MRI of the knee cost-efffective use

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MRI of the Knee
Cost-Effective Use

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CHAPTER 1

Introduction

1. Introduction

In The Netherlands every year approximately 300,000 knee injuries occur [1]. An injury to the knee is the second most common problem of the musculoskeletal system for which patients consult their general practitioner (48 per 1000 per year) [2]. Between the ages of 16 and 45 years the prevalence of knee complaints in primary care is 27 per 1000 [2]. Most of these injuries heal spontaneously, but in a minority of cases (18%) these complaints last more than four weeks and about 90,000 patients are referred to an orthopedic surgeon each year [2,3]. Because of the high prevalence of knee injuries in primary care several guidelines for general practitioners were issued in 1998 [4-6].

Approximately 20,000 arthroscopies are performed in patients aged between 16 and 45 years [7]. Arthroscopy offers direct visualization of all intra-articular structures with high diagnostic accuracy [8], the possibility to examine the stability of the knee under anesthesia and the possibility to perform a therapeutic procedure in the same session. However, arthroscopy is an invasive procedure that needs hospitalisation and comes with high costs, the risk of complications and the sick leave afterwards.

The complication rate of arthroscopy is reported to be between 0.56 and 8.2% [9-12]. Sherman at al. [12] found 126 serious complications in 2640 arthroscopies. Complications were: infection, hemarthros, adhesions, effusion, cardiovascular complications, neurological complications, sympathetic reflex dystrophia and broken equipment.

The percentage of non therapeutic arthroscopies varies and is being estimated between 27 and 61% [13-15]. In 12,000 (66.3%) out of 18,000 arthroscopies performed in The Netherlands in patients aged between 16 and 45 years no therapeutic procedure was registered. The number of arthroscopies per 100,000 inhabitants varied between regions in The Netherlands from 323 to 409 [16].

These two issues led the Dutch Orthopedic Society (NOV) in cooperation with the Centraal Begeleidingsorgaan voor de Intercollegiale Toetsing (CBO) to organize a consensus meeting with regards to arthroscopy of the knee [16]. This consensus concerns patients aged between 16 and 45 years with at least four weeks of knee complaints. The consensus was that it is useless to conclude an examination with an arthroscopy if not at least one of the following clinical criteria is met at physical examination: substantial joint effusion (more than bulging sign), passive extension deficit of at least 10°, passive flexion deficit of at least 20°, instability (ie, positive varus and valgus stress, Lachman, anterior and posterior drawer, and Pivot test results), a positive result of at least one meniscal provocation test (ie, McMurray, Apley, or squat test), and atrophy of at least 2 cm relative to the contralateral leg measured 15 cm above the medial joint line. Furthermore the consensus states that the clinician, after history taking, physical examination and if necessary diagnostic imaging, almost always can decide his treatment-strategy. For that purpose a purely diagnostic arthroscopy is not necessary.

Five years after this consensus meeting, in 1997, the percentage of purely diagnostic arthroscopies had risen from 66.3% to 72.9% ($p < 0.05$) [7].

Magnetic Resonance (MR) imaging was not taken into account in the consensus. In studies evaluating the diagnostic accuracy of MR, using arthroscopy as standard of reference, MR proved to have a high accuracy in detecting intra-articular knee pathology [17-21]. Other studies demonstrated that MR can be used in patients with knee complaints to limit the number of diagnostic arthroscopies and reduce costs [13-15, 22-27]. These studies all have three important shortcomings. All of these studies used intermediate outcome parameters, like diagnostic accuracy or therapeutic impact of MR in stead of clinical outcome parameters: 'impact on health' [28]. The 'impact on health' can be studied by following patients in time, using clinical outcome measures, like function and symptoms of the knee, to evaluate success or failure of diagnostic and therapeutic strategies. The second shortcoming of the aforementioned studies is that costs and savings were calculated using charges or fees and not the real cost-prices of procedures. Moreover, often only the medical costs and not the non-medical or productivity costs were taken into account in the analyses. The third shortcoming of the studies is that patients were not randomly assigned to the treatment strategies, thus introducing bias.

We started a prospective multicenter study in one academic and two teaching hospitals in The Netherlands with the purpose to evaluate the cost-effectiveness of MR imaging performed to exclude the need for arthroscopy in patients with nonacute knee symptoms and high clinical suspicion of intra-articular knee abnormality. To this end all consecutive patients aged 16-45 years, who had had knee symptoms (specifically pain, swelling, instability, and/or locking) for at least 4 weeks (nonacute) and were referred to one of the three participating hospitals were eligible for the study. All included patients underwent a standardized physical examination. Based on this physical examination, according to guidelines by the Dutch Orthopedic Society, patients were divided in two groups: patients with high and patients with low clinical suspicion on intra-articular knee pathology. All patients underwent MR imaging. MR was classified as being positive (ie, arthroscopy indicated on the basis of the MR findings) or negative (ie, arthroscopy not indicated on the basis of the MR findings alone). Patients with high clinical suspicion and positive MR result underwent arthroscopy. Patients with high clinical suspicion and negative MR result were randomized; half of these patients underwent arthroscopy and the other half was treated conservatively for at least three months. was assigned for diagnostic arthroscopy. All patients with high clinical suspicion were clinically evaluated at six months and costs were calculated in order to perform a cost-effectiveness evaluation. Patients with low clinical suspicion and positive MR result underwent arthroscopy. Patients with low clinical suspicion and negative MR result were conservatively treated. These patients were not clinically evaluated after six months.

This thesis describes the cost-effictiveness study and several substudies, using the same patient population. In chapter 2 we assessed the effectiveness of MR imaging in selecting patients with nonacute knee symptoms for arthroscopy of the knee.
In chapter 3 we discuss effectiveness and costs of MR imaging triaging these patients. In chapter 4 we determine in patients with nonacute knee symptoms and normal standardized physical examination the fraction of MR imaging studies showing arthroscopically treatable intraarticular pathology, thus evaluating whether one safely can refrain from MR imaging. In chapter 5 we discuss whether radiographs are needed when MR imaging is performed for nonacute knee symptoms anyway. The impact of bone bruise on presentation and short term course of knee complaints and the relation between bone bruise and (peri-)articular derangement is assessed in chapter 6.

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CHAPTER 2

Effectiveness of MR Imaging in Selection of Patients for Arthroscopy of the Knee at low field strengths

Based on article:

Effectiveness of MR Imaging in Selection of Patients for Arthroscopy of the Knee

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2.1. Abstract

Purpose To determine the effectiveness of 0.5-T magnetic resonance (MR) imaging in the appropriate identification of those patients with a high clinical suspicion of internal derangements of the knee who require arthroscopic therapy.

Materials and methods In a prospective multicenter study, MR imaging was performed at 0.5-T in 430 consecutive patients. The sensitivity and specificity of MR imaging in the patients who underwent arthroscopy and the corrected sensitivity and specificity of MR in all the study patients were calculated. For this correction, patients with negative MR and arthroscopic results were considered representative of the patients with negative MR results who were conservatively treated, and the number of the former was doubled. The standard errors of the corrected values were adjusted with the δ method.

Results At MR imaging, arthroscopy was indicated in 221 patients, 200 of whom underwent arthroscopy. Two hundred nine patients with negative MR imaging results were randomized for arthroscopic (105 patients) or for conservative treatment (104 patients). Of the 105 patients randomized for arthroscopy, 93 actually underwent arthroscopy. Arthroscopic treatment was necessary in 13 of 93 patients with a negative diagnosis at MR imaging. Arthroscopic treatment was necessary in 179 of 200 patients with a positive diagnosis at MR (sensitivity, 93.2%; specificity, 79.2%). Sensitivity and specificity corrected for randomization were 87.3% and 88.4%. Sensitivity and specificity corrected for randomization, respectively, were 84.1% and 94.2% for the diagnosis of medial meniscal tears and 69.5% and 94.5% for the diagnosis of lateral meniscal tears at MR.

Conclusion MR imaging is an effective tool in the selection of patients for arthroscopy from among a general population. Field strength is not a substantial factor in diagnostic performance of MR imaging of the knee.

2.2. Introduction

Magnetic resonance (MR) imaging of the knee has become a reliable tool in the detection of intraarticular knee injuries. Injuries to intraarticular structures like menisci and cruciate ligaments can be diagnosed at MR imaging with a high degree of sensitivity and specificity, but the accuracy of MR imaging decreases in patients with multiple injuries [1-3].

The clinical relevance of MR imaging, however, is determined in one way by its value in the selection of patients for or exclusion of patients from treatment with therapeutic arthroscopy. This overall assessment of the entire joint, also called composite diagnosis [4], is more relevant than the accurate diagnosis of all specific lesions of the various anatomic structures.

Determination of the clinical relevance of MR imaging can be affected by selection bias. Selection criteria for arthroscopy, results of which are used as the reference standard, play a role in most studies and potentially have a major influence on the interpretation of MR imaging results.

The aim of this prospective multicenter study was to determine the effectiveness of 0.5-T MR imaging of the knee for appropriately identifying patients who require arthroscopic therapy from among those in whom there is a high clinical suspicion of internal derangements of the knee.

2.3. Material and methods

2.3.1. Patients

Patients between the ages of 16 and 45 years who had experienced at least 4 weeks of symptoms that included pain, swelling, instability, and/or locking of the knee and who had been consecutively referred to the departments of orthopedics or surgery at our institutions between March 1997 and October 1998 were eligible for this study. Exclusion criteria were known joint disease (eg, rheumatoid arthritis), existence of a pathologic condition diagnosed earlier at MR imaging or arthrography, contraindication to MR (eg, claustrophobia, presence of a pacemaker) or arthroscopy, locked knee at presentation, a history of recurrent locking of the knee in combination with an extension deficit and a positive McMurray test at physical examination, previous knee surgery, presence of a radiographically confirmed fracture, severe osteoarthritis of the knee (grade 4, according to Kellgren), and a clinical diagnosis of retropatellar chondromalacia.

Patients were included in the study at the departments of orthopedics or surgery of three unaffiliated hospitals (one university and two general hospitals) involved in this cooperative study. In all three hospitals, our protocol received approval of the institutional review board. The study was funded by the Dutch Insurance Council. Informed consent was obtained from 613 patients.

All 613 patients underwent a standardized physical examination and anteroposterior and lateral radiography of the knee. Radiographs were not used in the clinical assessment. On the basis of the standardized physical examination results, the orthopedic surgeon categorized each patient as having clinical findings highly suggestive of internal knee derangement requiring arthroscopic treatment (category 1) or as having no need of arthroscopic treatment (category 2). For this assessment, we used the criteria of the Dutch Orthopedic Society. These criteria are as follows: the presence of marked joint effusion or at least a 'bulge sign' (ie, a visible bulge next to the patella caused by displacement of fluid) at physical examination; an extension deficit of at least 10°; a flexion deficit of at least 20°; instability at the varus and valgus stress test, Lachman test, anterior and posterior drawer test, and/or pivot test; at least one positive meniscal provocation test (McMurray, Apley, and squat tests); and atrophy of at least 2 cm relative to the contralateral leg measured 15 cm above the medial joint line. If at least one of these criteria was met (ie, the patient had clinical findings suggestive of knee derangement requiring arthroscopic treatment), the patient was included in the study.

Ultimately, 430 patients had a positive clinical diagnosis and were included. The patients had a mean age of 30.6 years; 299 (69.5%) of the patients were male.

2.3.2. Study design

MR imaging was performed in all patients within 2 weeks after inclusion in the study. The subsequent course of each patient's treatment was determined by the diagnosis at MR imaging (Fig 1). Patients with a positive MR imaging result (ie, those in whom arthroscopic treatment was indicated) proceeded to undergo arthroscopy. Patients with a negative MR result (ie, those in whom arthroscopic treatment was not

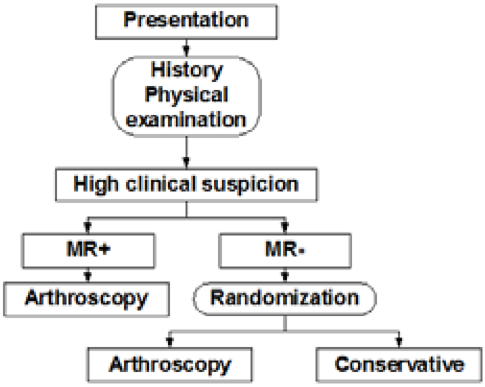

Figure 1. Schematic shows study design. MR+ = signs of major injury, arthroscopy indicated; MR- = normal MR images or signs of minor injury, arthroscopy not indicated.

indicated) were randomly assigned to treatment with one of two strategies. To this end we used random permuted tables. Half of these patients underwent arthroscopy; the other half was treated conservatively. Only those patients in whom arthroscopy was performed within 100 days of MR imaging were accepted for this study.

2.3.3. MR imaging

In all three hospitals, we performed MR imaging with an identical 0.5-T system (Gyroscan T5; Philips Medical Systems, Best, the Netherlands), the same software release (Release 3; Philips Medical Systems), and a dedicated transmitreceive knee coil. The standardized MR imaging protocol consisted of three sequences: a sagittal and a coronal dual spin-echo (SE) sequence and a sagittal T1-weighted threedimensional gradient-echo sequence with frequency-selective fat suppression. The following parameters were used for both SE sequences: 140-160-mm field of view and 20 and 80 msec echo times. The sagittal dual SE sequence had a repetition time of 2,350 msec, a matrix of 256 × 179, and a section thickness of 4 mm with a 0.4-mm intersection gap. The coronal dual SE sequence had a repetition time of 2,100 msec, a matrix of 256 × 205, and a section thickness of 5 mm with a 0.5-mm intersection gap.
The parameters for the sagittal T1-weighted three-dimensional gradient-echo sequence with frequency-selective fat suppression were as follows: repetition time msec/echo time msec, 70/13; flip angle, 45°; field of view, 160 mm; matrix, 256 × 205; and section thickness, 4 mm with 2-mm overlap.

The total time it took to perform the MR imaging examination (including the initial survey sequence) was 26 minutes.

2.3.4. Interpretation of MR Images

One of six appointed radiologists (including T.P.W.d.R., W.M.C.M., and J.L.B.) with at least 4 years of experience with musculoskeletal MR imaging prospectively and individually evaluated the MR images in each patient. The radiologist was informed about the patient’s history and the findings at physical examination because we tried to mimic the normal clinical situation as much as possible. After the radiologist had recorded the findings on a standardized case record form, the radiologist characterized the composite diagnosis at MR (Table 1) according to the following four categories: category 1, normal MR study; category 2a, some findings of injury but arthroscopy not indicated; category 2b, equivocal findings at MR imaging, after which the final diagnosis and therefore the decision to perform arthroscopy was based on the assessment of an experienced panel; and category 3, major findings of injury, arthroscopy indicated. For patients in category 2b, the members of the panel (ie, the radiologist who evaluated the MR images and an orthopaedic surgeon) decided, on the basis of the patient’s history and findings at physical examination and MR, whether the patient could potentially benefit from arthroscopic therapy (final positive diagnosis) or not (final negative diagnosis). Patients in the former group were selected for arthroscopy, whereas patients in the latter group were randomly selected for either arthroscopy or conservative treatment.

Table 1
Classification of pathology on MR, category 1 = normal

	Category 2a	Category 2b	Category 3
Menisci (Classification according to Lotysch [5])	Tear < 5mm Degeneration without tear Discoid meniscus		Tear ≥ 5mm Cyst
Cartilage (Classification according to Recht [6])	Grade 1-3 chondromalacia Nonisolated grade 4 chondromalacia Isolated grade 4 chondromalacia of a non-weight-bearing surface	OD with intact cartilage	Isolated grade 4 chondromalacia of a weight-bearing surface OD with cartilage fissure Loose body
Cruciate ligaments	Acute isolated tear Partial tear	Chronic tear with instability	Tear in combination with meniscal tear
Collateral ligaments	Isolated tear collateral ligament	Tear with capsular lesion	Tear in combination with meniscal tear
Synovia	Thickened plica Synovitis		Intraarticular PVNS
Other structures	Bone bruise	Tumor Extraarticular PVNS	

Note.—OD = Osteochondritis Disseccans; PVNS = Pigmented Villonodular Synovitis

We used a modified version of the classification system of Lotysch et al [5] to score meniscal injuries on MR images. A meniscal tear on MR images was defined as being of grade 3 signal intensity (ie, intrameniscal signal intensity unequivocally extending to an articular surface). These meniscal tears were further classified according to the following two categories: tears smaller than 5 mm without clinical importance (ie, not needing arthroscopy) and tears larger than 5 mm. We used this cutoff point of 5 mm because our orthopedic surgeons regard tears smaller than 5 mm to be stable tears, whereas they consider tears larger than 5 mm to be unstable in the majority of cases [7].

The anterior cruciate ligament (ACL) was considered normal when it appeared as a band of fibers of low to intermediate signal intensity on both sagittal and coronal dual SE images. The ACL was considered to be partially torn when there was abnormal signal intensity within the ligament or when otherwise intact fibers appeared wavy on sagittal or coronal dual SE images. The ACL was considered to be completely torn if there was disruption of all fibers or if it was not discernible at all on MR images [8-10]. For statistical analysis, we considered normal and partially torn ligaments as one group and complete tears as another group.

Commonly accepted criteria were used to establish a diagnosis of other abnormalities such as ligamental tears [11] and bone bruises [12,13].

2.3.5. Arthroscopy

All arthroscopic examinations were videotaped and were performed in the three participating hospitals by an experienced orthopedic surgeon or by a resident supervised by an orthopedic surgeon. A total of 17 surgeons participated in the study. Just like the radiologist, the surgeon was informed of the patient's history and of the findings at physical examination. The surgeon, however, was informed only of the diagnostic category at MR imaging, not the detailed MR diagnosis. The arthroscope, which had a 30° viewing angle, was introduced into the knee through an anterolateral or transpatellar portal. All structures were probed as well as visualized. After the diagnostic part of the examination, the arthroscopist recorded the arthroscopic diagnosis and therapeutic intentions, if any. To this end, a case record form was used that was identical to that used at the interpretation of the MR images. Subsequently, one of the authors (P.W.J.V. or B.P.M.t.B.), who was present at the arthroscopic examination, revealed the detailed diagnosis at MR imaging to the arthroscopist. In case of a discrepancy, the arthroscopist took a second look at the area during the same arthroscopic session. Next, depending on the diagnostic findings, the arthroscopist terminated the procedure or continued with the therapeutic part of the procedure.

2.3.6. Data analysis

The composite diagnosis at MR imaging (Table 1) and the MR imaging diagnosis of injuries to individual structures were compared with the outcome of arthroscopy. Arthroscopic findings were considered positive when a therapeutic intervention was performed. Arthroscopic findings were considered negative if the procedure was terminated without arthroscopic treatment. For each individual structure, the diagnosis at MR imaging was compared with the diagnosis at arthroscopy.

Because patients with a negative MR imaging result were randomly selected for one of two treatments, and thus only half of the patients with a negative MR result underwent arthroscopy, we introduced a verification bias by artificially increasing the prevalence of MR imaging findings of injury in the patients whose MR results could be correlated with arthroscopic results. We calculated the sensitivity and specificity of MR imaging in the patients who underwent arthroscopy, and we calculated a corrected sensitivity and specificity for all patients who were included in the study to eliminate this verification bias. For this correction, we presumed the two randomized groups of patients to be equal, which would be true if the randomization was successful. Thus, the findings in the patients with a negative MR result who underwent arthroscopy are representative of the findings expected in patients with a negative MR result who underwent conservative treatment. These findings were doubled to enable the calculation of corrected sensitivity and specificity values for all patients included in the study. Negative and positive predictive values are not influenced by the randomization process.

Because of the introduction of additional uncertainty by doubling the number of patients with negative MR imaging results and arthroscopic correlation, we had to adjust the standard errors of the corrected sensitivity, specificity, and negative and positive predictive values by means of a standard statistical method (δ method) [14]; this process resulted in adjusted CIs.

2.4. Results

On the basis of findings at MR imaging, arthroscopy was indicated in 221 (51.4%) of the 430 patients. Two of these patients (0.5%) had equivocal signs of injury at MR (category 2b) and were assigned to this group after a final diagnosis was rendered by the panel.

Thirteen of these 221 patients refused arthroscopy; among them was one of the two patients who had equivocal signs of injury at MR imaging. Eight patients were excluded because the interval between MR imaging and arthroscopy was longer than 100 days. Therefore, data from 200 patients with a positive MR imaging result who underwent arthroscopy according to our protocol were included in our final analysis.

MR imaging results were negative in 209 (48.6%) of 430 patients. Of these 209 patients with a negative MR result, 105 were randomly selected for immediate arthroscopy. Of these 105 patients, 93 actually underwent arthroscopy according to protocol. Eleven patients refused arthroscopy, and one patient underwent arthroscopy more than 100 days after MR imaging.

Thus, ultimately, data from 293 patients were analyzed. The mean interval between MR imaging and arthroscopy for these 293 patients was 29.5 days (median, 28 days; range, 3-87 days).

In these 293 patients, the sensitivity of MR imaging for detecting composite knee injury was 93.2% (179 of 192), the specificity was 79.2% (80 of 101), and the accuracy was 88.4% (259 of 293). The sensitivity of MR imaging for detecting medial meniscal tears was 90.4% (122 of 135), the specificity was 92.4% (146 of 158), and the accuracy was 91.5% (268 of 293). The sensitivity of MR imaging for detecting lateral meniscal tears was 74.7% (65 of 87), the specificity was 92.7% (191 of 206), and the accuracy was 87.4% (256 of 293). The sensitivity of MR imaging for detecting ACL ruptures was 75.0% (27 of 36), the specificity was 93.8% (241 of 257), and the accuracy was 91.5% (268 of 293).

The sensitivity and specificity of the composite diagnosis at MR and of the diagnosis of injuries to individual structures, corrected for verification bias, are presented in Table 2.

Table 2
Sensitivity, specificity, and predictive values corrected for bias for composite and individual-structure diagnoses at MR Imaging in 293 patients

Statistic	Composite Diagnosis	Medial Meniscus Injury	Lateral Meniscus Injury	Complete Rupture ACL
Sensitivity (%)	87.3 (81.7-92.9)	84.1 (77.1-91.2)	69.5 (60.3-78.6)	70.0 (55.2-84.7)
Specificity (%)	88.4 (84.2-92.6)	94.2 (91.8-96.5)	94.5 (92.2-96.8)	94.5 (92.7-96.3)
Positive PredictiveValue (%)	89.5 (85.3-93.7)	89.7 (85.3-94.6)	80.5 (71.7-89.2)	59.6 (45.3-73.8)
Negative PredictiveValue (%)	86.0 (79.0-93.1)	90.8 (85.9-957)	90.5 (86.5-94.5)	96.5 (94.6-99.4)

Note.—Data in parentheses are 95% CIs corrected for randomization. Diagnostic criteria are defined in Materials and Methods. Arthroscopic findings were the reference standard. Incidences of pigmented villonodular synovitis (*n* = 0), osteochondritis dissecans with cartilage fissure (*n* = 2 at MR imaging), loose body (*n* = 3 at MR imaging), and isolated grade 4 chondromalacia (*n* = 11 at MR imaging) were too low to enable calculation of sensitivity, specificity, and positive and negative predictive values of MR imaging for these findings.

