PhD Thesis

The effect of end-range Maitland mobilization on pain, pressure pain threshold and functional measures in knee osteoarthritis

Miklós Pozsgai

Head of Doctoral School: Prof. Lajos Bogár, MD., PhD.

Program Leader: Prof. Péter Than, MD. PhD.

Supervisors: Nóra Nusser, MD., Ph.D.

Prof. Péter Than, MD. PhD.

University of Pécs, Medical School

Pécs

2022

Table of contents

Abbreviations

CG	Control group
CTGr	Conservative therapy group
EMGr	End-range Maitland group
KOA	Knee osteoarthritis
nEMGr	Not end-range Maitland group
NPRS	Numeric Pain Rating Scale
M+CTGr	Maitland plus conservative therapy group
PPT	Pressure pain threshold
ROM	Range of Motion
TENS	Transcutan Electroneuro Stimulation
TUG	Timed Up and Go test
VAS	Visual Analogue Scale
6MWT	6-minute walking test

1. Introduction

1.1. Knee osteoarthritis

Knee osteoarthritis (KOA) is an irreversible condition involving structural deformation of the joint. The main symptoms in KOA are joint stiffness, pain, decrease of range of motion (ROM), appearing of different directions of contractures, crepitus, muscle atrophy, decrease of joint proprioception, crambling, restricted function and limited physical activity.

1.2. Pain sensitization

Pain is the most prevalent symptom limiting patients daily life in KOA. Previous studies suggest that the increased pain in KOA, i.e. hyperalgesia, can be attributed to peripheral and central sensitization. Peripheral sensitization involves increased biochemical processes at nociceptors, whereas central sensitization involves alterations in the biochemical properties of segmentally located secondary neurons, increased function of various brain areas and decreased function of descending pain inhibitory pathways. Sensitization can lead to distorted sensations, with some authors attributing sensitization to neuropathic-like pain during KOA and structural changes in joint innervation.

1.3. Pressure pain threshold examination

Out of several methods measuring sensitization, pressure pain threshold (PPT) is the most relevant in KOA. PPT measurement consists of an externally applied, controlled, gradually increased, in normal condition harmless stimuli performed until the onset of pain. PPT measurement can be performed locally around the knee for measuring peripheral sensitization and distant away from the knee for measuring central sensitization. Lower PPT suggests increased pain sensitivity, higher PPT proposes decreased pain sensitivity.

1.4. Conservative therapy

The guidelines prefer conservative therapy for the decrease of symptoms of KOA. The best-known conservative therapy modalities include land-based exercises, water-based exercises, electrotherapy and balneotherapy. In addition to the mainly suggested conservative therapy modalities, manual therapy is also preferred to decrease the symptoms of KOA.

2. Aim

1. Introducing Maitland manual therapy
2. Investigation of the efficacy of manual therapy based on a comprehensive, systematic literature search
3. Investigation of the combined effect of end-range Maitland mobilization and conservative therapy on pain and physical functioning in KOA
4. Investigation of the effect of sigle end-range Maitland mobilization on PPT and physical functioning in KOA
5. Investigation of the time-course of single end-range and not end-range Maitland mobilization on PPT and physical functioning in KOA.

3. Results

3.1. Maitland manual therapy

Maitland manual therapy was developed by Geoffrey D. Maitland (1924-2010), an Australian/English-born physiotherapist. Maitland manual therapy consists of a subjective patient examination (anamnesis, present complaint), an objective patient examination (inspection, examination, physical tests) and patient treatment.

Maitland manual therapy distinguishes between three different groups of patients during patient management. In the Pain Dominant group, patients are dominated by pain and are therefore able to move with minimal active movement; in the ROM problem group, patients are able to move with some pain; in the End Of Range problem group, patients only feel pain in a position close to the end-range of the joint ROM. Depending on each clinical group, the appropriate strength of manual intervention is applied.

Maitland manual therapy classifies the manual forces applied to a bone in the joint into grades I to IV. Grade I is a very gentle, careful and slow, tension- and pain-free movement in a pain-free position of the treated joint, applied only to the Pain Dominant group. Grade II is applied to the ROM problem group in the loose position of the joint and is used until the first resistance from the periarticular tissues appearing at one of the bone ends. Grades III and IV are used only in patients with End Of Range problems, with the aim of reducing resistance in the end-range position of the joint ROM. The difference between the two grades is that while grade IV treats the joint by staying close to the end-range position of the joint, grade III reduces the force applied during treatment more compared to the end-range position of the joint.

The use of Maitland manual therapy is recommended in cases of dysfunction of the neuro-musculo-skeletal system. The use of Maitland manual therapy is contraindicated in malignant tumours, spinal cord or cauda equina (S4 syndrome) compression and carotid problems, and end-range Maitland mobilization is also contraindicated in active inflammation.

