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Treatment using 448 kHz capacitive resistive monopolar radiofrequency improves pain and function in patients with osteoarthritis of the knee joint: A randomised controlled trial

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Abstract

Objective: This study investigated whether capacitive resistive monopolar radiofrequency (CRMRF)-based treatment improves pain and function among patients with osteoarthritis of the knee.

Design and setting: Three-group randomised controlled trial with concealed allocation, participant blinding and intention-to-treat analysis. Forty-five patients diagnosed with osteoarthritis, from the waiting list for physiotherapy at a local hospital were enrolled.

Intervention: Participants in the active and sham groups received eight sessions of CRMRF and sham-CRMRF respectively over four weeks, along with standard care. The control group received standard care only.

Assessment: Pain and function were measured at four time points: week zero (baseline), week four (post intervention), week eight and week 16 (two follow-ups) using visual analogue scale (VAS), Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index, timed up and go (TUG) test and knee range of motion (ROM).

Results: For pain (VAS), there were clinically significant changes in the active group at post treatment compared to sham (effect size: 1.3, 95% CI: 0.29–1.3) and control (effect size: 1.5, 95% CI: 0.32–1.3), and at one-month follow-up compared to control (effect size: 1.1, 95% CI: 0.10–1.3). For function (WOMAC), there was clinically significant change in the active group at post treatment compared to control (effect size: 0.94, 95% CI: 0.02–2.6), but not compared to sham. No meaningful differences were noted for TUG or knee ROM. No differences were noted at three-month follow-up for any outcomes.

Conclusion: CRMRF treatment can improve pain and function in patients with knee osteoarthritis in the short term.

Trial registration: NIHR-CRN study ID: 20264.

Contribution of the paper:

- The study demonstrated significant short-term improvements of pain and function in OA knee with a four-week CRMRF intervention when compared to sham and current standard departmental care.
- The study highlights the potential benefits of this relatively underused RF-based EPA in the management of OA knee and provides baseline data for future research.

Key words: Electrophysical agents; Radiofrequency treatment; Osteoarthritis of knee; Joint pain; Functional quality of life.

Introduction

Osteoarthritis (OA) is the commonest form of arthritis among people of all ethnicities and a leading condition affecting function and quality of life (QoL) among middle-aged and older adults.[1-3] Data suggest that about 40% of adults aged over 65 years may be affected by OA of hip or knee, OA knee being more prevalent.[4,5] Together they cause significant economic burden.[1,6] Reflecting on accepted clinical practice, the guidelines published by the American College of Rheumatology classified OA knee as a clinical syndrome in older adults characterised by knee pain, morning stiffness and crepitus.[7,8] The pain can be felt during activity or while resting and is often poorly localised. As it progresses, functional ability and QoL diminish and the individual may develop physical deformities.[1,9]

Since there is no cure for OA, current treatment plans are aimed at symptom management, improving function and enhancing QoL thereby delaying or avoiding invasive procedures such as total knee replacement (TKR).[10] With a rapidly growing evidence-base for OA, updated clinical guidelines emphasise on the importance of non-drug non-surgical treatments such as physiotherapy.[11-13] Exercise therapy is recommended by all clinical guidelines and recent reviews.[14-16] Nonetheless, there is no consensus on the optimal content of an exercise-programme.[17] Moreover, exercise alone may not be adequate in the long term since their benefits may diminish over time especially given the relatively modest treatment effect sizes reported.[14,18] The NICE guidelines in the UK states that therapeutic heat should also be considered for OA to improve the outcomes.[19]

Half of all non-pharmacological interventions suggested by European League against Rheumatism (EULAR) as potential treatments for OA knee are electrophysical agents (EPAs) such as laser, transcutaneous electrical nerve stimulation (TENS), ultrasound and pulsed electromagnetic fields (PEMF & pulsed shortwave therapy (PSWT)).[20] Bjordal and colleagues[21] questioned EULAR for the lack of recommendation for EPAs for OA knee management despite their same level of evidence as certain analgesics such as paracetamol, opioids and coxibs. The effect of shortwave therapy (SWT) on OA knee was also demonstrated in a recent review.[22]

Besides SWT which commonly operates at 27.12 MHz, other radiofrequency (RF)-based EPAs employing significantly lower operating frequencies (<1 MHz) have also been reported for the treatment of OA knee, despite their evidence base being minimal.[22,23] Capacitive Resistive Monopolar Radiofrequency (CRMRF) that operates at 448 kHz is an example. This mode of therapy is relatively new, but its clinical use is reported worldwide. The CRMRF differs from SWT mainly in two ways – firstly the operating frequency and secondly, unlike SWT it is applied using a coupling medium since CRMRF cannot be transmitted through air. Hence, one assumed advantage of CRMRF over SWT is that there is potentially considerably lower scattering of RF waves.

