

# Immediate and short-term effects of Mulligan's mobilization with movement on knee pain and disability associated with knee osteoarthritis – A prospective case series

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## ABSTRACT

Manual therapy has proven to be a benefit in the management of knee osteoarthritis (OA), but the effects of the method of Mulligan's mobilization with movement (MWM) have yet to be explored in knee OA. As a first step, this case series investigated MWM's immediate and short-term benefits over three occasions of treatment in 19 patients with knee OA. Patients (71.1 ± SD 13.9 years, 14 females and 5 males) received individually prescribed MWM and performed self-MWM. Outcome measures included: 1) pain intensity (visual analog scales) during walking, ascending and descending stairs, and sit-to-stand; 2) passive flexion and extension range of motion (ROM); and 3) Activities of Daily Living Scale of the Knee Outcome Survey (KOS-ADLS). Pain and ROM were assessed at baseline, after the initial treatment, before the second treatment and at exit following the fourth consultation. The KOS-ADLS was assessed at baseline and at exit. Significant improvements from baseline were detected in flexion ROM and pain scores in all tasks following the initial treatment ( $P < 0.05/3$ ). The KOS-ADLS score improved significantly from baseline (67.1% ± SD 16.6%) to exit (86.3% ± SD 12.6%) ( $P < 0.001$ ). MWM was associated with immediate pain relief and improved knee function, suggesting its potential as a component of early management of knee OA.

## INTRODUCTION

Knee osteoarthritis (OA) is a frequent cause of knee pain (Felson, Naimark, and Anderson, 1987) which can be successfully managed by physiotherapy (Page, Hinman, and Bennell, 2011). Joint mobilization has been shown to be a useful modality to reduce knee pain (Moss, Sluka, and Wright, 2007). Two recent systematic reviews demonstrated the usefulness of manual therapy and exercise for the management of knee OA (French, Brennan, White, and Cusack,

2011; Jansen et al, 2011). In addition, Deyle et al (2012) reported a preliminary clinical prediction rule which may help to identify the minority of knee OA patients who are unlikely to respond to this management approach.

Mulligan's concept of mobilization with movement (MWM) is a contemporary form of joint mobilization (Konstantinou, Foster, Rushton, and Baxter, 2002), consisting of a therapist-applied pain-free accessory gliding force combined with active movement (Mulligan, 2004). There are reports of immediate pain relief and improved function in response to these techniques in several musculoskeletal disorders (Abbott, Patla, and Jensen, 2001; Collins, Teys, and Vicenzino, 2004; Paungmali, O'Leary, Souvlis, and Vicenzino, 2003; Teys, Bisset, and Vicenzino, 2008; Vicenzino, Paungmali, Buratowski, and Wright, 2001). The

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mechanisms by which MWM achieves pain relief are not well understood; however, biomechanical and neurophysiological mechanisms are probably involved (Vicenzino, Hall, Hing, and Rivett, 2011).

To our knowledge, there have been no reports to date of the effects of MWM on knee pain and disability associated with knee OA. Although a prospective randomized controlled trial (RCT) is the appropriate methodology to investigate treatment effects of MWM on knee OA, it is advantageous to have preliminary evidence of the immediate and short-term positive effects of MWM on knee OA patients both to justify the cost of conducting a formal RCT and to assist the development of a well-designed trial. Thus as this first step, we conducted a prospective case series in which the immediate and short-term effects of MWM on OA knee pain and associated disability were evaluated prior to the introduction of a multimodal program inclusive of exercise at the fourth consultation.

## METHODS

### Patients

This case series reports on 19 patients with knee OA who attended an outpatient clinic at the Shinoro Orthopedic Hospital in Japan over a 2 month period from December 2010 to January 2011. Inclusion criteria for knee OA were grade 2 or 3 knee OA according to the Kellgren and Lawrence (1957) classification. The diagnosis was made by an experienced orthopedic surgeon based on X-ray and MRI findings using a standard classification of knee OA (Altman et al, 1986). The patients agreed to participate in this study before commencing pharmacological pain management and other modalities of management for knee OA. The most painful side was treated with MWM in patients with bilateral knee OA. Ethical principles were followed according to the declaration of Helsinki and all participants provided written informed consent following an explanation about the study.