2.4.1. Positive composite MR diagnosis (arthroscopy indicated)

Of the 200 arthroscopic procedures performed because of a positive MR imaging result, 179 were indeed therapeutic, while 21 procedures remained simply diagnostic and thus represented false-positive diagnoses at MR. Fourteen of these diagnoses were true mistakes at MR imaging, and arthroscopy could have been avoided. The 14 false-positive diagnoses that were not confirmed at arthroscopy consisted of medial meniscal tear (n = 4), lateral meniscal tear (n = 6), meniscocapsular separation (n = 1), and presence of loose bodies (n = 3). Other considerations affected the decision not to treat the remaining seven patients at arthroscopy. In three patients who had a meniscal tear at MR imaging, the tear was recognized at arthroscopy but was considered to be smaller than 5 mm. And although the diagnosis at MR imaging was confirmed at arthroscopy in the other four patients, who, according to protocol, were correctly treated arthroscopically, the orthopedic surgeon decided not to treat. In two of these patients, the tear was considered at arthroscopy to be stable despite being larger than 5 mm (one of these patients also had an unconfirmed tear in the other meniscus at MR imaging). One patient with an arthroscopically confirmed meniscal tear was considered to be too young to undergo partial meniscectomy. One patient who had a large synovial cyst behind the posterior cruciate ligament was initially not treated arthroscopically, but eventually the cyst was resected in a second procedure.

2.4.2. Negative composite MR diagnosis (arthroscopy not indicated)

Of the 93 arthroscopic procedures performed despite a negative MR imaging result, 80 remained purely diagnostic. In 13 patients, arthroscopy revealed a pathologic condition that was subsequently treated, indicating that the diagnosis at MR imaging was false-negative in these patients. Eight of these false-negative diagnoses were true mistakes at MR imaging; arthroscopy would not have been performed in these patients in clinical practice because of this false-negative diagnosis. The findings at arthroscopy that were not observed at MR imaging were medial meniscal tear (n = 3) and lateral meniscal tear (n = 5). Therapeutic arthroscopy was not indicated in the remaining five patients according to our protocol, but the arthroscopist decided to treat these patients anyway because of the following specific reasons: a medial meniscal tear smaller than 5 mm (missed at MR imaging, but by our definition not an indication for arthroscopy) in one patient, a lateral meniscal tear smaller than 5 mm (also diagnosed at MR) in one patient, displaced fibers of partial ACL tear in two patients (both partial tears were appreciated at MR imaging), and a thickened plica in the medial compartment in one patient.

2.4.3. Individual structures

Of the 134 medial meniscal tears diagnosed at MR imaging, 122 were confirmed at arthroscopy. In six of the 12 patients with a false-positive diagnosis of medial meniscal tear at MR imaging, other pathologic findings led to therapeutic arthroscopy. In two patients, a tear smaller than 5 mm (not an indication for arthroscopy) that was seen on MR images was not confirmed at arthroscopy. In the remaining four patients, a false-positive diagnosis of meniscal tear at MR imaging would have led to unnecessary arthroscopy (Fig 2). On the other hand, arthroscopy revealed 13 tears in 159 medial menisci that were considered to be normal at MR. Of these additional 13 tears, only six were treated arthroscopically. In two of the six treated meniscal tears, arthroscopy was also indicated on the basis of other pathologic findings at MR imaging. Thus, only four false-positive diagnoses at MR imaging and four false-negative diagnoses at MR would have had clinical consequences. Corrected for verification bias, the sensitivity of MR imaging for detecting medial meniscal tears was 84.1% (122 of 145; these numbers are corrected for randomization); the specificity was 94.2% (227 of 241; these numbers are corrected for randomization).

Of the 80 lateral meniscal tears diagnosed at MR imaging, 65 were confirmed at arthroscopy. Other findings of injury visualized at MR imaging led to arthroscopic treatment of seven of the 15 patients with a false-positive diagnosis of lateral meniscal tear at MR. In one patient, a tear smaller than 5 mm (not an indication for arthroscopy) seen at MR imaging was not seen at arthroscopy. Arthroscopy revealed an additional 22 tears in 213 lateral menisci that had been considered normal at MR. Of these additional tears, 14 were treated arthroscopically. In nine of these treated meniscal

Figure 2. Sagittal intermediate-weighted MR image (2,350/20) reveals a tear in the posterior horn of the medial meniscus (arrow) that extends to both upper and lower articular surfaces. This tear was not recognized at arthroscopy performed 16 days after the MR imaging examination and therefore constitutes a false-positive diagnosis at MR.

Figure 3. Sagittal intermediate-weighted MR image (2,350/20) reveals a tear in the posterior horn of the lateral meniscus (arrow) that extends to both upper and lower articular surfaces. This tear was not recognized at arthroscopy performed 14 days after the MR imaging examination and therefore constitutes a false-positive diagnosis at MR.

tears, arthroscopy was also indicated on the basis of other pathologic findings at MR. Thus, seven false-positive diagnoses at MR imaging (Fig 3) and only five false-negative diagnoses at MR would have had clinical consequences. Corrected for verification bias, the sensitivity of MR imaging for detecting lateral meniscal tears was 69.5% (66 of 95; these numbers are corrected for randomization); the specificity was 94.5% (275 of 291; these numbers are corrected for randomization).

Of the 43 ACLs diagnosed as completely ruptured at MR imaging, 27 were confirmed to be ruptured, 15 were considered to be partially ruptured (Fig 4), and one was normal at arthroscopy. An ACL rupture diagnosed at MR is an important indicator of the coexistence of other injuries. In 86% (37 of 43) of these patients, arthroscopy was indicated because of a diagnosis at MR imaging of medial meniscal tear (44%; 19 of 43), lateral meniscal tear (14%; six of 43), or tears in both menisci (28%; 12 of 43). Only six patients had an isolated complete ACL rupture at MR imaging; three of these ruptures were confirmed at arthroscopy as being complete, while the other three were considered to be partial tears.

An additional nine ACLs that were classified at MR imaging as either partially torn (n = 8) or normal (n = 1) were revealed to be completely ruptured at arthroscopy. Six of these nine patients were selected for arthroscopy because of a positive composite diagnosis at MR imaging.

In 30 (83%) of all 36 patients with arthroscopically proved complete ACL rupture, arthroscopy was indicated because of meniscal tear diagnosed at MR imaging (tear in medial meniscus, 56% [20 of 36]; tear in lateral meniscus, 14% [five of 36]; tear in both menisci, 14% [five of 36]). Four of the six arthroscopically proved isolated ACL ruptures were appreciated at MR imaging; one of these six ACLs was considered to be partially torn at MR.

The sensitivity, specificity, and negative and positive predictive values of MR imaging for the diagnosis of meniscal tear and complete ACL rupture are listed in Table 2.

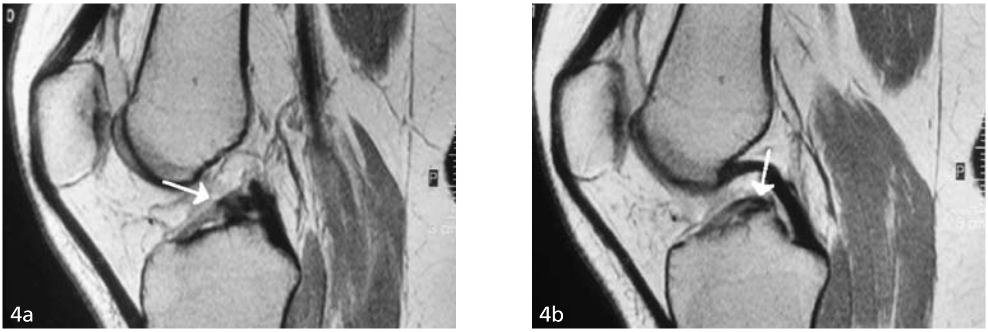

Figure 4 (a, b). Sagittal intermediate-weighted MR images (2,350/20) reveal what was thought to be a complete ACL rupture (arrow) that was not appreciated as a complete rupture at arthroscopy. The radiologist diagnosed a complete rupture extending toward the posterior cruciate ligament. According to the arthroscopist, however, it was a partial rupture that involved approximately 50% of the ligamentous body.

2.5. Discussion

We found a sensitivity of 93.2%, a specificity of 79.2%, and an accuracy of 88.4% for composite diagnosis at MR imaging. The positive predictive value was 89.5%; the negative predictive value was 86.0%. These results, however, do not measure the accuracy of MR imaging in the initially selected group of patients, because we introduced a verification bias by randomly selecting the patients with negative MR imaging results for one of two equal groups (one of which received arthroscopic treatment; the other received conservative treatment). This kind of verification bias leads to a sensitivity that is overrated and a specificity that is underrated. We have corrected for this bias by doubling the results in the group of patients in whom a negative diagnosis at MR imaging was correlated with arthroscopic findings. Only then can the true sensitivity and true specificity of MR imaging be appreciated. The corrected sensitivity, specificity, and accuracy for the composite diagnosis at MR imaging are 87.3%, 88.4%, and 87.8%, respectively. In nine of 34 erroneous diagnoses at MR imaging, no actual discordance existed between the MR findings and the arthroscopic findings. In these patients, various factors (described in the Results section) prompted the orthopedic surgeon to decide to treat the patient in a way that differed from that outlined in our protocol. The data for the composite knee diagnosis, rather than the data for diagnosis in specific structures, indicate why MR imaging is an effective tool in the selection of patients for arthroscopic treatment.

The sensitivity of the composite diagnosis at MR imaging is somewhat higher than that of the diagnosis in individual structures, while the specificity of the composite diagnosis is somewhat lower than that of the diagnosis in individual structures. The higher sensitivity is explained by the fact that in the concept of composite diagnosis at MR imaging, signs of injury in more than one individual structure can lead to a positive MR result, as well as by the fact that injuries are often not isolated. On the other hand, if patients are selected for therapeutic arthroscopy on the basis of the composite diagnosis at MR imaging and subsequent arthroscopy confirms the presence of injury but the arthroscopist does not deem it necessary to treat the injury, in hindsight the selection for arthroscopy was not correct: specificity will be low relative to that for individual structures.

Thus, the concept of a clinically relevant composite diagnosis at MR imaging can help correct for the low sensitivity of MR imaging for individual structures. In our study, the corrected sensitivity for lateral meniscal tear was 69.5%. This low sensitivity of MR imaging for the diagnosis of lateral meniscal tear, especially when associated with ACL injury, is well known [(3)]. However, because lateral meniscal tears were rarely isolated in our study, this low sensitivity was of little consequence; in 15 of the 22 lateral tears missed at MR imaging, arthroscopy was indicated anyway based on the presence of other injury.

The sensitivity of MR imaging for the detection of ACL ruptures, especially when corrected for randomization, was rather low in our study. This is probably secondary to the criteria used by the radiologist and orthopedic surgeon to distinguish between normal and partially and completely ruptured ACLs. Partial ruptures are especially difficult for the radiologist and the orthopedic surgeon to define in common terms. The arthroscopic definition of partial rupture is large and amorphous and ranges from the presence of some disrupted fibers to a subtotally ruptured ACL. Results could have been better if we had adopted a scoring system proposed by Rubin et al [1], which distinguishes between high and low-grade injuries and thereby discards the diagnosis of partial rupture. The fact that there was only one false-negative case and one false-positive case in the distinction between a normal and a completely torn ACL supports the approach used by Rubin et al.

The discordance between the MR imaging findings and the arthroscopic findings of partial rupture is of little clinical importance because only a minority of complete ACL ruptures are isolated. Therefore, 30 of the 36 patients with complete ACL rupture in our study were assigned to undergo arthroscopy because of accompanying meniscal tears.

In our study, we did not consider an isolated ACL tear to be an indication for arthroscopy. In the Netherlands, an isolated rupture of a cruciate ligament is not considered to be an indication for arthroscopy in a general population (as opposed to ACL tear in professional athletes). Fewer than 1% of our patients were athletes who performed on a high competitive level and trained on a daily basis.

If an isolated complete ACL rupture had been considered to be an indication for arthroscopy in our study, the effect on our results would have been minimal. Only six complete ACL ruptures proved to be isolated at arthroscopy. Four of these were diagnosed at MR imaging as complete tears.

Our selection of patients on the basis of their history and the findings at physical examination increases the prevalence of pathologic conditions revealed at MR imaging relative to a situation without such a selection. The positive predictive value will be higher and the negative predictive value will be lower relative to those in an unselected population, although the effect on sensitivity and specificity is minor.

Including larger fractions of older and male patients in a study will also increase the prevalence of pathologic conditions and will thus affect MR imaging results. These population characteristics are reflected in the percentages of negative MR examination results in the various studies. Study design also has a major effect on MR imaging results. When MR imaging is used in the selection of patients for arthroscopy, as is the case in many retrospective studies, sensitivity and specificity will be substantially influenced because not all patients with a negative MR imaging result will undergo arthroscopy. This leads to a sensitivity that is overrated and a specificity that is underrated. The true sensitivity and true specificity of MR imaging can only be calculated when all patients with a negative MR imaging result undergo arthroscopy as well.

Bui-Mansfield et al [4] found a sensitivity of 94% and a specificity of 93% for composite diagnosis at MR imaging in a group of 50 patients selected on the basis of criteria related to surgical indications for monitoring appropriateness. In this group, results of 15 MR imaging examinations (30%) were considered negative. Correction for verification bias was not necessary because all patients underwent arthroscopy. The population consisted of predominantly male (90%) military personnel between 18 and 50 years of age with a higher prevalence of pathologic conditions relative to that in the population in our study. Therefore, the percentage of negative MR imaging results was rather low compared with that in our study. The sensitivity and specificity were better than in our study. However, the CIs for the calculated sensitivity and specificity values in the study by Bui-Mansfield et al were rather large because of the relatively small number of patients studied. Our bias-corrected sensitivity and specificity levels (Table 2) are well within their confidence intervals.

Ruwe et al [15] found that, in a group of 103 patients with clinical findings that necessitated diagnostic arthroscopy, 62 (60%) had negative MR imaging results. Forty-one percent of the patients, who were between 11 and 72 years of age, were female. This could explain why the percentage of negative MR imaging results was rather high compared with that in our study. Of the 62 patients with negative MR imaging results, only 10 underwent arthroscopy. A total of 44 patients underwent immediate arthroscopy. The sensitivity of 100% and specificity of 83% were thus very much influenced by verification bias—the sensitivity was overrated and the specificity was underrated; both are therefore not comparable with our results. Ruwe et al, however, used clinical outcome rather than arthroscopy as the standard against which MR imaging was compared, so there was no reason to correct for verification bias.

Rappeport et al [16] examined 47 patients between 19 and 54 years of age, 68% of whom were male, who were suspected of having intraarticular knee injuries. All 20 (43%) patients who had negative MR imaging results underwent arthroscopy; therefore there was no verification bias. This population was most comparable to our study population. Rappeport et al found a sensitivity of 86% and a rather low specificity of 65%. This low specificity in part explains the rather low percentage of negative MR imaging results (43%) in the patients studied compared with those in our study and in the study of Ruwe et al.

Other studies [17-21] are difficult to compare with ours because they either did not include clearly described selection criteria, considered only individual structures without regard to therapeutic consequences, or did not define precisely which diagnoses at MR imaging indicated a need for arthroscopy.

The influence of field strength on diagnostic accuracy of MR imaging deserves some attention. We used a 0.5-T system. On one hand there has been a growing interest in cheaper and potentially more cost-effective dedicated low field MR systems. On the other hand there has been the more widespread clinical availability in recent years of MR systems of higher field strengths (3.0-T), with theoretical technical superiority. Several researches, comparing low field and high field strength systems (up to 1.5-T) suggest that field strength is not an important determinant of diagnostic accuracy [22-29]. A comprehensive systemic review by Oei et al. [30] with a meta-analysis of the diagnostic performance of MR imaging, using original articles published between January 1991 and December 2000 confirms these findings. Although they observed a trend toward better diagnostic performance for higher magnetic field strengths (field strengths of included articles ranged from 0.2 to 1.5-T), these differences were far from significant, except for ACL tears. Only Fischer et al [31] found a statistically significant difference between a 0.35-T and a 1.5-T system, and then only in imaging of the medial meniscus. This study, however, was biased by the use of a more extensive scanning protocol with the higher-field-strength unit.

More recent studies [32, 33] compare 3.0-T systems to 1.5-T systems and / or arthroscopy. These studies agree that there is the advantage of higher-resolution imaging at 3.0-T, compared to scanning at lower field strengths. They however disagree whether this translates in better diagnostic performance or not. Magee et al. [32] conclude that MRI of the knee performed at 3.0-T compares favorably in sensitivity and specificity with studies performed at 1.5-T field strength or lower. They however don't compare directly between different field strengths in one study population, but they compare their findings at 3.0-T with results reported in previous studies, published between 1987 and 1994. In our opinion this flaw undermines their conclusion. Krampla et al. [33] conclude that the technical superiority of 3.0-T, compared to 1.0-T and 1.5-T, did not lead to an increase in sensitivity or specificity. It is therefore unlikely that field strength differences are a substantial factor in diagnostic performance of MR imaging of the knee.

We conclude that, in a general population such as that described in this study, a composite diagnosis obtained at MR imaging after adequate clinical selection is accurate, despite the lower sensitivity of MR imaging for the diagnosis of injuries in individual knee structures. Therefore, the combination of clinical examination and 0.5-T MR imaging is useful in selecting patients for arthroscopy.

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CHAPTER 3

Effectiveness and costs regarding triage of patients with non-acute knee complaints

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3.1. Abstract

Purpose To prospectively evaluate the cost and effectiveness of magnetic resonance (MR) imaging performed to exclude the need for arthroscopy in patients with nonacute knee symptoms who are highly suspected clinically of having intraarticular knee abnormality.

Materials and methods The study was approved by the institutional review boards of three hospitals; informed patient consent was obtained. All 584 included patients (406 male, 178 female; mean age, 31.1 years ± 8.0 [standard deviation]) underwent MR imaging. Patients with an MR result positive for the diagnosis of intraarticular knee abnormality underwent arthroscopy (group A). Patients with a negative MR result were randomly assigned to undergo either conservative (group B) or arthroscopic (group C) treatment. Treatment was considered effective if the Noyes function score had increased 10% or more at 6 months. A cost analysis was performed from a societal perspective to compare the treatment strategy involving MR imaging with the strategy not involving MR imaging.

Results Of the 584 patients, 294 (50.3%) were assigned to group A; 149 (25.5%), to group B; and 141 (24.1%), to group C. At 6 months, the number of patients effectively treated in group B (conservative treatment) was a mean of 5.1% ± 10.0 larger than the number of patients effectively treated in group C (arthroscopy). Owing to savings in productivity costs, total societal costs were lower with use of the strategy involving MR imaging by a mean of $153 ± 488 ($P = 0.54$).

Conclusion MR imaging can be used without additional costs or disadvantageous effects on function to obviate arthroscopy in patients with nonacute knee symptoms who are highly suspected of having intraarticular knee abnormality.

3.2. Introduction

Arthroscopy of the knee is frequently used to diagnose and treat intraarticular abnormalities. Despite clinical selection by the orthopedic surgeon, based on history and physical examination findings, 39%-73% of arthroscopies remain diagnostic and are not used for therapy [(1-4)]. The objective is to use this invasive procedure primarily for treatment and to limit the number of nontherapeutic arthroscopies performed. During the past 15 years, magnetic resonance (MR) imaging of the knee has become available as an alternative to diagnostic arthroscopy. The purpose of our study was to prospectively evaluate the cost and effectiveness of MR imaging performed to exclude the need for arthroscopy in patients with nonacute knee symptoms who are highly suspected clinically of having intraarticular knee abnormality.

3.3. Materials and Methods

3.3.1. Patients

The study was approved by the institutional review boards of the three participating hospitals; informed patient consent was obtained. Between March 1997 and October 1999, consecutive patients aged 16-45 years who had had knee symptoms -specifically, pain, swelling, instability, and/or locking- for at least 4 weeks (nonacute) and were referred to one of the three participating nonaffiliated hospitals (one academic [Leiden University Medical Center], two teaching [MCH Westeinde Hospital and Leyenburg Hospital]) were eligible for the study. All patients underwent a standardized physical examination that consisted of, at least, knee inspection, instability and meniscal provocation tests, and measurement of the circumference of both legs 15 cm above the medial joint line. In addition, anteroposterior and lateral radiographs of the knee were obtained.

Exclusion criteria were known joint disease, abnormality diagnosed earlier with MR imaging or arthroscopy, contraindication to MR imaging or arthroscopy, locked knee at presentation, a combination of locked knee and either extension deficit or positive McMurray test results, prior knee surgery, a radiographically confirmed fracture, severe osteoarthritis of the knee (Kellgren grade 4), and/or a clinical diagnosis of retropatellar chondromalacia.

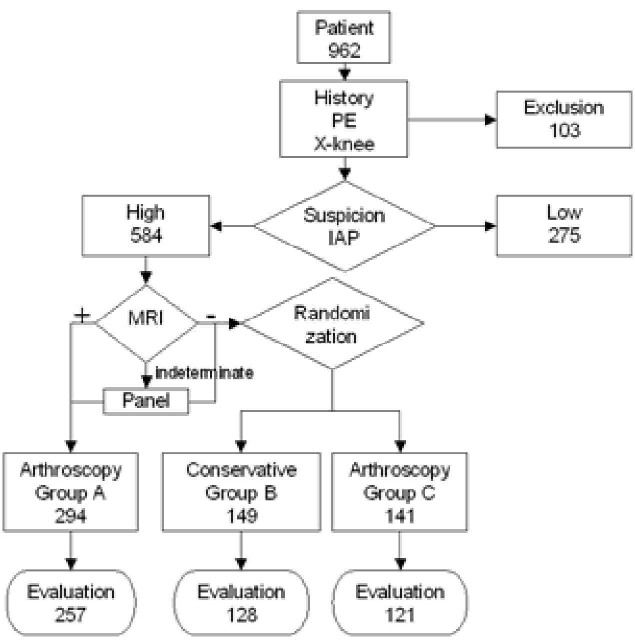
Patients were included in the study if they were highly suspected clinically of having an intraarticular knee abnormality and thus arthroscopy was indicated according to the guidelines of the Dutch Orthopedic Society [(5)]. Arthroscopy is warranted if at least one of the following clinical criteria is met at physical examination: substantial joint effusion (more than bulging sign), passive extension deficit of at least 10°, passive flexion deficit of at least 20°, instability (ie, positive varus and valgus stress, Lachman, anterior and

posterior drawer, and Pivot test results), a positive result of at least one meniscal provocation test (ie, McMurray, Apley, or squat test), and atrophy of at least 2 cm relative to the contralateral leg measured 15 cm above the medial joint line.
The threshold for arthroscopy is kept relatively low by the Dutch Orthopedic Society to avoid the rendering of too many falsenegative diagnoses on the basis of physical examination results.

3.3.2. Study Design

After study inclusion, all patients first underwent MR imaging. Patients with a positive MR result (ie, in which arthroscopy was indicated on the basis of the MR findings, in concordance with high clinical suspicion) were referred for arthroscopy (group A). Patients with a negative MR result (ie, in which arthroscopy was not indicated on the basis of the MR findings alone, despite high clinical suspicion, but rather on the basis of the Dutch Orthopedic Society guidelines) were randomly assigned, by using permuted block randomization, to undergo conservative (group B) or arthroscopic (group C) treatment. The MR result was reported to the central study center by telephone, after which the patients were assigned to the groups (Figure) by one of two research physicians (A.P.M.t.B., P.W.J.V.).

The mean interval between MR imaging and arthroscopy in groups A and C was 37.3 days ± 37.5 (standard deviation) (median, 28.0 days; range, 1-371 days). During the time intervals between study inclusion, MR imaging, and subsequent



Study design and number of patients enrolled in the study.
Note.- IAP = Intra Articular Pathology

arthroscopy or randomization (to conservative or arthroscopic treatment group), the patients received no treatment except analgesics. The regimen for conservative therapy was not standardized but rather left to the discretion of the orthopedic surgeon and/or the patient.