Studies conducted by the same authors on asymptomatic adults obtained a significantly more pronounced skin[24,25] and deep[26] physiological response from CRMRF when compared to PSWT. It was anticipated that such physiological response may lead to more pronounced clinical benefits. In this study the authors aimed to investigate the potential clinical benefits of 448 kHz CRMRF on pain and functional QoL among patients affected by chronic OA of the knee joint(s).

Method

Design

A placebo-controlled participant-blinded randomised controlled trial was conducted to address the aim. The study lasted four months with one-month intervention and three-month follow-up, and involved an experimental group, control group and a sham group. The patients were randomly allocated to one of the three study groups at the time of recruitment using computer generated block randomisation tables.^a The allocation was blinded by concealment using sealed envelopes; however, after allocation the study was not blinded for assessment since the same researcher carried out both intervention and assessments. All participants were assessed four times: pre-treatment (week zero), post treatment (week four), one-month post-intervention follow-up (week eight) and three-month post-intervention follow-up (week 16). The basic study design is illustrated in Figure 1. The ethics approval was granted by the NRES Committee North West - Greater Manchester South of the NHS UK Health Research Authority (HRA). The study was registered

with the National Institute of Health Research (NIHR) Clinical Research Network (CRN) (study ID: 20264).

Participants, clinicians and centres

This single-centre study involving one clinician (BK) was set at the Safari Therapy Unit, Hemel Hempstead General Hospital, Hemel Hempstead, (Hertfordshire Community NHS Trust, UK). Adult patients on the waiting list for physiotherapy treatment for OA knee were invited in writing seeking participation. Inclusion criteria were: symptomatic for a minimum of six months; and a prior clinical and/or radiological diagnosis of OA knee meeting the American College of Rheumatology criteria.[27] Exclusion criteria were: contra-indications to RF-based treatment (pregnancy, active cancer or malignancy, active tuberculosis, metal implant in the affected knee, pacemaker or other sensitive electronic implants present), significant comorbidities such as neurological impairment, active skin lesions around the affected knee, known hypersensitivity to heat, invasive treatment such as joint injections or surgical procedures within the last three months, invasive procedures planned during the study period, inability to attend the hospital for intervention or assessments and inability to sign informed consent. The participants were not required to make any changes to their normal lifestyle, medications, activities or exercising (or not) routine as a prerequisite to taking part in this study.

An a priori sample size analysis was not undertaken as no equivalent published data concerning the use of CRMRF on patients with OA knee was available.

Interventions

The active and sham groups received eight sessions of CRMRF and sham CRMRF treatments respectively in four weeks and current standard departmental treatment for OA knee. During the same period, the control group only received three sessions comprising the standard treatment currently followed in the department. Since the active and control groups received dissimilar number of treatment sessions, it raises the issue of non-equivalence between the groups. However, if the number of sessions for the control group was increased to match that of the active group it would not have reflected current

departmental care policy. Similarly, the active group number of sessions could not be reduced to match the control group since it would have been insufficient.

The CRMRF intervention

The CRMRF at 448 kHz was delivered using 'Indiba Activ 902',^b a new factory calibrated device with a peak power of 200 W, which delivered continuous-wave RF in two modes: Capacitive (CAP) and Resistive (RES), using metallic electrodes via a coupling medium. A moderately thermal dose of CRMRF was delivered to the active group participants. The intensity of delivery was adjusted according to patient feedback on their perception of moderate heating, based on previous experimentation.[26] Fifteen minutes of treatment comprising five minutes CAP and 10 minutes RES was delivered twice a week for four consecutive weeks providing eight sessions in total. The treatment was delivered to the whole knee joint area, although emphasis was given to the more symptomatic areas. The return electrode was placed under the calf one-fourth way down the distance between the fibular head and the lateral malleolus.

The sham CRMRF intervention

An additional sham setting was integrated into the device by the manufacturer for this study. The treatment technique was similar to the active intervention except that no verbal feedback was sought from the participants since there was no energy delivery. The machine display was identical in both active and sham modes.

Current standard departmental treatment

By default, all participants received the current evidence-based physiotherapy care offered by the department to patients with OA knee. This included tailored advice, education and home/gym-based prescription exercises. Participants were given this on their first visit. They were instructed to perform the exercise sets once a day. Subsequently, they were reviewed and re-emphasised at the second visit for the control group and fourth visit for the others. The exercises included open and closed chain knee ROM and strengthening exercises, and tailored gym-based tasks such as using a static bike. The advice included restricting activities

that place excessive load and shear forces on the knee. The participants were also urged to use proper supportive footwear while walking.