3.2. Investigation of the efficacy of manual therapy based on a comprehensive, systematic literature search

Comprehensive search was conducted on Clinical Trials database for representing the frequency of application and efficacy of manual therapy. The search aimed to collect registered, manual therapy-related clinical trials, in which manual therapy was used alone or

as a complementary intervention. Overall, 47 registered, manual therapy-related clinical trials were found. Amongst the 47 trials, 20 trials had results.

The effectiveness of manual therapy based on trials with results can be summarized as follows: The trials were conducted in many different musculoskeletal conditions, the most common being low back pain, neck pain, jaw joint disease and stroke. The length of trials also varied widely, from 1-2 days to a year. In all patient groups studied, measured variables improved, patients' pain decreased, range of motion of treated joints increased, and patients' functional status and quality of life improved. Overall, manual therapy improved both subjective and objective outcomes in the short and long term in a variety of diseases.

Among the studies without results, we consider it important to highlight one that focuses on the genetic background of the effectiveness of manual therapy treatments. This is the first registered clinical trial of manual therapy designed to investigate the molecular response to manual therapy in fibromyalgia and chronic fatigue syndrome. We hypothesise that this study may form the basis for further studies on genetics and manual therapy.

3.3. Investigation of the combined effect of end-range Maitland mobilization and conservative therapy on pain and patients' physical functioning in KOA

Study design

Non-randomized, assessor-blinded interventional trial was conducted in Harkány Termal Rehabilitation Centre. Overall, 30 patients (24 female and 6 male together) were included in the trial. Recruited patients were assigned to Maitland and conservative therapy group (M+CTGr: n=15) or to only conservative therapy group (CTGr: n=15). Outcome measures were assessed at arriving at the hospital and at the end of 3-week treatment.

Interventions

Patients in both groups received medical bath, water- and land-based exercises and Transcutan ElectroNeuro Stimulation (TENS) therapy. Medical bath and water-based exercises were applied a total of 15 sessions, land-based exercises and TENS therapy were used a total of 9 times (3-times per week). In addition, patients in M+CTGr received end-range Maitland mobilization for both knees a total of 6 times over the 3-week treatment period (2 times/week).

Outcome measures

Patients pain intensity in general (Visual Analogue Scale, VAS 1), during getting up from a chair (VAS 2), during getting in car (VAS 3), during turning while walking (VAS 4) and during stair descending (VAS 5) were assessed. Patients flexion and extension passive range of motion (PROM) of knee joints, peak voluntary isometric muscle force of quadriceps and hamstring muscles in both legs and patients functional performance representing the Timed Up and Go Test (TUG) and 6-Minute Walk Test (6MWT) were also measured.

Statistical analysis

For comparing differences between post- and pre- treatment values in both groups, paired sample t-test or Wilcoxon-test, for comparing differences amongst groups independent sample t-test or Mann-Whitney U-test was used. All p-values equal or below 0.05 were considered statistically significant.

Results

There were no differences in demographic data between the two groups. Significant difference was found in peak muscle force of the right hamstring muscle at baseline between the two groups. In both groups, all measured variables presented significant decrease as a result of the treatments compared to baseline. M+CTGr also showed decrease in all VAS scores compared to CTGr, increase in bilateral knee joint flexion PROM, right hamstring peak muscle force and distance measured during 6MWT. The VAS values are shown in Table 1, PROM, peak muscle force, TUG and 6MWT values are shown in Table 2.

Table 1: Pre-, and post-treatment results of the different visual analogue scale (VAS) pain scores.

VAS scores	**M+CG**				**CG**				**Between-group comparison**
	Pre	**Post**	**Percentage change (%)**	**p**	**Pre**	**Post**	**Percentage change (%)**	**p**	**p**
VAS 1	6 (5-8)	3 (0-5)	65.25 (30.44)	**<0.001**	6 (5-7)	4 (3-5)	22.97 (24.44)	**0.007**	**0.002**
VAS 2	7 (6-8)	2 (0-4)	65.85 (33.76)	**<0.001**	6 (4-6)	4 (3-6)	25.18 (26.90)	**0.003**	**<0.001**
VAS 3	6 (5-8)	2 (0-5)	60.70 (35.85)	**<0.001**	6 (5-6)	4 (3-5)	24.86 (22.12)	**0.004**	**0.004**

VAS 4	6 (2-7)	1 (0-3)	67.48 (36.72)	**<0.001**	4 (3-5)	3 (2-4)	32.05 (29.82)	**0.004**	**0.008**
VAS 5	7 (5-8)	2 (1-5)	58.20 (31.35)	**<0.001**	7 (5-8)	4 (3-7)	27.18 (23.57)	**0.005**	**0.004**

Values represent median with 25 and 75 percentiles and the percentage change is presented as mean±standard deviation. M+CTGr, Maitland plus conservative therapy group; CTGr, conservative therapy group; VAS 1, general pain; VAS 2, pain rising from a chair; VAS 3, pain getting in car; VAS 4, pain turning while walking; VAS 5, pain during stair descending.

