important predisposing factors for DISH. Their previous study involved patients from ethnic populations, including 667 white, 144 black, 72 Native American, 11 Hispanic, and 30 Asian patients. They showed that the Asian, black, and Native American populations had a remarkably lower prevalence of DISH; however, their study population was small. In a recent study, Kim et al. [18] reported that race influences the prevalence of DISH. Their prevalence of DISH was 5.4 % in men and 0.8 % in women aged over 80 years in a Korean population, which is remarkably lower than the prevalence in our study, despite the similar race. Our prevalence was similarly high as the white population in Weinfield's report. Therefore, it is believed that genetic factors influence the prevalence of DISH more than race.

The present study clarified that most cases of DISH were observed in the thoracic vertebrae. There were no cases of DISH located in only the cervical or lumbar region. All cases of DISH in the cervical region were categorised as diffuse-type. Even if subjects were categorised into diffuse-type DISH, thoracic vertebrae were found to be the most affected. In addition, among the thoracic vertebrae, we found the predilection site to be the middle thoracic vertebrae (Th7–Th9). Holton et al. [27] reported that the distribution of the lowest level of DISH in 298 male subjects aged ≥65 years was 38 % in the thoracic region, 49 % in the thoracolumbar region, and 13 % in the lumbar region. It is interesting that DISH has predilection sites, which might be due to anatomic alignment of the vertebrae. For example, the middle thoracic vertebrae are likely to be affected by compressive mechanical stress because the Th8 is located nearly at the top in physiologic kyphosis. DISH originates mainly from the thoracic spine and extends to the cervical and/or lumbar spine by mechanical stress. In the present cross-sectional study, we could not evaluate whether DISH tends to occur in the thoracic vertebrae and then forms in the lumbar spine secondarily; however, we were able to follow-up on the ROAD study and clarify the disease course of thoracic DISH.

Regarding the definition of DISH, it might be easy to imagine that LS, defined by KL2 (defined as radiographically definite osteophytes), is associated with DISH. However, there are few reports to confirm the association between DISH and severe LS with the criterion of KL3 or 4. In the present study, we confirmed the significant association between DISH and LS, not only with the criterion of KL2, but also with KL ≥3. In addition, there are few reports to clarify the association between DISH and OA of other sites. In the present study, we also confirmed the significant association between DISH and KOA. In fact, the OR of the presence of DISH for KOA significantly increased according to the severity of KOA. The effects of LS and KOA coexisted independently. This result suggests that DISH and OA might be in a similar vein of disease, for example, the so-called 'bone proliferative group'. There have been several reports regarding the association between DISH and OPLL [4–7]. Resnick et al. [4] described 4 patients with coexisting DISH and cervical OPLL, and found OPLL in 50 % of 74 additional patients with DISH after reviewing their cervical spine radiographs. However, there has been no report on the association of DISH and OA; thus the etiology of ossification might not be similar to that of OA. Therefore, with only the results of the present study, we cannot definitely claim that DISH and OA are in a similar disease group, even though DISH tends to have similar associated factors, such as age, overweight (bigger BMI), and mechanical stress, as OA.

Another hypothesis is that there might be hidden associated factors that might affect both DISH and OA. We considered risk factors for metabolic syndrome as potential confounders. Several constitutional and metabolic abnormalities have been reported to be associated with DISH including obesity, large waist circumference, hypertension, diabetes mellitus, hyperinsulinemia, dyslipidemia, and hyperuricemia [21, 28–30]. In addition, both LS and KOA are well known to be associated with obesity [31]. We have already reported on the presence of hypertension and impaired glucose tolerance, and shown that the accumulation of metabolic risk factors is associated with the presence and occurrence of KOA [32, 33]. In addition, we found that current smoking, a known risk factor for cardiovascular disease as well as metabolic risk factors, was significantly associated with DISH. These findings may indicate that DISH is a candidate surrogate index for metabolic risk factors as a predictor of OA, or vice versa. We could not evaluate this hypothesis at present, but we would clarify the association including the causal relationships between DISH, OA, and metabolic risk factors in a further study.

Alternatively, we considered associated factors for inflammation or cartilage metabolic turnover as potential confounders between DISH and OA. These factors might coexist as risk factors for DISH and OA. Thus, there might be a direct or indirect pathway between DISH and OA via hidden associated factors, which should be investigated in a further study.

This study has several limitations. First, although the ROAD study includes a large number of participants, these subjects may not truly represent the general population. To address this, we compared the anthropometric measurements and frequencies of smoking and alcohol consumption between study participants and the general Japanese population; no significant differences were found, with the exception that male ROAD study participants aged 70–74 years were significantly smaller in terms of body structure than the overall Japanese population ($p < 0.05$)

[25]. This difference should be considered when evaluating potential risk factors in men aged 70–74 years; factors such as body build, particularly greater weight, are known to be associated with LS and KOA. Therefore, our results may be an underestimation of the prevalence of these conditions. Second, in the present study, we used only the data of the baseline study. Thus, we were not able to confirm a causal relationship between DISH status and other associated factors, as mentioned above. Nevertheless, we have performed a follow-up study, so we will be able to clarify the causal relationship between DISH status and OA in the near future. Third, this study could not evaluate the cervicothoracic junction (C7–Th4) because we assessed only radiographs. Although most cases of DISH existed in the inferior thoracic spine, as Fig. 2 shows, the lack of findings in the C7/C1–Th3/Th4 levels might have underestimated the prevalence of DISH. To evaluate the cervicothoracic junction, it would be necessary to use computed tomography or magnetic resonance imaging of the whole spine, which appeared impossible to perform on more than 1,600 subjects. Fourth, LS defined by KL2 may have been included in cases of DISH, but there is no method to confirm the overlap of the presence of DISH and LS of KL2 using the radiographic diagnostic criteria. DISH is observed mainly in the thoracic region, and only the diffuse type expands partly into the lumbar region. Therefore, there is a small possibility that LS of KL2 might be contaminated into DISH. Finally, in the present study, we could not evaluate other sites of OA besides the knee and lumbar spine, such as the hands or hip. To evaluate DISH and other sites of OA, we should evaluate the presence or occurrence of OA at other sites in a further study.

In conclusion, in the present population-based study, we found that the prevalence of DISH was 10.8 % in the overall population. Prevalence was significantly higher in older subjects, and mainly distributed at the thoracic spine. Logistic regression analysis revealed that the presence of DISH was significantly associated with older age, male sex, higher BMI, and presence of severe KOA.

Acknowledgments This work was supported by Grants-in-Aid for Scientific Research B23390172 and B20390182 to NY, C20591737 to TA, and C20591774 to SM, for Young Scientists A18689031 to HO, and Collaborating Research with NSF 08033011-00262 (Director, NY) from the Ministry of Education, Culture, Sports, Science and Technology; and H17-Men-eki-009 (Director, KN), H18-Choujyu-037 (Director, TN), H20-Choujyu-009 (Director, NY), H23-Chojyu-002 (Director, TA), and H25-Chojyu-007 (Director, NY) from the Ministry of Health, Labour and Welfare in Japan. This study also was supported by grants from the Japan Osteoporosis Society (NY, SM, HO, and TA) and research aid from the Japanese Orthopaedic Association (JOA-Subsidized Science Project Research 2006-1 and 2010-2 [Director, HK]). The authors wish to thank Dr. Takako Nojiri and Mr. Kazuhiro Hatanaka of the Gobo Public Health Centre; Dr. Naoki Hirabayashi of the Kawakami Clinic, Hidakagawa Town; Mrs. Tomoko Takijiri, Mrs. Kumiko Shinou, Mrs. Rie Takiguchi, Mrs. Kyoko Maeda, Ms. Ikuyo Ueyama, Mrs. Michiko Mori, Mrs. Hisayo Sugimoto, and other members of the public office in Hidakagawa Town; Dr. Shinji Matsuda of the Shingu Public Health Centre; and Mrs. Tamako Tsutsumi, Mrs. Kanami Maeda, Mr. Shoichi Shimoichi, Mrs. Megumi Takino, Mrs. Shuko Okada, Mrs. Kazuyo Setoh, Mrs. Chise Ryouno, Mrs. Miki Shimosaki, Mrs. Chika Yamaguchi, Mrs. Yuki Shimoji, and other members of the public office in Taiji Town for their assistance in locating and scheduling participants for examinations. We also thank Ms. Kyoko Yoshimura, Mrs. Toki Sakurai, and Mrs. Saeko Sahara for their assistance with data reduction and administration.