Outcome measures

Self-reported pain

Pain was rated using a self-administered visual analogue scale (VAS). The level of pain was reported as 'pain over the last 24 hours' on a 10 cm VAS; and rated from 0–10, where 0 meant 'no pain' and 10 meant 'worst imaginable pain'. VAS is a reliable and valid tool for measuring pain.[28,29] A reduction in pain by around 1.9–2.0 out of 10 (19–20%) is generally accepted as its minimum clinically important difference (MCID).[30,31]

WOMAC osteoarthritis index

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) global score was used for the assessment of functional QoL.[32] The WOMAC is a questionnaire that assesses the levels of pain, stiffness and physical function in patients with OA of the hip/knee. The index consists of 24 items based on symptoms and physical function, divided into three subscales of pain, stiffness and physical function. The items were scored using five-point Likert scales with the responses ranging from 'none' to 'extreme'. A 16% reduction from the baseline WOMAC global score is considered its MCID.[33,34] The questionnaire is among the most widely used outcome measures in OA research with proven psychometric properties.[32,35]

Walking ability

Walking ability was assessed using Timed Up and Go (TUG) test.[36] The test measures the time taken to rise from sitting on a standard chair, walk three metres in a straight line, turn around, walk back and sit again. The participants were given standard instructions on how to perform the task at their normal speed when the assessor asks them to start. Walking aid was allowed if they used one. TUG is used widely in arthritic population, with proven psychometric properties.[37,38]

Knee joint range of movement

Active knee joint active ROM, within their level of pain, was measured using a universal goniometer with the participant positioned in supine. Assessor measured the flexion and extension using the greater trochanter, lateral condyle of the femur, head of the fibula and lateral malleolus as bony landmarks. For the analysis, ROM was taken as the total of flexion and extension movements. Universal goniometry is a valid and reliable tool widely used to obtain instant measure of joint ROM.[39]

Physiological and other measurements

Blood pressure (BP) and pulse rate (PR) were monitored using a digital BP monitor^c and core temperature using an infra-red (IR) tympanic thermometer.^d A body composition monitor^e was used to obtain the anthropometric data. Room temperature and humidity were monitored using an electronic thermohygrometer.^f These measures enabled to monitor the impact of CRMRF on systemic physiological responses as well as the influence of intrinsic and extrinsic factors on the treatment outcome.

Procedure

Informed consent was signed by both parties before the start of the study. Subsequently, their skin thermal sensitivity to heat and cold was tested using test tubes filled with water at different temperatures. A brief description about the assessment and treatment procedure was provided depending on their group allocation. The description for the active and sham groups remained the same. Then, the assessment data was collected in the following order: 1. Demographic and anthropometric data. 2. TUG test. 3. VAS and WOMAC. 4. Knee ROM. Subsequently the intervention was delivered.

If any CRMRF session was missed, the intervention was extended to complete all planned sessions. If more than two CRMRF sessions were missed (>25% of sessions) the intervention was considered invalid. If any control group participant missed their second session, they were contacted by phone to discuss any concerns and to reinforce the treatment. At sessions 2–7, the active/sham participants attended the clinic to receive their 15-minute CRMRF intervention. At session 8, all participants underwent the post treatment

assessments. All participants were advised to continue with the home exercises and self-management at least until the second follow-up.

Data analysis

The group data were compared on an intention to treat (ITT) basis using a mixed model analysis of variance (ANOVA)^a at four within-group time points: baseline, post treatment, one-month follow-up, three months follow-up, and three between-group conditions: active, sham, control. Where the data exhibited deviation from normality and/or inequality of variances, square root transformation of the data was performed before the analysis. The treatment effect sizes were determined using the Hedges' *g*. The statistical significance was set at $p \leq 0.05$ (0.8 P, 95% CI).

Results

Participant flow and baseline characteristics

The flow of participants through the study is shown in Figure 1. Two participants from the control group whose symptoms deteriorated due to unrelated causes and one participant from the sham group who lost interest withdrew from the study during the intervention phase. Hence 42 participants (93%) completed the study. All interventions and assessments were well tolerated with no reports of adverse events that might be a consequence of the intervention, including potential CRMRF-induced overheating. Good compliance was reported with the exercise intervention.

****Insert Figure 1 here****

The demographic and the mean (SD) anthropometric data are reported in Table 1. There were no significant differences between the groups in any characteristic.

****Insert Table 1 here****

CRMRF treatment dose

The mean (SD) CAP, RES and total dose received by the participants in the active group over the eight sessions were 17.3 (1.4) W, 61.1 (5.8) W and 46.5 (4.1) W respectively. The mean doses delivered over the eight sessions did not vary significantly.

Self-reported pain

Group-wise mean (SD) 24-hour pain results are plotted in Figure 2. Statistical analysis (4*3 mixed methods ANOVA (time, group)) revealed a significant main effect for time (within-group change) ($F(2.1, 88) = 16, p < 0.001$) and a significant interaction between group and time ($F(4.2) = 5.2, p = 0.001$). Therefore, the type of intervention made a significant difference to the reported pain scores and there was a significant overall difference between pre, post, and one-month and three-month follow-up pain scores. The baseline pain scores were not significantly different. Results of pairwise comparisons that showed a significantly more pronounced effect in the active group, both within and between groups are reported in Tables 2 & 3 respectively.