All MR findings were prospectively and individually evaluated by one of five available musculoskeletal radiologists (including J.L.B., W.M.C.M., T.P.W.d.R., and E.G.C., with 2-12 years experience in musculoskeletal MR imaging). The medical history, physical examination findings, and radiographs of each patient at study entry were available to the radiologist. All MR findings were recorded on a standardized case record form. The MR result was categorized as negative (arthroscopy not indicated), equivocal, or positive (arthroscopy indicated) according to the criteria outlined in Table 1. The term negative MR finding in this context does not imply that there was no intraarticular abnormality but rather that there was no intraarticular abnormality that necessitated therapeutic arthroscopy. By using all available information, a panel consisting of the radiologist who evaluated the MR result and the orthopedic surgeon assigned the patients with equivocal MR findings to group A or randomized group B or C.

Table 1
Classification of pathology on MR

	Negative MR diagnosis (i.e. arthroscopy not indicated)	Equivocal MR diagnosis	Positive MR diagnosis (i.e. arthroscopy indicated)
Menisci (Classification according to Lotysch)	Normal Meniscal tear < 5mm Meniscal degeneration without tear Discoid meniscus		Meniscal tear ≥ 5mm Meniscal cyst
Cartilage (Classification according to Recht)	Normal Chondromalacia grade 1-3 Non-isolated chondromalacia grade 4 Isolated chondromalacia grade 4 of a none-weight bearing surface	OD with intact cartilage	Isolated chondromalacia grade 4 of a weight bearing surface OD with cartilage fissure Loose body
Cruciate ligaments	Normal Isolated tear cruciate ligament Partial tear cruciate ligament	Isolated tear cruciate ligament with instability	Tear cruciate ligament in combination with meniscal tear
Collateral ligaments	Normal Isolated tear collateral ligament	Tear collateral ligament with capsule-lesion	Tear collateral ligament in combination with meniscal tear
Synovia	Normal Plica Synovitis		Intra-articular PVNS
Other structures	Normal Bone bruise	Tumor Extra-articular PVNS	

Note.- OD = Osteochondritis dissecans; PVNS = Pigmented Villonodular Synovitis

Patients who were treated conservatively (group B) were scheduled for arthroscopy if their symptoms had not diminished 3 months after the first clinical evaluation. Our analyses were based on the intention-to-treat principle, meaning that the patients in group A or C who did not undergo arthroscopy and the patients in group B who did undergo arthroscopy despite not having indications for it according to the protocol criteria remained in their respective designated group for the analyses.

3.3.3. MR Imaging

The MR examinations were performed at all three hospitals by using the same 0.5-T system (Gyroscan T5; Philips Medical Systems, Best, the Netherlands) and the same software with a dedicated transmit-receive knee coil.

The standardized MR imaging protocol consisted of three sequences: sagittal dual spin echo, coronal dual spin echo, and sagittal T1-weighted threedimensional gradient echo with frequency-selective fat suppression. A 140-160 mm field of view and an echo time of 20 or 80 msec were used for both spin-echo sequences. For coronal dual spin-echo imaging, a repetition time of 2100 msec, matrix of 256 × 205, and section thickness of 5 mm with a 0.5 mm intersection gap were used. For sagittal dual spin-echo imaging, a repetition time of 2350 msec, matrix of 256 × 179, and section thickness of 4 mm with a 0.4 mm intersection gap were used. The parameters for sagittal frequency-selective fat-suppressed T1-weighted three-dimensional gradient-echo imaging were 70-msec repetition time, 13-msec echo time, 45° flip angle, 160 mm field of view, 256 × 205 matrix, and 4 mm section thickness with a 2 mm overlap. The total imaging time for the standard MR imaging protocol (including the initial survey sequence) was 26 minutes.

3.3.4. Arthroscopy

All arthroscopic examinations were performed by an orthopedic surgeon or a resident supervised by an orthopedic surgeon. A total of 17 surgeons (including S.d.L., R.M.B., L.N.J.E.M.C., and P.A.v.L., with 1-21 years experience) participated in the study. At each participating hospital, one orthopedic surgeon was assigned to the panel that decided the diagnosis in the cases of equivocal MR findings.

Like the radiologist, the surgeon was informed of the patients' medical history and physical examination findings. The surgeon, however, was informed of the MR category (positive or negative findings) only -not the detailed MR diagnosis. An arthroscope with a 30° viewing angle was introduced into the knee through an anterolateral or transpatellar portal. All structures were not only visualized but also probed. After the standardized diagnostic part of the arthroscopic examination, the arthroscopist reported an arthroscopic diagnosis and the therapeutic intentions, if any. For this report, a standardized case record form identical to that used to record the MR findings was used. The researcher then revealed the detailed MR diagnosis to the arthroscopist. In cases of discrepancy, the arthroscopist then examined the joint again. Then, depending on the second-look findings, the arthroscopist either terminated the procedure or continued to the therapeutic portion of the examination.

3.3.5. Outcome Measures

All patient demographic data, clinical characteristics, MR findings, and findings of arthroscopy (if performed) were recorded. The MR and arthroscopic findings were considered to be intermediate outcome measures.

Effectiveness. -Knee function and symptoms were assessed during interviews with the patients at the time of MR imaging and at 3- and 6-month intervals by using Noyes function scores, which ranged from 200 (indicating poor function) to 550 (indicating good function), and Noyes symptom scores, which ranged from 0 (indicating serious symptoms) to 400 (indicating no symptoms) [6,7]. The patients were interviewed by one of two research physicians (A.P.M.t.B., P.W.J.V.).

The Noyes scale for symptoms was used in group B to determine whether the treatment for some patients should be changed to arthroscopy after 3 months of conservative treatment. Patients were scheduled for arthroscopy if the initial Noyes symptom score had not increased at least 10% at 3 months. The mean interval between MR imaging and arthroscopy in group B was 136.3 days ± 57.2 (median, 126.0 days; range, 83-321 days).

The Noyes function score at 6 months was chosen as the primary outcome parameter for determining the effectiveness of each treatment strategy. We considered a treatment strategy to be effective if the initial Noyes function score had increased at least 10% at 6 months. The orthopedic surgeons who were involved in the study design considered this value, on the basis of their experience, to be a realistic increase during a period of 6 months after successful therapy, whether this be conservative or arthroscopic treatment. The cutoff value was therefore empirically determined.

Costs. -The economic evaluation was performed from a societal perspective and included assessment of the medical and productivity costs during the initial 6 months after randomization to the treatment groups. Costs are reported in U.S. dollars and were updated to the 2005 price level by using the Dutch consumer price index (www.cbs.nl). The cost analyses involved the evaluation of volumes (ie, numbers of procedures and other cost elements) and prices.

Volumes were determined from the study registrations for initial consultation with the orthopedic surgeon, MR examination (including subsequent consultations), and arthroscopy (including hospital stays and postoperative consultations). These data were supplemented by volumes of secondary medical care (ie, consultations, physiotherapy sessions, hospitalizations, medications, and out-of-pocket expenses) and days of absenteeism (from work) reported by the patients in two quarterly cost diaries. These diaries were handed in and discussed with the patients at 3 and 6 months.

Detailed cost analyses of MR imaging and arthroscopy were performed at the three participating centers and included assessment of the costs of different staff members, equipment, material, housing, and overhead items and of the costs in time and travel of the patients. The money spent on medical aids was gleaned from the diaries.
The costs of other health care entities were determined according to standard Dutch prices that were designed to reflect societal costs and standardize economic evaluations [8,9]. The time and travel costs for medical care were based on national averages for the duration of health care and the travel distances calculated from postal codes. The costs for absenteeism were calculated by using the patients' reported actual gross income per day according to the friction cost method; for our study duration of 6 months, these values amounted to the costs for all reported absenteeisms.

3.3.6. Data and Statistical Analyses

All performed analyses were based on the intention to treat principle. The effectiveness of different treatment strategies was compared by using χ^2 tests. Costs were compared by using standard unequal-variance t tests. All analyses were performed by using SPSS for Windows (release 11.5.0; SPSS, Chicago, Ill).

Effectiveness. -We compared the effectiveness of the treatments performed in groups B (conservative treatment) and C (arthroscopy) to determine whether treatment B would not be inferior to treatment C. We expected treatment C to be effective in 90% of the patients. We allowed a noninferiority margin of 15% and accepted an effectiveness of 75%.

We computed a sample size of 91 patients per group ($\alpha = 5\%$ one sided, $1 - \beta = 0.90$) for the case in which treatment B was actually as effective as treatment C. Since we expected about 50% of the patients to be randomly assigned between groups B and C, we needed to include a total of 364 patients (two groups times two times 91 patients). To establish noninferiority of treatment B, we reported confidence intervals for the differences between treatments B and C.

Costs. -In our economic evaluation, we compared the results of a treatment scenario involving MR imaging with the results of a scenario not involving MR imaging. If in the strategy involving MR imaging φ denotes the fraction of patients with a negative MR examination result who do not require arthroscopic treatment, the difference in costs between the two strategies is calculated as follows:

$$
\begin{aligned}
&\{[(1 - \varphi) \cdot C_{A,in}] + (\varphi \cdot C_{B,in})\} \\
&- \{[(1- \varphi) \cdot C_{A,ex}] + (\varphi \cdot C_{C,ex})\} \\
&= C_{MR} + [\varphi \cdot (C_{B,ex} - C_{C,ex})],
\end{aligned}
$$

Where $C_{A,in}$ represents the costs for group A with MR imaging included; $C_{A,ex}$, the costs for group A with MR imaging excluded; $C_{B,in}$, the costs for group B with MR imaging included; $C_{B,ex}$, the costs for group B with MR imaging excluded; $C_{C,ex}$, the costs for group C with MR imaging excluded; and CMR, the costs for MR imaging.

The power calculation for the economic evaluations was based on the break-even fraction (φ_0), for which the difference in costs between the strategy with and the strategy without MR imaging is zero. On the basis of a priori data on average costs per patient, we estimated a φ_0 of 0.4. For larger values,the strategy with MR imaging is costeffective.

The sample size calculation was based on the results of testing φ equals φ_0 versus φ is greater than φ_0. To show a difference of 10%, we needed 206 patients ($\alpha = 5\%$ one sided, $1- \beta = 0.90$). In practice, we would not use estimated average costs but rather the actual costs per patient. Differences in cost between the strategy with and the strategy without MR imaging are reported as 95% confidence intervals of the mean costs.

The width of these intervals around the difference in costs between the strategies was calculated as φ times the width of the standard 95% confidence interval of the mean difference in costs between treatment groups B and C. This approach ignores the uncertainty in the estimated MR-negative fraction φ. Ignoring this uncertainty is justified because the much larger uncertainty in the cost difference dominates the uncertainty in their independent product.

Study sample size and sensitivity analysis. -On the basis of the computations described for effectiveness and costs, we determined that we needed to include about 400 patients. We performed univariate sensitivity analysis of our data on the percentage of negative-result MR examinations and the costs of MR imaging and arthroscopy.

3.4. Results

Of the 962 patients who agreed to participate in the study, 378 either were excluded (103 patients) or had negative physical examination findings according to the Dutch Orthopedic Society guidelines (275 patients). In the remaining 584 patients (178 female, 406 male; mean age, 31.1 years ± 8.0 [standard deviation]), arthroscopy was indicated according to Dutch Orthopedic Society guidelines. The data regarding 430 of these patients (those included between March 1997 and October 1998) had been used in a prior study [10]. The mean interval between study inclusion and MR imaging was 10.9 days ± 9.2 (median, 8.0 days; range, 0-77 days).

3.4.1. Effectiveness

All 584 patients were interviewed at the time of MR imaging (Figure). Initially, 289 patients had MR findings positive for intraarticular knee abnormality, 285 had negative MR findings, and 10 had equivocal MR findings. The panel concluded that five of the patients with equivocal findings needed arthroscopy (group A) and five did not (randomly assigned to group B or C). Thus, 294 (50.3%) patients were assigned to undergo arthroscopy (group A). The remaining 290 patients were randomly assigned to undergo conservative (group B, 149 [25.5%] patients) or arthroscopic (group C, 141 [24.1%] patients) therapy (Table 2). Two hundred seventy-seven (94.2%) group A patients, 126 (89.4%) group C patients, and 28 (18.8%) group B patients underwent arthroscopy. Seventeen group A patients and 15 group C patients did not undergo arthroscopy. Of these 32 patients, 17 were lost to follow-up and 15 refused to undergo or delayed undergoing arthroscopy for various reasons, including sufficient subsiding of symptoms during wait to undergo arthroscopy (eight patients).

The most prevalent abnormalities at MR imaging and arthroscopy are listed in Table 3. Furthermore, pigmented villonodular synovitis was suspected on the basis of MR imaging findings in two patients; one of these cases was confirmed at arthroscopy.

In one patient, a complete tear of the posterior cruciate ligament was found at MR imaging.

Table 2
Demographic and clinical characteristics at baseline

Group	Group A (n=294)	Group B (n=149)	Group C (n=141)
Mean age in years (SD); medians	33.0 (8.0); 34.0	29.6 (7.4); 30.0	28.5 (8.0); 31.0
No (%) of women	53 (18.0)	65 (43.6)	56 (39.7)
Duration of complaints in weeks (SD); medians	53.3 (107.6); 16.7	70.0 (176.4); 16.7	55.4 (125.9); 16.0
Trauma	175 (59.5)	93 (62.4)	93 (66.0)

Note.- Data in parentheses are percentages unless stated otherwise; n = number of patients

Table 3
Most important pathology found at MR imaging and arthroscopy. Results of arthroscopy are divided in patients that underwent arthroscopy because of a positive MR (group A) and patients with a negative MR (group B and C)

	MR (n=584)	Arthroscopy (n=431)	
		Group A (n=277)	Group B/Group C (n=154)
Medial meniscal tear	199 (34.1)	157 (53.4)	12 (7.8)
Lateral meniscal tear	90 (15.4)	77 (26.2)	8 (5.2)
Tear anterior cruciate ligament	75 (12.8)	38 (12.9)	11 (7.1)
Chondromalacia grade 4 (weight bearing surface)	19 (3.3)	23 (7.8)	4 (2.8)
Osteochondritis dissecans	10 (1.7)	5 (1.7)	0 (0.0)

Note.- Data in parentheses are percentages; n = number of patients

After undergoing MR imaging, 506 (86.6%) of the 584 patients were available for follow-up 6 months later: 257 (87.4%) patients in group A, 128 (85.9%) in group B, and 121 (85.8%) in group C. The majority of patients lost to follow-up had moved or did not provide correct addresses. At 6 months (Table 4), 105 (82.0%) of the 128 patients available for follow-up in group B were effectively treated according to our criteria. In group C, 93 (76.9%) of 121 patients who were available for follow-up were treated effectively. Therefore, the mean difference in effectiveness between the two groups, 5.1% ± 10.0, favored the conservative treatment (group B), with a 95% confidence interval of - 4.9% to 15.1% (P = 0.314). Thus, our data revealed conservative treatment to be noninferior to arthroscopic treatment in patients with negative MR findings.

3.4.2. Costs

Seventy-nine (13.5%) of the 584 patients did not return both cost diaries and thus were excluded from the cost analyses. The estimated medical and productivity costs in groups A and C were very similar (Table 5). Patients in group B underwent conservative treatment initially. As a result, their medical costs were considerably lower because only 18.8% of them subsequently underwent arthroscopy. Also, the absenteeism in group B was lower than that in group C by about 8 days. The costs of absenteeism were valued, on average, at $138 per day.

Table 4
Effectiveness of treatment strategy in randomization groups. Therapy is considered effective if Noyes function score increases more than 10% in six months.

Strategy	Group A	Conservative treatment (group B)	Arthroscopy (group C)	Difference between randomization groups
n	257	128	121	
Mean Noyes function score at t=0 (SD)	341.2 (65.4)	336.9 (67.7)	340.4 (70.4)	
Mean Noyes function score at t=6 (SD)	430.8 (85.1)	415.9 (84.7)	412.1 (89.4)	
% of treatment effective	84.4%	82.0%	76.9%	5.1% (-4.9;15,1)

Note.- Data in parentheses are 95% CIs unless stated otherwise; n = number of patients; Conservative treatment group = High clinical suspicion and negative MRI; randomized for conservative treatment (intention to treat); Arthroscopy group = High clinical suspicion and negative MRI; randomized for arthroscopy (intention to treat). Treatment is considered effective in case of a 10% increase in Noyes function score.

Table 5
Medical and productivity costs in study groups

		Group A (n=256)		Group B (n=125)		Group C (n=124)	
	unit prices	volume	costs	volume	costs	volume	costs
Medical costs							
Primary							
MR imaging (consultation not included)	593	100 %	593	100 %	593	100 %	593
Arthroscopy	889	94 %	835	19 %	169	89 %	791
Consultations (orthopedic) surgeon (including MR related consultation)	77	2.94 ×	227	2.19 ×	169	2.89 ×	222
Subtotal costs primary treatment			1,655		930		1,607
Secundary							
Physiotherapy		52%		62%		43%	
Physiotherapy 0-3 months	73	2.35 hr	172	4.50 hr	330	3.64 hr	267
Physiotherapy 3-6 months	73	2.63 hr	194	1.95 hr	143	1.81 hr	133
Consultations (orthopedic) surgeon (not scheduled)	77	0.66 x	50	0.91 x	70	0.69 x	53
General practitioner	31	0.72 ×	22	0.64 ×	21	0.69 ×	22
Other consultations	46	0.03 ×	1	0.02 ×	1	0.02 ×	1
Admissions	542	0.30 days	173	0.13 days	64	0.13 days	64
Medical aids		41 %	19	25 %	14	47 %	24
Medication		20 %	3	23 %	2	30 %	5
Subtotal costs secondary treatment			634		645		567
Total costs medical treatment			2,289		1,575		2,173
Productivity costs							
Employment		79 %		78 %		77 %	
Sick leave		56 %		32 %		60 %	
Sick leave 0-6 months		14.5 days	2,127	9.2 days	1,222	17.1 days	2,280

Note.- Costs in 2005 US Dollars; n = number of patients; number = mean number of hours/days per patient, mean number of consultations per patient, percentage of patients that underwent procedure or received treatment, percentage of patients that was employed / had sick leave or mean number of days of sick leave per patient; these results are calculated for each group as a whole, including patients without employment and therefore without sick leave; Group A = High clinical suspicion and positive MRI; Group B = High clinical suspicion and negative MRI; randomized for conservative treatment (intention to treat); Group C = High clinical suspicion and negative MRI; randomized for arthroscopy (intention to treat)

The projected costs for the strategy with and the strategy without MR imaging triage (Table 6) indicate that medical costs were significantly lower ($P < 0.001$) for the strategy without MR imaging because the MR costs outweighed the savings gained by not performing arthroscopy. However, productivity costs were significantly lower (P = 0.023) for the strategy with MR imaging. The aggregated results indicate that there was a nonsignificant mean difference in total societal costs of $153 in favor of the strategy involving MR imaging (P = 0.539).

Table 6
Frequency distribution of procedures and events and their associated costs for for strategies with and without MR imaging

	Strategy with MRI	Strategy without MRI	Difference	95% CI	
				Lower threshhold	Upper threshhold
MR imaging	100 %	0 %	100 %	100 %	100 %
Arthroscopy	57 %	92 %	-35 %	-39 %	-31 %
Costs primary treatment	1,296	961	334	294	375
Costs secundary treatment	640	600	39	-67	144
Subtotal costs medical care	1,934	1,561	373	255	490
Sick leave	44 %	58 %	-14 %	-20 %	-8 %
Sick leave	11.8 days	15.8 days	-4.0 days	-7.2 days	-0.7 days
Subtotal productivity costs	1,678	2,203	-525	-980	-72
Total costs society	3,612	3,765	-153	-641	335

Note.- Costs in 2005 US Dollars; Costs and percentages are arrived at using figures for group A, B and C as mentioned in table 4; Difference = Scenario with MRI triage - Scenario without MRI triage

3.4.3. Sensitivity Analysis

Univariate sensitivity analysis revealed that the estimated societal costs became more favorable without MR imaging triage (a) when the estimated 50% MR-negative fraction decreased to less than 40% -and became significantly more favorable when the fraction decreased to less than 25%, (b) when the costs of MR imaging increased from $593 to more than $746 -and became significantly more favorable when these costs increased to more than $1233, or (c) when the costs of arthroscopy decreased from $889 to less than $449 -but not significantly more favorable.

3.5. Discussion

MR imaging of the knee in patients with nonacute knee symptoms who are highly suspected clinically of having an intraarticular knee abnormality can be used to obviate arthroscopy, with nonsignificant differences in total societal costs. On the basis of the negative MR findings in our study, arthroscopy and conservative management had similar effectiveness and costs at 6 months.

To our knowledge, no other multicenter prospective randomized studies in which clinical outcome was used and total societal costs (including medical and productivity costs) were calculated have been published. However, investigators in several studies have addressed the question of whether MR imaging can be used cost effectively or assessed the value of MR imaging as a diagnostic examination [1-4,11-17]. In these studies, intermediate outcome parameters (eg, diagnostic accuracy of MR imaging) or the influence of MR imaging on therapy was used to assess the value of MR imaging.

We also used part of our patient group (those included between March 1997 and October 1998, hence the difference in the number of reported patients between the present study and our previous investigation) to compare the diagnostic accuracy of MR imaging with that of arthroscopy [10]. One study involving the use of clinical outcome was a single-center randomized controlled trial conducted by Bryan et al [18] in which 118 patients were randomly assigned to be examined with MR imaging or arthroscopy. That study had similar results: The use of MR imaging led to a decreased number of arthroscopies without increased overall costs or associated worsened outcomes.

Knowing the prevalence of treatable knee abnormalities in the given population is critical to the efficient application of MR imaging to exclude patients for arthroscopy. In our study population, which was selected by the orthopedic surgeon on the basis of clinical examination findings, the prevalence of treatable abnormalities seen at MR imaging was only 50%. The prevalences of abnormalities in other studies have been similar to the prevalence in our study. Ruwe et al [2] found, in a group of 103 patients with clinical findings that necessitated diagnostic arthroscopy, MR abnormalities in 41 (40%) patients. Rappeport et al [12] found in 47 patients suspected of having intraarticular knee injuries 27 (57%) patients with MR abnormalities. To our knowledge, only Bui-Mansfield et al [4] have observed, in a group of 50 patients, a prevalence of knee abnormality that was substantially higher (35 [70%] patients) than that observed in our study. The fact that their study population consisted predominantly of male military personnel might explain this difference.

The results of sensitivity analysis of our data suggest that use of the strategy involving MR imaging will significantly reduce societal costs when the prevalence of MR abnormalities is lower than 75%. The percentage of positive-result MR examinations in all of the preselected populations described was lower than 75%. Our economic evaluations were based on conditions in the Netherlands, and the generalization to other settings may be influenced by differences in economic climate and treatment patterns. However, our sensitivity analysis revealed that the costs of MR imaging can more than double, to $1233, before the societal costs of the strategy not involving MR imaging are significantly preferred, whereas lowering the costs of arthroscopy will not lead to a significant preference for the strategy not involving MR imaging.