Table 2: Pre- and post-treatment results of PROM, peak muscle force, TUG and 6MWT.

Variables			**M+CG**				**CG**				**Between-group comparison**
			Pre	**Post**	**Percentage change (%)**	**p**	**Pre**	**Post**	**Percentage change (%)**	**p**	**p**
PROM (degree)	Flexion	Right side	107 (96-116)	116 (110-136)	19.78 (18.65)	**0.002**	97 (90-104)	104 (90-107)	5.12 (5.09)	**0.002**	**0.010**
		Left side	110 (90-118)	120 (114-134)	19.39 (14.85)	**<0.001**	104 (96-115)	107 (100-118)	4.04 (3.15)	**0.002**	**<0.001**
	Extension	Right side	-4 (-6 - -1)	-1 (-4 - 0)	45.44 (44.30)	**0.007**	-5 (-6 - -2)	-4 (-6 - 0)	18,99 (35.76)	**0.039**	0.087
		Left side	-4 (-7 - -2)	-2 (-4 - 0)	38.08 (42.72)	**0.011**	-4 (-6 - -3)	-4 (-5 - -1)	19.52 (35.71)	**0.039**	0.174
Peak muscle force (N)	Hamstring	Right side	99.4 (53.4-113)	155 (128-202.6)	43.73 (50.26)	**<0.001**	76.7 (67.7-104)	84.7 (77.4-110)	11.47 (7.29)	**<0.001**	**0.045**
		Left side	88.4 (45-106)	114,4 (98-126)	72.03 (83.03)	**<0.001**	78.8 (67.8-111)	89.6 (80.4-128)	13.94 (6.32)	**<0.001**	0.089
	Quadriceps	Right side	131.6 (95-185.4)	155 (128-202.6)	35.12 (65.68)	**<0.001**	102 (89.5-148)	118.6 (107-187.5)	25.27 (17.34)	**<0.001**	0.436
		Left side	127.8 (61.4-156.4)	165 (136-198)	74.28 (106.71)	**<0.001**	122 (92-146)	145 (114-195)	26.27 (22.40)	**<0.001**	0.486
TUG (sec)			13.78 (11.44-17.71)	11.49 (9.58-12.8)	19.99 (12.95)	**<0.001**	12.86 (11-16.66)	11.74 (9.91-14.57)	10.78 (10.08)	**<0.001**	0.081
6MWT (m)			388 (288-465)	450 (358-601)	36.33 (51.98)	**<0.001**	371 (286-381)	376 (299-407)	4.88 (6.24)	**<0.001**	**<0.001**

Values represent median with 25 and 75 percentiles and percentage change is presented as mean±standard deviation; M+CTGr: Maitland plus conservative therapy group; CTGr: Conservative therapy group; PROM: passive range of motion; N: Newton; TUG: Timed Up and Go test; 6MWT: 6-minute walking test. ^Significant baseline difference between M+CTGr and CTGr.

3.4. Investigation of the effect of single end-range Maitland mobilization on PPT and physical functioning in KOA

Study design

Randomised, controlled, assessor-blinded clinical trial was conducted with overall 40 female patients. Twenty patients were assigned to end-range Maitland group (EMGr) and 20 patients were assigned to Control Group (CGr). Patients in EMGr received end-range Maitland mobilization and patients in CGr were treated with sham manual therapy technique (placebo). Outcome measures were assessed before treatment, 30 minutes and 1-week after treatment.

Interventions

Patients in EMGr received end-range Maitland mobilization performed in flexion and extension end-range position of the tibiofemoral joint. Patients in CGr received sham manual therapy, which consisted of hands-on cutaneous input technique performed in end-range positions of both knees without any movement.

Outcome measures

Outcome measures were PPT measured locally at the knee; distant PPT measured at the ipsilateral musculus extensor carpi radialis longus; general pain intensity during the previous week via VAS scale (this variable was determined only prior the treatment session and after 1-week period), pain intensity during dynamic balance measured with Numerating Pain Rating Scale (NPRS), dynamic balance measured with TUG test and the strength of passive resistance of the knee joint, which consisted of the maximal painfree passive knee flexion ROM and the degree of resistance of connective tissues during passive knee flexion at the same time.