****Insert Figure 2 here****

****Insert Table 2 here****

****Insert Table 3 here****

WOMAC osteoarthritis index

Group-wise mean (SD) WOMAC global scores are plotted in Figure 3. Statistical analysis revealed a significant main effect for time ($F(2.2, 91) = 18, p < 0.001$) and a significant interaction between group and time ($F(4.3) = 2.7, p = 0.031$). Therefore, like the pain scores the type of intervention made a significant difference to the reported results and there was a significant overall difference between pre, post, and one-month and three-month follow-up WOMAC global scores. The baseline scores were not significantly different. Results of pairwise comparisons that showed a significantly more pronounced effect in the active group, both within and between groups are reported in Tables 2 & 3 respectively.

****Insert Figure 3 here****

Walking ability

Group-wise mean (SD) TUG scores are plotted in Figure 4. Statistical analysis revealed a significant main effect for time ($F(2, 85) = 15, p < 0.001$); however, there was no significant interaction between group and time. Therefore, unlike the two outcomes reported above the type of intervention did not make a significant difference to the reported TUG scores, but there was a significant overall difference between pre, post, and one-month and three-month follow-ups. The baseline TUG scores were not significantly different. Results of within groups pairwise comparisons are reported in Table 2.

****Insert Figure 4 here****

Knee joint ROM

Group-wise mean (SD) knee ROM values are plotted in Figure 5. Statistical analysis revealed a significant main effect for time (within-group change) ($F(3, 126) = 9.1, p < 0.001$) and a significant interaction between group and time ($F(6) = 2.6, p = 0.023$). Therefore, the type of intervention made a significant difference to the observed knee ROM and there was a significant overall difference between pre, post, and one-month and three-month follow-up knee ROM. The baseline knee ROMs were not significantly different. Although there was a significant main effect for the interaction between time and group, pairwise comparisons did not reveal any significant interactions between any of the groups. Results of within-group pairwise comparisons are reported in Table 2.

****Insert Figure 5 here****

Post-hoc power and sample size calculation

Based on the obtained effect sizes for the VAS and WOMAC global scores, a total of 42 participants were required to demonstrate a statistically and clinically significant difference with 95% confidence and 80% power.^g Allowing for a drop-out of 20%, it was anticipated that 17 participants would be needed per group. With a total sample of 45, the sample size requirements for a power of 0.8 for all ANOVA main effects and interactions were met.

Discussion

This study investigated the effects of 448 kHz CRMRF on the clinical outcomes of patients affected by chronic OA of the knee, which to the authors' knowledge is the first such study. The results revealed significant improvements in OA-related pain and function in participants treated with active CRMRF in addition to exercise and advice, when compared to those who were treated with exercise and advice only. The fact that the sham group also improved at a greater rate than the control group notwithstanding the effect size being smaller than that of the active treatment indicated the presence of a placebo effect. This is unsurprising given that significant placebo effect may normally exist with perceived intervention, mainly due to expectation.[40]

The active group reported 66% reduction in pain from baseline to post treatment, 45% of which was sustained at the three-month follow-up. In contrast, the control group only reported 8% reduction in pain from baseline to post treatment, which improved to 12% at three-month follow-up. The sham group demonstrated a reduction in pain of 16% and 21% respectively for the same time points. It should be noted that only the pain reduction results in the active treatment group reached the MCID. Similarly, the active group reported 45% reduction in the WOMAC global score from baseline to post treatment, 38% of which was sustained at the three-month follow-up. These were significantly higher than the minimal post treatment change noted in the control group (4%); however, not significantly different to the changes at the follow-up in control group or any time points in the sham group, which were between 20–30%.

The two other outcome measures on walking ability and knee ROM only provided limited information regarding the usefulness of CRMRF for OA knee. TUG produced evenly matched results in all three groups with no significant difference between them although the overall trend showed significant improvements within all three groups. However, none of the results reached the proposed MCID. Knee ROM results were highly significant within the active group, but not within the other two groups. Based on verbal feedback, all patients in the active group could reduce their pain medication intake and many who were being considered for invasive procedures by their consultant were able to postpone the same.

Medication use in the remaining two groups either increased or remained unchanged (medication use was not documented as an outcome in the study).

The results from the participants who gained a greater reduction in pain and hence a greater improvement in physical function suggested that they could be more functionally active. Since pain relief and commensurate improvements in function were noted in the actively treated group in the short term, it is proposed that the CRMRF energy may potentially have promoted an anti-inflammatory effect in the articular and/or periarticular tissues. However, the decline in the effects a few weeks after treatment suggests that any such benefits might not be permanent. Besides, participants' increase in function may also have led to a return of symptoms in the weeks following the end of treatment (bounce back effect).