Conflict of interest All authors declare that (1) no author has received corporate support for the submitted work; (2) the authors have no relationships with companies that might have an interest in the submitted work in the previous 3 years; (3) the authors' spouses, partners, or children do not have financial relationships that may be relevant to the submitted work; and (4) the authors have no nonfinancial interests that may be relevant to the submitted work.

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J Orthop Sci
DOI 10.1007/s00776-014-0677-1

ORIGINAL ARTICLE

Improved accuracy of diagnosis of lumbar intra and/or extra-foraminal stenosis by use of three-dimensional MR imaging: comparison with conventional MR imaging

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Received: 9 July 2014 / Accepted: 19 November 2014

Abstract

Background The purposes of this study were to assess the reliability of 3-dimensional magnetic resonance (MR) imaging (3D MRI) and conventional MRI (CMRI) for detection of lumbar intra and/or extra-foraminal stenosis (LIEFS) and to compare the diagnostic accuracy of the 2 imaging modalities.

Methods A total of 60 sets of 3D MR and CMR images from 20 healthy volunteers and 40 LIEFS patients were qualitatively rated according to defined criteria by 3 independent, blinded readers. Kappa statistics were used to characterize intra and inter-reader reliability for qualitative rating of data. Multireader, multicase analysis was used to compare lumbar foraminal stenosis detection between the 2 modalities.

Results Intra-reader agreement for 3D MRI was excellent, with kappa = 0.90; that for CMRI was good, with kappa = 0.78. Average inter-reader agreement for 3D MRI was good, with kappa = 0.79, whereas that for CMRI was moderate, with kappa = 0.41. Average area under the ROC curve values (1st reading/2nd reading) for detection of lumbar foraminal stenosis using 3D MRI and CMRI were 0.99/0.99 and 0.94/0.92, respectively. Detection of LIEFS with 3D MRI was significantly better than with CMRI ($P = 0.0408/0.0294$).

Conclusions These results suggest that CMRI was of limited use for detection of the presence of LIEFS. Isolated imaging with CMRI may risk overlooking the presence of LIEFS. In contrast, reliability of 3D MRI for detection of LIEFS was good. Furthermore, readers' performance in the diagnosis of LIEFS can be improved by use of 3D MRI. Therefore, 3D MRI is recommended when using imaging for diagnosis of LIEFS.

Introduction

Most surgery for lumbar spinal stenosis is considered successful for relief of symptoms, but a significant number of failures occur. The term "failed back surgery syndrome" (FBSS) is used to designate persistent complaints of low back pain and/or leg pain among patients who have undergone surgical procedures intended to relieve those complaints. Burton et al. reported the most common reason for FBSS as failure to diagnose lateral spinal stenosis, which includes intra and/or extra-foraminal nerve root entrapment [1]. This diagnostic limitation seems to be the result of difficulty identifying the lesion outside the spinal canal with conventional imaging modalities [2]. When the site of nerve compression is peripheral to the root sleeves, myelography provides no information [3]. Therefore, parasagittal magnetic resonance (MR) images have long been the recommended method for investigation of any abnormality in the region of the intervertebral foramen. Obliteration of the perineural fat surrounding the nerve root has been reported to

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Published online: 11 December 2014

be the finding most suggestive of lumbar intra and/or extraforaminal stenosis (LIEFS). However, such MR images do not give complete information and sometimes result in false-positive or false-negative findings [4, 5].

The advent of 3-dimensional magnetic resonance imaging (3D MRI) has rapidly countered this difficulty in recent years [6, 7]. Direct visualization of the nerve root in the intervertebral foramen by use of 3D MRI has been a great benefit in the daily practice of spinal medicine. Nerve abnormalities outside the spinal canal can be easily diagnosed by using this modality. However, no reference standard for diagnosis of LIEFS on 3D MRI has been established, and the diagnostic performance of 3D MRI and conventional imaging modalities has not yet been directly compared.

The purposes of this study were to propose new diagnostic criteria for LIEFS on 3D MRI, to assess the reliability of 3D MRI and conventional MRI (CMRI) for the identification of LIEFS, and to compare LIEFS detection between the 2 imaging modalities.

Materials and methods

Patient population

The local ethics committee approved this retrospective study. Informed consent was obtained from all study participants. To collect CMRI and 3D MRI data samples for this reading study, positive images (radiographically abnormal cases) were obtained from patients who underwent surgery for LIEFS at our university hospital. To achieve uniform reading conditions, the responsible lesions were limited to the L5-S1 level, which is the most common site of involvement of LIEFS. To establish a clear diagnosis, only cases involving a single stenotic lesion were selected. That is, the patients had no concomitant intraspinal canal lesion at the time of surgery. Their leg symptoms were completely resolved after L5 nerve block, and the outcome of decompression surgery for LIEFS at L5–S1 was successful. LIEFS images that were of low diagnostic quality for the examinations, because of motion or other artifacts were excluded. After reviewing all the images and records, the final study group with positive images comprised 40 patients (22 male, 18 female; age 50–84 years, mean 70.0 years). The study group for negative images (radiographically normal cases) consisted of 20 normal healthy volunteers (10 male, 10 female; age 18–28 years; mean 21.3 years). These subjects had no current or previous history of low back pain and/or leg pain and no history of spinal disorders, and their spinal MRI revealed no disc degeneration over the entire lumbar spine. Thus, a total of 60 sets of 3D MRI and CMRI images from 20 normal healthy volunteers and 40 LIEFS patients were evaluated.

Imaging technique

MRI was performed with a 3.0 T MR scanner (Achieva; Philips Medical Systems, Best, Netherlands) using a 32-channel SENSE-Torso/Cardiac coil. The sequences for 3D MRI are called "Proset Myelo" in this system (3D FFE with, in principle, the selective excitation technique). The scanner settings were: TR = 20 ms, TE = 8 ms, flip angle = 15 degrees, slice thickness = 0.55 mm, field of view = 240 mm, and matrix = 256 × 512. Images were then subjected to postprocessing with multiplanar reformatting in a workstation to provide continuous longitudinal nerve images. For the conventional MRI procedure, the spin echo sequences of sagittal T1-weighted images were: TR = 650 ms, TE = 10 ms, flip angle = 90°, field of view = 280 mm, and matrix = 352 × 512.