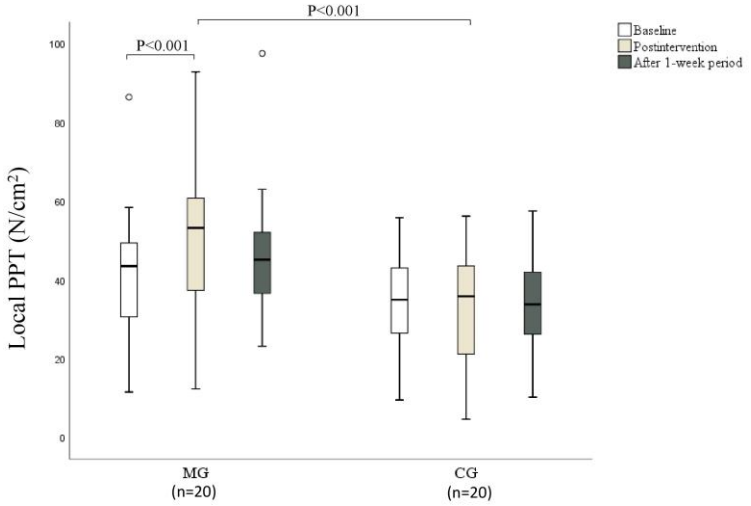
Statistical analysis

Wilcoxon signed-rank test was used to compare changes within-group measurements. Mann-Whitney U test was used to compare differences between-group measurements. Significance level was set at $p<0.05$.

Results

The demographic values of both groups presented no difference. Significant difference was found in strength of passive resistance in favor of EMGr at baseline. All outcome measure improved significantly in EMGr postintervention and no difference was revealed in CGr postintervention. Despite general pain VAS, between-group comparison revealed significant difference in all measured variables in favor of EMGr. Within-group comparison revealed no significant difference in EMGr and CGr at 1-week after treatment. Between-group comparison revealed significant difference in strength of passive resistance after 1-week period in favor of EMGr. Change of local PPT in both groups is presented in Figure 1, data of distant PPT, general pain VAS, NPRS, TUG and strength of passive resistance in both groups are presented in Table 3.

Figure 1: Change of local pressure pain threshold in both groups.



Local PPT: pressure pain threshold measured at the knee; N/cm^2: Newton/cm^2; EMGr: Maitland Group; CGr: Control Group.

Table 3: Results of distant PPT, general pain VAS, NPRS, TUG and strength of passive resistance in both groups.

	EMGr (n=20)	**p**	**CGr (n=20)**	**p**	**Between-group comparison p**
Distant PPT (N/cm^2)					
Baseline	31.65 (19.65-36.60)		21.90 (13.30-31.35)		
Postintervention	38.10 (28.45-50.15)	**<0.001**	21.40 (10.59-30.00)	0.151	**<0.001**
After 1-week period	29.95 (24.40-42.90)	0.198	20.35 (12.64-29.70)	0.507	0.383
General pain VAS					
Baseline	65.00 (44.00-70.00)		66.00 (53.50-68.00)		
After 1-week period	54.00 (30.50-72.00)	0.147	65.00 (54.50-68.50)	0.519	0.461
NPRS					
Baseline	4.50 (2.50-7.00)		4.00 (2.00-6.00)		
Postintervention	3.00 (0.50-5.00)	**0.005**	3.50 (2.80-6.80)	0.305	**0.006**
After 1-week period	4.00 (1.00-6.00)	0.153	3.50 (2.00-6.00)	1.000	0.429
TUG (sec)					
Baseline	14.25 (12.60-20.10)		12.95 (11.80-18.05)		
Postintervention	13.85 (11.25-15.00)	**<0.001**	12.80 (11.35-17.35)	0.085	**0.015**
After 1-week period	12.25 (10.45-14.90)	0.056	12.60 (11.00-16.45)	0.687	0.076
Degree of passive knee flexion					
Baseline	110.00 (86.00-117.00)		99.00 (87.50-114.00)		
Strength of passive resistance (N)					
Baseline |	28.65 (21.10-33.30)		17.05 (14.20-21.10)		
Postintervention	19.30 (14.20-23.50)	**<0.001**	16.25 (14.60-22.80)	0.569	**<0.001**
After 1-week period	25.20 (16.65-35.30)	0.054	22.05 (15.50-31.10)	0.053	**<0.001**

Data presented in median (lower IQR-upper IQR). EMGg: Maitland Group; CGr: Control Group; ECRL: Distant PPT: Pressure pain threshold of the m. extensor carpi radialis longus muscle; N/cm^2: $Newton/cm^2$; General pain VAS: General pain intensity measured with Visual Analogue Scale; TUG: Timed Up and Go Test; sec: secundum; NPRS: Numerating Pain Rating Scale; N: Newton; |: Significant baseline difference between EMGr and CGr.

3.5. Investigation of the timecourse of single end-range and not end-range Maitland mobilization on PPT and physical functioning test in KOA

Study design

Randomised, controlled, assessor-blinded clinical trial was conducted with overall 66 (50 female and 16 male) patients. Twenty-two patients were assigned to end-range Maitland group (EMGr), 22 patients were assigned to not end-range Maitland group (nEMGr) and 22 patients were assigned to Control Group (CGr). Outcome measures were assessed pre-, 30 minutes postintervention and on the following consecutive second days within 6-day period.