The findings from this study are limited to a moderately thermal dose of CRMRF application based on participant perception. It is likely that the clinical effects demonstrated were linked to the applied dose (dose-response relationship); however, this can only be confirmed with studies that employ contrasting treatment doses. A dose-response relationship for contrasting doses of CRMRF was demonstrated in the laboratory studies on asymptomatic adults that were reported earlier.[24,26] It remains a realistic possibility in clinical populations too.

On the final visit, all participants were asked to identify the study group they were allocated to, based on their perception about the treatment they received. Four participants (27%) in the active group were unsure what treatment they received. The remaining 11 participants believed they received the active CRMRF intervention. Eight participants (53%) from the sham group could not identify their treatments correctly. The others said they thought they had received the sham mainly due to their lack of improvement in the symptoms. Hence, participant blinding, which is challenging for such interventions, was only moderately achieved.

This study included adult participants regardless of age or gender and did not exclude any based-on OA in other joints. Such broad inclusion criteria may have acted as a confounder, but it has potentially made the study more reflective of real clinical world. Future research

should test CRMRF against other interventions, be double-blinded and investigate whether providing periodic follow-up treatment sessions (maintenance dose) would enhance and/or consolidate the obtained benefits. Further research should also investigate on the optimum dosing and intervention parameters. To understand the potential changes to the tissues in response to CRMRF treatment, future studies should consider employing outcome assessments that can monitor the changes in deeper tissues.

In summary, the study found that the treatment of OA with a moderately thermal dose of CRMRF produced clinically significant improvements in pain and functional QoL in the short term, which was significantly more pronounced than those obtained with current standard departmental treatment or a sham.

Ethics approval: NRES Committee North West - Greater Manchester South, NHS UK Health Research Authority (HRA). REC reference: 15/NW/0529.

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Footnotes: ^aIBM SPSS Statistics (Version 20), IBM Corporation, USA; ^bIndiba S. A., Barcelona, Spain; ^cOmron M2, Omron Healthcare Europe B.V., Netherlands; ^dBraun ThermoScan IRT 4520, Braun GmbH, Germany; ^eOmron BF508, Omron Healthcare Europe B.V., Netherlands; ^fRS 212-124, RS Components Pte Ltd., Singapore; ^gG*Power 3.1, University of Düsseldorf, Düsseldorf, Germany.

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Table 1: Demographic and mean (SD) anthropometric data from the 45 study participants

Study Group	Demographic data				Mean (SD) anthropometric data			
	Mean (SD) age (years)	Males	Females	Mean (SD) OA duration (years)	Height (m)	Weight (kg)	Body fat (%)	BMI
CRMRF	63 (10)	6	9	5.6 (4.1)	1.67 (0.10)	88 (17)	39 (7.6)	31 (3.8)
CRMRF Sham	63 (10)	6	9	4.3 (3.9)	1.63 (0.09)	82 (17)	38 (13)	31 (5.6)
Control	60 (6.2)	6	9	6.0 (5.7)	1.67 (0.07)	96 (16)	42 (8.5)	34 (5.7)

CRMRF – capacitive resistive monopolar radiofrequency; OA – osteoarthritis; BMI – body mass index

Table 2: Within-group comparisons from the three study groups on the four outcome measures

Outcome measure	Group	Baseline to post treatment			Baseline to one-month FU			Baseline to three-month FU		
		Mean* difference	Confidence interval (95%)	Effect size** (Hedges's g)	Mean* difference	Confidence interval (95%)	Effect size** (Hedges's g)	Mean* difference	Confidence interval (95%)	Effect size** (Hedges's g)
Pain	Active	1.2	0.81 to 1.5	2.5	1.1	0.63 to 1.5	1.9	0.76	0.18 to 1.3	1.4
	Sham	0.25	- 0.10 to 0.61		0.44	0.00 to 0.88	0.79	0.43	- 0.15 to 1.0	
	Control	0.11	- 0.25 to 0.47		0.15	- 0.29 to 0.59		0.30	- 0.28 to 0.88	
WOMAC	Active	1.9	1.1 to 2.8	1.5	2.2	1.2 to 3.1	1.7	1.7	0.41 to 2.9	1.2
	Sham	0.98	0.16 to 1.8	0.79	1.1	0.14 to 2.0	0.74	1.4	0.15 to 2.7	0.84
	Control	0.09	- 0.73 to 0.92		0.71	- 0.24 to 1.7		1.1	- 0.20 to 2.3	
Walking ability	Active	0.17	0.05 to 0.28	0.72	0.23	0.09 to 0.37	1.1	0.14	- 0.05 to 0.33	
	Sham	0.15	0.03 to 0.26	0.41	0.16	0.02 to 0.30	0.39	0.15	- 0.04 to 0.34	
	Control	0.14	0.02 to 0.25	0.33	0.18	0.04 to 0.32	0.45	0.16	- 0.03 to 0.35	
Knee ROM	Active	0.48	0.16 to 0.79	0.81	0.55	0.19 to 0.91	0.91	0.29	- 0.06 to 0.64	
	Sham	0.06	- 0.26 to 0.37		0.24	- 0.12 to 0.60		0.22	- 0.14 to 0.57	
	Control	0.02	- 0.30 to 0.34		0.17	- 0.20 to 0.53		0.26	- 0.09 to 0.61	