Imaging analysis

Images were provided to the readers on CDs and viewed with commercial software (Virtual Place Liberty; AZE, Japan). Display monitors were not standardized across readers. Qualitative ratings were performed according to defined criteria by 3 independent readers (orthopedic surgeons and board-certified spinal experts of the Japanese Orthopedic Association) with no knowledge of the patients' clinical information. Each reader attended a lecture explaining the standardized definitions of imaging features from the first author (H.Y.), and consensus for interpretation of 3D MRI and CMRI findings was obtained among the readers before the start of the study. The images were scored as "definitely showing LIEFS", "probably showing LIEFS", "probably not showing LIEFS", or "definitely not showing LIEFS". All 3D MRI and CMRI images were independently evaluated twice by the 3 readers with a 1-month interval between readings.

The following reference standards were used for each imaging modality. On CMRI, obliteration of the perineural fat surrounding the nerve root in the intervertebral foramen was taken into consideration (parasagittal MRI reading technique). If the perineural fat was clearly visible, the image was considered normal. If the perineural fat was diminished because of disc height loss, osteoarthritic changes in the facet joints, buckling of the ligamentum flavum, or protrusion of the annulus fibrosis, the image was considered abnormal [8].

No widely used diagnostic criterion or grading system exists for LIEFS on 3D MRI. Hence, the authors reviewed the images of all the surgical cases of LIEFS and selected 4 representative imaging features as an index of highly suspicious findings of LIEFS:

1. transverse path of the nerve root and/or spinal nerve (Fig. 1a);

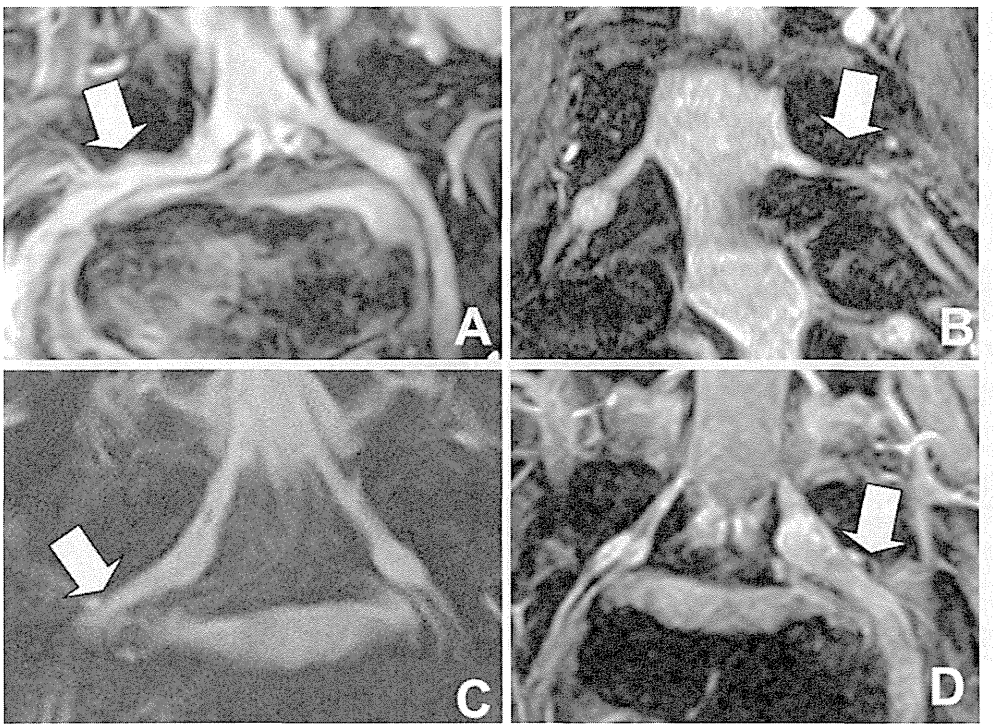

Fig. 1 Index of highly suspicious findings of LIEFS: **a** transverse path of the nerve root and spinal nerve, **b** obscurity of the spinal ganglion, **c** constriction of the spinal nerve, and **d** nerve swelling

2. obscurity of the dorsal root ganglion (DRG) (Fig. 1b);
3. spinal nerve indentation (Fig. 1c); and
4. nerve swelling (Fig. 1d).

These radiological findings on 3D MRI were highly consistent with the anatomical abnormalities in our surgical case series. Although all 4 radiological abnormalities were not always present on 3D MRI in cases with LIEFS, at least 1 imaging feature was always observed. Therefore, if any 1 of these 4 radiological findings was observed, it was regarded as abnormal. Images that did not have any of these radiological findings were considered normal.

As a basic step toward developing diagnostic criteria, we defined the area from the medial pedicle wall to the lateral pedicle wall as the intra-foraminal zone and the area beyond the lateral pedicle wall as the extra-foraminal zone. The spindle-shaped nerve root in the intra and/or extra-foraminal zone was defined as the DRG. The nerve root in the extra-foraminal zone beyond the DRG was defined as the spinal nerve. The nerve between the thecal sac and the DRG was defined as the nerve root [9]. Imaging features and their association with intraoperative findings were:

1. Transverse path of the nerve root and/or spinal nerve (Fig. 1a). The transverse path was defined as positive when either of the tilting angles of the nerve root and/or spinal nerve in the intra and/or extra-foraminal zone was larger than that of the normal contralateral side. The normal nerve root and spinal nerve basically run obliquely downward through the intervertebral foramina after branching from the dura mater. Hence, a transverse path is abnormal. The nerve root and/or spinal nerve were compressed and shifted upward by degenerating bulging discs. The transverse path of the nerve root and/or spinal nerve indicated the presence of up-down-type stenosis in the intra and/or extraforaminal zone [10, 11].
2. Obscurity of the DRG (Fig. 1b). Obscurity of the DRG was defined as positive when its configuration became unclear. DRGs are the largest neural structures around the intervertebral foramina and are ordinarily distinguishable from the nerve root and spinal nerve by their spindle shape on 3D MR images. Because the vast majority of DRGs are normally located in the intra-foraminal zone, morphological changes to the DRG imply significant diminishment of available space for the nerve root around the intervertebral foramen. Thus, when DRG configuration becomes unclear, the existence of LIEFS is strongly suspected. DRGs were compressed by degenerative bulging discs from the inferior and by superior articular facets from the posterior of the intra-foraminal zone. Obscurity of the DRG indicated circumferential-type stenosis in the intra-foraminal zone [4, 11].

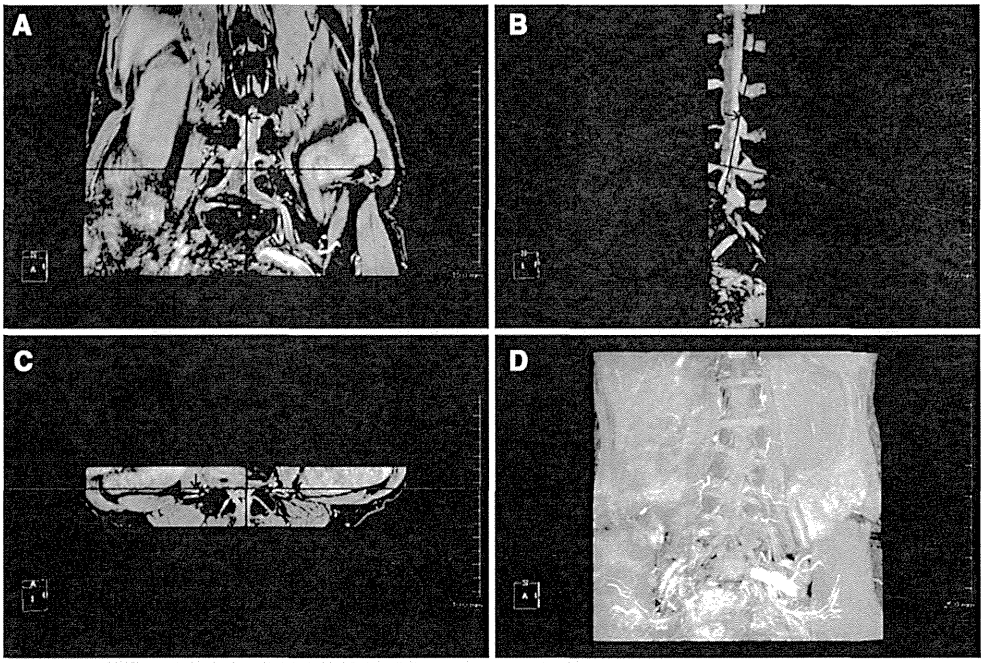

Fig. 2 An example of the 3D view of the 5th lumbar nerve roots and spinal nerves using MPR (multi-planar reconstruction) in **a** coronal view, **b** axial view, **c** sagittal view and the MIP (maximum intensity projection) technique (**d**)

