). Moreover, patients with isolated bone bruise (i.e. no concomitant internal knee lesions) were also included. Apparently, bone contusion is possible without ligament or meniscus damage or osteoarthritis. The severity of these bone bruise lesions did not differ from lesions in knees with accessory injuries.

No significant differences were found in the distribution of lesions between femoral condyles and tibia plateau. Lesions in the lateral compartment were more severe than lesions in the medial compartment. In two other studies, the prevalence of bone bruise was slightly higher in the lateral compartment, but these studies provided no information on the severity of lesions.[9, 10]

In our study, bone bruise severity is related to lateral located bruises and anterior cruciate ligament tears. This might explain why bone bruise was linked with lateral location and anterior ligament tears in the earlier publications;[5, 7, 8] because more severe bruises are more conspicuous, they are more easily detected on the less sensitive conventional T1 and T2-weighted images used in these earlier publications.

Davies et al. found no relation between volume of bone bruising and type of associated ligamentous or meniscal injury;[17] bone bruise volume was significantly larger only in patients with concomitant osteochondral lesions compared with patients without osteochondral lesions, but the study included only 30 patients.

For daily practice it is important to recognize that bone bruise is a frequent finding on MR imaging of posttraumatic knees in primary care. Further study is needed to clarify the clinical consequences and to define the long-term prognosis of such lesions.

In conclusion, in the present study bone bruise is found in 60% of patients seeking help from their general practitioner for posttraumatic knee complaints. Presence of bone bruise is related to medial meniscal lesions, anterior cruciate ligament tears and medial collateral ligament tears. Bone bruise is more severe in tibial, lateral, or reticular lesions, and in the presence of anterior cruciate ligament tears.

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Chapter 7

MRI follow-up of posttraumatic bone bruise in general practice

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ABSTRACT

Background Only little is known on the natural course of bone bruise in posttraumatic knees and determinants of this course.

Hypothesis Posttraumatic bone bruise lesions resolve within twelve weeks and possible prognostic factors of healing can be identified.

Study design Cohort study.

Methods Prospective MRI follow-up data of patients with bone bruise lesions after sustained knee trauma. Follow-up was ceased when bone bruise could no longer be discerned or after one year. Survival analyses were used to study the relationships between time to healing of all bone bruises (in each patient) and age, gender, obesity, workload, sports load, number of bone bruise lesions, osteoarthritis, and concomitant knee lesions. Logistic regression analyses for repeated measurements were used to study the relationships between resolution of individual bone bruise lesions at six and 12 months separately and lesion type, size and location, as well as the explanatory variables mentioned above.

Results In 80 patients, 157 bone bruise lesions were found. Median healing time was 42.1 weeks. Healing was prolonged in case of a higher number of bone bruise lesions and in the presence of osteoarthritis. Resolution of individual bone bruise lesions was prolonged in the presence of osteoarthritis and higher age. Reticular lesions were less likely to be present after 6 months than other bone bruise types. None of the remaining tested variables had prognostic value.

Conclusion The median healing time of bone bruise lesions is 42.1 weeks. Prognosis is influenced by the presence of osteoarthritis, age, type of bone bruise, and number of bone bruise lesions.

INTRODUCTION

After the introduction of MR imaging, many reports have described a new diagnosis: occult bone injury or occult intraosseous fracture.[1-3] These lesions are called occult because no abnormalities are seen on conventional radiographs, and in direct observation (arthroscopy) they would be hidden by the overlying cartilage. These lesions, later also referred to as bone bruises, are presumably the result of microfracture of the medullar trabeculae.

Mink et al. suggested that bone bruise is a benign disorder,[2] but later reports concluded that bone bruise is not entirely benign,[4] and is associated with increased disability in patients with anterior cruciate ligament ruptures.[5]

A recent systematic review showed that, in general, a healing response of bone bruise was often encountered and that bone bruise type appeared to have prognostic value.[6] However, comparison of the individual studies in that review was difficult due to differences in the time interval between the trauma and the initial MR images, and in the techniques used to detect bone lesions, as well as in classification systems, follow-up periods, and treatment protocols. Most studies supplied no information on initial lesion size or on the relation between concomitant lesions and bone bruise. In our opinion all these factors might influence the presence and identification of bone lesions, or might have prognostic value. The natural course of bone bruise and possible determinants thus remain unclear.

The aim of this study was to describe the natural course of bone bruise using a structured MR imaging follow-up, and to describe possible prognostic factors on the natural course.

SUBJECTS AND METHODS

Patients

The present study is part of a prospective observational cohort study of 1,068 patients with new knee complaints in primary care (HONEUR study). The design of the general cohort is presented in detail elsewhere.[7] The study was approved by the institutional review board of the Erasmus MC and the Medical Centre Rijnmond-Zuid, and written informed consent was obtained from each patient.

In the present study, we included consecutive patients with posttraumatic knee complaints seeking help from their general practitioner. Patients were found eligible if they had sustained an acute trauma of the knee less than five weeks before consultation and were 18 to 65 years of age. We excluded patients with contra-indications for MR imaging, or with severe trauma for which immediate hospital referral was necessary, and those referred for conventional radiographs showing sustained fracture. A total of 47 general practitioners participated in this study. A total of 134 patients were included.

MR Imaging

MR imaging was performed on a GE Signa Horizon LX 1T scanner (GE Medical Systems, Milwaukee, USA). The following MR sequences were acquired: sagittal T1-weighted fast spin-echo (FSE) sequences (TR/TE 575/min full; section thickness 3 mm; field of view (FOV) 180 x 135 mm; matrix 384 x 224), sagittal intermediate-weighted (3600/min full) and T2-weighted (3600/102) FSE sequences (section thickness 3 mm; FOV 180 x 135 mm; matrix 512 x 224); coronal gradient- echo T2* (325/min full; flip angle 30; section thickness 3 mm; FOV 180 x 135 mm; matrix 256 x 192) and T2-weighted fat suppressed sequences (12/3700/fatsat, section thickness 3 mm; FOV 180 x 135 mm; matrix 385 x 224); and axial intermediate-weighted FSE sequences (3500/20; section thickness 3 mm; FOV 170 x 127.5 mm; matrix 320 x 256). The presence of bone bruise was assessed and classified on the coronal T2-weighted fat suppressed images.

Follow-up measurements

A total of 157 bone bruise lesions in femur and tibia were identified in 80 patients. These patients were asked to participate in the follow-up study, consisting of repeat MR imaging after approximately three weeks, 10 weeks, six months and one year after the initial MR imaging. Follow-up was considered complete when bone bruise could no longer be discerned, or after one year of follow-up. For follow-up imaging only the coronal T2-weighted fat suppressed sequence was applied, using the same parameters.

Assessment of MR images and definitions

Two radiologists (DV and SSB) evaluated the MR images independently from each other and without knowledge of the physical examination. In case of disagreement, consensus was reached.

Bone bruise was identified as an area of abnormal high signal intensity in the subchondral bone or marrow on the T2-weighted fat suppressed images. Bone bruise was classified according to the Vellet classification: reticular lesions, geographic lesions and other lesions (i.e. impaction, osteochondral and subcortical fractures) (see Appendix 7).[8]

Bone bruise severity at baseline was classified according to the percentage of bone volume involved: none, minimal, <25%, 25 to 50%, 50 to 75%, and >75%. This was done for each possible site of bone bruise (i.e. lateral, or medial femur, lateral, or medial tibia). At follow-up, bone bruise was classified as present or absent.

Healing of bone bruise was defined as the total absence of bone bruise lesions in a patient at follow-up.

Menisci were classified as intact or torn. Cruciate ligaments and collateral ligaments were dichotomized as normal or (partially/totally) ruptured. Osteoarthritis of the knee was defined as absent (i.e. no abnormalities or minimal osteophytes of dubious significance at MR imaging) or present (i.e. osteophytes and/or joint space narrowing, possibly associated with sclerosis of the subchondral bone at MR imaging).

Workload and sports load were assessed according to the baseline questionnaire, identifying four workload categories: no occupation, sedentary occupation (e.g. office jobs), occupation in which the patient had to stand nearly all day (e.g. hairdressers), and heavy physical work (e.g. construction workers); and three sports load categories: no sporting activity, less than four hours of sporting activity per week, and four hours or more of sporting activity per week.

Data analyses

Previous analyses showed that the interobserver agreement for the bone bruise volume classification (none, minimal, <25%, 25 to 50%, 50 to 75%, and >75%) at baseline was very high (intraclass correlation coefficient 0.95 to 1.0) (Chapter 6). In the current study, interobserver agreement was assessed for the resolution of bone bruise at each follow-up MRI scan, using the kappa statistic.

The "survival" time to healing was estimated using a Weibull survival function, allowing for left and right censoring. First, we plotted the survival curve for all 80 patients and estimated the median healing time. Next, we estimated the univariable relationships between healing time and age (years), gender, obesity (body mass index >30 kg/m^2), workload, sports load, number of bone bruise lesions, osteoarthritis, and cruciate or collateral ligament tears, or meniscal ruptures. Finally, the relative healing time for different levels of each explanatory variable, adjusted for the other explanatory variables, was estimated using a multivariable model including all variables with a univariable p-value < 0.10.

In addition, we investigated the relation between resolution of the 157 individual bone bruise lesions at six and 12 months separately and the explanatory variables mentioned above. For this, we used logistic regression analyses for repeated measurements with so-called Generalized Estimating Equations in order to account for the multilevel structure of the data (lesions within patients). In these analyses, the presence of separate bone bruise lesions was used as the dependent variable. As independent variables we entered lesion-specific characteristics [i.e. type of bone bruise, location (femur vs. tibia, lateral vs. medial), severity (<25% vs. >25% of bone volume involved)], and the patient-specific characteristics mentioned above. We estimated odds ratios (ORs) for all explanatory variables using multivariable models with explanatory variables with a univariable p-value < 0.10. A p-value < 0.05 was considered significant.

All analyses were performed using SPSS (version 11.0.1, SPSS Inc., Chicago, Ill) and SAS (version 9.1, SAS Institute Inc., Cary, NC).

RESULTS

Table 7.1 gives the characteristics of the 80 patients included in this study. MR imaging was performed on average 5.3 weeks after the sustained trauma (range 2.0 to 11.1 weeks). The interobserver agreement for resolution of individual bone bruise lesions was high (initial agreement on 397 of 436 scores; kappa 0.82).