* Mean difference of the transformed (square root) data

** Effect sizes are reported only where the interaction was statistically significant at $p \leq 0.05$

WOMAC – Western Ontario and McMaster universities osteoarthritis index; ROM – range of motion; FU – follow-up

Table 3: Between-group comparisons from the three study groups on the four outcome measures

Outcome measure	Time points	Active versus control			Active versus sham			Sham versus control		
		Mean* difference	Confidence interval (95%)	Effect size** (Hedges's g)	Mean* difference	Confidence interval (95%)	Effect size** (Hedges's g)	Mean* difference	Confidence interval (95%)	Effect size** (Hedges's g)
Pain	Post treatment	0.82	0.32 to 1.3	1.5	0.79	0.29 to 1.3	1.3	0.03	- 0.47 to 0.53	
	One-month FU	0.68	0.10 to 1.3	1.1	0.50	- 0.08 to 1.1		0.17	- 0.41 to 0.75	
	Three-month FU	0.22	- 0.54 to 0.98		0.20	- 0.56 to 0.97		0.01	- 0.75 to 0.77	
WOMAC	Post treatment	1.3	0.02 to 2.6	0.94	1.0	- 0.27 to 2.3		0.29	0.99 to 1.6	
	One-month FU	0.89	0.53 to 2.3		1.1	- 0.30 to 2.5		0.21	- 1.2 to 1.6	
	Three-month FU	0.06	- 1.8 to 1.9		0.30	- 1.5 to 2.1		0.24	- 1.6 to 2.1	
Walking ability	Post treatment	0.15	- 0.12 to 0.42		0.18	- 0.09 to 0.45		0.03	- 0.24 to 0.30	
	One-month FU	0.17	- 0.11 to 0.46		0.23	- 0.05 to 0.51		0.06	- 0.22 to 0.34	
	Three-month FU	0.10	- 0.24 to 0.44		0.15	- 0.20 to 0.49		0.05	- 0.30 to 0.39	
Knee ROM	Post treatment	0.18	- 0.35 to 0.71		0.24	- 0.29 to 0.77		0.06	- 0.47 to 0.59	
	One-month FU	0.11	- 0.38 to 0.61		0.13	- 0.37 to 0.62		0.02	- 0.48 to 0.51	
	Three-month FU	0.25	- 0.24 to 0.73		0.11	- 0.38 to 0.59		0.14	- 0.35 to 0.62	

* Mean difference of the transformed (square root) data

** Effect sizes are reported only where the interaction was statistically significant at $p \leq 0.05$

WOMAC – Western Ontario and McMaster universities osteoarthritis index; ROM – range of motion; FU – follow-up