3. Spinal nerve indentation (Fig. 1c). Spinal nerve indentation was regarded as positive when the nerve diameter narrowed locally. Because the nerve thickness is the same other than at the dorsal root ganglion, indentation is evidence suggesting the presence of stenosis. Spinal nerve indentation indicated spinal nerve entrapment on operative findings, which was mainly observed in cases of extra-foraminal stenosis at the lumbosacral junction. This lesion had several etiologies, for example impingement of the transverse process of L5 against the ala of the sacrum [12], entrapment by the lumbosacral ligament [13, 14], and entrapment by osteophytes of the L5 vertebral bodies and sacral ala [15]. All these lesions occurred in the lumbosacral tunnel [16] in the extra-foraminal zone. The lumbosacral tunnel is an osteofibrotic tunnel for the exiting nerve of L5, which is formed by developing osteophytes and the degenerating hypertrophied lumbosacral ligament. This unique anatomical structure contributed to spinal nerve entrapment.
4. Nerve swelling (Fig. 1d). Swelling of the nerve root, DRG, or spinal nerve was defined as positive when the size of any of these structures exceeded that of the normal contralateral side. Although morphological changes to the nerve do not always indicate symptomatic radiculopathy, nerve swelling has been reported as a good indicator of symptomatic LIEFS in previous studies [7]. Thus, the existence of nerve swelling at any level from the entrance zone to the extraforaminal zone and at any range from local to total was considered abnormal. This finding was often observed in cases with clinical symptoms of severe spontaneous pain. Thus, nerve swelling may indicate the existence of nerve inflammation.

An example of the 3D view of the 5th lumbar nerve roots and spinal nerves using multi-planar reconstruction and the maximum intensity projection technique is shown in Fig. 2. The readers could observe many different views of the nerves by adjusting the screen to detect the intra and/or extra-foraminal lesion.

Statistical methods

First, reliability was measured by use of kappa statistics. This statistical analysis was performed by using JMP version 10 (SAS Institute Japan, Tokyo, Japan). Intra and inter-reader reliability was assessed with the kappa coefficient, which was characterized as: <0.0 = "poor" agreement, 0.0–0.2 = "slight" agreement beyond chance, 0.21–0.4 = "fair" agreement, 0.41–0.60 = "moderate" agreement, 0.61–0.80 = "substantial" agreement, and 0.81–1.00 = "almost perfect" agreement [17]. To analyze the data obtained, readers' ratings were classified into 2 categories: "positive," consisting of definite or probable LIEFS, and "negative," consisting of cases defined as probably or definitely not showing LIEFS. Second, to compare the diagnostic performance of the 2 imaging modalities, receiver operating

characteristic (ROC) analysis based on a sequential test method was used [18, 19]. To analyze the data, readers' ratings were converted into a numerical rating scale as follows: "definitely showing LIEFS" = 4, "probably showing LIEFS" = 3, "probably not showing LIEFS" = 2, and "definitely not showing LIEFS" = 1. The area under the ROC curve (AUC) and 95 % confidence intervals (CI) were obtained with a quasi-maximum likelihood estimation of binomial distribution by using DBM MRMC software (version 2.2). Accuracy was determined by using the AUC. An area of 1 represents a perfect test; an area of 0.5 represents a worthless test. An approximately guide for classifying the accuracy of a diagnostic test is the traditional academic point system, with AUC values 0.90–1 = "excellent", 0.80–0.90 = "good", 0.70–0.80 = "fair", 0.60–0.70 = "poor", and 0.50–0.60 = "fail" [20]. The significance of the different AUC for CMRI and 3D MRI was tested by use of the Dorfman–Berbaum–Metz method, which included both reader variation and case sample variation, by means of an analysis of variance approach. P values <0.05 were regarded as indicative of a significant difference.

Results

The first and second reading results of each reader are summarized in Table 1. Average sensitivity and specificity for 3D MRI (1st reading/2nd reading) were 85.8/90.0 and 98.3/98.3 %, respectively. Those for CMRI were 59.2/63.3 and 100/100 %, respectively. Intra-reader reliability for CMRI and 3D MRI is summarized in Table 2. Intra-reader reliability for 3D MRI showed agreement was excellent, with kappa = 0.90, whereas agreement for CMRI was good, with kappa = 0.78. Inter-reader reliability for CMRI and 3D MRI are summarized in Tables 3 and 4, respectively. Inter-reader agreement for 3D MRI was good, with kappa = 0.79, whereas agreement for CMRI was moderate, with kappa = 0.41. The AUC values of the ROC curves for 3D MRI and CMRI for individual observers are summarized in Table 5. The mean AUC of the ROC curves (1st reading/2nd reading) for the 3 observers was 0.99/0.99 for 3D MRI and 0.94/0.92 for CMRI (Figs. 3, 4). AUC values for the 2 imaging modalities were statistically significantly different (P = 0.0408/0.0294, 95 % CI 0.10009–0.00178/0.00803–0.11867).

Table 1 Sensitivity and specificity of CMRI and 3D MRI for individual observers

Statistic and reader	3D MRI (1st reading/2nd reading)	CMRI (1st reading/2nd reading)
Sensitivity (TP/TP + FN) (%)		
A	82.5/82.5	70.0/67.5
B	82.5/92.5	70.0/57.5
C	92.5/95.0	37.5/65.0
Average	85.8/90.0	59.2/63.3
Specificity (TN/TN + FP) (%)		
A	100/95.0	100/100
B	95.0/100	100/100
C	100/100	100/100
Average	98.3/98.3	100/100

TP indicates true positive, *FN* false negative, *TN* true negative, *FN* false negative

Table 2 Intra-reader reliability of CMRI and 3D MRI for individual observers

Imaging modality and observer	κ Statistic	Standard error	Agreement
3D MRI			
A	0.8986	0.1291	58
B	0.8275	0.1291	55
C	0.9644	0.1291	59
Average	0.8968		
CMRI			
A	0.8661	0.1291	57
B	0.6089	0.1291	49
C	0.8636	0.1291	57
Average	0.7795		

Table 3 Inter-observer reliability of 3D MRI

Observers	κ Statistic	Standard error	Agreement
1st reading			
A and B	0.3114	0.1291	41
A and C	0.3407	0.1291	42
B and C	0.4139	0.1291	45
2nd reading			
A and B	0.5567	0.1291	47
A and C	0.3407	0.1291	42
B and C	0.4920	0.1291	47
Average	0.4092		

Discussion

Failure to diagnose LIEFS continues to be the most common reason for FBSS [1]. The difficulty in identifying LIEFS with conventional imaging modalities is well-recognized. LIEFS tends to be overlooked rather than overestimated. Therefore, new imaging techniques to detect LIEFS with certainty are required.