Table 7.1. Characteristics of 80 patients with one or more bone bruise lesions at baseline MR imaging

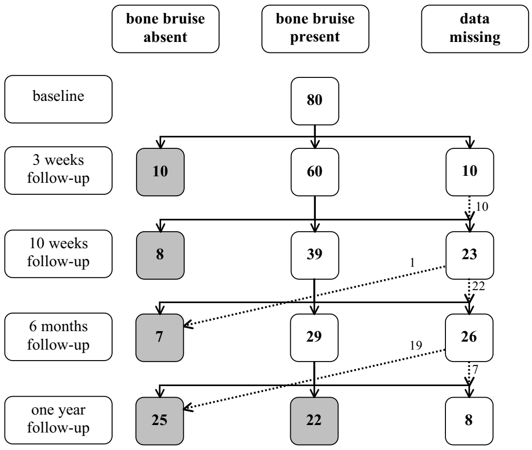
	n = 80
Age (years), mean (range)	43.5 (21.1 ; 63.8)
Gender, n (%)	
- female	35 (43.8)
- male	45 (56.3)
Obesity (body mass index > 30 kg/m^2), n (%)	15 (18.8)
Workload, n (%)	
- no working activities	25 (31.3)
- sedentary occupation	34 (42.5)
- primarily standing all day	17 (21.3)
- heavy physical work	4 (5.0)
Sports load, n (%)	
- no sport	23 (28.8)
- < 4 hours/week	33 (41.3)
- ≥ 4 hours/week	24 (30.0)
Knee lesions	
Number of bone bruise lesions, n (%)	
- one	37 (46.3)
- two	19 (23.8)
- three	14 (17.5)
- four	10 (12.5)
Meniscal rupture, n (%)	35 (43.8)
Cruciate ligament rupture, n (%)	21 (26.3)
Collateral ligament rupture, n (%)	33 (41.3)
Osteoarthritis of the knee, n (%)	12 (15.0)

Figure 7.1 shows follow-up was complete in 72 patients (i.e. bone bruise was absent, or the follow-up period was completed at one year). The eight patients with incomplete follow-up included three participants without any follow-up, three with one control MRI scan, one with two controls, and one with three control MRI scans after baseline measurements. Twenty-two participants showed bone bruise at one year follow-up; these participants had 36 bone bruise lesions (of the 66 initial lesions in this group). The eight participants with incomplete follow-up had 13 initial lesions, of which one had disappeared. Thus, of the 157 initial lesions, 12 lesions (7.6%) were lost to follow-up and 36 lesions (22.9%) were still present after one year.

Healing of bone bruise patients

Figure 7.2 shows the fraction of bone bruise patients that had not healed over time. The median healing time was 42.1 weeks for the total study population. Age, gender, obesity,

Figure 7.1. Presence of bone bruise in 80 posttraumatic patients until one year follow-up.



workload, and sports load were not related to healing on the patient level, neither was the presence of concomitant meniscal, cruciate ligament or collateral ligament rupture (Table 7.2, all p-values > 0.20). In patients with knee osteoarthritis the healing time was about twice that of patients without osteoarthritis (Table 7.2, multivariable analysis). The number of bone bruise lesions prolonged the healing time by approximately one third per additional lesion. In the multivariable analyses both osteoarthritis and the number of lesions showed a prolonged healing time but neither was statistically significant (p = 0.1).

Table 7.2. Relative healing time of bone bruise for explanatory variables (expressed in percentages)

	Percentage longer healing time ($CI_{95\%}$)		
Variable	Univariable	p-value	Multivariable
Age (per year)	1.6 (-1.0 ; 4.3)	0.22	NI
Gender (female vs. male)	23.9 (-35.0 ; 136.3)	0.51	NI
Obesity	51.8 (-41.9 ; 296.5)	0.39	NI
Workload (per increasing category)[a]	-10.3 (-29.4 ; 14.0)	0.37	NI
Sports load (per increasing category)[a]	-0.6 (-35.7 ; 53.7)	0.98	NI
Number of lesions (per category)	56.9 (10.4 ; 122.9)	0.01	34.6 (-5.1 ; 90.9)
Meniscal rupture	47.9 (-21.9 ; 180.2)	0.23	NI
Cruciate ligament rupture	17.7 (-45.2 ; 152.7)	0.68	NI
Collateral ligament rupture	-30.9 (-63.3 ; 30.1)	0.25	NI
Osteoarthritis of the knee	338.5 (15.9 ; 1558.3)	0.03	203.7 (-21.4 ; 1073.9)

Note - NI: not included in the multivariable model (univariable p-value > 0.10). $CI_{95\%}$: 95% confidence intervals. [a] for explanation of the different categories see Table 7.1.

Resolution of individual bone bruise lesions

Figures 7.3 and 7.4 present examples of the gradual resolution of bone bruise lesions over time. Of the initial 157 bone bruise lesions, six month follow-up data were available in 114 lesions and 12-month follow-up data in 145 lesions. Logistic regression with bone bruise lesions as units of analysis showed a relation between the presence of bone bruise after six and 12 months and older age (adjusted OR 1.0, $CI_{95\%}$ 1.0 to 1.1) (Table 7.3). Osteoarthritis was a clear prognostic variable for the presence of bone bruise at six months (adjusted OR 3.0, $CI_{95\%}$ 1.0 to 9.2) as well as at 12 months (adjusted OR 5.6, $CI_{95\%}$ 1.9 to 16.9). Reticular lesions were less likely to be present after six months (adjusted OR 0.2, $CI_{95\%}$ 0.0 to 1.1) than other bone bruise types. At 12-months follow-up, there was no statistically significant relationship between the presence of bone bruise and bone bruise type (Table 7.3). Number, location and severity of lesions, gender, obesity, workload, sports load, and concomitant meniscal, cruciate ligament and collateral ligament tears were not significantly related to resolution of the individual bone bruise lesions.

Figure 7.3.
Coronal T2-weighted fat suppressed images (TR/TE 12/3700/fatsat, section thickness 3 mm; FOV 180 x 135mm; matrix 385 x 224) showing gradual resolution of bone bruise (subcortical fracture) over time in a 57-year-old female.
Figure 7.3.A. (left) Baseline imaging;
Figure 7.3.B. (left below) After 3 weeks follow-up;
Figure 7.3.C. (right below) After 9 weeks follow-up.

Figure 7.2.
Fraction of bone bruise patients not healed over time

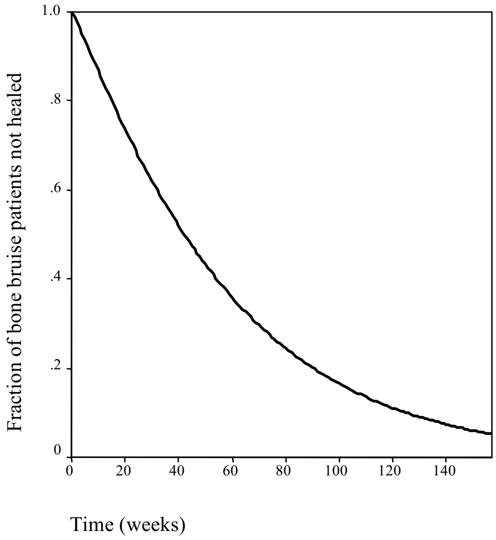


Figure 7.4.
Coronal T2-weighted fat suppressed images (TR/TE 12/3700/fatsat, section thickness 3 mm; FOV 180 x 135mm; matrix 385 x 224) showing fast resolution of bone bruise (reticular lesion) in a 31-year-old male.
Figure 7.4.A. (right) Baseline imaging;
Figure 7.4.B. (left below) after3-weeks follow-up;
Figure 7.4.C. (right below) after 9-weeks follow-up.

Table 7.3. Prediction of the presence (non-resolution) of individual bone bruise lesions at 6 months and at 12 months and its relationship with baseline variables

	6 months (n = 114)			12 months (n = 145)		
	Crude OR ($CI_{95\%}$)	p-value	Adjusted OR ($CI_{95\%}$)	Crude OR ($CI_{95\%}$)	p-value	Adjusted OR ($CI_{95\%}$)
Age (years)	1.1 (1.0;1.1)	0.01	1.0 (1.0;1.1)	1.1 (1.0;1.1)	0.009	1.1 (1.0;1.1)
Gender			NI			NI
- male (reference)	1.0			1.0		
- female	1.7 (0.7;4.1)	0.24		1.2 (0.5;3.1)	0.69	
Obesity	1.1 (0.4;3.6)	0.84	NI	1.7 (0.6;5.4)	0.33	NI
Workload			NI			NI
- no working activities (ref)	1.0			1.0		
- sedentary occupation	1.4 (0.5;3.8)	0.54		1.3 (0.5;3.8)	0.61	
- primarily standing	1.0 (0.3;3.1)	0.96		0.8 (0.2;3.2)	0.73	
- heavy physical work	0.5 (0.0;6.6)	0.60		0.9 (0.1;10.8)	0.96	
Sports load			NI			NI
- no sport (reference)	1.0			1.0		
- < 4 hours/week	1.7 (0.6;5.3)	0.34		1.2 (0.4;3.9)	0.76	
- ≥ 4 hours/week	0.8 (0.2;2.6)	0.65		0.7 (0.2;2.5)	0.53	
Bone bruise						
Number of lesions	1.2 (0.8;1.8)	0.36	NI	1.4 (0.9;2.1)	0.14	NI
Type						NI
- geographic	0.7 (0.2;2.7)	0.58	0.5 (0.1;2.0)	1.1 (0.4;3.1)	0.89	
- reticular	0.2 (0.0;1.2)	0.09	0.2 (0.0;1.1)	0.5 (0.1;1.5)	0.20	
- other (reference)	1.0		1.0	1.0		
Location			NI			
- femur	1.0			1.0		1.0
- tibia	0.9 (0.5;1.6)	0.69		0.5 (0.2;1.1)	0.09	0.4 (0.2;0.9)
Location			NI			NI
- lateral	1.0			1.0		
- medial	0.9 (0.5;1.7)	0.74		0.9 (0.4;2.0)	0.87	
Severity			NI			NI
- < 25%	1.0			1.0		
- 25% or more	1.6 (0.6;4.5)	0.33		1.1 (0.5;2.7)	0.78	
Knee lesions						
Meniscal[a]	1.9 (0.8;4.7)	0.16	NI	1.7 (0.7;4.5)	0.25	NI
Cruciate ligament[a]	0.4 (0.2;1.2)	0.11	NI	0.6 (0.2;1.7)	0.33	NI
Collateral ligament[a]	1.0 (0.4;2.4)	0.94	NI	1.1 (0.4;2.8)	0.84	NI
Osteoarthritis	4.3 (1.6;11.3)	0.003	3.0 (1.0;9.2)	8.5 (3.4;21.6)	<0.001	5.6 (1.9;16.9)

Note - OR: odds ratio for presence (i.e. non-resolution) of bone bruise lesion. Crude OR: univariable analyses; Adjusted OR: multivariable analyses with variables with univariable p-value < 0.10. $CI_{95\%}$: 95% confidence interval. NI: not included in the multivariable model (univariable analyses p>0.10). [a] rupture vs. no rupture.

DISCUSSION

To our knowledge, our study is the first structured prospective follow-up study of posttraumatic bone bruises detected on MR imaging. The median healing time of bone bruise patients of was 42.1 weeks, and healing time was prolonged in case of osteoarthritis and a higher number of initial bone bruise lesions. Resolution of individual bone bruise lesions is related to the presence of osteoarthritis, age and type of bone bruise. Concomitant knee lesions, gender, obesity, workload, sports load, location and severity of bone bruise were not related to the natural course of bone bruise.