Other considerations, in addition to effectiveness and cost, may guide the decision to use or not to use the MR imaging strategy. For instance, the wait to undergo both procedures may have a decisive role. When the wait to undergo arthroscopy is long, MR imaging can be used to reduce the number of arthroscopies performed and shorten the wait. On the other hand, if the wait to undergo MR imaging is long, no such gain is expected. In the Netherlands, MR units are commonplace in hospitals and waiting lists for MR imaging of the knee are short compared with these lists some years ago, when the wait to undergo this examination could be several months.

Apart from the societal considerations used to decide whether MR imaging should be performed to select patients for arthroscopy, on an individual level, the ability to prevent unnecessary arthroscopy by using MR imaging also may have a role in this decision. When an arthroscopic procedure is not performed for therapeutic purposes, no health gain can be expected from it. The prolonged morbidity after diagnostic arthroscopy, compared with that after MR imaging, and the risk of complications with arthroscopy may guide the decision of the orthopedic surgeon and the patient to use MR imaging initially.

There were some limitations in our study. As mentioned earlier, the generalization of our present study findings to other settings may be influenced by differences in not only the economic climate but also the treatment patterns of different countries. For instance, in the Netherlands, an isolated tear of the anterior cruciate ligament is not considered an indication for therapeutic arthroscopy for the general population because the initial therapy of choice is physiotherapy. In other countries, however, early anterior cruciate ligament reconstruction is considered the therapy of choice for certain patients, and, thus, isolated tear of the anterior cruciate ligament is an indication for arthroscopy. However, the number of these patients with isolated tears of the anterior cruciate ligament would be small, and these differences would not substantially alter our results.

Other possible limitations were our use of a 0.5-T MR system and the probability that MR and arthroscopy techniques have changed since 2000 (the year in which the last arthroscopies were performed in our study). A comprehensive review [(19)] revealed that the magnetic field strength does not significantly affect the performance of MR systems in the detection of meniscal abnormalities. In our study population, the majority of arthroscopies (90%, for 265 of 294 positive-result MR examinations) were indicated because of a meniscal abnormality [(10)]. To our knowledge, no important developments in the diagnosis and treatment of meniscal tears have been reported in the last couple of years. The most promising changes reported have been in the diagnosis and treatment of cartilage lesions, which were not prevalent in our study population.

We therefore conclude that in patients with nonacute knee symptoms who are highly suspected clinically of having an intraarticular knee abnormality, MR imaging can be used to obviate arthroscopy, without additional societal costs or disadvantageous effects on function.

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CHAPTER 4

Only MR can safely exclude Patients from Arthroscopy

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4.1. Abstract

Objective The aim of this study was to determine in patients with subacute knee complaints and normal standardized physical examination the fraction of magnetic resonance imaging (MRI) studies showing arthroscopically treatable intra-articular pathology.

Materials and methods There were 290 consecutive patients (between 16 and 45 years) with at least 4 weeks of knee complaints and low clinical suspicion of intra-articular pathology based on physical exam. Two hundred seventyfour patients were included. Sixteen patients with prior knee surgery, rheumatic arthritis, or severe osteoarthritis were excluded. MRI was used to assign patients to group 1 (treatable abnormalities) or group 2 (normal or no treatable findings), depending on whether MR demonstrated treatable pathology. Arthroscopy was performed in group 1 patients. If symptoms persisted for 3 months in group 2 patients, cross over to arthroscopy was allowed.

Results MR showed treatable pathology in 73 patients (26.6%). Arthroscopy was performed in 64 patients of 73 patients (group 1). In 52 patients (81.3%, 95% confidence interval (CI) 71.4-91.1%), arthroscopy was therapeutic. Of the 13 arthroscopies (6.5%) in group 2, four were therapeutic (30.8%, 95% CI 1.7-59.8). The highest fraction of MR studies showing treatable pathology was found in males, aged over 30 years, with a history of effusion (54.5%, six of 11 patients).

Conclusion Authors believe that the negative predictive value of clinical assessment in patients with subacute knee complaints is too low to exclude these patients from MR. MR should at least be considered in male patients aged 30 years and over with a history of effusion.

4.2. Introduction

The decision to perform arthroscopy or magnetic resonance (MR) imaging of the knee is based on clinical assessment. Diagnostic and/or therapeutic procedures are scheduled based on clinical assessment that is equivocal or that reveal abnormal findings. If clinical assessment is normal and the suspicion for intra-articular pathology is therefore low or absent, MR imaging is not indicated since the yield is expected to be low. This strategy relies on good positive and negative predictive values of clinical assessment of the knee. Among others, Terry et al. concluded that '…a thorough clinical assessment can provide sufficient information for the surgeon to make a definitive primary operative diagnosis...' without additional imaging in patients with knee complaints [(1)]. Ruwe et al. were one of the first to show that the positive predictive value of clinical assessment is limited [(2)]. These authors and others only studied patients undergoing arthroscopy based on abnormal clinical findings. Patients with a negative clinical assessment and therefore no arthroscopy were not included. The results are consequently skewed by verification bias [(3)].

The purpose of this study was to determine prospectively the fraction of MR imaging studies showing arthroscopically treatable intra-articular pathology in patients with subacute knee complaints who should, according to guidelines established by the Dutch Orthopedic Society and the Dutch Institute for Health Care Improvement [(4)], not proceed to additional diagnostic procedures because of normal standardized physical examination. In addition, we tried to identify clinical (sub-) groups with an above or below average yield of these MR studies.

4.3. Materials and methods

The internal review board of each participating hospital approved the study. We obtained written informed consent from all patients. During the first visit, the (orthopedic) surgeon took a standardized interview, including assessment of pain, history of trauma, joint effusion, instability, and locking. The impact of these data and the impact of gender and age (divided in two groups -30 years or younger and older than 30 years) of patients on the outcome of MR were studied using logistic regression (SPSS statistical package, version 10.0; SPSS Statistical Package, version 10.0).

Inclusion criteria were at least 4 weeks of knee complaints (pain, swelling of the joint, feeling of instability or giving way, history of locking), age between 16 and 45 years, and low clinical suspicion on intra-articular pathology based on normal standardized physical exam. A negative physical exam was defined as no soft tissue swelling, no marked joint effusion (no 'bulge sign' [ie, a visible bulge next to the patella caused by displacement of fluid and indicative for effusion]), no quadriceps muscle atrophy, no ligamental instability, no loss of range of joint motion, and negative meniscal provocation tests. Ligament instability was considered to be present if there was instability of the knee when applying varus and/or valgus stress. Joint instability was also considered to be present when the anterior and/or posterior drawer test and/or Lachman's test were positive [(5)]. Loss of range of motion was considered to be present when there was a difference of maximum flexion of more than 20° or extension of more than 10° between the symptomatic and asymptomatic extremity. Meniscal provocation tests were performed according to McMurray and Apley [(5)]. Pain in the popliteal fossa during hyperflexion (squad test) was also regarded as a positive meniscal provocation test.

Arthroscopy should not be performed in patients with a negative physical exam according to criteria established by the Dutch Orthopedic Society and the Dutch Institute for Health Care Improvement [(4)].

Exclusion criteria were previous surgery of the affected knee (including arthroscopy), fracture, rheumatoid arthritis, osteoarthritis Kellgren grade 4 [(6)], clinical retropatellar pain syndrome, previous MR imaging, or MR imaging unavailable for evaluation.

A total of 962 consecutive patients with at least 4 weeks of knee complaints visited the participating (orthopedic) surgical department of two general and one university hospital. Physical exam was performed by one of 17 (orthopedic) surgeons (with 1-21 years experience) or by residents under their supervision. Two hundred ninety patients had a negative physical examination according to the guidelines of the Dutch Orthopedic Society and thus were eligible for inclusion. Twenty-six patients (9.5%) were excluded because of the aforementioned exclusion criteria, leaving 274 patients as our study population. Mean age of the 274 included patients was 31.2 (standard deviation 7.8) years; 103 patients (37.6%) were female. Minimum duration of knee complaints was 4 weeks. Median duration of knee complaints was 29 weeks (95 percentile 254 weeks). The median interval between inclusion in the study and MR imaging was 8 days (95 percentile 26 days).

MR imaging was performed using three similar 0.5-T systems (Philips Medical Systems, Best, The Netherlands). The standardized scanning protocol consisted of three sequences: a sagittal and a coronal dual spin-echo (SE) sequence and a sagittal T1-weighted 3D gradiëntecho (GE) sequence with frequency selective fatsuppression. The following parameters were identical for both SE sequences: 140-160 mm field of view and 20/80 ms echo time (TE). The coronal dual SE had a repetition time (TR) of 2,100 ms, a 256×205 matrix, and a slice thickness of 5 mm with a 0.5-mm interslice gap. The sagittal dual SE had a TR of 2,350 ms, a 256×179 matrix, and a slice thickness of 4 mm with a 0.4-mm interslice gap. The parameters for the sagittal frequency selective fat-suppressed T1-weighted 3D GE were TR 70 ms, TE 13 ms, 45° flip angle, 160 mm field of view, 256×205 matrix, and 4 mm slice thickness with 2 mm overlap.

The total imaging time of the standard protocol (including the initial survey sequence) was 26 min. One of the six available radiologists, all with at least 5 years experience, used a case record form to evaluate the MR images according to established criteria (7-9).

We divided pathology found by MR imaging into two categories and patients were treated accordingly: group 1, abnormal findings requiring arthroscopic treatment (meniscal tears (≥5 mm), meniscal cysts, severe chondromalacia (grade 4 according to Recht (7)), osteochondritis dissecans with disrupted cartilaginous surface, loose bodies, or intraarticular pigmented villonodular synovitis). Group 2 consisted of patients without abnormalities or with findings not requiring arthroscopic treatment (small meniscal tears (< 5 mm), slight to moderate chondromalacia (grades 1 to 3 according to Recht (7)), isolated cruciate or collateral ligament tears, synovitis, synovial plicae, or bone bruises). We used the cutoff point of 5 mm in grading meniscal tears because our orthopedic surgeons regard tears smaller than 5 mm to be stable tears, whereas they consider tears larger than 5 mm to be unstable in the majority of cases. Patients with pathology equivocally requiring arthroscopic treatment such as osteochondritis dissecans with intact cartilaginous surface or capsular tear combined with ruptured collateral ligament could not be categorized initially. In these patients, the decision to perform arthroscopy was made after consulting the referring (orthopedic) surgeon. These patients were subsequently assigned to either group 1 or group 2.

According to protocol, arthroscopy had to be performed within 21 days after MR in all group 1 patients, but the time interval between MR and arthroscopy was not an exclusion criterion. If symptoms persisted for 3 months in group 2 patients, cross over to arthroscopy was allowed. All arthroscopic examinations were videotaped and were performed in the three participating hospitals by an experienced orthopedic surgeon or by a resident supervised by an orthopedic surgeon. A total of 17 surgeons participated in the study. Just like the radiologist, the surgeon was informed of the patient's history and of the findings at physical examination. The surgeon, however, was informed only of the diagnostic category at MR imaging, not the detailed MR diagnosis.
The arthroscope, which had a 30° viewing angle, was introduced into the knee through an anterolateral or transpatellar portal. All structures were probed as well as visualized. Chondromalacia was graded according to Outerbridge (10). After the diagnostic part of the examination, the arthroscopist recorded the arthroscopic diagnosis and therapeutic intentions, if any. To this end, a case record form was used that was identical to that used at the interpretation of the MR images. Subsequently, one of the authors (P.W.J.V. or B.P.M.t.B.), who was present at the arthroscopic examination, revealed the detailed diagnosis at MR imaging to the arthroscopist. In case of a discrepancy, the arthroscopist took a second look at the area during the same arthroscopic session. Next, depending on the diagnostic findings, the arthroscopist terminated the procedure or continued with the therapeutic part of the procedure. Results of arthroscopies were analyzed.

In the patients undergoing arthroscopy, assessment of knee function at study entry and at follow-up after at least 6 months was obtained using Noyes and Tegner questionnaires for assessing work-related and sport-related activities and functional limitations (11-13). Clinical outcome was assessed after at least 6 months.

4.4. Results

MR showed unequivocal abnormalities that required arthroscopy by protocol in 71 patients (25.9%). MR showed pathology equivocally requiring arthroscopic treatment in six patients (2.2%). After consulting the referring (orthopedic) surgeon, according to protocol, two of these six patients (0.7%) were assigned to group 1 (arthroscopy required). The other four patients (1.5%) were assigned to group 2 (conservative treatment). After assigning these six patients to the two groups, 73 patients (26.6%) were included in group 1 and 201 patients (73.4%) in group 2. Meniscal tear was the most frequent finding (Table 1); 76 tears were found with MR in 72 patients (26.2%). Of these tears, 68 in 65 patients were larger than 5 mm.

Table 1
MR imaging findings in 274 patients without abnormal findings at physical exam

		MR Group					
		1		2		Total	
Number of patients		73	(100.0)	201	(100.0)	274	(100.0)
Effusion		37	(50.7)	91	(45.3)	128	(46.7)
Medial meniscus	Small tear (< 5 mm)	0	(0.0)	3	(1.5)	3	(1.1)
	Large tear (≥ 5 mm, including bucket handle tears)*	44	(60.3)	0	(0.0)	44	(16.1)
	Discoid meniscus with* or without tear	1	(1.4)	0	(0.0)	1	(0.4)
	Meniscal cyst*	9	(12.3)	0	(0.0)	9	(3.3)
Lateral meniscus	Small tear (< 5 mm)	2	(2.7)	3	(1.5)	5	(1.8)
	Large tear (≥ 5 mm, including bucket handle tears)*	24	(32.9)	0	(0.0)	24	(8.8)
	Discoid meniscus with* or without tear	4	(5.5)	2	(1.0)	6	(2.2)
	Meniscal cyst*	5	(6.8)	0	(0.0)	5	(1.8)
Bone bruises		6	(8.2)	18	(9.0)	24	(8.8)
Severe chondromalacia*		5	(6.8)	1	(0.5)	6	(2.2)
Loose body*		2	(2.7)	0	(0.0)	2	(0.7)
Medial collateral ligament tear		7	(9.6)	16	(8.0)	23	(8.4)
Lateral collateral ligament tear		0	(0.0)	1	(0.5)	1	(0.4)
Anterior cruciate ligament tear		9	(12.3)	10	(5.0)	19	(6.9)
Posterior cruciate ligament tear		1	(1.4)	2	(1.0)	3	(1.1)

MR Group 1, pathology requiring arthroscopic treatment. MR Group 2, pathology not requiring arthroscopic treatment or normal knees. Ligamental tears include partial and total tears. Findings are not mutually exclusive. Percentage given in brackets
*Finding requiring arthroscopy as defined by our protocol.

A total of 77 arthroscopies were performed. Arthroscopy was performed in 64 of the 73 patients ofMR group 1 (87.7%; Table 2). The remaining nine patients of MR group 1 (12.3%) refused arthroscopy, mainly because of subsiding symptoms.

Table 2
Arthroscopy findings in 77 patients with negative physical exam who underwent arthroscopy.

		MR Group					
		1		2		Total	
Number of patients		64	(100.0)	13	(100.0)	77	(100.0)
Medial meniscus	Small tear (< 5 mm)	4	(6.3)	0	(0.0)	4	(5.1)
	Large tear (≥ 5 mm, including bucket handle tears)*	30	(46.9)	0	(0.0)	30	(39.0)
	Discoid meniscus with* or without tear	0	(0.0)	0	(0.0)	0	(0.0)
	Meniscal cyst*	0	(0.0)	0	(0.0)	0	(0.0)
Lateral meniscus	Small tear (< 5 mm)	0	(0.0)	1	(7.7)	1	(1.3)
	Large tear (≥ 5 mm, including bucket handle tears)*	17	(26.6)	1	(7.7)	18	(23.4)
	Discoid meniscus with* or without tear	2	(3.1)	0	(0.0)	2	(2.6)
	Meniscal cyst*	5	(7.8)	0	(0.0)	5	(6.5)
Severe chondromalacia*		9	(14.1)	1	(7.7)	10	(13.0)
Loose body*		1	(1.6)	0	(0.0)	1	(1.3)
Anterior cruciate ligament tear		13	(20.3)	4	(30.8)	17	(22.1)
Posterior cruciate ligament tear		0	(0.0)	0	(0.0)	0	(0.0)

MR Group 1, pathology requiring arthroscopic treatment. MR Group 2, pathology not requiring arthroscopic treatment or normal knees. Ligamental tears include partial and total tears. Findings are not mutually exclusive. Percentage given in brackets.
*Finding requiring arthroscopy as defined by our protocol.

The median interval between MR and arthroscopy in group 1 patients was 24 days (95 percentile 118 days).

In 13 of the 201 MR group 2 patients (6.5%), arthroscopy was performed. The median interval between MR and arthroscopy in these patients was 120 days (95 percentile 458 days). The study protocol was violated in four patients of group 2 (2.0%) who underwent arthroscopy within 3 months after normal MR.

The fraction of therapeutic arthroscopies in MR group 1 was 81.3% (95% confidence interval (CI) 71.4-91.1%) and this fraction was in MR group 2 statistically lower (30.8%, 95% CI 1.7-59.8, p value < 0.05). All but two of the 52 meniscal tears found at arthroscopy were present in MR group 1.

All but four of the 17 anterior cruciate ligament (ACL) ruptures seen at arthroscopy were present in MR group 1. All four patients with ACL ruptures diagnosed in MR group 2 were found to be isolated at arthroscopy. Because isolated ACL ruptures were no indication to perform arthroscopy in our study, these patients were rightly categorized as group 2.

Using binary logistic regression, gender, age (divided in two groups - 30 years or younger and older than 30 years), and a history of knee effusion appeared to be independent predictors of the fraction of MR studies showing arthroscopically treatable intra-articular pathology (chi-squared tests, p value < 0.05). The odds ratios of these three independent parameters for presence of intraarticular treatable pathology are 2.8 (95% CI 1.5-5.2) for male gender, 2.8 (95% CI 1.6-5.1) for age over 30 years, and 2.3 (95% CI 1.2-4.6) for a history of effusion. Combining gender, age, and a history of effusion, we found the highest fraction of MR studies showing arthroscopically treatable intra-articular pathology in male patients, aged over 30 years with a history of effusion - 54.5% (six of 11 patients). We found the lowest fraction of MR studies showing arthroscopically treatable intraarticular pathology in female patients aged 30 years or less without a history of effusion - 6.7% (three of 45 patients).

A history of trauma, pain, instability or locking proved not to be predictors of the fraction of MR studies showing arthroscopically treatable intra-articular pathology (p value > 0.05). We were able to assess functional outcome in 57 of 77 patients who underwent arthroscopy and to compare these data with data obtained at study entry. Mean interval between study entry and follow-up was 18 months. All scores improved significantly (p value < 0.05) after (therapeutic) arthroscopy.

4.5. Discussion

Normally, patients with subacute knee complaints but negative clinical tests do not proceed to additional diagnostic procedures. We found, however, in 26.6% of these patients abnormalities on MR that required arthroscopy. All these patients improved clinically following arthroscopy. The most frequent finding was meniscal tear. Arthroscopic treatment was performed in 81.3% (95% CI 71.4-91.1) of these patients.

In the literature, reported sensitivities and specificities of commonly used clinical tests of the knee, range from 10% to 95% and from 5% to 100%, respectively (5,14,15). A review by Scholten et al. stresses the poor methodological quality of the studies addressing diagnostic accuracy and limited clinical value of these tests (14). These tests perform worse in the ACL deficient knees (16) and also in the presence of effusion of the knee (14). The wide range of these test results is an indication of the limited clinical value of these tests.

Others report that more experienced examiners perform better than inexperienced examiners (17). This may be true, but we feel that the mixture of experienced and less experienced (orthopedic) surgeons, participating in this study, reflects usual care. It has also been suggested that a combination of test results improves the diagnosis of meniscal tears (5,14-16). In our study, we used a combination of six clinical tests. Although all six tests used were negative, we still found that 26.6% of patients had abnormalities on MR that required arthroscopy.

In a separate cost-effectiveness study (18), we included patients with high clinical suspicion on intra-articular knee pathology based on the aforementioned standardized physical exam (at least one of six tests positive). In this study group, 50.3% of patients had abnormalities on MR that required arthroscopy. So clinical assessment based on physical examination has only limited value in selecting patients for additional diagnostic procedures.

In the Dutch situation until recently, a general practitioner had no direct access to

MR of the knee. However, because of the limited additional value of (orthopedic) clinical assessment, direct access to MR and thus selection of patients for referral to an orthopedic surgeon could be a cost-effective policy [19, 20].

Not outcome of clinical assessment but gender, age, and history of effusion of the knee proved to be predictors for abnormal MR. We found the highest fraction of MR studies depicting arthroscopically treatable intra-articular pathology in male patients aged 30 years and over (54.5%). The importance of history taking in patients with knee complaints is stressed in textbooks. We could identify only one study reporting accuracy of medical history questions concerning intra-articular pathology [21]. Based on 30 questions that were not described, a diagnostic accuracy for intra-articular pathology of 85% was reported.

Assessing functional outcome of patients was not the primary goal of this study because we expected the frequency of arthroscopies required to be much lower than the observed 26.6%. We were able to analyze functional outcome using Noyes and Tegner questionnaires for assessing work-related and sport-related activities and knee limitations [11-13] in 57 of 77 patients who underwent arthroscopy and were able to compare these data with data obtained at study entry. Mean interval between arthroscopy and follow-up was 18 months. All scores improved statistically significantly after arthroscopy, suggesting that therapeutic arthroscopies were effective.

Isolated ACL tears in patients without high level sports activity are initially treated conservatively in The Netherlands. Arthroscopy is therefore not a routine procedure when an isolated ACL tear is diagnosed. A different treatment strategy does, in view of the accuracy of MR for diagnosing ACL tears, not affect our results. Twelve of the 17 knees with ACL tears, diagnosed at arthroscopy, had other findings requiring arthroscopy and were thus group 1 patients. The only isolated complete ACL tear in group 2 was diagnosed on MR; the others were partial tears.

A limitation of this study was that 12.3% of patients with positive MR did not proceed to arthroscopy mainly because of subsiding symptoms. These patients may have had false positive MRs or the findings on MR were not symptomatic to begin with. Another possibility is the well-known phenomenon of subsiding symptoms of patients on a waiting list [22]. In our study, patients waited on average 24 days (95 percentile 126 days). Another limitation was that a control group was not present since arthroscopy was only performed in patients with abnormal MR results. However, performing arthroscopy in patients with negative clinical assessment and negative MR results would have been considered unethical. A further limitation was the limited group of patients in which knee function at study entry and at follow-up was obtained. In conclusion, we believe that the negative predictive value of clinical assessment in patients with subacute knee complaints is too low to exclude these patients from MR. MR should at least be considered in male patients aged 30 years and over with a history of effusion, especially when symptoms do not subside within approximately 1 month.

4.6. References

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CHAPTER 5

Are radiographs needed when MR imaging is performed for non-acute knee symptoms in patients younger than 45 years of age?

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5.1. Abstract

Objective The objective was to determine the value of radiographs in young adults with non-acute knee symptoms who are scheduled for magnetic resonance imaging (MRI).

Materials and methods Nine hundred and sixty-one consecutive patients aged between 16 and 45 years with knee symptoms of at least 4 weeks' duration were prospectively included in three participating hospitals. After applying exclusion criteria, 798 patients remained. Exclusion criteria were previous knee surgery (including arthroscopy) or MRI, history of rheumatoid arthritis, clinical diagnosis of retropatellar chondromalacia, contra-indication for MRI and recent trauma. We identified two groups: group A with no history of trauma (n = 332), and group B with an old (> 4 weeks) history of trauma (n = 466). Patients had a standardized history taken, and underwent a physical exam, antero-posterior (AP) and lateral radiographs and MRI. We evaluated the radiographs and MRI for osseous lesions, articular surface lesions, fractures, osteoarthritis, loose bodies, bone marrow edema and incidental findings. Subsequently, patients with osseous abnormalities (Kellgren grade 1 and 2 excluded) on radiographs and a matched control group was evaluated again using MRI without radiographs.