Table 4 Inter-observer reliability of CMRI

Observers	κ Statistic	Standard error	Agreement
1st reading			
A and B	0.7634	0.1291	53
A and C	0.7943	0.1291	54
B and C	0.7586	0.1291	53
2nd reading			
A and B	0.7586	0.1291	53
A and C	0.7917	0.1291	54
B and C	0.8933	0.1291	57
Average	0.7933		

Table 5 AUC values of the ROC curves for 3D MRI and CMRI for individual observers

Reader	3D MRI (1st reading/2nd reading)	CMRI (1st reading/2nd reading)
A	1.00/0.98	0.96/0.92
B	0.96/1.00	0.91/0.96
C	1.00/0.99	0.93/0.89
Average	0.99/0.99	0.94/0.92

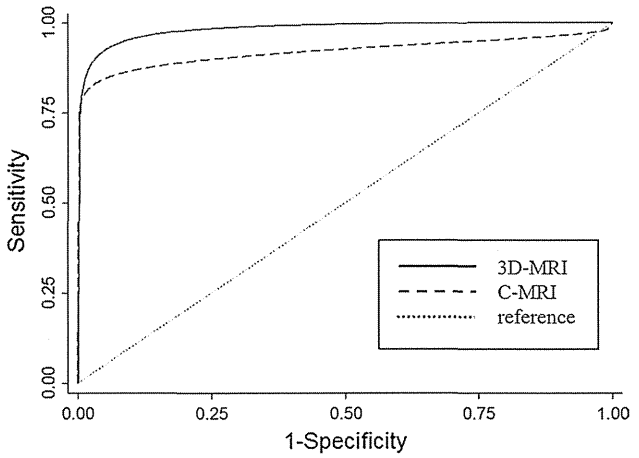

Fig. 3 Averaged ROC curves for 3 observers obtained from 1st reading results for 3D MRI and CMRI

This study confirms the low reliability of the parasagittal MRI reading technique for evaluating LIEFS reported in the past. Speciciale et al. [21] reported the lowest overall inter-observer reliability kappa value, 0.26, for ratings of stenosis severity, which included both foraminal and lateral recess and central stenosis. Lurie et al. [8] reported good agreement for intra-reader reliability for foraminal stenosis, with an overall kappa of 0.77, but moderate agreement for inter-reader reliability, with an overall kappa of 0.58. Our study also revealed good agreement for intra-reader

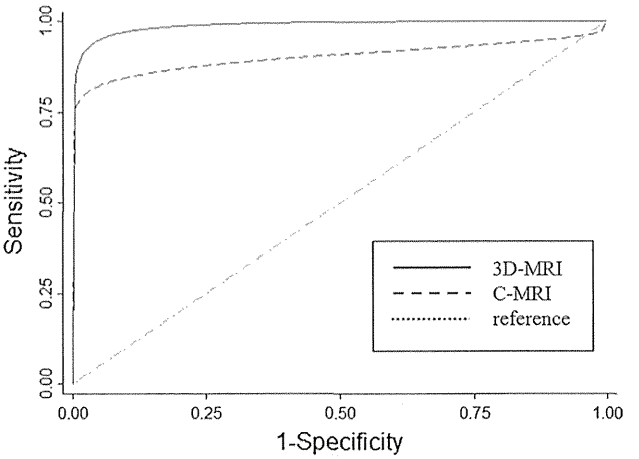

Fig. 4 Averaged ROC curves for 3 observers obtained from 2nd reading results for 3D MRI and CMRI

reliability and moderate agreement for inter-reader reliability, with overall kappa values of 0.78 and 0.41, respectively. Taking these findings into account, we conclude that parasagittal MRI reading of CMRI is not highly reliable for detection of LIEFS, especially with regard to inter-reader agreement. This situation is not ideal when considering surgical indications for LIEFS. Presurgical diagnosis may differ with different examiners, which may increase the number of FBSS patients.

The lower reliability of the parasagittal MRI reading technique for LIEFS identification has several possible causes. Evaluating a limited number of cross-sectional images is not sufficient to identify all abnormalities along the nerve pathways. This technique is limited to evaluation of foraminal stenosis and is inadequate for investigating extraforaminal pathology. Furthermore, accurate evaluation of nerve pathology in intra and/or extraforaminal zones where the nerve pathways progress in 3 dimensions is beyond the ability of 2-dimensional conventional imaging interpretation.

From this perspective, 3D MRI seems ideal for evaluating nerve lesions around the intervertebral foramen. Direct visualization of nerve morphology is very helpful for identifying nerve abnormalities with high reliability. As expected, this new imaging modality resulted in excellent agreement for intra-reader reliability, with overall kappa of 0.90, and good agreement for inter-reader reliability, with overall kappa of 0.79. In addition to improved imaging quality with high spatial resolution, we believe our diagnostic criteria for LIEFS on 3D MRI contributed to readers' understanding of the nerve pathology in the intra and/or extra-foraminal zone and served as a support tool for more reliable identification of nerve lesions.

No study comparing diagnostic performance between 3D MRI and CMRI using ROC analysis has been

conducted to date. ROC analysis is a crucial technique for evaluating diagnostic systems, and ROC curves have been regarded as imperative when comparing new imaging technology [22, 23]. Our study demonstrated that the AUC values of both imaging modalities were greater than 0.9, indicative of excellent diagnostic performance in clinical use, but the AUC of 3D MRI was significantly higher than that of CMRI. This result suggests that the detectability of LIEFS by 3D MRI is superior to that by CMRI. Although direct comparison of diagnostic performance between 3D MRI and conventional imaging studies has not been conducted previously, this study demonstrated that 3D MRI is superior to CMRI in reliability and detectability.

This study has some limitations. First, the number of imaging samples was small, but a significant difference was observed between 3D MRI and CMRI with regard to reliability and detectability. Second, this study only focused on comparing the detectability of abnormal morphology by the 2 imaging modalities. Therefore, we recruited control subjects with little or no degenerative changes for negative images (radiographically normal cases), whereas the study group for positive images was recruited from patients who had LIEFS surgery. LIEFS may be more difficult to distinguish radiologically from age-related changes, and future studies should examine the sensitivity and specificity of these changes for an age-matched control group.

Investigating the percentage of symptomatic nerve roots that are correctly identified as having these 3D MRI abnormalities is also very important. Several reports have indicated that abnormal CMRI findings of lumbar disc herniation or spinal stenosis are not always accompanied by symptoms [24, 25]. Radiographic abnormalities of the nerve are common, but symptomatic nerves are less prevalent. Therefore, the correlation between 3D MRI abnormalities and clinical symptoms must be investigated further. Otherwise, overdiagnosis may occur. To resolve this problem, functional diagnosis with use of selective nerve blocking, electromyographical study [26, 27], and diffusion MRI [28] may be help to improve the specificity of diagnosing symptomatic LIEFS. Nonetheless, improving the detectability of radiographic abnormalities indicative of LEIFS is important in daily spinal practice. Not all screening tests have been shown to benefit the person being screened; however, finding unrecognized LIEFS would be very beneficial for patients who are scheduled for nerve decompression surgery because misdiagnosis of LIEFS remains one of main reasons for FBSS.