In the past, the time to resolution of bone bruises has been debated. An early study on this subject suggested that bone bruises resolve within 12 weeks of the acute injury,[9] whereas more recent studies have shown that bone bruises can persist much longer.[4, 10-12] In the available follow-up studies on bone bruises, follow-up is nearly always restricted to one MR imaging scan. Only Bretlau et al. used two follow-up scans, showing that after a longer period of follow-up further healing is possible.[10] Comparison of the results of the studies is difficult because of differences in follow-up periods and the techniques used to detect bone lesions. None of the studies used a structured follow-up.[6]

We realize that the median healing time, as calculated in our study, is not an exact measure. The time period between the follow-up scans was not uniform. The rationale to perform follow-up scans at approximately three weeks, 10 weeks, six months and one year after the initial scan was that this schedule was expected to enable an accurate survival analysis taking into account both the fast-resolving lesions and the more slowly-resolving lesions. In addition, we felt it was important to keep patient compliance as high as possible. Had we also performed an additional scan at nine months, the calculated median healing time might have been even more precise; however, because only six patients (seven lesions) in our data set resolved unequivocally during this period, an extra follow-up scan would probably not have influenced the calculated healing time substantially. Censoring may have caused some inaccuracy in the estimated healing time but this is not likely to have had a major effect.

Healing was defined as the total absence of bone bruise lesions in a patient at follow-up. Small rest lesions, that in daily practice might be ignored or overlooked, were also counted. We decided not to exclude these small, insignificant looking lesions (exclusion would result in a shorter healing time) because we were interested in the complete healing of patients.

We hypothesized that the tested independent variables might be related to the natural healing of bone bruise. However, another potentially important variable, i.e. treatment protocol, was not tested. The main reason for this was that we followed an observational study design. The 47 GPs that participated in the present study used their own treatment strategies, making it difficult to compare patients. The GPs were not informed about the results of the MR images, and we did not want to interfere with these treatment strategies. Treatment choice is probably influenced by the severity of the complaints (reverse causation). Reliable information on the effect of treatment (e.g. load reduction) can only be obtained by means of an intervention study.

We performed our survival analyses on the patient level. Similar survival analyses on the resolution of individual bone bruise lesions showed (not surprisingly) a smaller median time to resolution (33 weeks), however we think this latter measure is not clinically meaningful. Moreover, this survival analysis does not take into account the correlation between several lesions within one knee.

Baseline severity of bone bruise appeared to have no significant prognostic value. We realize that our bone bruise volume measurements are only an approximation of true bone bruise volume. Others have described a computer-assisted method for quantification of bone marrow edema.[13] Although this is a more exact quantification technique with a very low intraobserver variation, this method has proved to be too time consuming for clinical use.[13] In the present study, we classified the severity of bone bruise according to the percentage of bone volume involved; this proved to be a quick method with good reproducibility (kappa 0.95 to 1.00) and can be used to compare bone bruise severity between individual patients. For statistical purposes (small groups in the more severe categories), we dichotomized bone bruise severity into light (<25% volume involvement) or severe (>25% involvement). The most severe category (>75% volume involvement) seems to have a longer healing time, but this could not be tested reliably due to the small groups.

Our results show that bone bruise healing is mainly related to the presence of osteoarthritis. Previous studies have described a relation between osteoarthritis and bone marrow edema pattern.[14-18] In our earlier study on determinants of bone bruise (Chapter 6) we showed that the prevalence of bone bruise lesions is higher in osteoarthritic patients (multivariable analyses: OR 3.3, $CI_{95\%}$ 0.8 to 14.1). In osteoarthritic patients, the bone bruise lesions might have been preexistent and may have worsened as a result of trauma. On the other hand, bone bruise lesions may persist longer because of reduced cartilage thickness (and therefore reduced absorption of compressive forces) or altered subchondral bone quality.[19] The design of the present study does not allow to prove causality.

We found that lesions within one patient do not heal at exactly the same speed. Therefore the influence of the number of bone bruise lesions on healing time was expected: the higher the number, the more likely that there will be one slowly-resolving lesion.

Healing time was slightly prolonged in case of associated cruciate ligament or meniscal injury but the difference was not statistically significant. This finding is in line with a previous study of Davies et al.[4]

Bone bruise type appeared to have prognostic value (OR at six months follow-up was 0.2 for reticular lesions). This is in line with the results from our systematic review on the follow-up of posttraumatic bone bruises detected on MR imaging.[6] In that review, we found a consistent good prognosis for reticular lesions; the reported prognosis for geographic lesions differed between studies. At 12-months follow-up, reticular lesions again showed smaller ORs, but the difference between lesion types was not statistically significant.

For daily practice, it is important to recognize that bone bruise lesions take a relatively long time to dissipate (longer than suggested in the earliest studies on this subject). Prognosis is mainly influenced by the presence of osteoarthritis, but the type of bone bruise and age also appear to have prognostic value.

Future studies must establish whether the presence of bone bruise is related to clinical symptoms, such as pain. Moreover, the long-term prognosis of these lesions should be determined, with particular focus on the overlying cartilage. Histopathological studies have reported a profound effect of trauma on cartilage metabolism.[20-22] The chondral surface could undergo chondrolysis and death proportionate to an impactive force and its distribution;[8] this may lead to premature degeneration even in the absence of other substantial soft tissue trauma. When the presence of bone bruise is related to clinical symptoms or a worse long-term prognosis, studies on the effect of different treatment strategies seem appropriate.

In conclusion, the estimated median healing time in our patients with posttraumatic bone bruise lesions in the knee is 42.1 weeks. Prognosis is particularly influenced by the presence of osteoarthritis, but age, type of bone bruise and number of bone bruise lesions also have prognostic value.

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APPENDIX 7

Different types of bone bruise according to the Vellet classification

Reticular lesion: serpiginous region of increased T2W fat suppressed signal distant from subchondral bone plate;
Geographic lesion: discrete confluent focus of high signal contiguous to the subchondral plate;
Subcortical fracture: discrete linear zone of increased T2W fat suppressed signal < 2 mm width with sharp zone of transition to adjacent marrow fat;
Impaction fracture: depression of articular surface in conjunction with a geographic type lesion;
Osteochondral fracture: geographic lesion with a discrete interface marginating the lesion from the surrounding trabecular bone and communicating with the joint space

Chapter 8

Clinical consequences of posttraumatic bone bruise in the knee

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ABSTRACT

Background Bone bruise is often seen in posttraumatic knees, but the clinical relevance is unclear.

Hypothesis The presence of bone bruise is associated with increased pain severity in patients with sustained knee trauma.

Study design Cohort study.

Methods Prospective data of 132 patients visiting their general practitioner after sustained knee trauma. Patients with bone bruise underwent an MR imaging follow-up study that was ceased when bone bruise could no longer be discerned or after one year of follow-up. Bone bruise was assessed on MR imaging, and pain severity was scored on a numerical rating scale (ranging from zero to 10) at baseline, and three, six, and 12 months after trauma. The presence of bone bruise and pain severity (over time) were compared using linear regression analyses for repeated measurements. Adjustment was made for possible confounders: presence of meniscal tears, cruciate or collateral ligament ruptures, severe effusion, osteoarthritis, obesity, age, gender, workload and sports load.

Results At baseline as well as during follow-up, bone bruise was associated with a slightly higher pain score. The differences, however, were very small (adjusted difference in pain severity 0.34 or less) and not statistically significant nor clinically relevant.

Conclusion There is no statistical significant relationship, nor a clinical relevant relationship between the presence of bone bruise and pain severity in patients with sustained knee injury in general practice.

INTRODUCTION

Since the introduction of MR imaging, many studies have described the occurrence of so-called bone bruises in posttraumatic knees. These lesions are seen on MR imaging as areas of signal abnormality in the subchondral bone and marrow, particularly as a high signal intensity on T2-weighted fat suppressed images. There is little histological evidence of such bone lesions; after trauma, they are presumably the result of microfracture of medullar trabeculae.[1, 2] In histological studies, hemorrhage and edema are found in the region of signal abnormalities.[3-5]

One might assume that bone bruises cause pain, even in the absence of other substantial soft tissue injury. Little is known, however, about the clinical consequences of these lesions. In the few studies that give information on the subject, it is often not possible to distinguish between symptoms caused by bone bruise and symptoms caused by other lesions, such as ligament ruptures or meniscal tears. Moreover, most studies that do give clinical information use combined symptom scores (e.g. the Noyes symptom score, which assesses pain, swelling, instability and locking);[6-8] thus, because no isolated pain scores are given, no conclusions can be made about a possible relation between pain and bone bruise.

The purpose of our study was to investigate the possible relationship between pain severity (as scored on a numerical pain scale) and the presence of bone bruise, in patients with sustained knee injury.

SUBJECTS AND METHODS

Patients

The present study is part of a prospective observational cohort study of 1,068 patients with new knee complaints in primary care (HONEUR study). The design of the general cohort is presented in detail elsewhere.[9]

In the present study, we included consecutive patients with posttraumatic knee complaints seeking help from their general practitioner. In the Netherlands, patients first visit their general practitioner before going to a hospital. Patients were alerted to the existence of the study through posters in the waiting room. During consultation, the general practitioner briefly informed the patient on the existence of the study and handed over written information and a baseline questionnaire. Patients forwarded their contact details to the researchers. The researchers contacted the patients to further inform them about the study and to make an appointment for signing informed consent, performing a standardized physical examination of both knees, and, when eligible, to make an appointment for MR imaging. Patients were recruited between March 2002 and October

2003 and found eligible if they had sustained an acute trauma of the knee less than five weeks before consultation and were 18 to 65 years of age. Trauma of the knee was defined as a sudden impact or wrong movement of the knee. We excluded patients with contra-indications for MR imaging or with severe trauma for which immediate hospital referral was necessary, and those referred for conventional X-rays showing sustained fracture.

MR imaging

All patients underwent MR imaging of the posttraumatic knee. MR imaging was performed on a GE Signa Horizon LX 1T scanner (GE Medical Systems, Milwaukee, USA). The following MR sequences were acquired: sagittal T1-weighted fast spin-echo (FSE) sequences (TR/TE 575/min full; section thickness 3 mm; field of view (FOV) 180 x 135 mm; matrix 384 x 224), sagittal intermediate-weighted (3600/min full) and T2-weighted (3600/102) FSE sequences (section thickness 3 mm; FOV 180 x 135 mm; matrix 512 x 224); coronal gradient- echo T2* (325/min full; flip angle 30; section thickness 3 mm; FOV 180 x 135 mm; matrix 256 x 192) and T2-weighted fat suppressed sequences (12/3700/fatsat; section thickness 3 mm; FOV 180 x 135 mm; matrix 385 x 224); and axial intermediate-weighted FSE sequences (3500/20; section thickness 3 mm; FOV 170 x 127,5 mm; matrix 320 x 256). The presence of bone bruise was assessed and classified on the coronal T2-weighted fat suppressed images. For follow-up MR imaging only the coronal T2-weighted fat suppressed sequence was applied, using the same parameters.