Results Median duration of symptoms was 20 weeks. In group A, radiographs showed 36 osseous abnormalities in 332 patients (10.8%). Only 13 of these, all Kellgren grade 1 osteoarthritis, were not confirmed on MRI. MRI showed 72 (21.7%) additional abnormalities not confirmed on radiographs. In group B, radiographs showed 40 osseous abnormalities (8.6%) in 466 patients. Only 15 of these, all Kellgren grade 1 osteoarthritis, were not confirmed on MRI. MRI showed 194 (41.6%) additional abnormalities not confirmed on radiographs. The second evaluation of MRI without radiographs in 34 patients was identical to the first MRI evaluation. Common lesions were significantly more often diagnosed with MRI than with radiographs.

Conclusion Radiographs should not be obtained routinely when MRI is being performed in young adults with nonacute knee complaints because the yield and added value to MRI are low.

5.2. Introduction

Radiographs in patients with acute knee problems that are obtained at, or close to, the time of trauma serve mainly to exclude fractures and most of these radiographs are normal. To reduce the total number, and especially the number of normal radiographs, clinical decision rules that identify patients with a high risk of fracture have been developed and validated [(2-4)]. In patients with non-acute knee symptoms radiographs are the mandatory minimal initial exam in patients with non-traumatic knee pain, according to ACR appropriateness criteria [(5)]. Magnetic resonance imaging (MRI) is frequently obtained if additional imaging is clinically needed to search for suspected intra-articular abnormalities. The value of radiographs relative to MRI in a heterogeneous group of patients was recently reported [(6)]. Radiographs were rated 'essential' or 'very important' in 46-58% of cases and added 'not needed information' in 14-29% of cases. However, the value of radiographs relative to MRI in young adults presenting with non-acute knee symptoms has, to our knowledge, not been established. If in these patients radiographs could be omitted, or obtained only when needed when reading MRI, this could possibly lead to a significant reduction of the volume of knee radiographs with ensuing reduction in radiation dose and costs.

The purpose of our prospective study was to determine the value of radiographs in young patients with non-acute knee symptoms and suspected intra-articular pathology who are scheduled for MRI based on the results of a physical exam. We therefore determined the prevalence of osseous abnormalities visible on radiographs and MRI and the yield of MRI compared with that of radiographs. In addition, we measured the radiation dose of standard radiographs of the knee.

5.3. Materials and methods

Over 3 years, 961 patients referred from general practitioners to the outpatient surgery or orthopedic surgery clinics of three hospitals (two general hospitals and one university hospital) because of non-acute knee symptoms agreed to participate in our prospective study. The symptoms had to have been present for at least 4 weeks. The institutional review board of each hospital approved the study. We obtained written informed consent from all patients. At study entry a standardized history, including inventory of traumatic events and other knee-related events such as morbidity and medical procedures was taken. Physical exam was performed by one of 15 (orthopedic) surgeons or by residents under their supervision. All the patients included underwent MRI and radiographs of the knee. Recent radiographs taken for the same complaints that were obtained prior to study inclusion were not repeated.

We included patients who met the following inclusion criteria: knee symptoms (pain, swelling of the joint, feeling of instability or giving way, history of locking) of at least 4 weeks' duration and age between 16 and 45 years. To obtain a homogenous study population without co-morbidity we did not include patients who had had previous surgery of the affected knee (including arthroscopy) or previous MRI, a history of rheumatoid arthritis, and clinical diagnosis of retropatellar chondromalacia, contra-indication for MRI, or an incomplete data set. One hundred and sixtythree patients (17.0%) were eventually excluded (Table 1), leaving 798 patients as our study group. Of these excluded patients a substantial number should not have been included by the orthopedic surgeons in the first place according to our study protocol, for instance, because they were either too young, too old or had knee complaints of less than 4 weeks' duration.

Table 1
Excluded patients. Of the 961 eligible patients, 163 (17.0%) patients were excluded

Exclusion criteria	n
Symptoms of less than 4 weeks' duration	65
Aged under 16 years	1
Aged over 45 years	6
Previous surgery	8
Retropatellar chondromalacia	14
Previous MRI	1
Radiographs unavailable or not obtained	65
MRI or arthroscopy prohibited	2
Immediate arthroscopy required	30

Criteria are not mutually exclusive.

One out of six musculoskeletal radiologists (all with at least 5 years' experience) evaluated the radiographs without knowledge of the MR images and recorded their findings on a Case Record Form (CRF).

The radiation dose of standard antero-posterior and lateral radiographs was determined in two of the three hospitals using flat ionization chambers. We used PCXMC software (STUK, Finland) to convert the measured radiation doses into effective doses.

The radiologist evaluated the radiographs for articular surface lesions, using the classification developed by Bohndorf [(7)]. Osteoarthritis was scored using the scoring system developed by Kellgren et al. [(1)]. In the analysis, grades 1 to 3 were considered as one group, with osteoarthritis being present.

Radiographs were also evaluated for fractures [(8-10)], loose bodies, and incidental findings. A loose body was defined as a radiodense circumscriptive lesion located in the femorotibial, patellofemoral jointline or suprapatellar pouch. Incidental findings, such as non-ossifying fibromas and enchondromas were diagnosed using established criteria [11, 12]. On radiographs a lesion was considered a non-ossifying fibroma if it met the following criteria: asymptomatic, cortical metaphyseal location, and radiographically non-aggressive. A lesion was considered an enchondroma if it met the following criteria: central metaphyseal location, chondroid matrix, geographic pattern of destruction with or without sclerotic margin.

We performed the MR studies in all three hospitals on an identical 0.5-T system (Gyroscan T5, Philips Medical Systems, Best, the Netherlands), with the same software release using a dedicated transmit-receive knee coil.

The standardized scanning protocol consisted of three sequences: a sagittal and a coronal dual spin-echo (SE) sequence and a sagittal T1-weighted 3D gradient-echo (GE) sequence with frequency selective fat suppression. The following parameters were identical for both SE sequences: field of view 140-160 mm, echo time (TE) 20/80 ms. The coronal dual SE had a repetition time (TR) of 2,100 ms, a 256×205 matrix and a slice thickness of 5 mm with a 0.5 mm interslice gap. The sagittal dual SE had a TR of 2,350 ms, a 256×179 matrix and a slice thickness of 4 mm with a 0.4 mm interslice gap. The parameters for the sagittal frequency selective fat-suppressed T1-weighted 3D GE were: TR 70 ms, TE 13 ms, 45° flip angle, field of view 160 mm, 256×205 matrix, 4 mm slice thickness with a 2 mm overlap.

The total imaging time of the standard protocol (including the initial survey sequence) was 26 min.

After reading the radiographs one out of six radiologists evaluated MR images and reported his findings on a CRF. In accordance with usual management the observer had access to the radiographs, but not to the reports, when evaluating MR images. The CRF was similar to the one used for radiographs [8-12], except that bone marrow edema was added as an item [13]. For articular surface lesions we again used the classification developed by Bohndorf [7]. For osteoarthritis we used the scoring system developed by Recht et al. [14]. For the purpose of this study, grades 1 to 4 were considered as one group, with osteoarthritis being present.

To overcome bias in the reading of MR studies, introduced by knowledge of the results of conventional radiographs, one radiologist (JLB) re-evaluated MR studies of patients with abnormalities on conventional radiographs with the exception of osteoarthritis of Kellgren [1] grades 1-2. We used the same CRF format. At this second evaluation, MR studies of patients with osseous abnormalities on conventional radiographs were mixed with age- and gender-matched MR studies of patients without abnormalities on conventional radiographs. The radiographs and the findings on the CRF were not available at that time.

We divided the completed CRFs over two groups: group A had no history of trauma, and group B had a history of trauma of more than 4 weeks before presentation at the hospital.

We used the Chi-squared test to identify significant differences between the yield of radiographic and MR diagnoses, and between the number of findings in group A and that in group B. To look for statistically significant differences between the yield of radiographs and MRI within groups A, B and the study population as a whole, we used McNemar's Chi-squared test.

5.4. Results

The median age of the 798 patients included was 31 years (range 16-45 years), and 261 patients (32.7%) were female. Minimal and median duration of symptoms were 4 and 20 weeks respectively (range 4-1,490 weeks). Three hundred and thirty-two patients reported no history of trauma (group A), and 466 patients reported an old (more than 4 weeks prior to consultation) history of trauma (group B).

Magnetic resonance imaging depicted arthroscopically treatable intra-articular pathology in 341 patients (42.7%). Medial and lateral meniscal tears were found in 225 (28.2%) and 111 patients (13.9%) respectively. The average radiation dose of supine antero-posterior and lateral radiographs was 0.2 and 0.3 mSv respectively. The median duration of the interval between radiographs and MRI was 8 days (95 percentile, 85 days). In 196 patients (24.6%)radiographs were obtained prior to inclusion in the study. These radiographs were not repeated since the knee complaints had not changed between the moment they were obtained and inclusion in this study.

In group A, radiographs showed 36 osseous abnormalities in 332 patients (10.8%, Table 2). All these abnormalities, except 13 Kellgren [(1)] grade 1 osteoarthritis cases, were also depicted on MRI. There were 23 concordant radiographic and MRI diagnoses (Fig. 3; Table 2). One incidental finding (enchondroma) was demonstrated on radiographs and MRI. The majority of the 72 diagnoses made only with MRI were osteoarthritis and bone bruising (Table 2). Most osseous lesions (osteoarthritis, articular surface lesions, loose bodies and bone marrow edema) with the exception of incidental findings (one case) and old fractures (not present in this group) were significantly more often diagnosed with MRI than with radiographs (Table 2).

In group B, radiographs showed 40 osseous abnormalities in 466 patients (8.6%, Table 3). All these abnormalities, except 15 Kellgren [(1)] grade 1 osteoarthritis cases, were also depicted on MRI. There were 25 concordant radiographic and MRI diagnoses (Figs. 1, 4, 5 and 6; Table 3). Four of the six incidental findings were diagnosed on radiographs and MRI (1 non-ossifying fibroma and 3 enchondromas, Fig. 7). Two enchondromas were depicted on MRI only (Fig. 8). The majority of the 192 diagnoses made only with MRI were bone marrow edema (Fig. 2), osteoarthritis and articular surface lesions (Table 3). These three diagnoses were significantly more often diagnosed with MRI than with radiographs (Table 3). There was no significant difference between MRI and radiographs in the diagnosis of loose bodies, old fractures and incidental findings.

Table 2
Osseous abnormalities detected on radiographs only, on radiographs and MRI, and on MRI only in 332 patients with non-acute nontraumatic knee complaints

Osseous abnormality	R (%)	R and MR (%)	MR (%)	Total (%)	McNemar Test, p-value
OA	13 (3.9)	18 (5.4)	39 (11.7)	70 (21.1)	0.00
ASL	0 (0)	3 (0.9)	7 (2.1)	10 (3.0)	0.02
LB	0 (0)	1 (0.3)	6 (1.8)	7 (2.1)	0.03
Fractures	0 (0)	0 (0)	0 (0)	0 (0)	NA
Incidental finding	0 (0)	1 (0.3)	0 (0.0)	1 (0.3)	1.00
Bone marrow edema	0 (0)	0 (0)	20 (6.0)	20 (6.0)	NA
Total	13 (3.9)	23 (6.9)	72 (21.7)	108 (32.5)	0.00

OA: osteoarthritis grade 1 or higher according to Kellgren [1] on radiographs and according to Recht [14] on MRI ; ASL: articular surface lesion with or without disrupted cartilage; LB: loose body; R: abnormality detected with radiographs only; R and MR: abnormality detected with both radiograph and MRI; MRI: abnormality detected with MRI only; NA: not applicable. Categories are not mutually exclusive.

Table 3
Osseous abnormalities detected on radiographs only, on radiographs and MRI, and on MRI only in 466 patients with non-acute traumatic knee complaints

Osseous abnormality	R (%)	R and MR (%)	MR (%)	Total (%)	McNemar Test, p-value
OA	15 (3.2)	13 (2.8)	65 (13.9)	93 (20.0)	0.00
ASL	0 (0)	3 (0.6)	22 (4.7)	25 (5.4)	0.00
LB	0 (0)	1 (0.2)	4 (0.9)	5 (1.1)	0.13
Fractures	0 (0)	4 (0.9)	3 (0.6)	7 (1.5)	0.25
Incidental finding	0 (0)	4 (0.9)	2 (0.4)	6 (1.3)	0.5
Bone marrow edema	0 (0)	0 (0)	96 (20.6)	96 (20.6)	NA
Total	15 (3.2)	25 (5.4)	192 (41.2)	232 (49.8)	0.00

Categories are not mutually exclusive.

Table 4
Osseous abnormalities detected on radiographs only, on radiographs and MRI, and on MRI only in 798 patients with non-acute knee complaints

Osseous abnormality	R (%)	R and MR (%)	MR (%)	Total (%)	McNemar Test, p-value
OA	28 (3.5)	31 (3.9)	104 (13.0)	163 (20.4)	0.00
ASL	0 (0)	6 (0.8)	29 (3.6)	35 (4.4)	0.00
LB	0 (0)	2 (0.3)	10 (1.3)	12 (1.5)	0.00
Fractures	0 (0)	4 (0.5)	3 (0.4)	7 (0.9)	0.25
Incidental finding	0 (0)	5(0.6)	2 (0.3)	7 (0.9)	0.5
Bone marrow edema	0 (0)	0 (0)	116 (14.5)	116 (14.5)	NA
Total	28 (3.5)	48 (6.0)	264 (33.1)	340 (42.6)	0.00

Categories are not mutually exclusive.

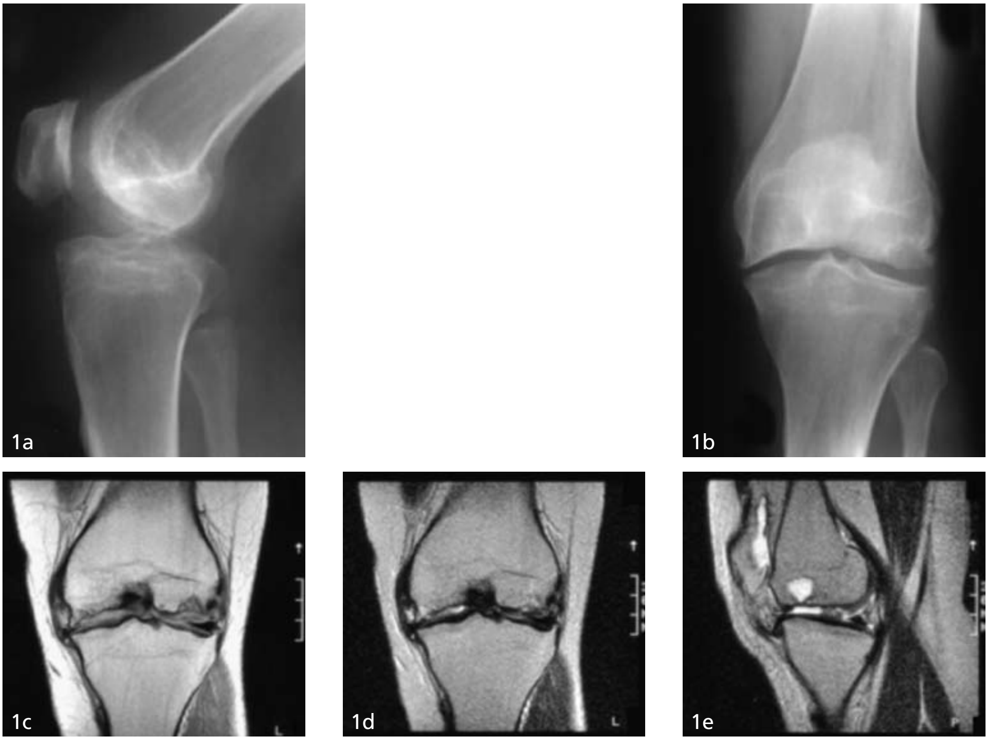

Figure 1. Severe osteoarthritis on both radiographs and MRI. **1a,b** Lateral and antero-posterior radiographs showing deformation of the femoral condyles and tibia plateau with marked subchondral cyst formation and osteophyte formation in a 44-year-old female patient with a history of knee trauma (group B). **1c,d** Coronal proton density and T2-weighted spin-echo (SE) images and of the same lesion showing, in addition to the deformities and changes already noted on the radiographs, the osteochondral defect to a better extent. **1e** Sagittal T2-weighted SE image showing the same features, but also focal fullthickness cartilage loss.

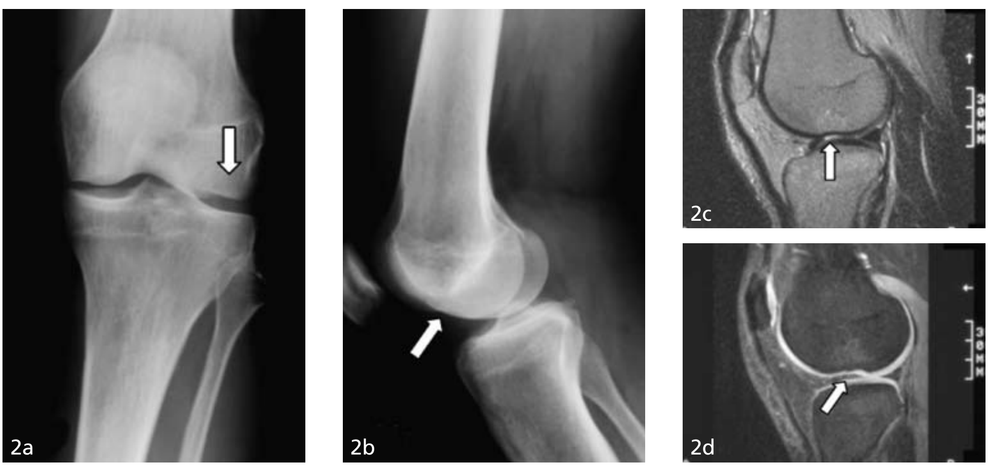

Figure 2. Three-month-old transchondral fracture on both radiographs and MRI. **2a,b** Antero-posterior and lateral radiograph showing irregularity and deformation of the lateral femoral condyle consistent with a transchondral fracture of the lateral femoral condyle in a 40-year-old male with a history of knee trauma (group B). **2c,d** Sagittal T2-weighted SE images and T1-weighted 3D gradientecho (GE) with fat suppression showing subtle contour deformity of the lateral femoral condyle with kissing bone bruises in the lateral femoral condyle and tibial plateau.

Osseous abnormalities were more frequently encountered in group B than in group A ($p < 0.001$). This difference is explained by a significant difference in the number of old fractures ($p < 0.05$, no old fractures were seen in group A), and patients with bone marrow edema ($p < 0.001$).

Bone marrow edema was demonstrated with MRI in 116 patients (14.5%, Table 4); 96 of these were found in group B (82.8% of patients with bone marrow edema, Table 3).

In 6 (30%) of the 20 group A patients with bone marrow edema, it was either associated with intra-articular damage of non-osseous origin or it was an isolated finding. The associated osseous abnormalities in the other 14 patients were as follows: bone marrow edema was found in 4 of the 10 patients with articular surface lesions, in 1 of the 7 patients with a loose body, and in 9 of the 70 patients with osteoarthritis.

In 89 (92.7%) of the 96 group B patients with bone marrow edema, it was either associated with intra-articular damage of non-osseous origin or it was an isolated finding. The associated osseous abnormalities in the other 7 patients were as follows: bone marrow edema was found in 4 of the 5 patients with articular surface lesions (Fig. 2), in 1 of the 5 patients with a loose body and in 2 of the 93 patients with osteoarthritis.

In our population we did not find any other osseous lesions like osteopenia or femoropatellar disease. Also, we did not find chondrocalcinosis on radiographs.

Subsequently, all patients with radiographically detected abnormalities with the exception of Kellgren [(1)] grade 1 and 2 osteoarthritis were identified. MRI studies of the 17 patients with 18 radiographically detected osseous abnormalities were mixed with 17 gender- and age-matched MRI studies of patients without abnormalities on radiographs. There were 6 females in each group, and the mean age in each group was 33.1 years, SD 7.9 years). At revision, the reader (JLB) was blinded to all information and had no access to the radiographs. All 18 osseous abnormalities (1 case of osteoarthritis Kellgren grade 3 [Fig. 1], 6 articular surface lesions [Figs. 2, 3], 2 loose bodies [Fig. 4], 4 old healed fractures [Figs. 5, 6] and 5 incidental findings [4 enchondromas and 1 non-ossifying fibroma, Figs. 7, 8]) were all diagnosed on MRI.

5.5. Discussion

Key characteristics of our population such as age, gender, clinical suspicion of intra-articular abnormalities, intraarticular abnormalities detected with MRI, and history suggest that our conclusions can be applied to typical populations scheduled for MRI to analyze non-acute knee problems.

The yield of radiographs in patients with subacute or chronic knee symptoms who are otherwise healthy and who are scheduled for MRI based on the results of a physical exam suggesting the presence of intra-articular damage is only 9.5% (76 patients).

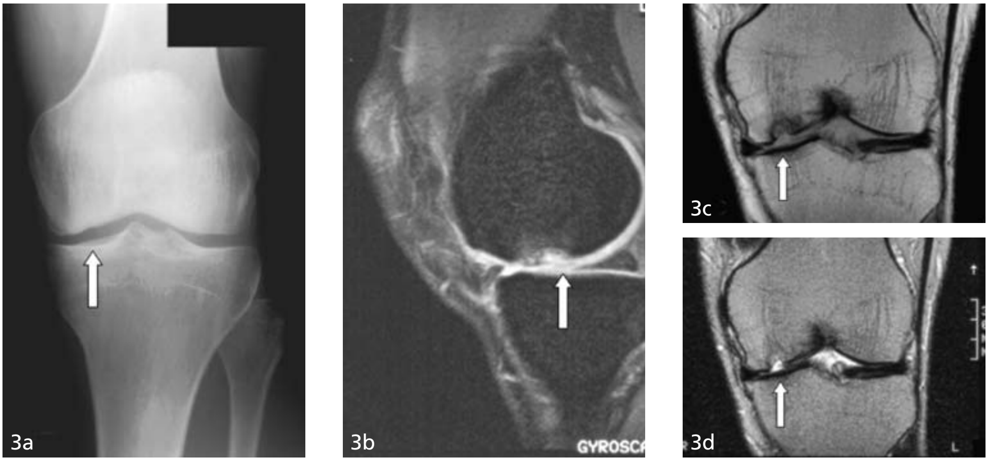

Figure 3. Twenty-six-month-old transchondral fracture on both radiographs and MRI. **3a** Anteroposterior radiograph showing abnormal density, subtle irregularity and deformation of the medial femoral condyle in a 35-yearold male patient with no history of knee trauma (group A). **3b-d** Sagittal T1-weighted 3D GE with fat suppression and coronal proton density and T2-weighted SE images of this knee showing the transchondral fracture.