### Outcome measures

Outcome measures included pain severity during performance of four functional tasks using a visual analog scale (VAS), passive knee joint range of motion (ROM), and level of disability determined by the Activities of Daily Living Scale of the Knee Outcome Survey (KOS-ADLS) Japanese version (Yoshida, Kubo, Irrgang, and Snyder-Mackler,

2010). Pain severity and ROM were evaluated by an independent assessor who remained blinded to the previous scores on the outcome measures. The measures were performed at baseline prior to the intervention on day 1, immediately after treatment on day 1, before the second treatment session and at final follow-up before other modalities were added at the fourth consultation. This allowed us to examine immediate and carry over effect of the initial treatment as well as the effects of MWM in the short-term after three treatments. As the KOS-ADLS asks participants to rate knee symptoms and function over the previous few days, it was not appropriate to administer this questionnaire at the second consultation. Thus, the KOS-ADLS was completed at baseline and at the final follow-up only.

### VAS pain score

A 100-mm VAS (0 mm = no pain, 100 mm = worst pain ever) is considered a valid and reliable measure for pain intensity (Hawker, Mian, Kendzerska, and French, 2011; Sindhu, Shechtman, and Tuckey, 2011; Williamson and Hoggart, 2005) and its test-retest reliability in individuals with knee and hip OA is generally acceptable (intra-class correlation coefficients [ICC] = 0.55–0.89) (Grafton, Foster, and Wright, 2005; Wessel, 1995). Previous studies of knee OA have assessed pain (VAS) during functional tasks, including walking, ascending and descending stairs, and sitting-to-standing (Aglamış, Toraman, and Yaman, 2008; Azlin and Lyn, 2011; Huang et al, 2011; Moss, Sluka, and Wright, 2007) and this measure was adopted in this case series. Hence, patients were asked to rate their knee pain using a VAS, during four tasks undertaken at their usual pace: Task 1 – a 20-m walk test; Task 2 – ascending and Task 3 – descending seven stairs without using a handrail and with alternating steps; and Task 4 – five repetitions of sit-to-stand from a standard height chair with arms folded across their chest.

### ROM

Passive ROM for knee flexion and extension was measured in supine lying using a standard goniometer. A systematic review demonstrated generally acceptable inter-rater reliability (ICC = 0.59–0.90) for this goniometric measurement (van Trijffel, van de Pol, Oostendorp, and Lucas, 2010). In this study, three repetitions were performed in each direction and the average value recorded for analysis.

### KOS-ADLS

The KOS-ADLS is a valid and reliable (test-retest reliability; ICC = 0.97) self-rating questionnaire used

for various painful knee conditions to evaluate symptoms and functional limitations over the previous few days (Irrgang et al, 1998). The symptom section has six questions regarding pain, stiffness, joint swelling, giving way, weakness, and limping. In this section, patients rated their disability level on a 6-point Likert scale (0 = complete loss of function due to the symptoms, 5 = no symptoms). The functional limitation section has eight questions regarding walking, ascending and descending stairs, standing, kneeling, squatting, sitting, and rising from a chair and patients rate their disability level on a 6-point Likert scale (0 = inability to perform it, 5 = no limitation). The total score (KOS-ADLS<sup>total</sup>) is presented in percentiles (0% = the highest disability, 100% = no disability). The KOS-ADLS<sup>total</sup> also reflects psychological reactions such as fear of movement and anxiety (Scopaz, Piva, Wisniewski, and Fitzgerald, 2009). The KOS-ADLS<sup>total</sup> was used as a measure of total disability level in this study and scores of the symptom (KOS-ADLS<sup>symptom</sup>) and functional limitation sub-sections (KOA-ADLS<sup>function</sup>) were used to inform on the levels of symptom and functional limitation, respectively, as secondary measures.

## Intervention

Patients completed a course of therapist and self-applied MWM only for the first three clinic visits. There was a 2–3 day interval between each consultation, and the total duration of the intervention period in this study ranged from 13 to 16 days. At the fourth clinic visit, participants commenced a multimodal program inclusive of therapeutic exercise.