Follow-up measurements

When bone bruise was identified on MR imaging (see further on), these patients were asked to participate in the follow-up MR imaging study. The follow-up consisted of repeat MR imaging at six weeks, three months, six months, and one year after trauma. Follow-up was complete when bone bruise could no longer be discerned during the follow-up period or after one year of follow-up.

Pain scores

Pain intensity was determined using a numerical rating scale ranging from zero (no pain) to 10 (unbearable pain). Numeric rating scales have compared favorably to visual analogue scales.[10] Baseline pain scores were filled in by the patients on the day of the baseline MR imaging. In case of bone bruise, patients also filled in the pain score on the day of the first follow-up MRI scan. All participants received follow-up questionnaires by mail: three, six, and 12 months after the trauma. These questionnaires contained the pain score and were returned by mail.

A total of 47 general practitioners participated in this study and 134 patients were included. The study was approved by the institutional review board of the Erasmus MC and the Medical Centre Rijnmond-Zuid, and written informed consent was obtained from each patient.

Assessment of MR imaging and definitions

MR images were evaluated independently from each other and from physical examination data by two radiologists (DV and SB). In case of disagreement, consensus was reached.

Bone bruise was identified as an area of abnormal high signal intensity in the subchondral bone or marrow on the T2-weighted fat suppressed images. Menisci were classified as intact or torn. Cruciate ligaments and collateral ligaments were dichotomized as normal or (partial/total) rupture. Effusion was dichotomized as non-severe (absent or without bulging of the knee capsule) or severe (bulging of the knee capsule). Osteoarthritis of the knee was defined as absent (i.e. no abnormalities or minimal osteophytes of dubious significance) or present (i.e. osteophytes and/or joint space narrowing, possibly associated with sclerosis of the subchondral bone).

Workload was assessed and classified according to the baseline questionnaire. We identified four categories: no occupation, sedentary occupation (e.g. office jobs), occupation in which the patient had to stand nearly all day (e.g. hairdressers), and heavy physical work (e.g. construction workers). Sports load was also assessed and classified according to the baseline questionnaire: no sporting activity, less than four hours of sporting activity per week, and four hours of sporting activity or more per week. We assumed that a patient returned to his/her baseline occupation and sporting activity as soon as possible.

Data analysis

We describe the baseline characteristics of patients with and without bone bruise in the knee on baseline MR images. The prevalence of bone bruise during follow-up was estimated. As at each point in time, some data were missing, we also estimated the prevalence using a best case and a worst case scenario. In the best case scenario, we assumed that bone bruise was absent in all missing data. In the worst case scenario, we assumed that bone bruise was present in all missing data.

To investigate whether the presence of bone bruise is related to pain, we performed several analyses. Firstly, we compared the pain severity at baseline between patients with and without bone bruise, using linear regression (with the pain score as dependent variable). Secondly, we compared the differences concerning the course of pain during follow-up between participants with and without bone bruise at baseline. For this, we used linear regression for repeated measurements with the pain severity as the dependent variable, assuming a compound symmetry structure for the variance/covariance matrix. Thirdly, we investigated in patients with bone bruise on the baseline MR images the relationship between pain severity during follow-up and the presence of bone bruise on the follow-up MR images.

Some patients did not return their mail questionnaire (three, six, and 12 months after trauma) precisely on the day of the follow-up MRI scan. Data were included only if the period of time between the follow-up MRI scan and filling out of the questionnaire did not exceed four weeks. In all other cases, we corrected for this time period. Again, we used linear regression for repeated measurements, with the pain severity as the dependent variable.

Next, we adjusted all three analyses for the presence of variables with a hypothesized relation to pain and pain sensation. These 'pain-related variables' were: concomitant meniscal tears, cruciate or collateral ligament ruptures, severe effusion, osteoarthritis, obesity (body mass index > 30 kg/m^2), age, gender, workload and sports load. Pain-related variables that showed a significant relationship with pain severity (p-value < 0.05) and pain-related variables that changed the difference in pain scores between bone bruise versus non-bone bruise patients by more than 10% were included in a multivariable model. The study did not intend to describe all determinants of pain in posttraumatic patients, but to adjust the univariable relationship between pain and bone bruise for possible confounders.

Bone bruise can be present in patients with osteoarthritis, even without trauma. Although in the abovementioned analyses, statistical correction is made for the presence of osteoarthritis, osteoarthritis can (potentially) influence the data. Therefore, we performed all analyses also on a subgroup of participants without osteoarthritis (n = 117). The group of participants with osteoarthritis (n = 15) was too small for statistical analyses.

All analyses were performed using SPSS (version 11.0.1, SPSS Inc., Chicago, Ill) and SAS (version 9.1, SAS Institute Inc., Cary, NC).

RESULTS

Of the 184 eligible patients, 134 (73%) were included in the current study. Reasons for non-participation were lack of time for participation or travel distance to the research facility was too long (n = 14), injury too small for participation according to the patient (7), non-compliance with the study design (8), and lack of interest or missing appointments (21).

Two patients had sustained a bilateral acute knee trauma; they were excluded in the final analyses because of inconsistencies in their questionnaires (e.g. sometimes referring to the right and sometimes to the left knee). This leaves us with 132 patients, 79 (59.8%) of which showed one or more bone bruise lesions in femur, tibia or fibula.

Mean age of the participants was 40.6 years (range, 18.8 to 63.8 years). MR imaging was performed on average 5.4 weeks after the trauma (range, 1.3 to 11.6 weeks; 75th

Table 8.1. Characteristics of participants with and without bone bruise

	bone bruise present (n=79)	bone bruise absent (n=53)
Age (years), mean (range)	43.1 (21.1-63.8)	36.9 (18.8-62.3)
Gender, n (%)		
-female	44 (55.7)	28 (52.8)
-male	35 (44.3)	25 (47.2)
Obesity (body mass index > 30 kg/m^2), n (%)	15 (19.0)	9 (17.0)
Sports load, n (%)		
- no sport	22 (27.8)	14 (26.4)
- < 4 hours per week	34 (43.0)	23 (43.4)
- 4 hours per week or more	23 (29.1)	16 (30.2)
Workload, n (%)		
- no working activities	25 (31.6)	10 (18.9)
- sedentary occupation	33 (41.8)	20 (37.7)
- primarily standing all day	17 (21.5)	15 (28.3)
- heavy physical work	4 (5.1)	8 (15.1)
Knee lesions		
Severe effusion, n (%)	7 (8.9)	2 (3.7)
Meniscal rupture, n (%)	34 (43.0)	11 (20.8)
Cruciate or collateral ligament rupture, n (%)	44 (55.7)	14 (26.4)
Osteoarthritis of the knee, n (%)	12 (15.2)	3 (5.7)

Table 8.2. Prevalence of bone bruise during follow-up in participants with bone bruise at baseline; for the total study population and for subjects without osteoarthritis

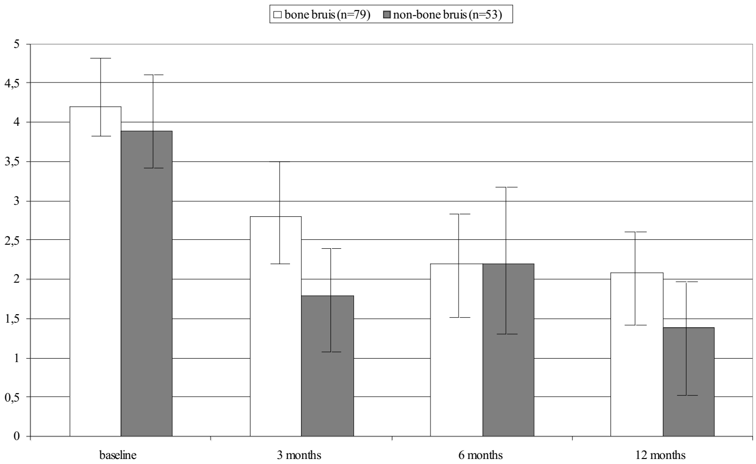
	total study population (n = 79)			subjects without osteoarthritis (n = 69)		
follow-up	prevalence[a]	best case[b]	worst case[c]	prevalence[a]	best case[b]	worst case[c]
3 weeks	85.3	73.4	87.3	83.1	71.0	85.5
10 weeks	67.3	46.8	77.2	62.2	40.6	75.4
6 months	51.9	34.2	68.4	45.2	27.9	66.2
one year	28.6	25.3	36.7	21.3	18.8	30.4

Note - [a] prevalence estimated from available data; [b] best case scenario: none of missing data contained bone bruise; [c] worst case scenario: all missing data contained bone bruise.

percentile 6.7 weeks). Table 8.1 shows the baseline characteristics of patients with and without bone bruise. Table 8.2 shows the prevalence of bone bruise during follow-up for all participants with bone bruise at baseline, as well as for the bone bruise patients without osteoarthritis. After one year 28.6% ($CI_{95\%}$ 25.3 to 36.7%) of the participants with bone bruise at baseline still had one or more bone bruise lesions.

Figure 8.1 shows the mean pain scores (with confidence intervals) of patients with and without bone bruise at baseline MR images and during follow-up. For all participants (n = 132), pain score decreased from 4.1 ($CI_{95\%}$ 3.7 to 4.5) at baseline to 1.9 ($CI_{95\%}$ 1.4 to 2.5) after one year. For subjects without osteoarthritis, pain score decreased from 4.1 ($CI_{95\%}$ 3.6 to 4.7) at baseline to 1.9 ($CI_{95\%}$ 1.1 to 2.6) after one year.

Figure 8.1. Pain scores (mean and 95% confidence intervals) of participants with and without bone bruise at baseline.



Note - Mean pain score on a scale from 0 to 10 where 0 means no pain and 10 means unbearable pain.

Baseline

Table 8.3 shows the differences in pain scores between patients with and without bone bruise at baseline. The mean pain score at baseline was 4.15 in patients with bone bruise and 3.88 in patients without bone bruise (difference 0.28; p = 0.45). Adjustment for the presence of severe effusion and sports load did not change this difference in average pain scores, whereas age, obesity, osteoarthritis, ligament lesions, meniscal tears, and work load gave a more than 10% change in outcome in the univariable analysis. Gender did not result in a 10% change of the outcome, but was statistically related to pain score (p = 0.007). Adjustment for all these variables resulted in a slightly higher (but still not statistically significant) difference in pain score between patients with and without bone bruise (difference 0.34; p = 0.38). For subjects without osteoarthritis, the unadjusted difference was 0.23 (p = 0.56). After adjustment for age, gender, obesity, workload, sports load, ligamentous tear, and severe effusion, this difference was 0.16.