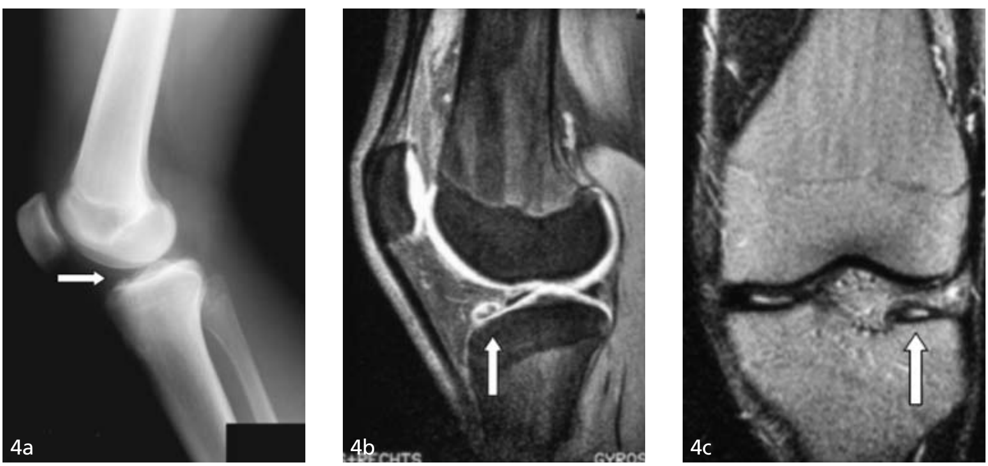

Figure 4. Loose body on both radiography and MRI. **4a** Lateral radiograph showing a ventrally located loose body in the left femorotibial joint in an 18-year-old male professional skater with a history of knee trauma (group B). **4b,c** Sagittal T1-weighted 3D GE with fat suppression and coronal proton density SE images of the same patient, also showing the loose body that is ventrally located in the lateral compartment of the femorotibial joint. At subsequent arthroscopy this loose body was removed.

The majority of these patients (77.6%) have osteoarthritis. We failed to confirm with MRI the radiographic diagnosis of Kellgren [1] grade 1 osteoarthritis in 28 patients, but none of the other abnormalities were diagnosed only with radiographs. This was confirmed in a second reading of MRI blinded to clinical and radiographic information. Radiographs do not, in the setting of this study, contribute to clinical decisionmaking or clinical management of the patient. Although the dose administered when obtaining radiographs of the knee is small, the size of the population with knee complaints make the reduction of an administered dose a relevant issue. Radiographs can therefore be omitted in this specific population when the decision to perform MRI is taken based on clinical assessment. The disadvantage of occasionally missing Kellgren [1] grade 1 osteoarthritis is limited when we realize that because of the lack of a gold standard these radiographic diagnoses may also be false-positive.

Taljanovic et al. [6] rated radiographs as 'essential' or 'very important' in 46-58% of cases and radiographs added 'not needed information' in 14-29% of cases. They conclude in their study that radiographs are an important, and sometimes essential initial, complementary study for reading musculoskeletal MR examinations. This apparently different conclusion can be explained by the differences in study populations. Taljanovic et al. [6] analyzed a large variety of diagnosis (trauma, infection, tumors, degenerative or miscellaneous) in all anatomical locations in patients of all ages. We only analyzed patients between 16 and 45 years of age with non-acute knee symptoms lasting at least 4 weeks, excluding amongst others patients with acute knee symptoms (ie, less than 4 weeks), history of rheumatoid arthritis, and clinical diagnosis of retropatellar chondromalacia. Other major methodological differences are mainly related to this difference.

The concordance between radiographs and MRI is not high because of the large number of diagnoses (77.6%) made only with MRI. In groups A and B osteoarthritis, articular surface lesions, and bone marrow edema were significantly more often diagnosed with MRI than with radiographs. Loose bodies were significantly more frequently diagnosed with MRI in group A only. This higher yield of MRI is no surprise, since abnormalities such as articular surface lesions and bone marrow edema are known to be better, or even exclusively appreciated on MRI. These findings have, in addition to the intra-articular abnormalities detected with MRI, potential clinical significance in view of the patients' presenting symptoms.

The advantage and comprehensiveness of MRI is illustrated by its ability to demonstrate bone marrow edema that is associated with other abnormalities. In the patients with a history of old trauma, bone marrow edema was mainly (92.7%) associated with intra-articular damage. In the group with no history of trauma, however, bone marrow edema was mainly (70%) seen in association with osseous abnormalities, thus facilitating the diagnosis of articular surface lesions and osteoarthritis.

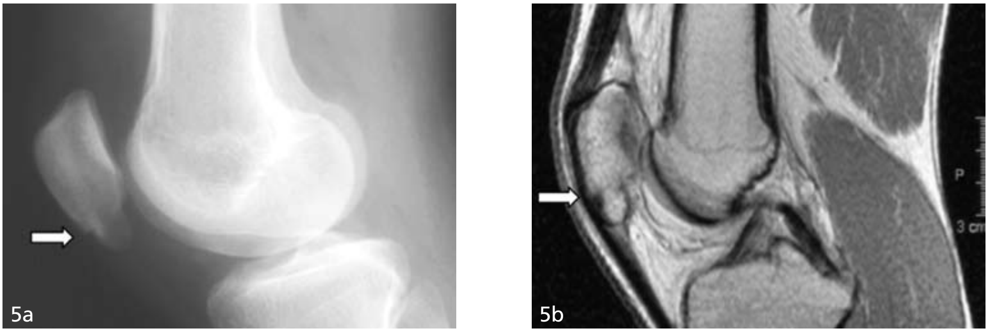

Figure 5 Eight-month-old healed fracture on both radiograph and MRI. **5a** Lateral radiograph showing a healed fracture of the inferior patellar pole in an 18-yearold male patient with a history of knee trauma (group B). **5b** Sagittal proton density SE image of the same patient, also delineating the healed fracture of the inferior pole of the patella.

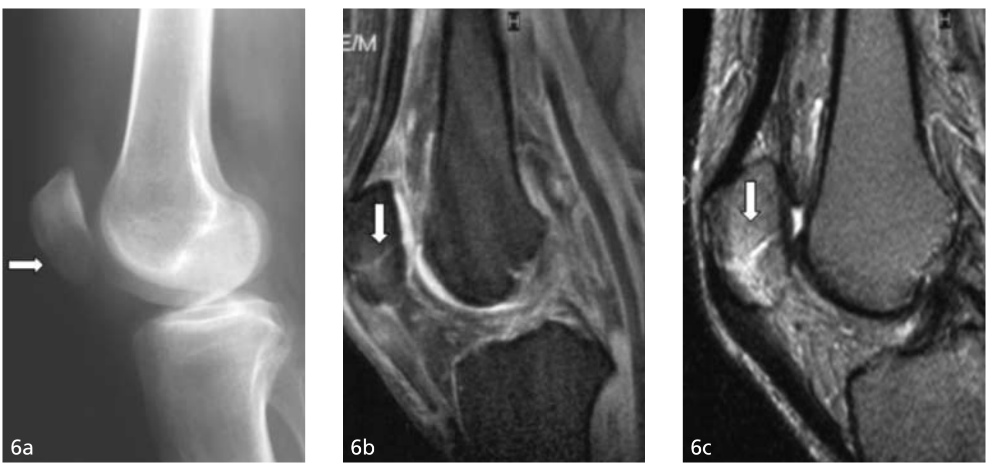

Figure 6. Two-month-old healing fracture on both radiograph and MRI. **6a** Lateral radiograph showing a healing fracture of the left inferior patellar pole in a 40-year-old male patient with a history of knee trauma (group B). **6b,c** Sagittal T1-weighted 3D GE with fat suppression and T2-weighted SE images of the same patient, also delineating the healing fracture of the inferior pole of the patella without cartilaginous irregularities. Around the fracture line bone marrow edema can be appreciated.

This prospective study has several limitations that are mainly related to the decision to follow usual care. This means that radiographs were available at the time of MRI. To overcome this limitation, one radiologist (JLB) reevaluated MR studies of patients with abnormalities on conventional radiographs without knowledge of the radiographs, as described.

Another limitation is that we could not determine accuracy because of the absence of a reference standard. If we look at the discordant cases, there are no potentially false-negative MRI diagnoses (with the exception of Kellgren [1] grade 1 osteoarthritis), but the number of potential false-positive MRI diagnoses (abnormal finding on MRI in combination with a normal radiograph) is substantial, mainly because of the high prevalence of bone marrow edema.

Another possible limitation of this study is the selection bias introduced by including only patients between 16 and 45 years of age and excluding patients with co-morbidity. The study design was not tailored toward assessment of the value of conventional radiographs only. The overall goal of this multicenter study was to evaluate the efficacy of MRI compared with direct arthroscopy in patients with subacute knee complaints, based on clinical outcome. To this end we tried to obtain a homogenous study population without comorbidity. This is most likely the reason we encountered only 1 patient with high-grade osteoarthritis (Kellgren [1] grade 3). However, because the majority of MR examinations performed in our institutions will be of patients in this age range without known co-morbidity, we do not think this selection bias will alter our overall conclusions.

We tried to mimic usual care as much as possible in this study. However, in our study MRI was performed within 2 weeks of inclusion in the study. Due to the limited availability of MRI compared with conventional radiographs in most hospitals, MRI often cannot be performed at such short notice. This can lead to a considerable waiting time for MR examinations and this may direct physicians to prior conventional radiographs to rule out gross pathology and reassure the patient. To prevent these unnecessary radiographs, the waiting time for MRI must be as short as possible. In the Netherlands waiting times for MRI in most institutions are down from several months a couple of years ago to several weeks nowadays.

We conclude that radiographs should not be obtained routinely when MRI is being performed in non-acute young patients with knee complaints because the number of clinically relevant lesions detected on radiographs is low. In addition, the small number of abnormalities found on radiographs is, with the exception of an occasional case of Kellgren [1] grade 1 osteoarthritis, also depicted on MRI. Reduction of costs and radiation dose is small in the individual patient, but, because of its size, substantial in the entire population with subacute and chronic complaints suspected to be knee injury.

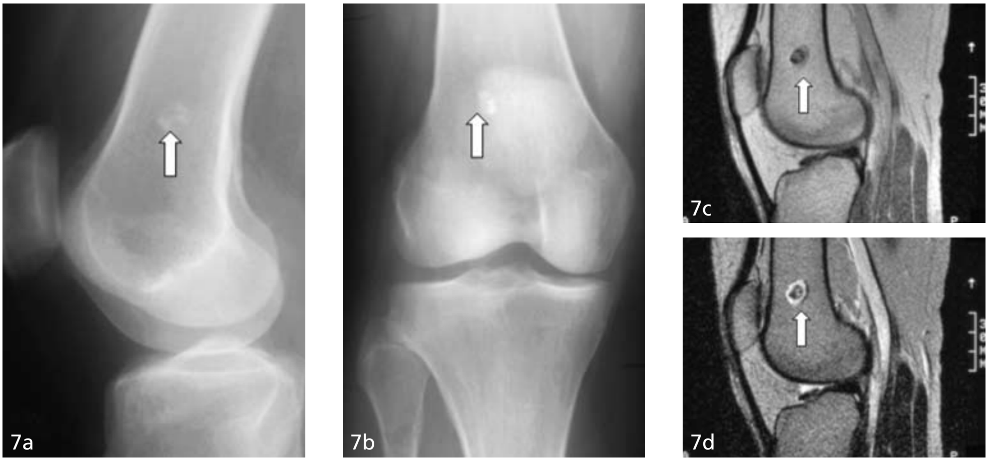

Figure 7. Incidental finding depicted on both radiographs and MRI. **7a,b** Lateral and antero-posterior radiographs showing a central, metaphyseally located lesion with chondroid matrix consistent with enchondroma in the femur in a 44-year-old female patient with a history of knee trauma (group B). **7c,d** Sagittal proton density and T2-weighted SE images of the same lesion.

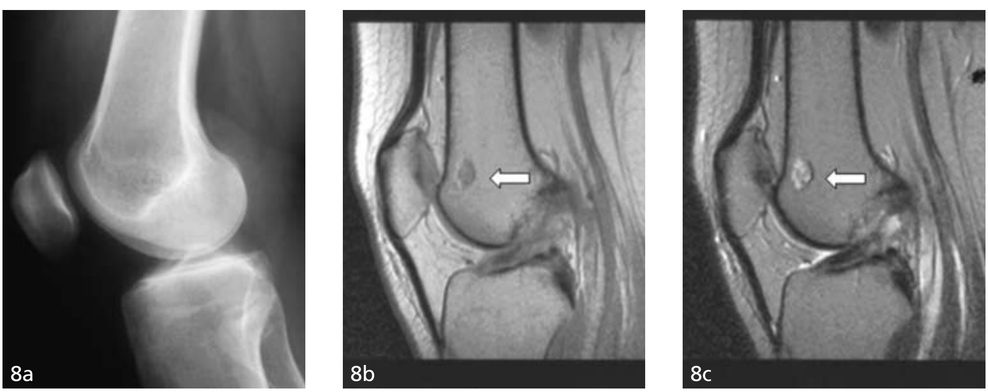

Figure 8. Incidental finding depicted on MRI only. **8a** Lateral radiograph showing no femoral osseous lesion in a 40-year-old female patient with a history of knee trauma (group B). **8b,c** Sagittal proton density and T2-weighted SE images showing a metaphyseal lesion consistent with an enchondroma.

5.6. References

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CHAPTER 6

Clinical consequences of bone bruise around the knee

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6.1. Abstract

Objective The aim of this study is to evaluate the relation between bone bruise and (peri-)articular derangement and to assess the impact of bone bruise on presentation and short term course of knee complaints.
Materials and methods We recorded MR abnormalities in 664 consecutive patients with sub-acute knee complaints. Patients were divided in four groups: patients with and without intra-articular knee pathology, subdivided in patients with and without bone bruise. We assessedfunction and symptoms at the time of MR and 6 months thereafter.
Results Bone bruises were diagnosed in 124 of 664 patients (18.7%). Patients with bone bruise had significantly more complete ACL, lateral meniscal, MCL and LCL tears. Both with and without intraarticular pathology patients with bone bruise had a significantly poorer function at the time of MR (Noyes score of, respectively, 313.21 versus 344.81 and 306.98 versus 341.19). Patients with bone bruise and intraarticular pathology showed significantly more decrease in activity (decrease of Tegner score from 6.28 to 2.12 versus 5.70–2.55). At 6 months there were no significant differences in clinical parameters between the four groups.
Conclusion We concluded that bone bruise in combination with MCL tear is an important cause of initial clinical impairment in patients with sub-acute knee complaints. Clinical improvement within 6 months is more pronounced than in patients without bone bruise.

6.2. Introduction

With the advent of magnetic resonance (MR) imaging bone bruise was introduced as a new radiologic diagnosis [1, 2]. A bone bruise is defined as a traumatically involved geographic, and non-linear area of signal loss involving the subcortical bone on T1-(short TE) weighted images and increased signal intensity on T2-weighted images. The term 'bruise" indicates the traumatic origin of these bone marrow changes. These signal alterations are thought to represent trabecular (micro-) fractures associated with edema and hemorrhage. MR imaging findings are therefore also referred to as bone marrow edema pattern. The clinical relevance of this finding has been an issue of discussion ever since the first reports on bone bruise. Clinically, bone bruises can have the same symptoms as meniscal or other intra-articular injury. Traumatic events resulting in bone bruise and/or intra-articular injury are also similar. Therefore, bone bruises may trigger decisions to perform arthroscopy in patients without internal derangement of the knee [3]. On the other hand, there also is an association between bone bruise and intra-articular pathology [4-9].

The aim of this prospective multicenter study is to evaluate the relation between bone bruise and (peri-)articular derangement and to assess the impact of bone bruise on presentation and short term course of knee complaints inpatients with clinically suspected internal derangement of the knee. We addressed this issue using a general MR knee protocol that is commonly used, rather than a dedicated protocol with a higher sensitivity to bone bruise.

6.3. Materials and methods

6.3.1. Patients and study design

In this prospective multicenter study, primarily designed to evaluate the efficacy of MR compared to direct arthroscopy, all consecutive patients, aged between 16 and 45 years, with at least 4 weeks of knee complaints, consisting of pain, swelling, instability and/or locking of the knee, who were referred to the departments of Orthopedics or Surgery of three unaffiliated hospitals (one university and two general hospitals) were eligible. In all three participating hospitals, the study received approval of the Institutional Review Board (IRB).

Informed consent was obtained from 962 patients. All these patients had standardized physical examination and antero-posterior and lateral radiographs of the knee. Patients were included if internal derangement was suspected based on the presence of at least one of the following clinical abnormalities: the presence of marked joint effusion or at least a 'bulge sign' (ie a visible bulge next to the patella caused by displacement of fluid and indicative for effusion); an extension deficit of at least 10°;

a flexion deficit of at least 20°; instability (varus and valgus stress, Lachman, anterior and posterior drawer and Pivot test); at least one positive meniscal provocation test (McMurray, Apley and squat test); and atrophy of at least 2 cm relative to the contralateral leg measured 15 cm above medial joint-line. Because of the criterion of at least 4 weeks of complaints, acute trauma was not included, whereas patients with chronic trauma could be included.

Exclusion criteria were known joint disease (for instance rheumatoid arthritis), pathology diagnosed earlier with MR imaging, contra-indication for MR imaging (claustrophobia, pacemaker) or arthroscopy, locked knee at presentation, recurrent locking of the knee in combination with extension deficit and/or positive McMurray test, prior surgery of the knee, a radiographically confirmed fracture, severe osteoarthritis of the knee (Kellgren grade 4) and a clinical diagnosis of retro-patellar chondromalacia. These patients were excluded because MR imaging will not play a role in the decision to perform arthroscopy either because arthroscopy will be performed on clinical criteria alone or because arthroscopy is contraindicated.

Ultimately 664 of 962 patients met our criteria and were included. All these patients underwent subsequent MR imaging within 2 weeks after inclusion. Of the 664 included patients in our study, 460 (69.3%) were male. The median age was 31.0 years.

As mentioned above, the study design was not tailored towards the issue of bone bruises only, because the overall goal of this multicenter study was to evaluate the efficacy of MR compared to direct arthroscopy in patients with subacute knee complaints, based on clinical outcome. The treatment following inclusion was determined by the MR diagnosis (see MR evaluation). Patients with abnormal intra-articular findings on MR proceeded to arthroscopy. Patients without intra-articular MR abnormalities were randomized over two treatment strategies. Half of these patients had arthroscopy, the other half were treated conservatively. This data set was subsequently also used to address the issue of bone bruises.

For the purpose of determining the influence of bone bruise on clinical presentation and course of complaints in patients with and without intra-articular knee pathology we divided patients in two groups: patients with and patients without relevant intra-articular knee pathology. We considered as relevant intra-articular knee pathology: all meniscal tears, complete anterior and posterior cruciate ligament tears, chondromalacia grade 3 or 4, osteochondritis dissecans with cartilage fissure or loose body.
In the patients who underwent arthroscopy (with or without positive MR diagnosis) the arthroscopic and not the MR diagnosis was used to categorize a patient as having intra-articular injury or not. In patients without arthroscopy the MR diagnosis was used to categorize the patient. Ultimately, 273 patients had no intra-articular pathology (152 based on arthroscopic findings, 121 based on MR findings), while 391 patients had internal derangement (345 based on arthroscopic findings, 46 based on MR findings).We identified in each of the two categories the patients with bone bruises.

6.3.2. MR imaging

In all three hospitals, we performed MR imaging with an identical 0.5-T system (Gyroscan T5; Philips Medical Systems, Best, the Netherlands), with the same software release (Release 3; Philips Medical Systems) using a dedicated transmit-receive knee coil.

The standardized scanning protocol was designed to address internal derangement and not bone bruise in particular and consisted of three sequences: a sagittal and a coronal dual spin-echo (SE) sequence and a sagittal T1-weighted three-dimensional gradient-echo sequence with frequency-selective fat suppression. The following parameters were identical for both SE sequences: 140-160 mm field of view and 20 and 80 ms echo times. The coronal dual SE had a repetition time of 2100 ms, a matrix of 256×205 and a section thickness of 5 mm with a 0.5 mm intersection gap. The sagittal dual SE had a repetition time of 2350 ms, a matrix of 256×179 and a section thickness of 4 mm with a 0.4 mm intersection gap. The parameters for the sagittal frequency-selective fat suppressed T1-weighted three-dimensional gradient-echo sequence were: repetition time ms/echo time ms, 70/13; flip angle, 45°; field of view, 160 mm; matrix, 256×205; and section thickness, 4 mm with 2 mm overlap.

The total imaging time of the standard protocol, including the initial survey sequence was 26 min.

6.3.3. MR evaluation

A group of six radiologists (W.M.C.M., E.G.C., J.L.B.) experienced in musculoskeletal imaging was available for reading MR images. Each MR study was prospectively and individually evaluated by one radiologist. We decided to accept the ensuing variation between observers because we preferred to follow real life clinical practice as closely as possible. After the radiologist had recorded his findings on a standardized case record form (CRF), he categorized the MR diagnosis depending on the observed pathology. We defined three categories (Table 1): category 1: normal MR examination or pathology not needing arthroscopic treatment; category 2: equivocal pathology; in these patients the orthopedic surgeon decided based on MR and clinical findings to perform arthroscopy or not; and category 3: pathology requiring arthroscopy.

The presence of bone bruise or bone marrow edema pattern, including the location, was also recorded. Bone bruise or bone marrow edema pattern were, irrespective of etiology, grouped together under the title of bone bruise. A bone bruise was defined as an ill defined geographic, and non-linear area of signal loss involving the subcortical bone on intermediate (short echo time) weighted images and increased signal intensity on T2-weighted images (2). On fat-suppressed T1-weighted images, these areas show increased signal intensity compared to suppressed normal fatty bone marrow. Small bone bruises that can only be detected using dedicated STIR-sequences were ignored.

We distinguished bone bruises from radiographic occult fractures using previously described criteria (linear areas of signal loss involving the subcortical bone with or without cortical interruption and osteochondral fractures)[4, 10]. These occult fractures were separately recorded.

Table 1
Classification of pathology on MR. Category 1 normal MR examination or pathology not needing arthroscopic treatment; category 2 equivocal pathology; category 3 pathology requiring arthroscopy, OD osteochondritis dissecans; PVNS pigmented villonodular synovitis

	Category 1	Category 2	Category 3
Menisci (Classification according to Lotysch)	Normal Meniscal tear < 5mm Meniscal degeneration without tear Discoid meniscus		Meniscal tear ≥ 5mm Meniscal cyst
Cartilage (Classification according to Recht)	Normal Chondromalacia grade 1-3 Non-isolated chondromalacia grade 4 Isolated chondromalacia grade 4 of a none-weight bearing surface	OD with intact cartilage	Isolated chondromalacia grade 4 of a weight bearing surface OD with cartilage fissure Loose body
Cruciate ligaments	Normal Acute isolated tear cruciate ligament Partial tear cruciate ligament	Chronic tear cruciate ligament with instability	Tear cruciate ligament in combination with meniscal tear
Collateral ligaments	Normal Isolated tear collateral ligament	Tear collateral ligament with capsule-lesion	Tear collateral ligament in combination with meniscal tear
Synovia	Normal Plica Synovitis		Intra-articular PVNS
Other structures	Normal Bone bruise	Tumor Extra-articular PVNS	

6.3.4. Assessment of function and symptoms

One of two research physicians (B.P.M.t.B., P.W.J.V.) assessed function and symptoms during an interview at the time of MR and 6 months thereafter, using Noyes scale for function (range: 200 [poor]-550 [good]) and symptoms (range: 0 [poor] - 400 [good]) (see Appendix 1)[11, 12]. In addition, we recorded, using a structured interview, the level of activity before the onset of complaints (in retrospect), at the time of MR and 6 months thereafter. To this end, we used the Tegner activity scale (range: 10 [competitive sports]-0 [sick leave]) (see Appendix 1)[13, 14]. History of traumatic events was also recorded.