### *Identification of the glide direction for the MWM treatment technique*

A physiotherapist, with 2 years experience in using MWM, applied all treatments for each patient. MWM consisted of a sustained manual glide of the tibia (either medial, lateral, anterior, posterior, or rotation) during active knee flexion and extension. These techniques are described in detail in a textbook of MWM (Mulligan, 2004). Each patient was tested with sustained manual glides in each of the possible directions during active knee flexion and extension in supine lying. Frontal plane glides were tested first and then sagittal plane glides followed by rotation. The glide direction that reduced pain to the minimum level and improved range of knee motion most was chosen as the glide for the MWM treatment technique. Overpressure was included at end range if ROM was pain-free. If pain was not present in

supine lying, then the glide direction for the MWM treatment technique was assessed in a weight-bearing position in a similar manner. If in supine lying more than one glide direction had similar beneficial effects, then these assessments were repeated in weight-bearing to identify the most effective glide direction for the treatment technique.

### *Procedures for the intervention*

At the first consultation, a therapist-applied MWM was performed (two sets of 10 repetitions) during active knee flexion and extension. The therapist initially applied the pain-free manual glide force on the tibia with the knee resting in a mid range position. The glide force was sustained while the patient performed 10 repetitions of self-paced active full range knee flexion and extension. Either of two protocols was used depending on the assessment of the patient's pain during active knee flexion and extension in lying:

1. For patients with pain during active knee flexion and extension in lying, the technique was performed initially in lying. The technique was progressed to weight-bearing positions when the movement in lying became pain-free. The patient was taught a self-applied MWM in weight-bearing position.
2. For patients without pain during active knee flexion and extension in lying, a therapist-applied MWM (two sets of 10 repetitions) was performed in the weight-bearing position. Patients were similarly instructed in the self-applied MWM in the weight-bearing position (Figure 1).

The self-management regime involved at least 20 movement repetitions, performed every 3 hours (or at least four to five times per day). Patients could perform the MWM exercise more frequently if they experienced any increase in pain with daily activities. Patients were also advised to stop the self-applied MWM if this exercise caused pain, or their knee showed signs of increasing inflammation such as swelling, heat, and/or redness greater than pre-treatment levels.

On the subsequent two consultations, the therapist-applied MWM intervention was repeated. Patients were treated in lying if they continued to have pain during movement in the non-weight-bearing position. Otherwise, the therapist-applied MWM was performed in the weight-bearing position. The glide direction was again checked prior to application of the intervention. Patients' self-applied MWM were checked for their correctness at each visit.



FIGURE 1. An example of self-applied mobilization with movement for knee flexion in a weight bearing position (lateral glide in this example). The direction of glide is presented with a red arrow and a fixation point is shown with a blue star.

## Statistical analysis

Outcomes were analyzed using an intention to treat analysis. Preliminary analysis (Shapiro–Wilk test) revealed that data were not normally distributed. Therefore, comparisons of the pain and ROM outcome measures across the assessment points were analyzed using Friedman tests. As therapeutic effects of MWM were expected a priori, one-tailed analyses were used for comparison. The one-tailed Wilcoxon signed-rank test with Bonferroni adjustments was used to examine improvements in pain and ROM between the baseline and each assessment point (three time points). The one-tailed Wilcoxon signed-rank test was also used to analyze KOS-ADLS data. All statistical analyses were performed with SPSS version 19.0 (IBM Corporation, New York, USA). Significance level was set at  $<0.05$ .

## OUTCOMES

Eleven patients began treatment in lying at the initial consultation. After one set of 10 repetitions of the therapist-applied MWM, the technique was progressed to weight-bearing positions in these patients as the movement in lying became pain-free. The other eight patients were treated with a therapist-

TABLE 1. Patients' demographics and the direction of glide chosen for the MWM intervention.

Variables	Patients with knee OA ( <i>n</i> = 19)
Age, mean (SD), years	71.1 (13.9)
Time since diagnosis of OA, mean (SD), months	92.8 (100.8)
Female, <i>n</i> (%)	14 (73.7)
Treated side, right <i>n</i> (%)	16 (84.2)
OA grade <sup>†</sup> , number of grade 2 (%)	9 (47.4)
OA grade <sup>†</sup> , number of grade 3 (%)	10 (52.6)
<i>MWM: glide direction on the tibia</i>	
Lateral, <i>n</i> (%)	9 (47.4)
Lateral + internal rotation, <i>n</i> (%)	2 (10.5)
Lateral + external rotation, <i>n</i> (%)	4 (21.1)
Medial, <i>n</i> (%)	2 (10.5)
Medial + internal rotation, <i>n</i> (%)	2 (10.5)
Anterior, <i>n</i> (%)	0 (0)
Posterior, <i>n</i> (%)	0 (0)

<sup>†</sup>Based on the Kellgren and Lawrence (1957) grading system.

applied MWM in weight-bearing position from the outset. Following the therapist-applied MWM, all patients were instructed a self-applied MWM at the end of the initial consultation.