In conclusion, CMRI demonstrated limitations in identifying the presence of LIEFS, and isolated imaging by use of CMRI may risk overlooking the presence of LIEFS. In contrast, use of 3D MRI for diagnosis of LIEFS resulted in good reliability and detectability. Our new diagnostic criteria for LIEFS on 3D MRI enable reliable discrimination between a normal root and LIEFS. This study demonstrated that reader performance in diagnosis of LIEFS can be improved by use of 3D MRI. Therefore, 3D MRI is recommenced when using imaging for diagnosis of LIEFS.

Acknowledgments The authors wish to thank Dr Hiroko Ihara, Dr Misato Okouchi, and Mr Yuji Nakao in Wakayama-minami radiology clinic for their technical assistance and for collecting data, and Dr Junji Shiraishi in School of Health Sciences, Kumamoto University for his comment on the study design and interpretation of the data.

Conflict of interest The authors declare that they have no conflict of interest.

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JAPAN JOURNAL OF NURSING SCIENCE

Japan Journal of Nursing Science (2014) doi:10.1111/jjns.12065

REVIEW ARTICLE

Literature review of pain management for people with chronic pain

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Abstract

Aim: Multimodal approaches toward relieving pain, patients' participation, and improving self-efficacy are important for chronic pain management. The aims of this review were to identify possible options of nursing strategies for pain management in individuals with chronic pain and to determine the effectiveness of these strategies for pain relief/pain-related problems; therefore, nurses and researchers could consider and/or adopt multimodal chronic pain management strategies.

Methods: A Systematic Integrated Literature Review was conducted. Published work related to pain management in individuals with chronic pain was identified by searching databases and reviewed.

Results: Among the studies reviewed, we identified 35 studies that focused on pain management strategies. In 10 studies, interventions such as integrated and multidisciplinary pain management programs were associated with significant decreases in pain intensity. However, they reported that the long-term effectiveness of pain relief was not satisfactory. Individuals with chronic pain reported that strategies including pharmacotherapy, physical activity, social support from friends and family, acupuncture, heating, rest, diets, or life-style changes helped them to effectively manage their pain.

Conclusion: We identified possible options of pain management strategies and explored effectiveness of chronic pain interventions. The long-term effects of pain relief interventions and social support for individuals with chronic pain require further investigation.

Key words: chronic pain, pain management, review, self-efficacy, self-management.

INTRODUCTION

Pain is an important health alert for human beings that could inform them of potential health problems. However, pain is sometimes persistent and exceeds the normal healing process, which can lead to unpleasant feelings and negative consequences for their lives. Many people suffer from chronic pain; the prevalence of chronic pain was reported as 45.2% in people living in the Japanese community (Nakamura, Nishiwaki, Ushida, & Toyama, 2014). Furthermore, chronic pain can cause physical disability, depression, a lower quality of life, or financial and employment difficulties (Achterberg *et al.*, 2010; Gillespie & Friedman, 2007; Johannes, Le, Zhou, Johnston, & Dworkin, 2010). Appropriate pain management was extremely important for individuals with chronic pain to maintain their daily activities as much as possible, as individuals incapacitated by chronic pain are prone to inactivity and focus their attention on their pain throughout the day.

Pain management is defined as the intention to modulate patients' pain or their response to pain using

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Received 24 June 2014; accepted 16 September 2014.

multimodal approaches in a collaborative relationship with the patient, with the aim of self-efficacy (Larsen, 2007). Because of the refractory nature of chronic pain, the goal of pain management may not depend on the level of pain the patient experiences (Richardson, Adams, & Poole, 2006).

Rather, relieving pain as much as possible in individuals with chronic pain is considerably important to motivate them to engage in new or positive behaviors, such as physical activity and exercise (Oliver & Ryan, 2004). Pharmacological therapy for pain relief could be effective, however, side-effects and adverse events of pharmacological therapy for pain were also reported among people undergoing long-term therapy for chronic pain (Finnerup, Sindrup, & Jensen, 2010; Planton & Edlund, 2010). Therefore, a combined strategy with alternative and pharmacological therapies are often needed for individuals with chronic pain.

The patient's participation in pain management also is necessary (Austrian, Kerns, & Reid, 2005); however, multimodal approaches in a collaborative relationship with patients have not been fully explored. Health professionals need to understand patients' perception toward their pain management and provide options to manage pain according to them.

In particular, knowing the effectiveness of chronic pain management strategies and their long-term effects in individuals with chronic pain are important. Nurses should access reviews of chronic pain management, such as self-management programs for musculoskeletal pain (Du *et al.*, 2011; Nuñez, Keller, & Ananian, 2009; Reid *et al.*, 2008) and the nurse's role in pain management (Courtenay & Carey, 2008; Dewar, 2006; Richardson *et al.*, 2006; Shin & Kolanowski, 2010). However, these reviews mainly focus on the nurse's role and self-management of musculoskeletal pain. There are no recent reviews regarding the management of other types of chronic pain, such as neuropathic pain. It is important that nurses understand multimodal strategies available for chronic pain management.

Therefore, the aims of this review are to identify pain management strategies for/by individuals with chronic pain from quantitative and qualitative studies, and to examine the effectiveness of these pain management strategies for pain relief/pain-related problems. A greater understanding of the strategies would help Japanese nurses to develop nursing systems for managing chronic pain and explore research areas that require further investigation.

METHODS

This review was conducted as a Systematic Integrated Literature Review, as described by Im and Chang (2012). This type of review is defined as systematic based on the methods used to retrieve, sort, and analyze the studies; the explicit description of the methods; and the comprehensive inclusion of all available sources of information.

To identify areas relating to chronic pain management strategies and their effectiveness, we selected reports on trials (e.g. randomized clinical trials [RCT], quasi-experimental design trials, and single group studies) and cross-sectional studies that examined pain management strategies. We aimed to identify the areas of strategies/interventions for chronic pain management that nurses could consider using; we also selected reports of qualitative research, through in-depth interviews and descriptive studies, which explored perceptions of effective pain management strategies.

Published work related to pain management for individuals with chronic pain was collected by searching PubMed and the Japan Medical Abstracts Society's web database in August 2013. We searched abstracts and titles of manuscripts written in English or Japanese that were published in the last 8 years (2006–2013) using key words such as pain "management", "chronic pain", and "nursing". In this study, pain resulting from a non-life-threatening cause that persisted for more than 6 months was defined as chronic pain (West, Usher, & Foster, 2011). This search identified 394 reports.

Studies were included if they met the following inclusion criteria: they involved targeted patients with chronic non-malignant pain as a study population; patients were at least 18 years of age; they were written in English or Japanese; they were interventional studies of patients with chronic pain, which could possibly be adopted by Japanese nurses; and they were qualitative or descriptive studies exploring patient preferences and/or evaluations regarding strategies for their chronic pain.

Published work was excluded if it was related to medical strategies for treatment that were not normally performed by nurses in Japan ($n = 2$); related to strategies for malignant cancer pain ($n = 21$); related to neonates and children ($n = 8$); related to acute pain only ($n = 19$); related to strategies involving nursing staff only ($n = 6$); related to symptoms/conditions other than pain ($n = 20$); was not written in English or Japanese ($n = 28$); did not focus on chronic pain management interventions or strategies ($n = 105$); was a scale

development study ($n = 6$); was a case report with a small sample size (e.g. one or two cases; $n = 4$); or was a published work review/opinion paper ($n = 131$).