Table 8.3. Difference in pain scores between participants with and without bone bruise at baseline

	baseline		follow-up of all participants	
	univariable analyses	multivariable analyses	univariable analyses	multivariable analyses
total study sample (n = 132)	0.28 (0.37)	0.34 (0.39)[a]	0.43 (0.30)	0.34 (0.31)[c]
participants without osteoarthritis (n = 117)	0.23 (0.40)	0.16 (0.41)[b]	0.29 (0.31)	0.29 (0.32)[d]

Note - scores present mean differences (standard errors). Data derived from ANOVA (baseline) and linear regression for repeated measurements (follow-up; including all available information during follow-up). [a] adjusted for age, gender, obesity, workload, meniscal tears, ligamentous tear and osteoarthritis; [b] adjusted for age, gender, obesity, workload, sports load, ligamentous tear, and severe effusion; [c] adjusted for age, obesity, sports load, ligamentous tears and osteoarthritis; [d] adjusted for age, obesity, sports load, and ligamentous tears.

Follow-up pain scores of all patients

During follow-up, patients with bone bruise at baseline experienced somewhat more pain than patients without bone bruise (on average 0.43 points more on the pain score), but the difference was not statistically significant ($p = 0.16$). Successive adjustment for age, osteoarthritis and ligamentous tear showed more than 10% change of the difference in pain score. Obesity and sports load were significantly related to pain score. Multivariable adjustment for these variables showed that the difference in follow-up pain scores between patients with and without bone bruise at baseline was on average 0.34 ($p = 0.27$). For subjects without osteoarthritis, the unadjusted difference was 0.29 ($p = 0.36$). Adjustment for age, obesity, sports load, and the presence of ligamentous tears did not change this difference (Table 8.3).

Table 8.4. Difference in follow-up pain scores between healed and non-healed bone bruise patients (n=79)

	univariable analyses	multivariable analyses
total study sample (n = 79)	0.41 (0.40)	0.25 (0.40)[a]
participants without osteoarthritis (n = 67)	0.51 (0.45)	0.45 (0.45)[b]

Note - scores present mean differences (standard errors). Data derived from linear regression analyses for repeated measurements (including all available information during follow-up). [a] adjusted for age, gender, sports load and osteoarthritis; [b] adjusted for age, gender and meniscal tears.

Follow-up pain scores of bone bruise patients

The repeated measurements model, using the pain score as the dependent and healing of bone bruise as the independent variable, showed that healing of bone bruise was associated with a somewhat lower pain score compared to persisting bone bruise (the pain score was on average 0.41 lower), but the difference was not statistically significant ($p = 0.32$) (Table 8.4). Successive adjustment for age, osteoarthritis and gender showed more than 10% change of the difference in pain score. Sports load was significantly related to pain score ($p = 0.02$). The multivariable analyses including these variables resulted in a mean difference in pain scores between healing and non-healing of bone bruise of 0.25 ($p = 0.53$). For subjects without osteoarthritis, the unadjusted difference was 0.51 ($p = 0.26$). Adjustment for age, gender and meniscal tears resulted in a slightly smaller difference (0.45, Table 8.4).

DISCUSSION

In this study in primary care no clear relation emerges between the presence of bone bruise in posttraumatic knees and pain severity. That is, no significant difference in pain scores was found between bone bruise patients and non-bone bruise patients. In the past, studies have used a 30 to 50% difference in pain scores as being clinically relevant.[11] Using this criterion, the described small differences in pain scores between bone bruise versus non-bone bruise patients was neither statistically significant nor clinically relevant.

The purpose of this study was to investigate the possible relationship between pain severity and bone bruise. We adjusted for those variables that might confound this relationship, to get a valid estimate for the true relationship between pain severity and the presence of bone bruise. We found that particularly age is a confounder of this relationship; this is of importance for future studies on posttraumatic knee pain.

At the start of our study, we did expect to find an association between pain severity and the presence of bone bruise. In the past, it has been shown that bone and bone marrow are rich in nociceptive fibers, suggesting that bone could contribute to pain.[12] In our opinion, the hemorrhage and edema in the region of signal abnormalities (as described in histological studies),[3-5] could lead to intraosseous hypertension and thus cause pain. In osteoarthritis, a relationship between intraosseous hypertension and pain has also been suggested.[13]

Earlier studies gave some conflicting results on the relationship between symptoms and posttraumatic bone bruises. In many studies, it is not clear whether the symptoms are caused by bone bruise or by concomitant knee lesions. Moreover, most studies used combined symptom scores, and no separate pain scores. Some authors suggested a positive relationship between symptoms and posttraumatic bone bruise,[6, 7, 14, 15] while others did not find such an association.[8, 16]

Bone bruises are seen on MR imaging as regions with an edema signal intensity in the subchondral bone and marrow of posttraumatic patients (i.e. low signal intensity on T1-weighted images and high signal intensity on T2-weighted images). The relation between bone marrow edema pattern and pain has also been investigated in other musculoskeletal disorders. Koo et al. concluded that marrow edema in osteonecrotic hips is strongly associated with pain, even in the absence of collapse.[17] In patients with sickle cell anemia, such a correlation has also been shown.[18] Most reports on this subject however concern patients with osteoarthritis. Felson et al. found a positive association between bone marrow lesions in osteoarthritic knees and pain. In their study on 401 patients with radiographically established osteoarthritis, they found bone marrow lesions in 77.5% of the 351 participants with knee pain, compared with only 30.0% of participants without knee pain ($p < 0.001$).[19] This relation was confirmed by Sowers et al.; however, they suggested that bone marrow edema must be linked to a cartilage defect and bone ulcer to be associated with pain.[20] Because in our study, nearly all patients (93.9%) reported knee pain, we could not reliably test the differences in bone marrow lesions between patients with and without pain. In our study, the association between pain severity and the presence of bone bruise was not significant. This is in line with another study in which bone marrow edema pattern also showed no significant correlation with pain scores in 50 osteoarthritic patients, nearly all with knee pain (WOMAC score).[21] Also, in the study of Felson et al. no association was found between pain severity and the presence of edema within the group of osteoarthritic patients with pain.[19] In the current study, we have corrected for the presence of osteoarthritis in the analyses on the total study sample. Additionally, we have performed analyses in a subgroup of patients without osteoarthritis. The outcome of the latter analyses did not differ relevantly from the outcome of the analyses on the total study population (Tables 8.3 and 8.4). The group of patients with osteoarthritis was too small for subgroup analyses.

We believe our study had enough power to detect a clinically relevant association between pain severity and the presence of bone bruise, if any existed. Our failure to find a significant relationship might be caused by the fact that pain after trauma can arise from many different structures; bone bruise is only one of the many possible causes. Perhaps our adjustments failed to cover all possible sources of pain. But apart from the fact that the differences were not statistically significant, we believe that the small differences in pain scores between bone bruise and non-bone bruise patients are hardly clinically relevant.

In one of the earliest studies on the subject of posttraumatic bone bruise, it was suggested that it is a benign condition.[1] The fact that we could not find a close correlation between the presence of bone bruise and the severity of pain may support this assumption. But to answer the question whether bone bruise is really of little clinical importance, studies with longer follow-up are needed to show long-term consequences, if indeed these exist. Trauma has been shown to have a profound effect on cartilage metabolism.[22-24] Perhaps the underlying bruised bone cannot support the overlying cartilage as it should, thus leading to premature degeneration even in the absence of other substantial soft tissue trauma.

In conclusion, the presence of bone bruises in the posttraumatic knee is not significantly related to the experienced severity of knee pain.

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Part Four

Chapter 9

General discussion

In the second and third chapters of this thesis, systematic reviews are presented focusing on the natural course of posttraumatic knee lesions, i.e. meniscal and ligamentous tears, and bone bruise. These reviews showed that there might be a healing response in cruciate ligament tears and bone bruises, but there still remain important gaps in the available knowledge, particularly with respect to the natural course of meniscal and collateral ligament tears. To address some of these gaps, we conducted our MR imaging study of patients with knee injury that were included in the HONEUR study.[1] In the fourth chapter of this thesis the design of this study is presented, whereas the results of the study are presented in chapters 5 to 8. The data provide important information on the possible pre-existence of internal knee lesions, and on determinants, natural course and clinical consequences of bone bruises. The results can be applied in daily practice and expand the knowledge on posttraumatic knee lesions.

In this general discussion, we will first comment on our study population of patients with sustained knee injury. Next, we discuss the strengths and drawbacks of the study design. Thereafter, we discuss the main findings of this thesis and put them in a broader perspective. Finally, we will give recommendations for future research.

STUDY POPULATION

The study population described in this thesis is part of a large descriptive prospective cohort study on knee disorders in primary care: the HONEUR knee cohort.[1] In the current study, 134 of the 184 eligible patients (73%) were included. Reasons for non-participation were distance to study facility or lack of time (n = 14), injury too small for participation according to the patient (7), non-compliance with the study design in which the general practitioner was not informed about the results of the MRI scan (8), and lack of interest or missing appointments (21). Because the current study was part of a larger cohort study, we were able to compare various characteristics between participants and non-participants. From this it appeared that the participants did not differ statistically from non-participants with respect to age, gender, and activities during which the trauma occurred (data not presented). The experienced pain severity as scored on the numeric rating scale was somewhat smaller in non-participants than it was in participants (mean difference 0.83; ANOVA, p = 0.046), which is in accordance with one of the self-reported reasons for non-participation ("minor trauma"). Thus, the pain severity might have influenced the interest of patients concerning participation in our study.

Of the 134 patients (60 females), two had sustained a bilateral acute knee trauma, resulting in 136 symptomatic and 132 asymptomatic knees. All patients underwent MR imaging of both the symptomatic and the asymptomatic knee. Mean age of the participants was 40.8 years (range 18.8 to 63.8 years). MR imaging was performed on average 5.4 weeks after the trauma (range 1.3 to 11.6 weeks; 75th percentile 6.7 weeks).

In 80 patients, the initial MR images showed one or more bone bruise lesions in femur and/or tibia. We tried to obtain a complete MRI follow-up study in all of these patients. Initially, we had planned only two follow-up MRI scans, approximately three weeks and one year after the baseline scan (initial study design). Because we found persisting bone bruises in many patients three weeks after the initial MRI scan, we decided to perform four follow-up scans, approximately three weeks, 10 weeks, six months and 12 months after the baseline scan. We considered follow-up to be complete when no bone bruise could be discerned any more, or after one year of follow-up.

Of all 80 participants with one or more bone bruises in femur and/or tibia, 28 had missed one or more follow-up scans (Figure 7.2). Of these, however, the majority had at least one follow-up; only three participants with bone bruise at baseline had no follow-up images at all; 10 had missed three scans, 10 missed two appointments, and in five cases one MRI scan was missing. Reasons for incomplete follow-up were: initial study design (n = 7), the small rest lesion was overlooked by the investigators, therefore no appointment for further follow-up was made (7), patient refusal (3), pregnancy (2), and missing appointments or unknown (9). Twenty-three patients with incomplete follow-up did return for MR imaging one year after inclusion. We believe that the incompleteness of the data does not hamper drawing conclusions based on the included patients.