At each of the following consultations, no patient reported either exacerbation of pain or inflammation following the therapist and self-applied MWM. The 11 patients, who had pain during active knee flexion and extension in lying and therefore began treatment in lying at the initial consultation, had no pain during active knee flexion and extension in lying at the second visit. Hence, all patients were treated in the weight-bearing position. Examination confirmed that the direction of glide applied in the MWM at the initial consultation was appropriate.

Patients' characteristics and the direction of glide applied in the MWM are summarized in Table 1. There were no complications arising from the MWM intervention. All patients completed each treatment session (no drop-outs). All patients verbally reported that they had undertaken the prescribed self-applied MWM home exercise program.

## VAS pain score during functional tasks

Table 2 presents the mean (SD) values of the pain VAS scores in the four tasks over the four assessment points. Significant time effects ( $P < 0.001$ ) were detected. The pain VAS scores were significantly lower than baseline over all assessment points in each task (all  $P < 0.001$ ). The greatest change occurred immediately after the first treatment and pain was minimal at the final assessment.

TABLE 2. 100-mm VAS during four tasks over the four assessment points and statistical outcomes.

Measures	Assessment 1 Baseline	Assessment 2 Immediately after treatment 1	Assessment 3 Prior to treatment 2	Assessment 4 Exit at fourth consultation	<i>P</i> -value*	<i>P</i> -value <sup>†</sup> [Z-score]
Walking	31.3 (23.6)	3.9 (4.6)	2.9 (5.4)	1.3 (2.8)	<0.001	Assessment 1 <i>vs.</i> Assessment 2; <0.001 [3.5] Assessment 1 <i>vs.</i> Assessment 3; <0.001 [3.5] Assessment 1 <i>vs.</i> Assessment 4; <0.001 [3.5]
Ascending stairs	45.0 (21.5)	8.9 (11.6)	5.5 (8.3)	1.1 (2.7)	<0.001	Assessment 1 <i>vs.</i> Assessment 2; <0.001 [3.6] Assessment 1 <i>vs.</i> Assessment 3; <0.001 [3.7] Assessment 1 <i>vs.</i> Assessment 4; <0.001 [3.7]
Descending stairs	50.5 (19.5)	10.3 (17.5)	8.9 (18.6)	2.6 (5.6)	<0.001	Assessment 1 <i>vs.</i> Assessment 2; <0.001 [3.8] Assessment 1 <i>vs.</i> Assessment 3; <0.001 [3.8] Assessment 1 <i>vs.</i> Assessment 4; <0.001 [3.8]
Sit-to-stand	32.6 (21.6)	4.5 (7.8)	6.1 (13.5)	0.3 (1.1)	<0.001	Assessment 1 <i>vs.</i> Assessment 2; <0.001 [3.4] Assessment 1 <i>vs.</i> Assessment 3; <0.001 [3.2] Assessment 1 <i>vs.</i> Assessment 4; <0.001 [3.4]

Note: Mean (SD) values in millimeter are presented.

\*Friedman test.

<sup>†</sup>One-tailed Wilcoxon signed-rank test with Bonferroni adjustments (significant level < 0.05/3 = 0.017).

### Passive knee ROM

Table 3 presents the mean (SD) values for knee flexion and extension range. Significant time effects ( $P = 0.007$ ) were detected in knee flexion ROM.

The one-tailed Wilcoxon signed-rank tests demonstrated that there was significant improvement from baseline in knee flexion ROM immediately after the initial treatment ( $P = 0.012 < 0.05/3$ ) and at the final assessment point ( $P = 0.013 < 0.05/3$ ). However,

TABLE 3. Knee ROM over the four assessment points and statistical outcomes.