Interventions

Patients in EMGr received end-range Maitland mobilization. End-range Maitland mobilization was performed in flexion and extension end-range position of the tibiofemoral joint. Patients in nEMGr received not end-range Maitland mobilization performed in loose position of the joint (approx. 20-30° flexion). Patients in CGr received sham manual therapy, which consisted of hands-on cutaneous input technique performed in both end-range positions of the knee without any movement.

Outcome measures

Outcome measures consisted of the previously mentioned local and distant PPT, TUG test and strength of passive resistance.

Statistical analysis

Analysis was performed with mixed model for calculation differences. Results are compared to baseline showing percentage change in case of all variable. A two-sided p value of<0.05 was regarded as statistically significant.

Results

Local PPT increased significantly postintervention in all groups compared to pre-intervention, but the significant increase persisted until day 6 only in EMGr. Between-group comparison revealed significant improvements postintervention and on the 2nd day in favor of EMGr compared to CGr. EMGr presented significant difference at all measurement points

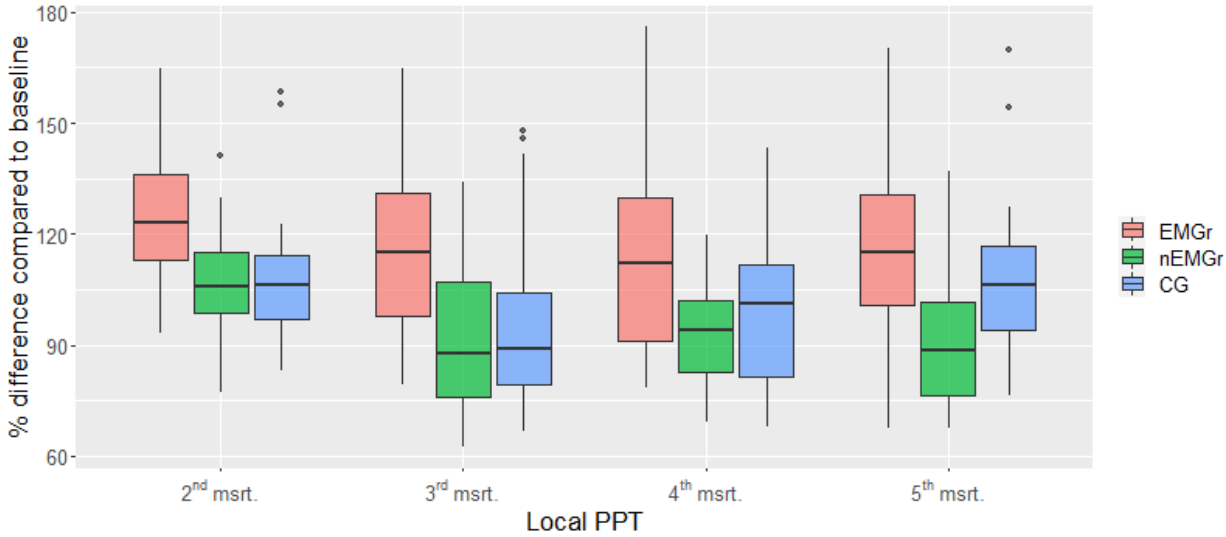
compared to nEMGr. No difference was found in favor of nEMGR compared to CG (Figure 2).

Distant PPT increased significantly postintervention compared to pre-intervention in EMGr and this significant increase persisted until the day 4 measurements. Distant PPT did not change at all in nEMGr and CG. Between-group comparison revealed significant difference in favor of EMGr compared to CG and nEMGr postintervention and in all measurement points except 6th day. There is not any difference in favor of nEMGr compared to CG (Figure 3).

TUG time decreased significantly postintervention compared to pre-intervention in EMGr and the significant decrease was maintained on every consecutive follow-up. Despite no change was revealed postintervention compared to pre-intervention in nEMGr and CGr, significant decrease was found on every consecutive follow-up in both of these groups. Between-group comparison presented no difference postintervention and on every consecutive follow-up in either groups (Figure 4).