The studies reviewed here examined strategies implemented for individuals with chronic pain or that patients used for their chronic pain and/or perceived as effective pain management. For chronic pain management studies of patients with chronic pain that were conducted using a trial or quasi-experimental design, we reviewed reports that focused on pain management strategies, participants, and settings, and study findings relating to pain intensity, and other variables; these have been reported in Table 1. When included studies used any theoretical framework/interventional approaches, they were also reported in Table 1. In order to identify perceptions of effective pain management strategies in individuals with chronic pain, qualitative, and descriptive studies focusing on patient perceptions regarding chronic pain management strategies were reviewed by focusing on data collection methods, participants, pain types or causes, and findings (Table 2).

RESULTS

Study characteristics

Of the 394 studies reviewed, 35 met the criteria for this study and were selected for further analysis. The studies were conducted in the USA ($n = 10$), Canada ($n = 5$), Taiwan ($n = 4$), Norway ($n = 4$), Australia ($n = 3$), Hong Kong ($n = 2$), China ($n = 1$), Denmark ($n = 1$), Iceland ($n = 1$), New Zealand ($n = 1$), Spain ($n = 1$), Switzerland ($n = 1$), and the UK ($n = 1$).

For the reviewed studies, participants were recruited from outpatient medical centers, clinics, and general practitioners' offices ($n = 16$); the community ($n = 12$); long-term care facilities and nursing homes ($n = 4$); and inpatient facilities and hospitals ($n = 3$). Many studies included subjects who were 18 years old and over ($n = 14$), and nine studies focused on older adults. Eight studies excluded people with a history of mental disorders or cognitive impairment.

Some studies focused on specific conditions, such as pain related to osteoarthritis ($n = 5$), back pain ($n = 4$), fibromyalgia pain ($n = 4$), headache ($n = 1$), chronic angina pain ($n = 1$), chronic deep nipple pain ($n = 1$), pain among people undergoing hemodialysis therapy ($n = 1$), and pain related to rheumatic disease ($n = 1$).

There were several types of studies reported, including RCT ($n = 8$), quasi-experimental ($n = 15$), and qualitative or descriptive studies ($n = 12$).

Intervention for chronic pain management in trials and quasi-experimental designs

Interventional strategies

Fourteen studies used multidisciplinary or multimodal strategies in which subjects adopted self-management strategies for chronic pain; two of these studies included patient intervention and staff education together (Haller *et al.*, 2011; Tse & Ho, 2013). Relaxation and guided imagery ($n = 2$), and music therapy ($n = 1$) were also used. A pain diary was used in three studies, which aimed to facilitate effective communication between healthcare professionals and individuals with chronic widespread pain and to assess patient pain and conditions (Hager & Brockopp, 2007; Kristjánsdóttir *et al.*, 2013; Nes, Eide, Kristjansdottir, & van Dulmen, 2013); two of these studies included web-based or smartphone-based interventions.

Effectiveness of pain relief

Eighteen studies reported the effects of their interventions on pain intensity in individuals with chronic pain. Ten studies reported that their intervention statistically significantly decreased pain intensity or provided pain relief. For example, an integrated pain management program for older residents' pain (Tse & Ho, 2013), Kinesio Taping for low back pain (Castro-Sánchez *et al.*, 2012), a multidisciplinary pain management program (Dysvik, Kvaløy, & Natvig, 2012), a collaborative quality improvement program (Haller *et al.*, 2011), music intervention for people suffering from fibromyalgia pain (Onieva-Zafra, Castro-Sánchez, Matarán-Peñarrocha, & Moreno-Lorenzo, 2013), a small multidisciplinary chronic pain management program (Burnham, Day, & Dudley, 2010), relaxation and guided imagery for people with fibromyalgia pain (Menzies & Kim, 2008), the Calgary Headache Assessment and Management Program (Sauro & Becker, 2008), the Arthritis Self-Help Course and the Chronic Disease Self-Management Program (Goeppinger, Armstrong, Schwartz, Ensley, & Brady, 2007), and an arthritis self-management program (Yip *et al.*, 2007) were reported. The studies that used Kinesio Taping (Castro-Sánchez *et al.*, 2012), music interventions (Onieva-Zafra *et al.*, 2013), and self-management programs (Yip *et al.*, 2007) used RCT. Long-term effects were also reported in two studies. Dysvik *et al.* (2012) reported that the score of bodily pain for the SF-36 improved after implementing a multidisciplinary pain management program for 12 months, but these changes were not significant after Bonferroni correction.

Table 1 Chronic pain management studies for patients with chronic pain by using a trial or quasi-experimental design

Authors, (published year), country	Sample and settings	Pain types/ causes	Design	Frameworks/ interventional approach	Intervention	Pain intensity scales	Results: pain intensity	Results: other variables
Tse and Ho (2013), Hong Kong	Nursing home residents, IG = 48, CG = 42	NA	Quasi-experimental pretest and post-test control group study	Snoeselen	Integrated pain management program, received instruction in gardening activities and physiotherapy activities for 8 weeks and 8 week physiotherapy program and acupressure and massage	Geriatric Pain Assessment	The residents in the IG reported significantly lower pain scores and used more non-drug strategies for pain relief compared with the control group (week 8)	Happiness, loneliness, life satisfaction, and geriatric depression had significantly improved among the residents in the IG
Barrett *et al.* (2013), USA	Patients diagnosed as having Raynaud's phenomenon of the nipple at a dermatological referral center ($n = 18$)	Chronic deep nipple pain during lactation	Retrospective medical record review	CBT and acceptance and commitment therapy	Treatment and counseling: (i) wear warm clothing; (ii) take hot showers twice daily before breast-feeding; and (iii) avoid caffeine and vasoconstrictive drugs to prevent precipitation of vasospasm	A 25 question follow-up survey (the quality of pain and symptoms experienced)	10 (83%) reported decreased or resolution of pain	All patients reported marked improvement of symptoms and were able to continue breast-feeding
Nes *et al.* (2013), Norway	Patients in the hospital, IG = 48, CG = 37	Chronic widespread pain	RCT	CBT and acceptance and commitment therapy	Three web-based interventions incorporating electronic diaries and situational feedback consisting of one face-to-face session and 4 weeks of web-based communication	VAS	NA	After the follow-up period, the IG reported less catastrophizing compared with the CG. Between-group effect size on catastrophizing was large (Cohen's d = 0.87, $P < 0.001$) and remained moderate (0.74, $P = 0.003$) 6 months after discharge from the inpatient program

Kristjánsdóttir *et al.* (2013), Norway	Female patients in the rehabilitation center, IG = 48, CG = 64	Chronic widespread pain	RCT	CBT and acceptance and commitment therapy	Smartphone intervention consisting of one face-to-face session and 4 weeks of written communication via a smartphone	VAS	No effect was found on pain level between intervention and control groups (effect size, −0.05 and −0.04, respectively)	Immediately after the intervention, the IG reported less catastrophizing than the CG, yielding a large effect size (Cohen's d = 0.87, $P < 0.001$) for study completers. At 5 months of follow up, the between-group effects size remained moderate for catastrophizing (0.74, $P = 0.003$), acceptance of pain (0.54, $P = 0.02$), and functioning and symptom levels (0.75, $P = 0.001$)
Onieva-Zafra *et al.* (2013), Spain	Sixty patients from fibromyalgia associations, IG = 30, CG = 30	Fibromyalgia pain	RCT	NA	Music interventions consisted of listening to music once a day for 4 consecutive weeks using two types of CDs	McGill Pain Questionnaire VAS	The participants in IG reported a significant reduction in pain at week 4 compared with the baseline interview, whereas CG participants reported no reduction in their pain at week 4 versus baseline scores. Differences in the IG regarding VAS at baseline and at week 4 also were significant	Mean depression scores from baseline to week 4 improved for the IG