Measures	Assessment 1 Baseline	Assessment 2 Immediately after treatment 1	Assessment 3 Prior to treatment 2	Assessment 4 Exit at fourth consultation	<i>P</i> -value*	<i>P</i> -value <sup>†</sup> [Z-score]
Flexion	123.2 (10.6)	126.3 (7.6)	125.8 (8.0)	127.1 (7.1)	0.007	Assessment 1 <i>vs.</i> Assessment 2; 0.012 [2.3] Assessment 1 <i>vs.</i> Assessment 3; 0.042 [1.7] Assessment 1 <i>vs.</i> Assessment 4; 0.013 [2.2]
Extension	4.2 (7.1)	1.8 (4.2)	3.4 (7.5)	2.9 (7.3)	0.059	–

Note: Mean (SD) values in degree are presented.

\*Friedman test.

<sup>†</sup>One-tailed Wilcoxon signed-rank test with Bonferroni adjustments (significant level < 0.05/3 = 0.017).

TABLE 4. KOS-ADLS at baseline and the exit and statistical outcomes.

Measures	Assessment 1	Assessment 4	<i>P</i> -value* [Z-score]
	Baseline	Exit at fourth consultation	
KOS-ADLS <sup>total</sup>	67.1 (16.6)	86.3 (12.6)	<0.001 [3.8]
KOS-ADLS <sup>symptom</sup>	79.9 (13.7)	96.0 (5.2)	<0.001 [3.8]
KOA-ADLS <sup>function</sup>	57.5 (22.4)	79.3 (18.6)	<0.001 [3.6]

Note: Mean (SD) values in percentile are presented.

\*One-tailed Wilcoxon signed-rank test (significant level < 0.05).

significant time effects were not detected in knee extension ROM ( $P = 0.059$ ).

## KOS-ADLS

Table 4 presents the mean (SD) values for the KOS-ADLS<sup>total</sup>, KOS-ADLS<sup>symptom</sup>, and KOA-ADLS<sup>function</sup>. Analysis revealed that the KOS-ADLS<sup>total</sup> and its components, KOS-ADLS<sup>symptom</sup> and KOA-ADLS<sup>function</sup> improved significantly from baseline ( $P < 0.001$ ).

## DISCUSSION

This short-term prospective case series revealed that MWM was associated with an immediate reduction in pain during performance of functional tasks. Such positive effects are similar to those reported for MWM administered for other extremity joint problems (Backstrom, 2002; O'Brien and Vicenzino, 1998; Paungmali, Vicenzino, and Smith, 2003; Vicenzino and Wright, 1995). Pain intensity scores in the functional tasks were minimal on presentation for the fourth consultation, representing changes from baseline ranging from 30 to 48 mm on the VAS, which are clinically relevant improvements (Grafton, Foster, and Wright, 2005).

Interestingly, the greatest reduction in pain occurred after the initial treatment application. The reduction was maintained until the second consultation. Pain continued to decline after treatments 2 and 3 and most subjects had minimal or no pain on their final assessment. However, the changes in pain between these subsequent assessment points were minimal. The reduction in pain intensity and its maintenance probably reflects a combination of the effect of the therapist and patient-applied MWM, but we are unable to separate the effects in this instance.

Nevertheless, the pain-relieving effect of MWM for knee OA achieved predominantly at the initial application, suggests that MWM could be applied at the first treatment session to reduce pain and that exercise programs may be able to be commenced at the second consultation. The pain relief afforded by MWM might limit its de-motivating effects (Fraenkel and Fried, 2008) to start exercise and would position the patient well to undertake exercise programs, which are recommended for the management of knee OA (Altman, Hochberg, Moskowitz, and Schnitzer, 2000; Roddy et al, 2005). It would be interesting to compare recovery time and compliance with exercise programs between a management plan where MWM is performed for one or two sessions to decrease pain prior to starting exercise and a plan where MWM treatment and the exercise program both start at the initial visit.

The treatment with MWM resulted in significant improvement in KOS-ADLS scores. The KOS-ADLS scores at baseline are consistent with other reports of disability in knee OA patients (Courtney et al, 2009; Piva et al, 2004; Zeni, Axe, and Snyder-Mackler, 2010; Zeni and Snyder-Mackler, 2010). Scores following the three treatments were representative of normal or nearly normal functional levels (Irrgang et al, 1998) and were comparable with those documented following surgery for knee OA (Briem et al, 2007; Mizner et al, 2005) or knee hyaluronic acid injections (Briem, Axe, and Snyder-Mackler, 2009). Changes of the mean KOS-ADLS<sup>total</sup> values were 19.2 in this study. Irrgang et al (1998) showed that patients who achieved great improvements and somewhat improvements on a 5-point global perceived change after 4-week physiotherapy had mean changes of approximately 25 and 11, respectively. Thus, the treatment with MWM resulted in clinically relevant improvement in disability due to knee pain and malfunction.