6.3.5. Arthroscopy

All arthroscopies were videotaped and performed in one of the three participating hospitals by an experienced (orthopedic) surgeon or a trainee supervised by a (orthopedic) surgeon. The scope was introduced in the knee through an antero-lateral or transpatellar portal, using an arthroscope with 30° viewing angle. All structures were not only visualized, but also probed if necessary.

6.3.6. Data analysis

In two categories of patients (with and without intra-articular knee pathology) we compared patients with and without bone bruise. With an independent samples t-test we compared both Noyes and Tegner scales at the time of MR and 6 months thereafter. We also evaluated the influence of individual (peri-)articular pathology on the Noyes and Tegner scales at the time of MR and 6 months later.

With univariate variance analysis, we evaluated the influence of bone bruise and other (peri-)articular pathology on the Noyes function and symptoms score and Tegner activity score at the time of MR and 6 months later.

6.4. Results

Bone bruises (Fig. 4) were diagnosed in 124 of 664 patients (18.7%). In addition, radiographically occult fractures (Fig. 5) were diagnosed in five patients (three patients without, two with concomitant intra-articular knee pathology). These five patients were not included in the analysis. Thus remained 659 patients in the analysis.

A traumatic event was reported in 106 of 124 patients with bone bruise (85.5%). In 535 patients without bone bruise, 308 (57.5%) reported a trauma prior to the start of their knee complaints. This difference in incidence of traumatic events between patients with and without bone bruise is significant ($P < 0.001$).

Eighty-one out of 389 patients (20.8%) with intra-articular pathology had bone bruise(s). Of these 81 patients, 36 (44.4%) had a bone bruise in one location. Twenty-nine patients (35.8%) had two bone bruises and 16 (19.8%) had more than two bone bruises. Bone bruises were located in the lateral femoral condyle in 44 patients (54.3%), in the lateral tibial plateau in 43 (53.1%), in the medial tibial plateau in 31 (38.3%), in the medial femoral condyle in 27 (33.3%), in the patella in six (7.4%) and intercondylar in one patient (1.2%).

Forty-three out of 270 patients (15.9%) without intraarticular pathology had bone bruise(s). Of these 43 patients, 29 (67.3%) had a bone bruise in one location. Eleven patients (25.6%) had two bone bruises and three (7.0%) had more than two bone bruises. Bone bruises were located in the lateral tibial plateau in 20 patients (46.5%), in the lateral femoral condyle in 16 (37.2%), in the medial tibial plateau in 11 (25.6%), in the patella in eight (18.6%), in the medial femoral condyle in six (14.0%) and intercondylar in one patient (2.3%).

In patients with intra-articular pathology, the number of bone bruises per patient was significantly higher than in patients without intra-articular pathology ($P = 0.034$).

Table 2 lists intra- and peri-articular abnormalities in patients with and without bone bruise. Patients with bone bruise did not have significantly more intra-articular injuries than patients without bone bruise (81 of 124 patients or 65.3% versus 308 of 535 patients or 57.6%, $P = 0.129$). However, patients with bone bruise had significantly more complete anterior cruciate ligament tears ($p = 0.001$) and lateral meniscal tears ($P = 0.033$) than patients without bone bruise. Of the peri-articular injuries both (partial) medial collateral ligament tears ($P < 0.001$) and (partial) lateral collateral ligament tears ($P < 0.001$) occurred significantly more frequent in patients with bone bruise (Table 2). We found no patients with complete medial or lateral collateral ligament tears. In Table 3, we provide the most frequent pathology of individual structures with the function, symptoms and activity scores.

Table 2
Articular and peri-articular abnormalities in relation to presence or absence of bone bruise. Data on seven subgroups of five of the main injuries (medial meniscal tear, lateral meniscal tear, ACL tear, MCL tear, LCL tear and chondromalacia) are given in italics. *n* number of patients, percentage (%) in parenthesis; * significant differencebetween groups

	No bone bruise	Bone bruise	p
N	535	124	
Intra-articular knee pathology	308 (57.6)	81 (65.3)	0.129
Medial meniscal tear	191 (35.7)	45 (36.3)	0.917
Lateral meniscal tear	96 (17.9)*	33 (26.6)*	0.033
Tear in both menisci	27 (5.0)	10 (8.1)	0.195
ACL tear	50 (9.3)*	26 (21.0)*	0.001
Isolated ACL tear	21 (3.9)	10 (8.1)	0.024
ACL combined with meniscal tear	29 (5.4)	16 (12.9)	0.016
Chondromalacia	71 (13.3)	17 (13.7)	0.884
MCL tear	85 (15.9)*	55 (44.4)*	<0.001
MCL tear (with intra-articular pathology)	59 (19.2)*	38 (46.9)*	<0.001
MCL tear (without intra-articular pathology)	26 (11.5)*	17 (39.5)*	<0.001
LCL tear	8 (1.5)*	10 (8.1)*	<0.001
LCL tear (with intra-articular pathology)	8 (2.6)	5 (6.2)	0.154
LCL tear (without intra-articular pathology)	0 (0.0)*	5 (11.6)*	<0.001

6.4.1. Clinical evaluation in patients with intra-articular pathology

At the time of MR, patients with bone bruise had a significantly poorer function than patients without bone bruise (P = 0.001; Table 4, Figs. 1, 2, 3). Although symptoms and activity were not significantly different at the time of MR, the decrease in activity level relative to the level of activity before onset of complaints of patients with bone bruise was significantly larger (P = 0.003) than in patients without bone bruise, because of a (not significant) higher activity level before onset of complaints (decrease from 6.28 to 2.12 in patients with bone bruise and from 5.70 to 2.55 in patients without bone bruise).

Table 3
Pathology of individual structures in relation to clinical parameters. *n* number of patients; SD standard deviation

	Noyes function score at time of MRI	Noyes function score six months after MRI	Noyes symptom score at time of MRI	Noyes symptom score six months after MRI	Tegner score before onset of complaints	Tegner score at time of MRI	Tegner score six months after MRI
Medial meniscal tear							
Yes (N = 236)	341.40 (SD 68.75)	436.32 (SD 83.56)	243.61 (SD 86.79)	348.84 (SD 76.64)	5.74 (SD 2.41)	2.42 (SD 2.13)	4.16 (SD 2.28)
No (N = 423)	334.86 (SD 65.56)	414.68 (SD 78.93)	232.21 (SD 88.05)	330.47 (SD 85.32)	5.64 (SD 2.48)	2.43 (SD 2.25)	4.06 (SD 2.23)
Lateral meniscal tear							
Yes (N = 129)	331.55 (SD 62.66)	415.31 (SD 80.09)	228.99 (SD 85.04)	328.85 (SD 85.48)	6.02 (SD 2.58)	2.46 (SD 2.07)	3.67 (SD 2.23)
No (N = 530)	338.58 (SD 67.70)	424.33 (SD 85.69)	238.12 (SD 88.34)	339.21 (SD 81.93)	5.60 (SD 2.42)	2.42 (SD 2.24)	4.20 (SD 2.25)
ACL tear							
Yes (N = 76)	340.00 (SD 64.00)	429.68 (SD 74.36)	244.21 (SD 70.83)	345.08 (SD 61.48)	7.17 (SD 1.98)	2.91 (SD 2.27)	4.26 (SD 2.22)
No (N = 583)	336.84 (SD 67.15)	421.66 (SD 85.83)	235.25 (SD 89.71)	336.18 (SD 84.93)	5.48 (SD 2.44)	2.36 (SD 2.20)	4.08 (SD 2.26)
MCL tear							
Yes (N = 140)	327.93 (SD 65.48)	424.04 (SD 84.09)	250.50 (SD 80.01)	335.26 (SD 81.68)	6.26 (SD 2.34)	2.32 (SD 2.18)	4.44 (SD 2.28)
No (N = 519)	339.71 (SD 67.00)	422.13 (SD 84.92)	232.34 (SD 89.44)	337.50 (SD 83.04)	5.53 (SD 2.46)	2.45 (SD 2.22)	4.01 (SD 2.24)
LCL tear							
Yes (N = 18)	301.67 (SD 53.16)	440.67 (SD 97.50)	234.44 (SD 81.98)	325.33 (SD 111.73)	5.67 (SD 2.93)	1.83 (SD 1.86)	4.87 (SD 2.33)
No (N = 641)	338.18 (SD 66.95)	421.93 (SD 84.41)	236.53 (SD 87.98)	337.29 (SD 81.94)	5.68 (SD 2.45)	2.44 (SD 2.22)	4.08 (SD 2.25)

Patients in both groups (with and without bone bruise) had significantly improved function, symptoms and activity 6 months after MR (P = 0.001 for all three scores). There were no significant differences between the two groups for the three parameters at 6 months (Table 4). There also were no differences between the two groups in amount of improvement of the three clinical parameters measured over 6 months.

Table 4
MR findings in relation to clinical parameters. *n* number of patients; SDstandard deviation

	No intra-articular knee pathology		Intra-articular knee pathology	
	No bone bruise	Bone bruise	No bone bruise	Bone bruise
N	227	43	308	81
Number of patients available at follow up	201	35	268	69
Noyes function score at time of MRI	341.19* (SD 66.08)	306.98* (SD 55.44)	344.81* (SD 67.59)	313.21* (SD 61.86)
Noyes function score six months after MRI	415.00 (SD 89.62)	436.18 (SD 78.93)	427.57 (SD 81.78)	418.26 (SD 82.72)
Noyes symptom score at time of MRI	234.53 (SD 89.14)	213.81 (SD 86.95)	243.82 (SD 88.01)	224.50 (SD 80.63)
Noyes symptom score six months after MRI	328.14 (SD 85.61)	350.86 (SD 84.76)	342.76 (SD 79.38)	334.49 (SD 84.57)
Tegner score before onset of complaints	5.46 (SD 2.45)	5.58 (SD 2.67)	5.70 (SD 2.44)	6.28 (SD 2.34)
Tegner score at time of MRI	2.39 (SD 2.33)	2.33 (SD 2.40)	2.55 (SD 2.12)	2.12 (SD 2.07)
Tegner score six months after MRI	4.10 (SD 2.29)	4.71 (SD 2.42)	4.08 (SD 2.24)	3. 88 (SD 2.06)

*Significant difference between patients with or without bone bruise within the category intra-articular knee pathology and within the category intra-articular knee pathology. In each group all scores improved significantly after 6 months

The initial clinical differences between patients with and without bone bruise, as mentioned above, were not associated with tears in ACL, lateral meniscus and collateral ligaments, that were more frequent in patients with bone bruise.

Both in patients with and without bone bruises that underwent arthroscopy (respectively 70 patients [86%] and 273 patients [89%]) the fraction of therapeutic arthroscopies (ie an arthroscopy during which an intervention with therapeutic intentions was performed) was almost equal: respectively 86% (60 patients) and 88% (240 patients).

6.4.2. Clinical evaluation in patients without intra-articular pathology

At the time of MR, patients with bone bruise had the same level of activity and symptoms, but significant (P = 0.002) lower level of function compared to patients without bone bruise (Table 4, Figs. 1, 2, 3). The decrease in activity level relative to the level of activity before onset of complaints was not significantly different between both groups.

Patients in both groups (with and without bone bruise) had significantly improved function, symptoms and activity 6 months after MR (P = 0.001 for all three scores). There were no significant differences between the two groups for the three parameters

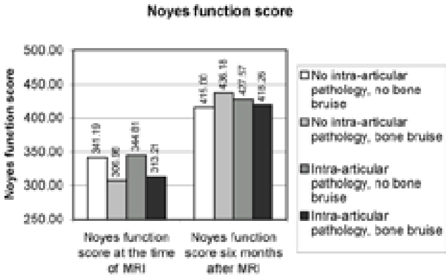

Fig. 1 Noyes function score at the time of MRI and six months later.

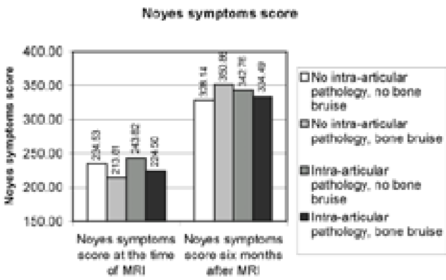

Fig. 2 Noyes symptoms score at the time of MRI and six

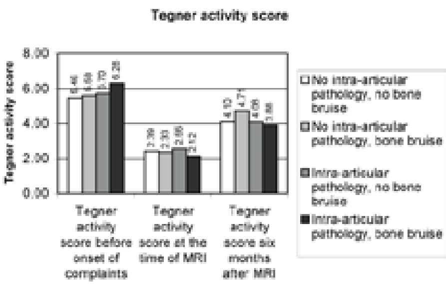

Fig. 3 Tegner activity scale before onset of complaints, at the time of MRI and six months later.

at 6 months (Table 4). However, the increase in function (from 306.98 to 436.18), measured over 6 months, was significantly (P = 0.001) larger in patients with bone bruise than in those without (from 341.19 to 415.00). Patients with bone bruise also had significantly (P = 0.039) more decrease of symptoms (from 213.81 to 350.86) measured over 6 months than those without bone bruise (from 234.53 to 328.14) (Table 4).

The improvement in activity, measured over 6 months, was not significantly different between the two groups.

The aforementioned relatively poor function at the time of MR and subsequent improvement 6 months later, as well as the decrease in symptoms, in patients with bone bruise were associated with the presence of partial MCL tears. The above-mentioned significant differences existed between two subgroups of patients with MCL ruptures: patients with (17 patients) and without bone bruises (26 patients). There were no significant differences in function and symptoms without MCL abnormalities at the time of MR or in improvement in function or symptoms over 6 months between 201 patients without and 26 patients with bone bruise.

Figure 4. 4a-c Coronal and sagittal T2-weighted (respectively 2100/80 and 2350/80) image and sagittal frequency-selective fat suppressed T1-weighted (70/13; flip angle 45°) image of bone bruise in lateral femoral condyle and lateral tibial plateau in a 26 year old patient 2 months after sports injury. Arthroscopy showed a medial meniscal tear and partial ACL rupture.

Because of the small number of LCL ruptures, the difference in incidence of this injury between patients with and without bone bruise had no significant effect on level of function, symptoms and activity of both groups.

Initially (at the time of MR), there were no significant differences in symptoms, function and activity between patients that underwent arthroscopy and those that did not. Patients whom underwent arthroscopy had, compared to those that did not have arthroscopy, significantly more symptoms (Noyes symptoms 344.8 versus 321.6, P = 0.036) 6 months after MR. There were no differences in function and activity. Arthroscopy probably has no impact on the reported differences between the patients with and without bone bruise, since the fraction of arthroscopies in both groups is not significantly different (60% [26 patients] in patients with bone bruise and 55% [125 patients] in patients without bone bruise).

6.4.3. Univariate variance analysis

The presence of bone bruise was in the univariate variance analysis the only variable that had a statistically significant effect on function (P = 0.001) at the time of MR. Intra- and peri-articular pathology had no significant effect on function. Both bone bruise and the presence of MCL injuries were the variables with significant effect on symptoms at the time of MR (both P = 0.004). Intra- and peri-articular pathology had no significant effect on symptoms. Bone bruise and intra- and peri-articular pathology had no significant effect on the level of activity at the time of MR. The presence of bone bruise had no significant effect on the function, symptoms and activity 6 months after MR.

6.5. Radiographically occult fractures

Four of the five occult fractures were located in the lateral femoral condyle, the fifth in the medial tibial plateau. Two occult fractures in the lateral femoral condyle were accompanied by bone bruise in the lateral tibial plateau. Two patients had concomitant intra-articular pathology. Initial mean function score (318.0) was similar to that of patients with bone bruise. Initial mean symptoms score (280.0) was somewhat higher than in patients with bone bruise. All patients had improved considerably after 6 months (function and symptoms scores respectively 474.0 and 380.0). The same trend was visible in the Tegner activity score. Tegner activity score before onset of complaints was 6.6, decreased to 3.2 at the time of MR and increased again to 5.2 6 months later.

6.6. Discussion

The prevalence of bone bruise in our population (124 out of 664 patients [18.7%]) is lower than that reported by others (2, 5, 6, 10, 15). A possible explanation for this difference could be the used MR sequence. Our sequence was tailored towards addressing the issue of internal derangement and related disorders including bone bruise in a general population in a time-effective way. We therefore did not use a dedicated sequence such as Short Tau Inversion Recovery (STIR) to detect bone bruise (7, 16). It is therefore likely that we missed small bone bruises that otherwise would have been diagnosed. Another explanation for the relative low prevalence of bone bruises in patients with intra-articular pathology may be that our patients had at least 4 weeks of knee complaints, whereas only acute patients were included in other studies (5, 6, 10, 15). In our study population, 64% had a history of trauma prior to the start of their knee complaints. A history of trauma was significantly more common (85%) in patients with bone bruise than in patients without bone bruise (59%). This confirms the relationship between trauma and bone bruise, also in our population without acute trauma.

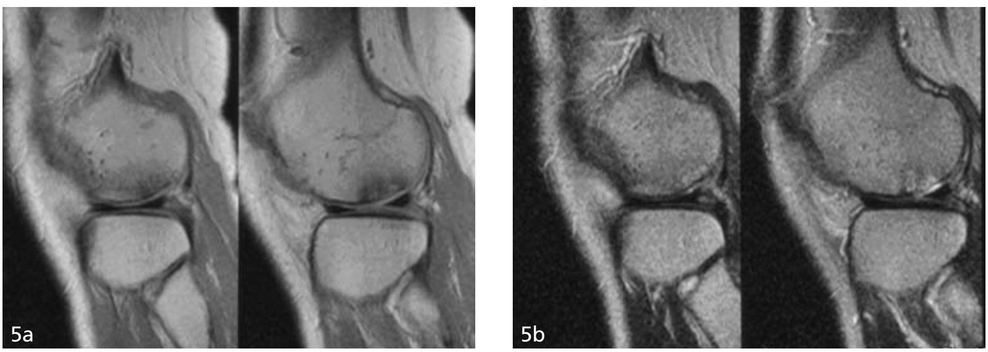

Figure 5 a, b Sagittal PD-weighted (2350/20) and sagittal T2-weighted (2350/80) image of subchondral fracture in the lateral femoral condyle, in a 32 year old female patient after trauma. Note the subchondral hypointense area of low signal intensity on the PD-weighted image, representing impacted cancelous bone. MR imaging showed no concomitant intra-articular pathology.

As did others, we found a predominance of bone bruises in the lateral femoral condyle and lateral tibial plateau (5, 6, 8-10, 15, 19). This can be explained by the usual mechanism of injury, ie anterior subluxation of the lateral tibial plateau relative to the lateral femoral condyle and valgus stress. The significant correlation of multiplicity of bone bruises in a single patient with intra-articular pathology confirms that severity of trauma determines, in addition to trauma mechanism, the pattern of bone bruises.

Presence of bone bruise, on the other hand, is no predictor for the presence of intra-articular pathology. Prevalence of bone bruise is not significantly different between patients with (21%) and those without (16%) intra-articular pathology.

A tear of the medial meniscus is the most common injury, but is not associated with bone bruise. As did others [4-9, 17] we found, in patients with bone bruise, a higher incidence of less common injuries, ie tears in anterior cruciate ligament, collateral ligaments and lateral meniscus (Fig. 4; Table 2).

Presence of bone bruise is associated with a higher level of presenting symptoms. In the univariate variance analysis, in which all 664 patients are taken as a whole, without dividing them into subgroups, bone bruise is the only MR abnormality that has a significant effect on function at the time of presentation. Bone bruise and medial collateral ligament tear are the only parameters that have a significant effect on symptoms at the time of presentation. Thus, bone bruise and MCL tear have more impact on function and symptoms at the time of MR than intra-articular pathology such as (medial) meniscal tears. Bone bruise does not have an effect on function, symptoms and activity at 6 months. These results of the univariate variance analysis are in accordance with the detailed analysis in patients with and without intra-articular pathology.

Function (Noyes function score, Table 4, Fig. 1) is, both in patients with and without intra-articular knee pathology, at the time of MR significantly lower in patients with bone bruise than in patients without bone bruise. The decrease in activity at the time of MR (Tegner activity score, Table 4, Fig. 3) is significantly larger when patients with intra-articular pathology also have bone bruises.

During the 6 months follow-up time, significant differences are observed within the category of patients without intra-articular pathology. The increase in function and decrease of symptoms in patients with bone bruise is significantly larger than in patients without bone bruise.

At 6 months, all four groups (with or without intraarticular pathology, with or without bone bruise) display significant improvement in all three clinical parameters (function, symptoms and activity). At 6 months, the clinical differences between all four groups have disappeared. This is in accordance with the aforementioned univariate variance analysis. Wright et al. reported similar results in a retrospective study on 12 patients [18]. A recent study of Davies et al. showed that in 30 patients, all but one reported some degree of pain 12-14 weeks post-injury. In all patients, bone bruises were still present on repeat MRI [20]. No follow-up beyond this 3-month period was reported. Because of this shorter follow-up period, a direct comparison with our study regarding clinical improvement is not possible.

In the category of patients without intra-articular pathology, the clinical differences between patients with and without bone bruise are only significant in the presence of medial collateral ligament ruptures. From a clinical perspective, therefore, bone bruise and medial collateral ligament tear act as one unit.

Patients with radiographically occult fractures (Fig. 5) have impaired function and symptoms at the time of MR comparable to that of patients with bone bruise.

Six months later, these patients have improved considerably without sequelae.

The choice to follow usual care has resulted in two limitations of this study. The participation of six radiologists has introduced differences between observers that we have not measured. We feel that the large sample size and the similarity to usual practice does not impair the clinical conclusions of this study. The second limitation is the use of an MR imaging protocol tailored towards detecting intra-articular pathology. Although we used a fat-suppressed GE sequence that is sensitive to susceptibility changes, we did not use the STIR sequence. It is likely that we missed small bone bruises. It is therefore possible that the clinical relevance at the time ofMRimaging is smaller when small bone bruises are included that are below the threshold of multiplanar SE and GE imaging. It is not likely that the inclusion of these small bone bruises will have an impact on the conclusion that no clinical sequelae are detectable at 6 months.

In conclusion, we found, using a general imaging protocol, that bone bruise in combination with medial collateral ligament tear is an important cause of clinical impairment in patients with sub-acute or chronic knee complaints. It has, initially, a higher impact on clinical parameters than articular pathology, including meniscal tears. Because of the fast improvement of function, symptoms and level of activity in 6 months time prognosis is good and bone bruise has no impact on clinical parameters later on.