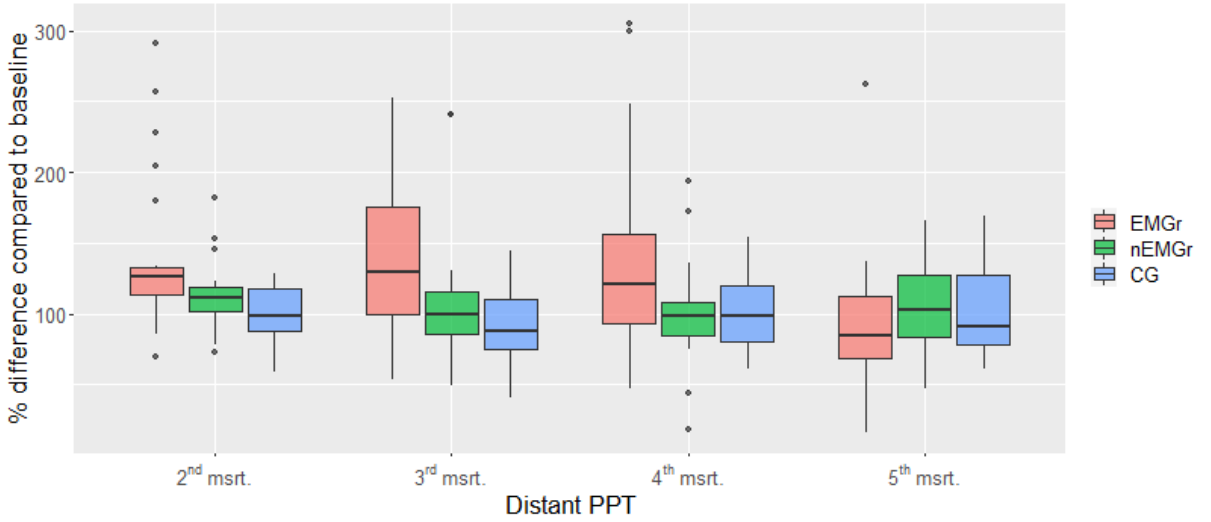
Both within-, and between-group comparison revealed significant decrease of passive resistance postintervention in EMGr, but no decrease was found later on every consecutive follow-up. Both within-, and between-group comparison did not show any change in strength of passive resistance at any measurement points in nEMGr and CG (Figure 5).

Figure 2: Results of local PPT.



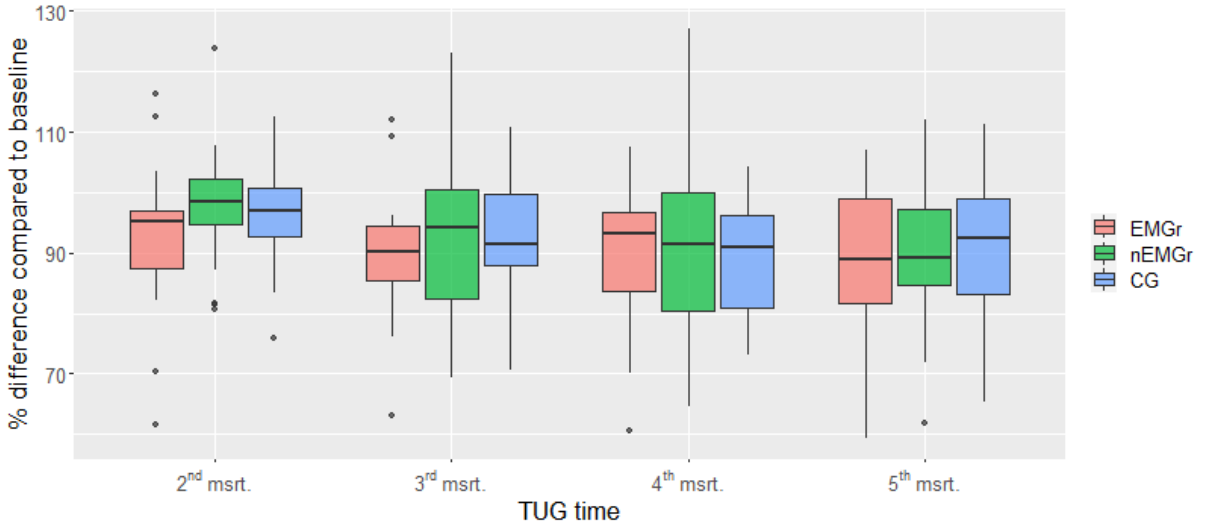
Local PPT: pressure pain threshold measured at the knee; EMGr: End-range Maitland group; nEMGR: Not end-range Maitland mobilization; CGr: Control group; 2nd msrt.: post-intervention measurement; 3rd msrt.: 2-day measurement; 4th msrt.: 4-day measurement; 5th msrt.: 6-day measurement.

Figure 3: Results of distant PPT.