Figure 1

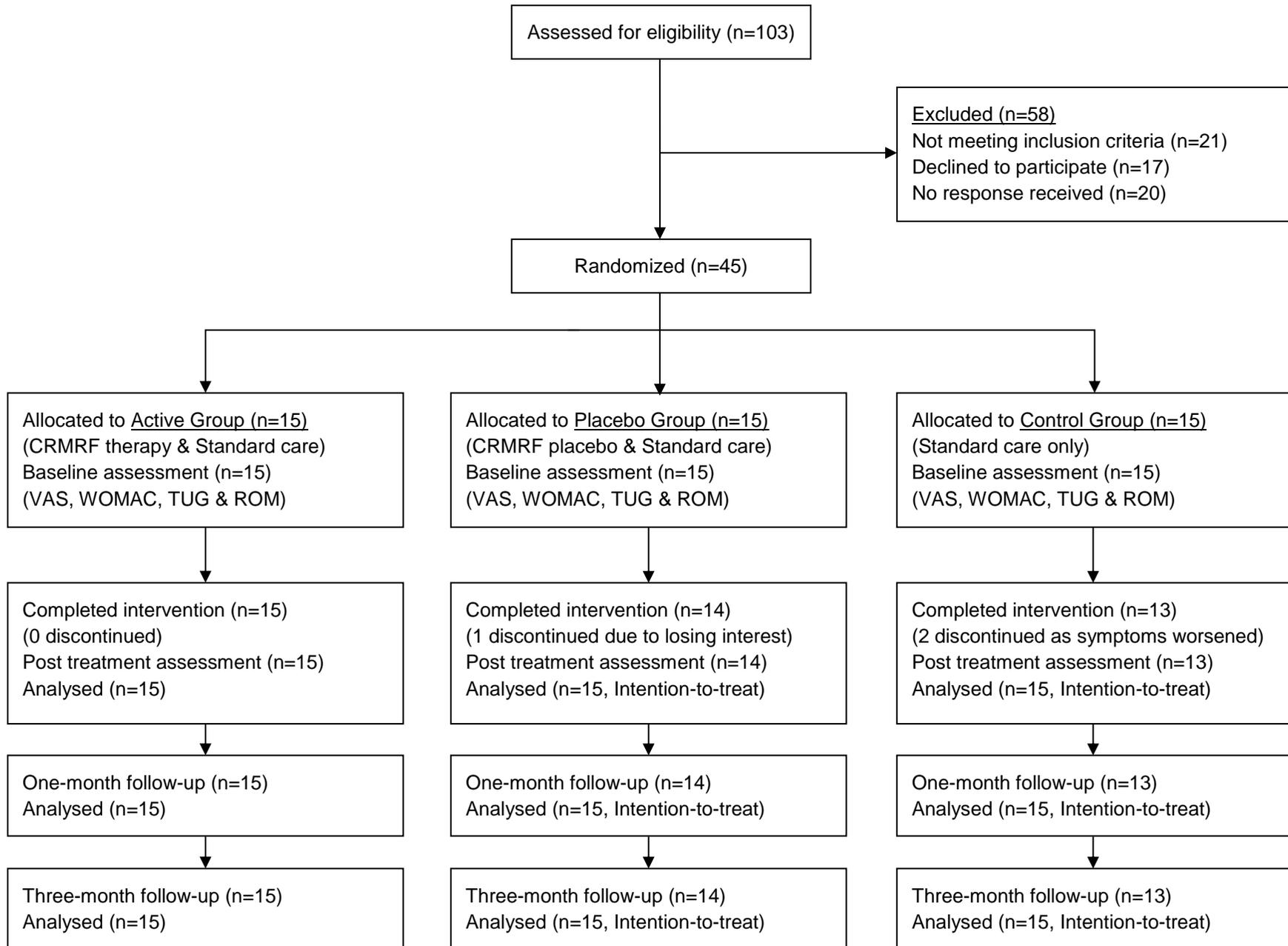


Figure 2

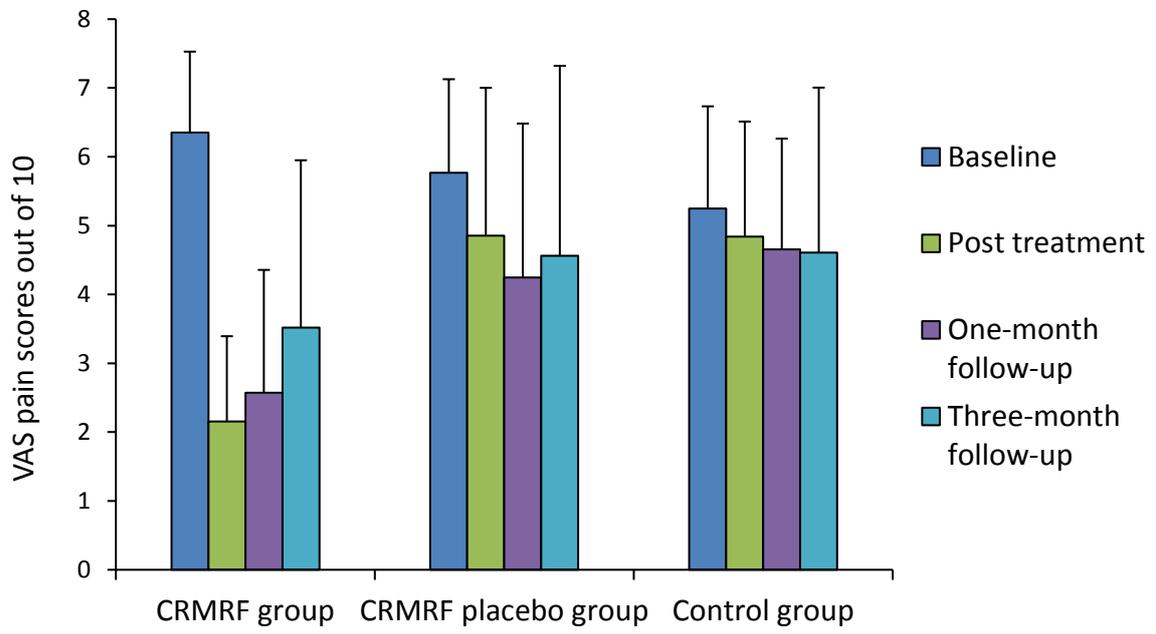