In our opinion, our study population is a good representation of patients with new knee trauma in general practice. We used a prospective study design, which is generally considered the preferred study design. We describe the first study cohort in which the findings in posttraumatic symptomatic and contralateral knees of general practice patients can be correlated. Our follow-up study on the natural course of bone bruise encompasses the largest patient cohort thus far. Moreover, our study is the first structured follow-up study.

STRENGTHS AND DRAWBACKS

With respect to the two review articles (Chapters 2 and 3), comparison of the results of the individual studies was difficult because of heterogeneity in study design and data presentation. The observed study populations were generally small and the quality of the included studies was generally poor. Pooling of data was not possible and no summary statistics could be given, other than percentages mentioned in the underlying articles. The literature search was restricted to the Medline database. Using additional databases might be of value. The Embase database contains additional journals (the overlap of journals with MEDLINE is about 60%) but, compared to Medline, Embase has a better coverage of pharmacological and medication studies as well as studies on healthcare policy and management. Furthermore, (national) European journals are better represented in the Embase database. For our topic, we did not expect to obtain additional studies to be included with an additional search in Embase, but we cannot state that with 100% certainty. An important problem of the Embase database is that it is not available for free, as is the Medline database. Such searches can therefore not be reproduced by every reader/reviewer. Despite all these potential problems, we think that these reviews were very useful to gain insight into the available knowledge on the topic of the natural course of posttraumatic knee lesions and to identify the gaps that need to be addressed.

With respect to our clinical studies, although we tried our best to set up a well-founded study design, we also acknowledge some drawbacks in our own prospective study design. In our study on abnormalities seen on MR imaging in posttraumatic and contralateral knees (Chapters 4 to 8), all MR images were evaluated independently by two radiologists and interobserver variability was assessed. In case of disagreement, the findings were discussed until consensus was reached. On the posttraumatic side more MR series were performed than on the contralateral side, implying that the radiologists were not blinded to information concerning which side was potentially affected by the trauma. This may have caused some underestimation of lesions in the contralateral asymptomatic knee. However, our study results of the contralateral knee are in line with those of studies in asymptomatic volunteers,[2-5] and we therefore think that the influence of 'non-blinding' is small. Although for an optimal study design we think that investigators should be blinded for symptomatic and asymptomatic sides by using identical MR sequences, this would require a longer duration and higher costs of the MR imaging.

The prevalence and severity of bone bruise found in the study on posttraumatic bone bruise in general practice - as described in Chapter 6 - may be underestimates of the true prevalence and severity in general practice, because patients with more severe knee lesions might have been referred directly to a hospital without being included in the study. On the other hand, the prevalence and severity may have been overestimated because non-participants might have had no or smaller bone bruise lesions due to minor trauma. The impact of under- and overestimation on the true prevalence and severity of bone bruise in general practice remains uncertain. We also acknowledge the possible influence of time between trauma and MR imaging on bone bruise lesions. In this period (ranging from 1.3 to 11.6 weeks), natural healing of lesions might have occurred. However, because we found that this period appeared to have no influence on the prevalence and severity of bone bruise, we believe that this relatively broad time interval did not significantly influence our study results.

We realize that the mean healing time of bone bruises, as calculated in Chapter 7, is not an exact measure. The event 'healing' presumably occurs unnoticed. More follow-up scans, with smaller time intervals between scans, would have resulted in a more precise calculated healing time. However, this would have been more troublesome for the patients with, in our opinion, a higher risk of non-participation in the follow-up study. Moreover, more follow-up scans would have been an unacceptable workload for the already full MR imaging schedule. We expected that with the used schedule, we would be able to perform an accurate survival analysis that does justice to the fast resolving lesions as well as the more slowly resolving lesions; moreover, we kept patient compliance as high as possible. The accuracy of the calculated median healing time is further influenced by censoring. Many missing data were caused by patients themselves, who found the follow-up scans too bothersome and who missed appointments. Some patients missed appointments due to holidays or working trips. Most of these patients with some missing data could be motivated, however, to return one year after trauma, for a final follow-up scan. Two patients had to stop participation because of pregnancy. The investigators were also a source of censoring, because when we evaluated the follow-up scans on the day they were made, we did not compare them with the former scans. Some very small rest lesions were overlooked, and no appointment for further follow-up was made. At the final evaluation of the follow-up scans, we compared all scans together and at that moment, the very small rest lesions were recognized and counted as present for the analyses. In future research, it is advisable that all the former scans be available when new follow-up appointments are made.

In our study, we describe the MR imaging findings for the total population of patients visiting their GP for posttraumatic knee symptoms. In daily (general) practice, only a few patients undergo MR imaging of the knee after trauma. Although it is unclear how our results translate to patients undergoing MR imaging of the knee after referral to a specialist, we believe that our data (especially, our findings in contralateral knees) may serve as reference data for these populations.

MAIN FINDINGS

Natural course of posttraumatic knee lesions; reviews

In our systematic review on the natural course of ligamentous and meniscal knee lesions detected at MR imaging (Chapter 2), we showed that the anterior cruciate ligament (ACL) and the posterior cruciate ligament (PCL) can regain continuity with conservative treatment after suffering partial or complete rupture. In case of a PCL rupture, a continuous ligament more often results in a firm endpoint with a posterior drawer test than does a discontinuous ligament. In case of an ACL rupture, a moderate association between normalization of ACL appearance and normal function is described. Despite the fact that there seemed to be a weak association between ligamentous continuity on MR imaging and clinical stability at follow-up, we have to keep in mind that apparent continuity at follow-up MR images does not guarantee normalization of the physical examination. When radiologists discuss results of MR imaging of individual patients with a traumatologist, it is important that they acknowledge this possible incongruity between imaging and physical examination. There is as yet no knowledge on the natural course of collateral ligament ruptures and meniscal lesions detected at MR imaging.

In our systematic review on the follow-up of posttraumatic bone bruises (Chapter 3), we found a natural healing of these lesions; a disappearance of bone bruise signal intensity was seen in most cases. In the few patients with persistent bone bruise, lesion size had clearly decreased. Other lesions can occur as a consequence of initial bone bruise; in such cases, the typical bone bruise pattern (low signal intensity on T1-weighted images and high signal intensity on T2-fat suppressed weighted images) has disappeared, but some rest lesions (e.g. fibrosis or fatty replacement of cancellous bone) often remain. The clinical meaningfulness of these findings is, as yet, unclear. Classification of bone bruise seemed to have prognostic value. The studies suggested a good prognosis for reticular lesions, but cartilage loss in all cases of initially disrupted articular surfaces. The reported prognosis of geographic lesions differed between studies. The clinical prognosis of bone bruise is good. With the available literature, no conclusions can be drawn about the effect of different treatment strategies on the course of bone bruise. All that can be stated is, that with non-operative treatment, bone bruise signal intensity disappears in most cases.

With our systematic reviews we have shown that, after sustained cruciate ligament rupture or bone bruise, a normalization of the initial abnormal MR appearance is possible. Arthroscopy studies have shown that tears of the meniscus, even when they occur in association with a cruciate ligament injury, can heal morphologically with non-surgical treatment.[6, 7] Many reports have addressed the healing potential of medial collateral ligament tears, as assessed with physical examination.[8, 9] All these results suggest natural repair mechanisms, in ligaments and menisci as well as in bone. This supports the watchful waiting policy, advised in the Dutch guideline for general practitioners (NHG guideline) on the management of posttraumatic knee symptoms.[10] Especially in eligible patients (higher age, low physical demands, high operation risk) one could wait and see if there is a natural healing response and a spontaneous reduction of complaints before referring these patients to secondary care.

MRI abnormalities in posttraumatic and contralateral knees; HONEUR study

Our study on MR imaging in posttraumatic (symptomatic) knees and contralateral knees - as described in Chapter 5 - also suggests that a wait and see policy in symptomatic knees may be justified. We have shown that ligament lesions in posttraumatic knees are most probably the result of the recent trauma because such lesions are exclusively seen in symptomatic knees. In contrast, meniscal lesions and effusion may be pre-existent in many cases. Especially, horizontal meniscal tears seem to be unrelated to recent trauma. From our analyses it appears that radial, longitudinal and complex tears are related to recent trauma, but we have shown that these lesions can also be seen in asymptomatic knees. We did not analyze the relationship between the presence of meniscal lesions, as shown on MR imaging, and physical symptoms. Looking at our study results, it is questionable whether especially horizontal meniscal tears could be the cause of posttraumatic knee complaints, if these lesions are the only visualized abnormality on MR imaging. There might be subtle differences between symptomatic and asymptomatic meniscal tears that cannot be detected by current MR imaging, but may account for the presence or absence of symptoms. Pending further investigation, our study results suggest that horizontal meniscal tears should not be treated just because of their presence on posttraumatic MR imaging.

We have also shown that many asymptomatic knees show an effusion, particularly a small effusion. Moderate and large effusions are related to trauma, but moderate effusions can also be seen in contralateral knees. In symptomatic knees, a small effusion in itself need not be of clinical importance. On the other hand, the absence of effusion does not rule out other intra-articular knee lesions. Whether the combination of moderate to severe effusion and meniscal tears is of prognostic value (compared to meniscal tears without effusion) needs to be clarified.

Bone bruises

Many previous studies reported on posttraumatic bone bruises, most of the time concerning bone bruise location in relation to trauma mechanism and concomitant knee lesions. Only a few studies, concerning secondary care patients, described the prevalence of bone bruises.[11-16] To our knowledge, we have performed the first study on posttraumatic bone bruise in general practice (Chapters 6 to 8). We found bone bruise in 60% of the posttraumatic patients. We believe this to be a high prevalence. However, the lesions were generally small: in 76% of all lesions less than 25% of the bone volume was involved. With our study, we gave insight into determinants of bone bruise (Chapter 6). The presence of bone bruise was related to medial meniscus lesions, anterior cruciate ligament tears, and medial collateral ligament tears. The severity of bone bruise was related to bone bruise type (reticular lesions were more severe), bone bruise location (tibial and lateral lesions were more severe) and concomitant knee lesions (patients with anterior cruciate ligament generally showed more severe bone bruises).

In the past, there has been some debate about the time to resolution of bone bruises. In one of the earliest studies on the subject, it was suggested that bone bruises resolve within 12 weeks of the acute injury.[13] However, more recent studies have shown that bone bruises can persist for a much longer period of time.[14, 15, 17, 18] In the available follow-up studies on bone bruises, follow-up is nearly always restricted to one MRI scan. To our knowledge, our study is the first structured prospective follow-up study of healing of posttraumatic bone bruises (Chapter 7). We found a median healing time of bone bruise patients of 42.1 weeks. Healing of patients is delayed in case of osteoarthritis and a higher number of bone bruise lesions. The likelihood of resolution of individual bone bruise lesions is higher in the absence of osteoarthritis (at six months and 12 months follow-up), in patients of younger age (at six months and 12 months follow-up) and in cases of reticular type of bone bruise (at six months follow-up). Concomitant knee lesions, gender, obesity, sports load, workload, and location and severity of bone bruise appear to have no prognostic value on the natural course of bone bruise.