6.7. References

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6.8. Appendix

Noyes assessment of function

Activity	Scale	Points
Walking	Normal, unlimited	50
	Some limitations	40
	Only 1 km possible on even surface	30
	Less than 500 m possible	20
	Less than 100 m possible	0
Stairs	Normal, unlimited	50
	Some limitations	40
	Only 21-30 steps possible	30
	Only 11-20 steps possible	20
	Less than 10 steps possible	0
Squatting/kneeling	Normal, unlimited	50
	Some limitations	40
	Only 6-10 possible	30
	Only 0-5 possible	20
	Impossible	0
Straight running	Fully competitive	100
	Some limitations, guarding	80
	Half-speed, definite limitations	70
	Less than 200 m	60
	Not able	50
Sprinting	Fully competitive	100
	Some limitations	80
	Half-speed, definite limitations	70
	Only a couple of times in short time period	60
	Not able	50
Jumping	Fully competitive	100
	Some limitations	80
	Half-speed, definite limitations	70
	Limitations in every sport	60
	Not able	50
Twisting/cutting	Fully competitive	100
	Some limitations	80
	Definite limitations	70
	Limitations in every sport	60
	Not able	50

Noyes assessment of symptoms

Symptom	Scale	Points
Pain	None	100
	Able to do moderate work/sports; pain with strenuous work/sports	80
	Able to do light work/sports; pain with moderate work/sports	60
	Able to do activities of daily living (ADL); pain with light work/sports	40
	Moderate pain (frequent, limiting) with ADL	20
	Severe pain (constant, not relieved) with ADL	0
Swelling	None	100
	Able to do moderate work/sports; swelling with strenuous work/sports	80
	Able to do light work/sports; swelling with moderate work/sports	60
	Able to do activities of daily living (ADL); swelling with light work/sports	40
	Moderate swelling (frequent, limiting) with ADL	20
	Severe swelling (constant, not relieved) with ADL	0
Instability/giving way	None	100
	Able to do moderate work/sports; instability with strenuous work/sports	80
	Able to do light work/sports; instability with moderate work/sports	60
	Able to do activities of daily living (ADL); instability with light work/sports	40
	Moderate instability (frequent, limiting) with ADL	20
	Severe instability (constant, not relieved) with ADL	0
Locking	No locking and no catching sensation	100
	Less than monthly catching sensation but no locking	80
	More than once a month catching sensation but less than monthly locking	60
	Monthly locking	40
	Weekly locking	20
	Daily locking	0

Tegner Activity Score

Activity		Points
Competitive sports		10
	Soccer, national and international elite	
Competitive sports		9
	Soccer, lower divisions Ice hockey Wrestling Gymnastics	
Competitive sports		8
	Bandy Squash or badminton Athletics (jumping, etc.) Downhill skiing	
Competitive sports		7
	Tennis Athletics (running) Motorcross, speedway Handball Basketball	
Recreational sports		
	Soccer Bandy and Ice hockey Squash Athletics (jumping) Cross-country, both recreational and competitive	
Recreational sports		6
	Tennis and badminton Handball Basketball Downhill skiing Jogging, at least five times per week	
Work		5
	Heavy labor (e.g., building, forestry)	
Competitive sports		
	Cycling Cross-country skiing	
Recreational sports		
	Jogging on uneven ground at least twice weekly	
Work		4
	Moderately heavy labor (e.g., truck driving, heavy domestic work)	
Recreational sports		
	Cycling Cross-country skiing Jogging on even ground at least twice weekly	
Work		3
	Light labor (e.g., nursing)	
Competitive and recreational sports		
	Swimming	
Walking in forest possible		
Work		2
	Light labor	
Walking on uneven ground possible but impossible to walk in forest		
Work		1
	Sedentary work	
Walking on even ground possible		
Sick leave or disability pension because of knee problems		0

CHAPTER 7

Summary

7. Summary

Chapter 1 provides a general introduction. The main aim of this thesis is to evaluate the costs and effectiveness of magnetic resonance (MR) imaging performed to exclude the need for arthroscopy in patients with nonacute knee symptoms with high clinical suspicion of having intraarticular knee pathology.

In **Chapter 2** we determine the effectiveness of MR imaging in the identification of those patients with a high clinical suspicion of internal derangement of the knee who require arthroscopic therapy. In a prospective multicenter study, MR imaging was performed at 0.5-T in 430 consecutive patients. The sensitivity and specificity of MR imaging in the patients who underwent arthroscopy and the corrected sensitivity and specificity of MR in all the study patients were calculated. For this correction, patients with negative MR and arthroscopic results were considered representative of the patients with negative MR results who were conservatively treated, and the number of the former was doubled. The standard errors of the corrected values were adjusted with the δ method.

At MR imaging, arthroscopy was indicated in 221 patients, 200 of whom underwent arthroscopy. Two hundred nine patients with negative MR imaging results were randomized for arthroscopic (105 patients) or for conservative treatment (104 patients). Of the 105 patients randomized for arthroscopy, 93 actually underwent arthroscopy. Arthroscopic treatment was necessary in 13 of 93 patients with a negative diagnosis at MR imaging. Arthroscopic treatment was necessary in 179 of 200 patients with a positive diagnosis at MR (sensitivity, 93.2%; specificity, 79.2%). Sensitivity and specificity corrected for randomization were 87.3% and 88.4%.

We conclude that 0.5-T MR imaging is an effective tool in the selection of patients for arthroscopy.

In **Chapter 3** the cost-effectiveness of MR imaging in patients with nonacute knee symptoms with a high clinical suspicion of intraarticular knee abnormalities is evaluated prospectively.

All 584 included patients underwent MR imaging. Patients with an MR result positive for the diagnosis of intraarticular knee abnormality had arthroscopy (group A). Patients with a negative MR result were randomly assigned to have either conservative (group B) or arthroscopic (group C) treatment. Treatment was considered effective if the Noyes function score had increased 10% or more at 6 months. A cost analysis was performed from a societal perspective to compare the treatment strategy involving MR imaging with the strategy not involving MR imaging. Of the 584 patients, 294 (50.3%) were assigned to group A; 149 (25.5%), to group B; and 141 (24.1%), to group C. At 6 months, the number of patients effectively treated in group B (conservative

treatment) was a mean of 5.1% ±10.0 larger than the number of patients effectively treated in group C (arthroscopy). Due to savings in productivity costs, total societal costs were lower using the strategy involving MR imaging by a mean of \$153 ± 488 (P = .54).

This proves MR imaging can be used without additional costs or disadvantageous effects on function to obviate arthroscopy in patients with nonacute knee symptoms who are highly suspected of having intraarticular knee abnormality. This conclusion is fairly robust and new dedicated MR systems, with comparable diagnostic accuracy and lower costs probably will favour MR triage even more.

The objective of **chapter 4** is to determine the fraction of MR imaging studies showing arthroscopically treatable intra-articular pathology in symptomatic patients with a normal standardized physical examination. Of 290 consecutive patients (between 16-45 years) with at least 4 weeks of knee complaints and low clinical suspicion on intra-articular pathology based on physical exam, 274 patients were included.
Sixteen patients with prior knee surgery, rheumatic arthritis or severe osteoarthritis were excluded. MRI was used to assign patients to group1 (treatable abnormalities) or group 2 (normal or no treatable findings), depending on whether MR demonstrated treatable pathology. Arthroscopy was performed in group 1 patients. If symptoms persisted for three months in group 2 patients cross over to arthroscopy was allowed.

MR showed treatable pathology in 73 patients (26.6%). Arthroscopy was performed in 64 patients of 73 patients (group 1). In 52 patients (81.3%, 95%-CI 71.4 - 91.1%) arthroscopy was therapeutic. Of the 13 arthroscopies (6.5%) in group 2, 4 were therapeutic (30.8%, 95%-CI 1.7 - 59.8%). The highest fraction of MR studies showing treatable pathology was found in: male gender, aged over 30 years, with a history of effusion (54.5%, 6 of 11 patients).

We believe that the negative predictive value of clinical assessment in patients with sub-acute knee complaints is too low to exclude these patients from MR. MR should at least be considered in male patients aged 30 years and over with a history of effusion. Because of the limited additional value of clinical assessment by an orthopedic surgeon we believe that there is no reason to deny a general practitioner direct access to MR of the knee.

In **chapter 5** the value of radiographs in young adults with non-acute knee symptoms who are scheduled for MR imaging is determined.

Nine hundred and sixty-one consecutive patients aged between 16 and 45 years with knee symptoms of at least 4 weeks' duration were eligible for inclusion.
After applying exclusion criteria, 798 patients remained. Exclusion criteria were previous knee surgery (including arthroscopy) or MRI, history of rheumatoid arthritis, clinical diagnosis of retropatellar chondromalacia, contra-indication for MRI and recent trauma. Included patients were divided in two groups: group A with no history of trauma

(n = 332), and group B with an old (> 4 weeks) history of trauma (n = 466). Patients had a standardized history taken, and underwent a physical examination, antero-posterior (AP) and lateral radiographs and MRI. We evaluated the radiographs and MRI for osseous lesions, articular surface lesions, fractures, osteoarthritis, loose bodies, bone marrow edema and incidental findings. Subsequently, patients with osseous abnormalities (Kellgren grade 1 and 2 excluded) on radiographs and a matched control group were evaluated again using MRI without radiographs. In group A, radiographs showed 36 osseous abnormalities in 332 patients (10.8%). Only 13 of these, all Kellgren grade 1 osteoarthritis, were not confirmed on MRI. MRI showed 72 (21.7%) additional abnormalities not confirmed on radiographs. In group B, radiographs showed 40 osseous abnormalities (8.6%) in 466 patients. Only 15 of these, all Kellgren grade 1 osteoarthritis, were not confirmed on MRI. MRI showed 194 (41.6%) additional abnormalities not confirmed on radiographs. The second evaluation of MRI without radiographs in 34 patients was identical to the first MRI evaluation. Common lesions were significantly more often diagnosed with MRI than with radiographs.

We conclude that radiographs should not be obtained routinely when MRI is being performed in young adults with nonacute knee complaints because the yield and added value to MRI are low.

In chapter 6 the relation between bone bruise and (peri-)articular derangement is evaluated and the impact of bone bruise on presentation and short term prognosis is assessed. We recorded MR abnormalities in 664 consecutive patients with nonacute knee complaints. Patients were divided in four groups: patients with and without intra-articular knee pathology, subdivided in patients with and without bone bruise. We assessed function and symptoms at the time of MR and 6 months thereafter. Bone bruises were diagnosed in 124 of 664 patients (18.7%). Patients with bone bruise had significantly more complete ACL, lateral meniscal, MCL and LCL tears. Both with and without intraarticular pathology patients with bone bruise had a significantly poorer function at the time of MR (Noyes score of, respectively, 313.21 versus 344.81 and 306.98 versus 341.19). Patients with bone bruise and intra-articular pathology showed significantly more decrease in activity (decrease of Tegner score from 6.28 to 2.12 versus 5.70 to 2.55). At 6 months there were no significant differences in clinical parameters between the four groups.

We conclude that bone bruise in combination with MCL tear is an important cause of initial clinical impairment in patients with sub-acute knee complaints. Clinical improvement within 6 months is more pronounced than in patients without bone bruise.

General conclusions

MR imaging is an effective tool in excluding or selecting patients with nonacute knee complaints who are highly suspected of having intraarticular knee abnormality for arthroscopy. Using MR as method for triage creates no additional costs and has no negative effects on function. This conclusion is fairly robust and new dedicated MR systems, with comparable diagnostic accuracy and lower costs probably will favour MR triage even more.

The negative predictive value of clinical assessment in patients with nonacute knee complaints is too low to exclude patients with a normal physical examination from MR. That is why there is no reason to deny a general practitioner direct access to MR of the knee.

Bone bruise is an important cause of initial clinical impairment in patients with sub-acute knee complaints. Clinical improvement is more pronounced than in patients without bone bruise.

When MR is performed, radiographs should not be obtained routinely in young adults with nonacute knee complaints because the yield and added value to MRI are low.

CHAPTER 8

Samenvatting

8. Samenvatting

Hoofdstuk 1 is een algemene introductie. Doel van dit proefschrift is om de kosten en effectiviteit van magnetische resonantie (MR) te evalueren indien deze wordt ingezet om niet therapeutische arthroscopieën te voorkomen bij patiënten met niet acute knieklachten en een hoge klinische verdenking op intra-articulaire kniepathologie.

In **hoofdstuk 2** bepalen we de effectiviteit van MR in de identificatie van die patiënten die arthroscopische therapie nodig hebben.

In een prospectieve multi-center studie werd bij 430 patiënten met hoge klinische verdenking een MR verricht. De sensitiviteit en specificiteit van MR bij patiënten die arthroscopie ondergingen en de gecorrigeerde sensitiviteit en specificiteit van MR bij alle patiënten in de studie werden berekend. Voor deze correctie werden patiënten met een negatieve MR die een arthroscopie ondergingen als representatief beschouwd voor die patiënten met een negatieve MR die conservatief werden behandeld en het aantal van de eerstgenoemde groep werd verdubbeld. De standaard fout van de gecorrigeerde waarden werd aangepast met de δ methode.

Op grond van de bevindingen bij dit MR onderzoek was arthroscopie geïndiceerd bij 221 patiënten, van wie er 200 daadwerkelijk een arthroscopie ondergingen. Tweehonderd en negen patiënten met een negatief MR onderzoek werden gerandomiseerd verdeeld over twee behandelstrategieën: arthroscopie (105 patiënten) of conservatieve therapie (104 patiënten). Van de 105 patiënten gerandomiseerd voor arthroscopie ondergingen er 93 daadwerkelijk arthroscopie. Arthroscopie was therapeutisch bij 13 van 93 patiënten met een negatief MR onderzoek. Arthroscopie was therapeutisch bij 179 van 200 patiënten met een positief MR onderzoek (sensitiviteit, 93,2%; specificiteit, 79,2%). Sensitiviteit en specificiteit gecorrigeerd voor randomisatie waren 87,3% en 88,4%.

Wij concluderen dat 0.5-T MR een effectief middel is bij de selectie van patiënten voor arthroscopie.

In **hoofdstuk 3** wordt de kosten-effectiviteit van MR bij patiënten met niet acute knieklachten en een hoge klinische verdenking op intra-articulaire kniepathologie prospectief geëvalueerd. Bij alle 584 geïncludeerde patiënten met niet acute knieklachten werd een MR verricht. Patiënten bij wie de MR de diagnose van intra-articulaire pathologie bevestigde ondergingen een arthroscopie (groep A). Patiënten met een negatieve MR werden gerandomiseerd verdeeld over twee behandelingen: conservatieve therapie (groep B) of arthroscopie (groep C). De behandeling werd als effectief beschouwd indien de Noyes function score 10% of meer was gestegen na 6 maanden. Er is een kostenanalyse vanuit maatschappelijk perspectief uitgevoerd, waarbij een behandelstrategie met en een behandelstrategie zonder een rol voor

MR werd vergeleken. Van de 584 patiënten kwamen 294 patiënten (50,3%) in groep A, 149 (25,5%) in groep B en 141 (24,1%) in groep C. Na 6 maanden was het aantal effectief behandelde patiënten in groep B (conservatieve therapie) 5,1% ±10,0 hoger dan in groep C (arthroscopie). Ten gevolge van een besparing in productiviteitskosten waren de totale maatschappelijke kosten $153± 488 (*P* = 0,54) lager als de strategie zonder MR werd gebruikt.

Dit bewijst dat MR kan worden gebruikt om het aantal arthroscopieën te verminderen bij patiënten met niet acute knieklachten en een hoge klinische verdenking op intra-articulaire kniepathologie zonder additionele kosten en zonder nadelige gevolgen voor het functioneren van de patiënt. Deze conclusie is vrij robuust en met nieuwe kleine MR systemen met vergelijkbare diagnostische accuratesse en lagere kosten zal MR triage zelfs nog meer voordeel bieden.

Het doel van **hoofdstuk 4** is om de fractie van patiënten te bepalen met knieklachten en een normaal klinisch onderzoek waarbij met MR wel behandelbare intra-articulaire kniepathologie wordt gezien.

Van 290 consecutieve patiënten (leeftijd tussen 16 en 45 jaar) met minimaal 4 weken knieklachten en lage klinische verdenking op intra-articulaire kniepathologie werden 274 patiënten geïncludeerd. Zestien patiënten met eerdere knieoperaties, rheumatoïde arthritis of ernstige arthrose werden geëxcludeerd. In deze groep van 274 patiënten toonde MR behandelbare pathologie bij 73 patiënten (26,6%). Arthroscopie werd uitgevoerd bij 64 van deze 73 patiënten (groep 1). Bij 52 patiënten (81,3%, 95%-CI 71,4 - 91,1%) was de arthroscopie therapeutisch. Van de 13 arthroscopieën (6,5%) bij 201 patiënten met normale of niet behandelbare MR bevindingen (groep 2), waren er maar 4 therapeutisch (30,8%, 95%-CI 1,7 - 59,8%). Mannelijk geslacht, leeftijd en een anamnese van hydrops waren voorspellers van de MR uitslag ($p < 0,05$). De grootste fractie MR onderzoeken met intra-articulaire pathologie werd gevonden bij mannen, ouder dan 30 jaar met anamnese van hydrops: 54,5% (zes van 11 patiënten).

Wij zijn van mening dat de negatief voorspellende waarde van lichamelijk onderzoek bij patiënten met niet acute knieklachten te laag is om patiënten uit te sluiten van MR. MR moet op zijn minst overwogen worden bij mannelijke patiënten ouder dan 30 jaar met een anamnese van hydrops. Vanwege de beperkte aanvullende waarde van lichamelijk onderzoek uitgevoerd door een orthopedisch chirurg is er geen reden om huisartsen de directe toegang tot het aanvragen van een MR van de knie te ontzeggen.

In **hoofdstuk 5** wordt de waarde van conventionele röntgenopnamen bij jonge volwassenen met niet acute knieklachten, waarbij een MR gepland is, bepaald.
Van 961 consecutieve patiënten met een leeftijd tussen 16 en 45 jaar en knieklachten gedurende minimaal 4 weken werden er 798 geïncludeerd. Exclusiecriteria waren

eerdere knieoperaties (inclusief arthroscopie) of MRI, rheumatoïde arthritis, klinische diagnose van retropatellaire chondropathie, contra-indicatie voor MRI en recent trauma. De geïncludeerde patiënten werden in twee groepen verdeeld: groep A zonder trauma in voorgeschiedenis (n = 332) en groep B met trauma meer dan 4 weken geleden in voorgeschiedenis (n = 466). Bij alle patiënten werd een gestandaardiseerde anamnese afgenomen, een gestandaardiseerd lichamelijk onderzoek uitgevoerd, een antero-posterieure (AP) en laterale röntgenopname van de knie gemaakt en tenslotte een MR vervaardigd. Wij evalueerden de röntgenopnamen en MR op ossale laesies, kraakbeenlaesies, fracturen, arthrose, corpora libera, beenmergoedeem en incidentele bevindingen. Vervolgens werden patiënten met ossale afwijkingen op de conventionele opnamen (Kellgren graad 1 en 2 uitgezonderd) en een controlegroep opnieuw geëvalueerd met alleen MR. In groep A toonden röntgenopnamen 36 ossale afwijkingen bij 332 patïenten (10,8%). Slechts 13, allen Kellgren graad 1 arthrose, werden niet gezien op MR. MR toonde 72 (21,7%) additionele afwijkingen, niet gezien op het conventionele röntgenonderzoek. In groep B toonden röntgenopnamen 40 ossale afwijkingen bij 466 patïenten (8,6%). Slechts 15, allen Kellgren graad 1 arthrose, werden niet gezien op MR. MR toonde 194 (41,6%) additionele afwijkingen, welke niet waren gezien op het conventionele röntgenonderzoek. De tweede evaluatie op basis van MR alleen bij 34 patiënten was identiek aan de eerste evaluatie. De meest voorkomende afwijkingen werden significant meer gediagnosticeerd met MR dan met röntgenopnamen.

Wij concluderen dat conventionele röntgenopnamen niet routinematig moeten worden vervaardigd bij jonge volwassenen met niet acute knieklachten als er ook een MR wordt verricht. De opbrengst en additionele waarde ten opzichte van MR is te gering.

In **hoofdstuk 6** wordt de relatie tussen botcontusie en (peri-)articulaire afwijkingen geëvalueerd en wordt de impact van botcontusie op presentatie en korte termijn prognose bepaald. Wij noteerden MR afwijkingen bij 664 consecutieve patiënten met niet acute knieklachten. Patiënten werden ingedeeld in vier groepen: patiënten met en zonder intra-articulaire kniepathologie, onderverdeeld in patiënten met en zonder botcontusie. Wij bepaalden functie en symptomen ten tijde van de MR en zes maanden later. Botcontusies werden gediagnosticeerd bij 124 van de 664 patiënten (18,7%). Patiënten met botcontusies hadden significant meer totale voorste kruisband scheuren, laterale meniscus scheuren, mediale en laterale collaterale band scheuren. Zowel met als zonder intra-articulaire pathologie hadden patiënten met botcontusies een significant slechtere functie ten tijde van de MR (Noyes scores van respectievelijk 313,21 versus 344,81 en 306,98 versus 341,19). Patiënten met botcontusies en intra-articulaire pathologie toonden een significant grotere daling in activiteit (daling van Tegner score van 6,28 tot 2,12 versus 5,70 tot 2,55). Na zes maanden waren er geen significante verschillen meer in klinische parameters tussen de vier groepen.

Wij concluderen dat botcontusie in combinatie met mediale collaterale band letsel een belangrijke oorzaak is van initiële klinische verslechtering bij patiënten met niet acute knieklachten. Klinische verbetering binnen zes maanden is meer uitgesproken dan bij patiënten zonder botcontusie.

Algemene conclusies

MR is een effectief middel bij de selectie van patiënten met niet acute knieklachten en een hoge klinische verdenking op intra-articulaire pathologie voor arthroscopie, zonder additionele maatschappelijke kosten en zonder negatieve effecten op het functioneren van patiënt. Dit is een robuuste conclusie en met nieuwe kleine MR systemen met vergelijkbare diagnostische accuratesse en lagere kosten zal MR triage zelfs nog meer voordeel bieden.

De negatief voorspellende waarde van lichamelijk onderzoek is te laag om patiënten met een negatief lichamelijk onderzoek uit te sluiten van MR. Derhalve is er geen reden om huisartsen de directe toegang tot het aanvragen van een MR van de knie te ontzeggen.

Botcontusie is een belangrijke oorzaak van initiële klinische verslechtering bij patiënten met niet acute knieklachten, waarna de klinische verbetering meer uitgesproken is. Indien een MR wordt verricht dient een conventionele röntgenopname niet routinematig te worden vervaardigd bij jonge volwassenen met niet acute knieklachten omdat de opbrengst en additionele waarde ten opzichte van MR gering is.

Curriculum Vitae

De auteur van dit proefschrift werd op 14 april 1967 geboren in Blerick. Hij behaalde het diploma Gymnasium β aan het Sint Thomascollege te Venlo in 1985. In datzelfde jaar begon hij aan de studie Geneeskunde aan de Katholieke Universiteit Nijmegen. In 1992 behaalde hij het artsexamen. Van 1992 tot en met 1993 werd de militaire dienstplicht vervuld als arts op de Legerplaats Harskamp. Van 1994 tot en met 1996 was hij werkzaam als arts-assistent niet in opleiding in het Groot Ziekengasthuis te 's-Hertogenbosch, het Pasteurziekenhuis te Oosterhout en de Sint Maartenskliniek te Nijmegen. Vanaf 1 februari 1997 trad hij in dienst van de afdeling Radiologie van het Leids Universitair Medisch Centrum, waar hij zich van 1997 tot 1 oktober 2000 als arts-onderzoeker bezig hield met het Ontwikkelingsgeneeskunde project 'MRI-Triage voor Arthroscopie' waaruit dit proefschrift is voortgekomen. Vanaf 1 oktober startte hij de opleiding tot radioloog, eveneens op de afdeling Radiologie van het Leids Universitair Medisch Centrum (Prof. Dr. J.L. Bloem en Prof. Dr. A. de Roos), welke op 30 september 2005 werd afgerond. Hierna bleef hij als radioloog verbonden aan de afdeling Radiologie van het Leids Universitair Medisch Centrum, aanvankelijk voltijds en vanaf 1 juli 2006 deeltijds nadat hij tevens als radioloog toetrad tot de Maatschap Radiologie in het Rijnland Ziekenhuis te Leiderdorp.