The mechanisms by which MWM achieves pain relief are not well understood, however biomechanical and neurophysiological mechanisms may be involved (Vicenzino, Hall, Hing, and Rivett, 2011). Biomechanically it was initially proposed that MWM may address joint partner bone alignment (i.e., positional fault) (Mulligan, 2004) and some observations of positional faults have been made (Hsieh et al, 2002; Hubbard and Hertel, 2008; Hubbard, Hertel, and Sherbondy, 2006). However, there is currently insufficient evidence to support correction of a positional fault as the mechanism of action for pain relief following MWM (Vicenzino, Paungmali, and Teys, 2007). Potential neurophysiological mechanisms include changes in descending pain inhibitory systems (Paungmali, O'Leary, Souvlis, and Vicenzino, 2004;

Paungmali, Vicenzino, and Smith, 2003; Skyba et al, 2003), and changes in central pain-processing mechanisms (Hall, Hardt, Schafer, and Wallin, 2006; Paungmali, O'Leary, Souvlis, and Vicenzino, 2004; Sterling et al, 2010). In addition, the large range movement used in the application of MWM with our patients might alter concentrations of inflammatory mediators (Schmidt, 1996) and result in deactivation of silent/sleeping nociceptors activated by such inflammatory mediators (Sambajon, Cillo, Gassner, and Buckley, 2003).

While the pain relief afforded by MWM would be associated with improvements of disability level (Schein et al, 2008), other factors may also contribute to the immediate improvements in disability level following MWM. The MWM was largely conducted in a weight-bearing position and patients received simultaneous feedback of painless joint movements. This feedback might modulate psychological features such as fear of movements (Vicenzino, Hall, Hing, and Rivett, 2011), resulting in an increased activity level. In addition, MWM in a weight-bearing position requires muscle activity, which might have resulted in improved motor performance, which would position the patient well to gain long-term benefits from a formal exercise program. Further research into the possible psychological and motor benefits of MWM is required.

Knee flexion ROM improved from baseline at post initial treatment and the final assessment point but there was no statistically significant change in knee extension ROM across the four assessment points. Generally, knee ROM appeared to improve less than improvements in pain and disability. This may reflect the small number of patients who presented with limited passive knee ROM in our group (8/19 and 6/19 were regarded clinically as having limited knee flexion and extension, respectively). Knee ROM was assessed in supine lying rather than in a weight-bearing position. Perhaps, if assessment had been undertaken in a functional weight-bearing position, greater limitation and changes of movement might have been detected. Such measures might be more useful than our measure of passive ROM in future studies of treatment effects.

In our cases, there were no patients who responded to an anterior or posterior glide. This finding corresponds with the clinical experience of Mulligan, who mentioned that the typical direction of beneficial glide for hinge joints was usually medial or lateral (Mulligan, 2004). However, the explanation why anterior or posterior glides are not beneficial for patients with knee OA remains unclear.

Case series represent one of the lowest levels of evidence. One limitation is the potential for bias

within the sample population who were not randomly selected and the lack of a control group. Our patients may not represent the entire population of people with knee OA and effects may have reflected, for example, patients' positive responses arising from their decision to consult an orthopedic surgeon for their knee pain. Such factors underpin the need for a formal RCT. Nevertheless, this case series has demonstrated the potential benefit of MWM for knee OA sufficiently we believe to justify a future RCT. In addition, outcomes also point to the need for future research into the mechanisms of action of MWM.

A multimodal treatment approach incorporating manual therapy, muscle strengthening, stretching, ROM, and home exercise has been shown to be beneficial for the long-term recovery of knee function and reduction of pain (Deyle et al, 2000, 2005, 2012; Jansen et al, 2011; Ko, Lee, and Lee, 2009). Given the effective pain relief associated with MWM in our cases, further studies could not only explore the most optimal application of joint mobilization for relief of knee OA pain but also investigate the inclusion of MWM into promising comprehensive management approaches for this chronic and widespread condition.

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