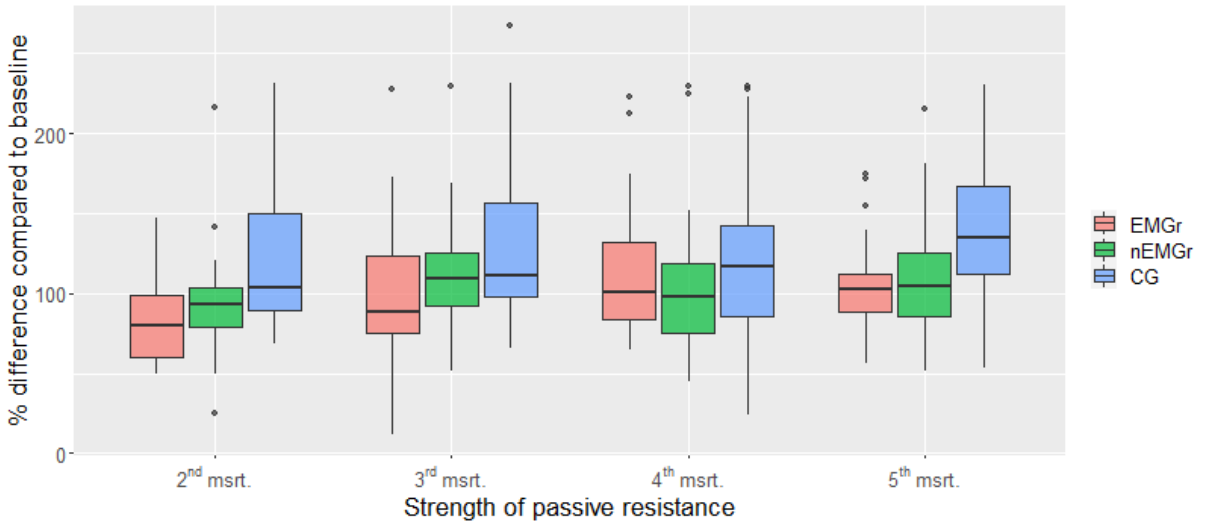
Distant PPT: pressure pain threshold measured at the musculus extensor carpi radialis longus; EMGr: End-range Maitland group; nEMGR: Not end-range Maitland mobilization; CG: Control group; 2nd msrt.: post-intervention measurement; 3rd msrt.: 2-day measurement; 4th msrt.: 4-day measurement; 5th msrt.: 6-day measurement.

Figure 4: Results of TUG time.



TUG time: Timed Up and Go test time; EMGr: End-range Maitland group; nEMGR: Not end-range Maitland mobilization; CG: Control group; 2nd msrt.: post-intervention measurement; 3rd msrt.: 2-day measurement; 4th msrt.: 4-day measurement; 5th msrt.: 6-day measurement.

Figure 5: Results of strength of passive resistance.



Strength of passive resistance: Strength of passive resistance at the onset of knee pain; EMGr: End-range Maitland group; nEMGR: Not end-range Maitland mobilization; CG: Control group; 2nd msrt.: post-intervention measurement; 3rd msrt.: 2-day measurement; 4th msrt.: 4-day measurement; 5th msrt.: 6-day measurement.

4. Conclusion

In our work, we first reviewed the literature for registered studies of manual therapy. We found that manual therapy is a widely used method, effective in alleviating variety of symptoms in many diseases, and there is no summary study describing the wide range of manual therapy trends in the international or national literature. Therefore, an overview and systematization of manual therapies and a positioning and detailed description of Maitland manual therapy were undertaken first. We then focused on investigation the effectiveness of Maitland manual therapy in terms of pain, hyperalgesia and reduction in physical function during KOA. As the prevalence of KOA is high in the population and it has very high impact on the adult population, causing a serious deterioration in quality of life, in some cases severe impairment and overburdening of the health care system, therefore it is important to investigate the treatment modalities for KOA.

Previous studies have demonstrated the beneficial effects of manual therapy in combination with physiotherapy modality one by one among many for knee and shoulder complaints, but the methodological presentation of manual therapy in these studies was not uniform and well defined. Since balneotherapy and physiotherapy is widely used in Hungary, most often in a complex way, in combination of several treatments, we considered it important to prove the efficacy of the combined use of complex balneotherapy and physiotherapy and end-range Maitland mobilization to reduce symptom of patients with KOA in clinical trials. Our studies to this end have provided new information on the subject, building on and concordant with previous studies, and can be seen as a further refinement of them.

Previous studies have investigated the immediate effects of a single manual therapy treatment on local and distant PPT and physical function in KOA, but neither the change in TUG test nor knee joint tension measured at maximal pain-free passive ROM have been examined. As pain is the most common symptom and often leads to loss of function, and there is proven the role of hyperalgesia in the development of severe pain, we further aimed to investigate hyperalgesia during KOA from a different perspective. Pain is very difficult to measure objectively due to its subjective nature. However, due to sensitization, the pain pressure threshold test is a relevant method in KOA. We demonstrated that the application of end-range Maitland mobilization immediately after treatment reduces local and central sensitization causing hyperalgesia and, as a consequence, there was immediate improvement in the functional status of the knee joint as well. We also confirmed that the decrease in