Figure 3

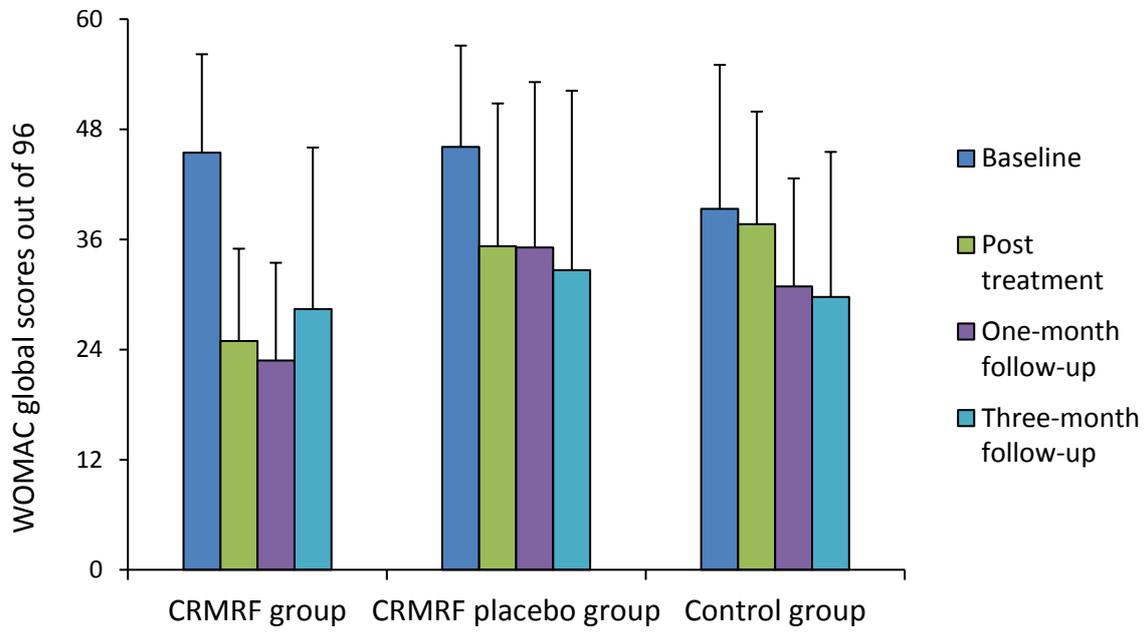


Figure 4

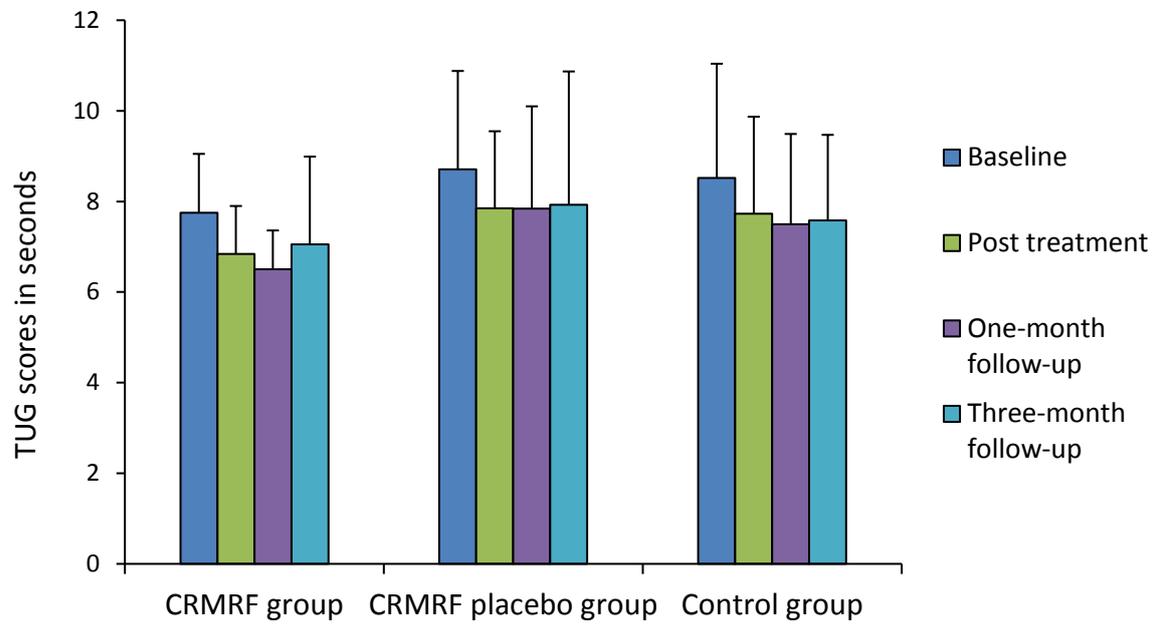


Figure 5