Table 1 *Continued*

Authors, (published year), country	Sample and settings	Pain types/ causes	Design	Frameworks/ interventional approach	Intervention	Pain intensity scales	Results: pain intensity	Results: other variables
Ryan, Packham, Dawes, and Jordan (2012), UK	Fibromyalgia patients at clinics and community rheumatology services, IG = 60, CG = 74	Chronic musculoskeletal pain	A retrospective study	Goal-setting and self-management principle and skills acquisition	Pain clinic attendance	NA	NA	In the 3 years following attendance at the pain clinic, the mean number of hospital appointments fell significantly. The mean reduction seen in hospital clinic attendances in the first year improved in the second and third years
Castro-Sánchez *et al.* (2012), Australia	Adults attended a clinic, n = 60	Chronic non-specific low back pain	RCT	NA	Kinesio Taping	VAS	Experimental group also had a greater decrease in pain than the control group immediately after treatment, which was maintained 4 weeks later	At 1 week, the experimental group had significantly greater improvement in disability, however, these effects were not significant 4 weeks later.
Dysvik *et al.* (2012), Norway	Participants, excluded older adults, were recruited through their general practitioners, n = 104	Chronic non-malignant pain	Follow-up quasi-experimental design and a previous control group	CBT	Pain management program based on CBT consisting of an 8 week basic course and follow up at 6 and 12 months	Brief Pain Inventory (BPI)	Indications of further improvements were seen in bodily pain and maintenance after 12 months, although these changes disappeared after a Bonferroni correction. No important differences were found when the changes in the SF-36 and pain intensity scores from post-test to 12 months were compared between the present studies	Findings suggest that this follow-up program can potentially maintain the positive results of the basic program in terms of reduced pain perception, improved health-related quality of life, and movement towards self-management

Wu *et al.* (2011), Taiwan	Aged 50 years and over recruited in the community health centers, n = 215	OA pain of the knee	Quasi-experimental study	CBT based on Bandura's concept of self-efficacy and behavior change	This program trial was a 4 week arthritis program followed by an 8 week follow-up assessment. There were four 80 min classes held once a week, each with 10–15 participants	NA	NA	At post-intervention, significant differences were found in pain beliefs and pain days. At 8 week follow up, there was a significant improvement in arthritis self-efficacy: pain and other symptoms subscales, pain beliefs and number of unplanned medical consultations
Kristjánsdóttir *et al.* (2011), Norway	Female participants ($n = 6$) diagnosed with CWP or FMS in the rehabilitation center or by GP	Chronic widespread pain	Pre- and post-test study	Mindfulness-based CBT Bandura's concept of self-efficacy	The intervention included daily online entries and individualized written feedback, grounded in a mindfulness-based CBT approach. The participants registered activities, emotions and pain cognitions three times daily using the mobile device	NRS	No differences	Intervention was rated as supportive, meaningful, and user-friendly by the majority of the women. The response rate to the daily registration entries was high and technical problems were few
Haller *et al.* (2011), Switzerland	All adult patients at a teaching hospital, n = 1237 in pre-program, n = 1113 in post-program	NA	Pre- and post-test study	NA	Implementation of a collaborative quality improvement program using multifaceted interventions (staff education, opinion leaders, patient education, audit, and feedback) to improve pain management at hospital level	A question: "Do you think the hospital staff did everything they could to help control your pain?"	For the patients who did not undergo surgery, 70.4% stated "Yes, definitely" (post-program) vs 57.3% (pre-program) of patients reported full pain relief ($P = 0.008$)	Among non-surgical patients, improvements were observed for pain assessment, pain management, and pain relief

Table 1 *Continued*

Authors, (published year), country	Sample and settings	Pain types/ causes	Design	Frameworks/ interventional approach	Intervention	Pain intensity scales	Results: pain intensity	Results: othervariables
Chen and Francis (2010), Australia	People aged between 25 and 65 years recruited through newspapers, n = 19	Chronic pain	RCT	Bernstein and Borkovec's individualized scripts	A 6 week combined abbreviated progressive relaxation technique (APRT) and guided imagery (GI) intervention	The McGill Pain Questionnaire (MPQ)	Not statistically significant	Regarding outcomes for mental health, the results indicated a lack of statistically significant improvements for IG. Results from the quality of life measure indicated that there was a consistent trend of improvement for IG
Burnham *et al.* (2010), Canada	Patients at a clinic Full multidisciplinary management, n = 29 Supervised medication management, n = 53	Chronic spinal pain	Pretest and post-test control group study	NA	Supervised medication management or full multidisciplinary management.	NRS	There was significant reduction in pain intensity in the full multidisciplinary group and medication management group, but not significantly different between groups	
Davis and White (2008), USA	Residents at three independent-living residential settings, n = 17	Chronic musculoskeletal pain related to rheumatic disease	Repeated measures pretest–post-test design	CBT and self-efficacy	This preliminary testing of the Goal Attainment Pain Management Program	NA	Not statistically significant	Results showed that older individuals could successfully participate in setting and attaining individual goals. Exercise and distraction were identified as significantly more helpful
Menzies and Kim (2008), USA	Patients recruited through brochures and newspaper advertisements, n = 10	Fibromyalgia pain	Repeated-measures pretest–post-test design	CBT/mind–body approach	Three 20 min relaxation and GI audiotapes used in a prescribed order for 6 weeks and in any order for weeks 7–10	VAS A short form of the McGill Pain Questionnaire (SF-MPQ)	Significant improvement was observed over time (baseline, 6 weeks and 10 weeks) in the scores of the PPI subscale of the SF-MPQ	

McGillion *et al.* (2008), Canada	Patients living in the community, IG = 57, CG = 60	Chronic angina	RCT	Cognitive–behavioral self-management techniques Bandura's Self-Efficacy Theory	Standardized psych education program given in 2 h sessions weekly, over a 6 week period	SF-36 (bodily pain)	No statistically significant	Significant improvements in IG: physical functioning and general health aspects of generic HRQL. Angina frequency, angina stability, and self-efficacy to manage disease were also significantly improved at 3 months
Sauro and Becker (2008), Canada	Patients are referred to a program by a general practitioner or a specialist, n = 132	Headache	Pre- and post-test study	CBT	The Calgary Headache Assessment and Management Program (CHAMP) 1. Education Session 2. Lifestyle Assessment 3. Self-Management Workshop 4. Nursing Contact and Advice 5. Physician Visit	VAS	Both the number of headache days and the intensity of headaches decreased following Self-Management ($n = 99$). The average intensity of the headaches decreased from baseline to post-workshop	Statistically reliable short-term improvements in HRQL and self-efficacy were found for those who participated in the CHAMP as compared with the control group; specific components of HRQL significantly improved included overall physical functioning and general health (SF-36) and frequency and stability of angina pain symptoms (SAQ)
Sørensen and Frich (2008), Denmark	Adult patients at the Multidisciplinary Pain Center. IG = 52, CG = 49	Chronic non-malignant pain	RCT	NA	The first nurse follow-up visit took place immediately after discharge from the Multidisciplinary Pain Center; further visits were at 4, 8, 12, 16, 20, and 24 months	VAS	Not statistically significant between groups	No statistically significant differences in health status were observed between the two groups after the 2 year intervention period. The costs were no statistically significant between control and intervention groups