We were particularly surprised that we could not find a statistically significant relation between the natural course and the severity of bone bruise at baseline; we expected a worse prognosis in case of more severe lesions. We realize that our bone bruise volume measurements are only an approximation of true bone bruise volume. We classified severity of bone bruise according to the percentage of bone volume involved. It proved to be a quick method with good reproducibility (kappa 0.95 to 1.00). For statistical purposes (because of low frequencies in the more severe categories), we dichotomized bone bruise severity into light (<25% volume involvement) and severe (>25% involvement). The most severe category (75% volume involvement or more) could not be tested separately, because only four lesions were included in this group.

In our study on determinants of bone bruise, we saw that reticular lesions were generally more severe than other types of bone bruise (Chapter 6). In the study on prognosis of bone bruises we saw a higher likelihood of resolution in case of reticular bone bruise lesions (Chapter 7). Therefore, we also performed stratified analyses to rule out any interaction between lesion type and severity. These analyses, stratified on reticular and geographic lesions, also showed no statistical significant relationship between severity of bone bruise lesions and prognosis.

We were also interested in the clinical consequences of bone bruises. Bone bruise patients experienced a little more pain than non-bone bruise patients, at baseline as well as during follow-up, but the differences were not statistically significant (Chapter 8). Our failure to find a significant relationship might be caused by the fact that pain after trauma can arise from many different structures; bone bruise is only one of the many possible causes. Perhaps our adjustments failed to cover all possible sources of pain. But apart from the fact that the differences were not statistically significant, we believe that the small differences in pain scores between bone bruise and non-bone bruise patients are hardly clinically relevant.

The data from our study suggest that the clinical consequences of bone bruise are small (there is a natural healing response and there is at most a weak relation between bone bruise and pain). Patients can be better informed with this information. It is important to acknowledge, however, that there are no studies that provide long-term clinical follow-up. Bone bruises might be associated with premature cartilage degeneration and osteoarthritis. If this should be the case, bone bruises are not so clinically benign as they now appear.

FUTURE RESEARCH

In our systematic review (Chapter 2), we found a few studies on the natural course of cruciate ligament tears detected through MR imaging, showing that the ligaments can regain continuity, after suffering partial or total rupture. There is, however, very little knowledge on the association between the MR imaging appearance, functional outcome scores and pain. Looking at arthroscopy and clinical studies, it is very likely that there is also a healing potential of meniscal tears and collateral ligament ruptures. To date, however, there are no studies that describe the MR imaging evaluation of this healing capacity. Subsequent analyses on the natural course of posttraumatic knee lesions will be performed in our prospective study cohort.

With our study, we have offered additional information on the determinants, course and clinical consequences of posttraumatic bone bruises (Chapters 6 to 8). Future long-term follow-up studies are necessary to demonstrate long-term consequences, if there are any, in cartilage or bone. These studies should use a longer follow-up period than we used in our study, e.g. five years. If these studies should demonstrate adverse long-term consequences, treatment effect studies are also needed to demonstrate the beneficial effects of different treatment strategies.

Nowadays, patients with posttraumatic knee symptoms who are referred to secondary care, may undergo arthroscopy, MR imaging or both. The chance for any patient to undergo MR imaging of the knee strongly depends on the local situation. In some hospitals, most patients with posttraumatic knee symptoms undergo MR imaging, while in other hospitals this occurs in only a minority of such patients. In the Netherlands, multidisciplinary guidelines for arthroscopy are available,[19] but guidelines for the use of MR imaging in patients with sustained knee trauma are lacking. Moreover, in the arthroscopy guideline, indications for arthroscopy are based on history taking and physical examination; MR imaging is not mentioned in this guideline. The same holds for the general practitioners guideline that was published in 1998, in which only plain radiographs are advised in some patients.[10] Therefore, future research and consensus meetings should clarify which patients should undergo MR imaging of the knee or arthroscopy, or both.

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Chapter 10

Summary & Conclusions
Samenvatting & Conclusies

SUMMARY

Every year, many patients seek medical treatment for sustained knee injury. The reported incidence in general practice ranges from 1.1 to 1.4%. Since the introduction of MR imaging, several studies have reported on the appearance of normal and abnormal cruciate ligaments, collateral ligaments and menisci. Compared to arthroscopy, which is considered the reference standard, the sensitivity and specificity of MR imaging are high for detecting abnormalities in these structures. Therefore, MR imaging is widely used to evaluate knee symptoms, and clinical decision-making is influenced by the results of these scans.

It has been shown that abnormalities in menisci, ligaments, and bone are found after knee trauma in approximately two thirds of patients. Such abnormalities (especially meniscal lesions) are also present in up to one third of asymptomatic knees, especially in those of older age. Therefore, in the trauma setting it is questionable which visualized lesions are the result of the recent trauma and which lesions might have been pre-existent. There is little knowledge on the natural course and functional outcome of posttraumatic knee lesions. However, this information is necessary for making managements decisions and to inform patients about their prognosis. This study was conducted to provide additional information in this field of posttraumatic knee lesions.

This thesis consists of four parts. Part I (Chapter 1) forms the introduction. Part II (Chapters 2 and 3) presents two studies in which we systematically summarized the available literature addressing the natural course of posttraumatic knee lesions. Part III describes the design (Chapter 4) and the results (Chapters 5 to 8) of our MR imaging study on patients with sustained knee trauma presenting in primary care. Part IV (Chapters 9 and 10) contains the general discussion and summaries.

In Chapter 2 we described the results of our systematic review of the literature on the natural course of posttraumatic ligamentous and meniscal knee lesions. Eleven studies were included: five concerning the posterior cruciate ligament (PCL), five concerning the anterior cruciate ligament (ACL), and one the menisci. Using a 14-item criteria list, only four studies received eight points or more and were considered 'high quality'. The results showed that between 77% and 93% of the partial or complete PCL ruptures regained continuity at follow-up MRI scanning. In case of partial or total ACL rupture, repair of continuity is also possible. There was a possible association between MRI continuity and clinical stability. Based on this review, no conclusions could be drawn about the natural course of meniscal or collateral ligament injury as seen on MRI.

In Chapter 3 we presented our review of the literature on the follow-up of MRI-detected posttraumatic occult bone lesions. Eight of the 13 included studies scored eight points or more of the 15 available quality points and were considered 'high quality'. The study results suggested a generally good clinical prognosis of bone bruises. Normalization

of MR imaging appearance is possible and most often encountered after reticular lesions (i.e. serpiginous region of diminished T1W signal distant from subchondral bone plate, according to the Vellet classification). Cartilage loss at follow-up is often found in case of initial cartilage damage (impaction or osteochondral fracture).

In Chapter 4 we described the design of our MRI study on patients presenting to their general practitioner with posttraumatic knee complaints.

In Chapter 5 we found that, after sustained knee trauma, ligamentous lesions were found almost exclusively at the posttraumatic side. Meniscal lesions and effusion were almost equally found in posttraumatic and contralateral knees. Multivariable analyses revealed that moderate to severe effusion was related to recent trauma and osteoarthritis, but not to history of trauma and age. The presence of any meniscal tear had a statistically significant association with recent trauma, a history of old trauma and age, but not with osteoarthritis. History of trauma was more strongly related to the group of radial, longitudinal and complex meniscal tears than to horizontal tears. Recent trauma was not related to horizontal meniscal tears but was strongly related to other types of meniscal tears.

In Chapter 6 we described the prevalence, severity, and determinants of bone bruise for the study population. In 81 of 136 posttraumatic knees (60%), 160 bone bruise lesions were found; 63% concerned reticular lesions, 55% geographic lesions, and 8% impaction, subcortical or osteochondral fractures. The lesions were almost equally divided over femur condyles and lateral and medial tibia plateau. Presence of bone bruise was related to medial meniscal lesions, anterior cruciate ligament, and medial collateral ligament tears. Bone bruises were more severe in the tibial or lateral location, in case of reticular lesion type, and in the presence of anterior cruciate ligament tears.

In Chapter 7 we performed a structured MR imaging follow-up study of the patients with bone bruise in the posttraumatic knee. Follow-up was ceased when no bone bruise could be discerned any longer, or after one year follow-up. The median healing time of bone bruise patients was 42.1 weeks. Healing was prolonged in case of a higher number of bone bruise lesions and osteoarthritis. Resolution of individual bone bruise lesions was prolonged in the presence of osteoarthritis and higher age. Reticular lesions were less likely to be present after six months than other bone bruise types. Bone bruise lesion size and location, concomitant ligamentous or meniscal knee lesions, gender, obesity, workload, and sports load had no prognostic value.

In Chapter 8 we looked for a possible relationship between the presence of bone bruise in posttraumatic knees and pain. All patients underwent MR imaging of the posttraumatic knee at baseline and received a pain score at baseline and approximately three months, six months and 12 months after trauma. Patients with bone bruise underwent follow-up MR imaging. Firstly, we compared the pain scores at baseline of bone bruise patients to the baseline pain scores of non-bone bruise patients. Secondly, we analyzed the differences in the follow-up pain scores between participants with and without bone bruise at baseline. Thirdly, we investigated the relationship between pain and the presence of bone bruise at follow-up in patients with bone bruise on the baseline MRI scan. None of these analyses showed a statistically significant relationship between the presence of bone bruise and pain.

In Chapter 9 we have discussed the main findings of this thesis and placed them in a broader perspective.

CONCLUSIONS

1. The available literature shows that the anterior cruciate ligament and the posterior cruciate ligament can regain continuity, after suffering partial or complete rupture.
2. In the available literature, a healing response is described after sustained posttraumatic occult bone lesions. The initial MRI appearance appears to have prognostic value.
3. Ligamentous lesions in posttraumatic knees are most probably the result of recent trauma. Radial, longitudinal and complex meniscal tears are strongly related to trauma, whereas horizontal meniscal tears and effusion may be pre-existent in many cases.
4. Bone bruises are encountered in 60% of patients presenting in primary care with posttraumatic knee complaints. Presence and severity of bone bruise are related to concomitant knee lesions. Severity is also related to location and lesion type.
5. The median healing time of patients with bone bruise lesions in the posttraumatic knee is 42.1 weeks. Prognosis is particularly influenced by the presence of osteoarthritis. Age, type of bone bruise and number of bone bruise lesions also have prognostic value.
6. There is no statistically significant relationship between pain and the presence of bone bruise in the posttraumatic knee.

SAMENVATTING

Posttraumatische knieklachten zijn een frequente aanleiding tot het zoeken van medische hulp. De gerapporteerde incidentie in de huisartspraktijk varieert van 1,1 tot 1,4%. Sinds de introductie van de MRI scan, is in meerdere onderzoeken het beeld beschreven van normale en abnormale kruisbanden, collaterale banden en menisci. Vergeleken met arthroscopie (wat beschouwd wordt als de gouden standaard), heeft de MRI scan een hoge sensitiviteit en specificiteit voor het detecteren van knieletsels. Beeldvorming met MRI wordt daarom veelvuldig toegepast bij de evaluatie van knieklachten en de klinische besluitvorming wordt beïnvloed door de resultaten van deze scans.

Eerder onderzoek heeft reeds aangetoond dat, na trauma, bij ongeveer 66% van de patiënten afwijkingen worden gevonden in menisci, ligamenten en bot. Maar dergelijke laesies (met name meniscuslaesies) worden ook gezien in asymptomatische knieën, tot in ongeveer 33% van de gevallen. Deze letsels in asymptomatische knieën komen met name voor op hogere leeftijd. Na trauma is het daarom niet duidelijk welke laesies het gevolg zijn van het recente trauma en welke laesies mogelijk reeds preëxistent aanwezig waren. Daarnaast bestaat er weinig kennis over het natuurlijke beloop en het functionele herstel van posttraumatische knieletsels. Maar al deze informatie is wel noodzakelijk om een behandelplan te kunnen opstellen en om patiënten goed te kunnen informeren over de prognose. Deze studie werd opgezet om kennis bij te dragen op dit terrein van posttraumatische knieletsels.

Dit proefschrift bestaat uit vier delen. Deel I (Hoofdstuk 1) vormt de introductie. Deel II (Hoofdstukken 2 en 3) presenteert 2 studies waarin wij een systematische samenvatting geven van de beschikbare literatuur met betrekking tot het natuurlijke beloop van posttraumatische knieletsels. Deel III beschrijft de opzet (Hoofdstuk 4) en de resultaten (Hoofdstukken 5 tot 8) van onze MRI studie waarin patiënten werden geincludeerd, die zich presenteerden bij de huisarts met posttraumatische knieklachten. Deel IV (Hoofdstukken 9 en 10) omvat de discussie en de samenvattingen.

In Hoofdstuk 2 geven wij een systematisch overzicht van de beschikbare literatuur met betrekking tot het natuurlijke beloop van posttraumatische ligament en meniscus laesies in de knie. Elf studies werden geincludeerd: vijf met betrekking tot de achterste kruisband, vijf met betrekking tot de voorste kruisband en één met betrekking tot de menisci. Gebruik makend van een 14-item scorelijst, bleek dat slechts vier studies acht punten of meer scoorden en werden beschouwd als 'studies van hoge kwaliteit'. De resultaten toonden dat tussen 77% en 93% van de partieel of totaal gescheurde achterste kruisbanden een herstel toonden van de continuïteit bij vervolg MRI onderzoek. Ook in geval van een partiële of totale voorste kruisband ruptuur was herstel van de continuïteit mogelijk. Er bestond een mogelijk verband tussen continuïteit op het MRI onderzoek en klinische stabiliteit. Gebaseerd op de uitkomsten van deze review, zijn er geen uitspraken mogelijk over het natuurlijke beloop van meniscus of collateraal band letsel, zoals dit kan worden gezien op een MRI scan.

Hoofdstuk 3 geeft een overzicht van de literatuur met betrekking tot het natuurlijke beloop van posttraumatische occulte botlaesies, zoals dit wordt gezien op MRI scans. Acht van de 13 geincludeerd studies scoorden acht punten of meer van de 15 beschikbare kwaliteitspunten en werden beschouwd als 'studies van hoge kwaliteit'. De resultaten suggereerden een goede klinische prognose van botoedeem. Een normalisatie van het MRI beeld bleek mogelijk en werd het meest frequent gezien na het doormaken van een reticulair type letsel (slingervormig gebied van afgenomen signaal intensiteit op T1 gewogen opnamen, op enige afstand van het subchondrale bot, volgens de Vellet classificatie). Bij vervolgonderzoek werd vaak kraakbeenverlies gezien nadat bij het eerste onderzoek kraakbeenschade is vastgesteld (impactie of osteochondrale fractuur).

In Hoofdstuk 4 beschrijven we de opzet van onze MRI studie, waarin we patiënten hebben geincludeerd die zich bij hun huisarts presenteerden met posttraumatische knieklachten.

In Hoofdstuk 5 beschrijven we dat ligamentletsels na trauma vrijwel exclusief voor kwamen aan de posttraumatische zijde. Meniscuslaesies en hydrops waren vrijwel gelijk verdeeld over de posttraumatische en contralaterale knieën. Multivariate analyses toonden dat matige tot ernstige hydrops gerelateerd is aan recent trauma en artrose, maar niet aan een trauma in de voorgeschiedenis of leeftijd. De aanwezigheid van een meniscusscheur bleek statistisch significant gerelateerd aan recent trauma, trauma in de voorgeschiedenis en leeftijd, maar niet aan artrose. Het hebben van een trauma in de voorgeschiedenis bleek sterker gerelateerd aan de groep van radiaire, longitudinale en complexe meniscusscheuren dan aan horizontale meniscusscheuren. Het hebben doorstaan van een recent trauma was niet gerelateerd aan horizontale meniscusscheuren, maar was wel sterk gerelateerd aan de overige typen meniscusscheuren.

In Hoofdstuk 6 beschrijven we de prevalentie en determinanten van botoedeem in onze studiepopulatie. In 81 van de 136 posttraumatische knieën (60%), vonden wij 160 botoedeem laesies. In 63% van de laesies betrof het reticulaire laesies, in 55% geografische laesies en in 8% impactie, subcorticale of osteochondrale fracturen. De laesies waren vrijwel gelijk verdeeld over de femurcondylen en het mediale en laterale tibiaplateau. De aanwezigheid van botoedeem bleek gerelateerd aan mediale meniscuslaesies, voorste kruisband en mediale collaterale band rupturen. De botoedeem laesies waren in het algemeen ernstiger wanneer zij zich lateraal of in de tibia bevonden, wanneer het een reticulair type letsel betrof en wanneer er tevens een voorste kruisbandruptuur aanwezig was.

In Hoofdstuk 7 beschrijven we de data van ons gestructureerde MRI vervolgonderzoek van patiënten met botoedeem in de posttraumatische knie. Het vervolgonderzoek werd gestaakt indien het botoedeem was verdwenen of na een jaar. De mediane genezingsduur van botoedeem patiënten bedroeg 42,1 weken. Genezing verliep trager in geval van een groter aantal oedeemlaesies bij het initiële onderzoek, en in geval van bijkomende artrose. Het verdwijnen van individuele botoedeemlaesies duurde langer in aanwezigheid van artrose en in geval van een hogere leeftijd. Reticulaire laesies hadden een grotere kans afwezig te zijn bij zes maanden dan andere typen botoedeem laesies. Grootte en locatie van de botoedeem laesie, bijkomend ligament of meniscusletsel in de knie, geslacht, obesitas, werkbelasting en sportbelasting hadden geen prognostische waarde.

In Hoofdstuk 8 zoeken we naar een mogelijke relatie tussen de aanwezigheid van botoedeem in posttraumatische knieën en pijn. Bij aanvang van het onderzoek ondergingen alle patiënten een MRI scan van de posttraumatische knie en vulden zij een pijnscore in. Daarnaast ontvingen zij allen een pijnscore formulier ongeveer drie maanden, zes maanden en 12 maanden na het trauma. Patiënten met botoedeem ondergingen een gestructureerd MRI vervolgonderzoek. Ten eerste vergeleken we de baseline pijnscores van patiënten met botoedeem met de baseline pijnscores van patiënten zonder botoedeem. Ten tweede analyseerden wij het verschil in pijnbeloop tussen patiënten met en patiënten zonder botoedeem bij aanvang van de studie. Ten derde onderzochten wij in de patiënten die botoedeem toonden op het eerste MRI onderzoek, de relatie tussen pijn en de aanwezigheid van persisterend botoedeem. Geen van deze analyses toonde een statistisch significant verband tussen de aanwezigheid van botoedeem en pijn.

In Hoofdstuk 9 bespreken we de belangrijkste bevindingen van dit proefschrift en plaatsen we ze in een breder perspectief.

CONCLUSIES

1. Uit de beschikbare literatuur blijkt dat de continuïteit van de voorste en achterste kruisband kan herstellen na partiële of totale scheur.
2. In de beschikbare literatuur wordt een genezingsrespons beschreven na een doorgemaakt posttraumatisch occult botletsel. Het initiële MRI beeld lijkt prognostische waarde te hebben.
3. Ligamentletsels in posttraumatische knieën zijn het meest waarschijnlijk het gevolg van het recent knietrauma. Radiaire, longitudinale en complexe meniscusscheuren zijn sterk gerelateerd aan trauma, terwijl horizontale meniscusscheuren en hydrops in veel gevallen preëxistent aanwezig kunnen zijn.
4. Patiënten die zich presenteren bij de huisarts met posttraumatische knieklachten tonen in 60 procent van de gevallen botoedeem. De aanwezigheid en ernst van botoedeem zijn gerelateerd aan bijkomend knieletsel. De ernst is ook gerelateerd aan locatie en laesie type.

5. De mediane genezingsduur van patiënten met botoedeem in de knie bedraagt 42,1 weken. De prognose wordt met name beïnvloed door de aanwezigheid van artrose. Leeftijd, type botoedeem en het aantal botoedeem laesies binnen een patiënt hebben ook prognostische waarde.
6. Er bestaat geen statistisch significante relatie tussen de ernst van de ervaren pijn en de aanwezigheid van botoedeem in de posttraumatische knie.

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CURRICULUM VITAE

Simone Salomé Boks werd geboren op 23 augustus 1974 te Lieren (gemeente Apeldoorn). In 1992 behaalde zij haar VWO-diploma aan de Christelijke Scholengemeenschap De Heemgaard te Apeldoorn, waarna zij begon aan de studie geneeskunde aan de Erasmus Universiteit Rotterdam. Aansluitend op het behalen van haar artsexamen in 1998, werkte zij drie maanden op de afdeling radiologie van het Clara Ziekenhuis te Rotterdam als arts-assistent. Vervolgens werd zij op 1 januari 1999 toegelaten tot de opleiding radiologie. Tijdens haar opleiding begon zij in 2002 aan het onderzoek zoals beschreven in dit proefschrift. Na het afronden van haar specialisatie tot radioloog op 1 januari 2004, werkte zij nog acht maanden als chef de clinique in het Medisch Centrum Rijnmond-Zuid. Vervolgens was zij ruim een jaar werkzaam als chef de clinique radiologie in de Isala Klinieken, locatie De Weezenlanden te Zwolle. Na enkele maanden volledig aan haar onderzoek te hebben gewerkt, startte zij als radioloog in het Diaconessenhuis te Meppel, alwaar zij nog steeds werkzaam is.

Simone Boks is getrouwd met Marco Blanker en samen hebben zij een zoontje, genaamd Sjoerd.