peripheral sensitisation persists for 2 days and the decrease in central sensitisation for 4 days. In contrast, the patient's perception of pain over the past week, as defined by the VAS scale, did not change after a single end-range Maitland mobilization. The patients' dynamic balance (TUG test) improved immediately after end-range mobilization, whereas it did not improve after not end-range mobilization. The improvement observed from day 2 in all groups can be explained by the fact that patients gained practice during the bi-daily test and that the performance of the test itself improved their dynamic balance. In contrast, in our first study, another TUG test was performed only after one week, which did not give the opportunity to practice. Therefore, we conclude that the outcome of the first study is realistic and that neither not end range mobilization nor placebo treatment actually has any effect on dynamic balance. The effect of end range Maitland mobilization results in the reduction in passive tension in the tissues around the knee joint immediately after treatment, whereas not end-range mobilization has no effect. This reduction in passive tension was observed in women even after one week too. When men were included in the study, the reduction was no longer significant after one week, which may be due to the increased connective tissue tightness that is characteristic of men.

Our future goals are to study the short- and long-term effects of end-range Maitland mobilization in various diseases and to study its use in combination with complex physiotherapy, especially land-based exercises.

5. Summary

1. We surveyed the studies using manual therapy in the literature and showed the effectiveness of the use of manual therapy.
2. We demonstrated that end-range Maitland mobilization used in combination with conventional physiotherapy enhances the effect of physiotherapy, both in terms of reducing pain and improving knee function in patients with TOA.
3. We demonstrated that local and central sensitization decreases immediately upon exposure to end-range Maitland mobilization and that this effect lasts for 2 days and 4 days respectively, whereas non-end-range mobilization has only an immediate effect. A single treatment temporarily improved the functional condition of the knee joint, which was no longer detectable after two days.

6. Acknowledgements

I would like to thank my supervisors, Prof. dr. Péter Than and dr. Nóra Nusser that they provided an opportunity for a deeper elaboration on the topic of manual therapy and that they also contributed to the exploration of manual therapy from a medical point of view.

Thanks to dr. Iván Antal Péter, the general director of the Harkány Thermal Rehabilitation Center, all the employees of the hospital, especially the physical therapist team of the hospital for all the help. I am also grateful to all my co-authors who have contributed to the published papers.

I am specially grateful to dr. Nelli Farkas for her all-time help regarding statistics.

I am also grateful to my family and everyone who supported me throughout my doctoral work.

7. Publication list

Publications in connection with the thesis

M Pozsgai, P Than, N Nusser: Manuálterápia, Balneológia, Gyógyfürdőügy, Gyógyidegenforgalom, 2021; 39(1): 35 – 44.

M Pozsgai, IA Péter, N Nusser: A véghelyzeti Maitland mobilizáció kiegészítő hatása térdartrózis esetén, Fizioterápia, 2021; 30(2–3): 38 – 45.

M Pozsgai, E Kövesdi, B Németh, I Kiss, N Farkas, T Atlasz, M Váczi, N Nusser: Clinical effect of End-range Maitland mobilization in the Management of Knee Osteoarthritis – A Pilot Study, In Vivo, 2021; 35(3): 1661 – 1668. **IF: 2,155 (Q2)**

M Pozsgai, I Szabo, N Nusser, R Varnai, Cs Sipeky: Overview of Registered Clinical Trials on Manual Therapy: Implications of Genetic Testing for Personalized Treatment, In Vivo, 2022; 36(1): 294 – 305. **IF: 2,155 (Q2)**

M Pozsgai, IA Péter, N Farkas, P Than, N Nusser: End-range Maitland mobilization decreasing pain sensitivity in knee osteoarthritis: randomised, controlled clinical trial, European Journal of Physical and Rehabilitation Medicine, 2022; . **IF: 2,874 (Q1)**

M Pozsgai, K Udvarácz, IA Péter, P Than, N Nusser: Time-curve of single end-range Maitland mobilization on pressure pain threshold and functional measures in knee osteoarthritis: randomised, controlled clinical trial, European Journal of Physical and Rehabilitation Medicine (under review process)

Publications not in connection with the thesis

AM Briggs, JG Persaud, ML Deverell, S Bunzli, B Tampin, Y Sumi, O Amundsen, EMg Houlding, A Cardone, T Hugosdottir, S Rogers, M Pozsgai, H Slater: Integrated prevention and management of non-communicable diseases, including musculoskeletal health: a systematic policy analysis amongst OECD countries, BMJ Global Health, 2019; 4(5): e001806. **IF: 4,28 (Q1)**

M Pozsgai, P Than, N Nusser: A véghelyzeti Maitland mobilizáció azonnali hatása a lokális és távoli fájdalomnyomás-küszöbértékre aspecifikus nyakfájdalom esetén, Fizioterápia, 2022; 31(1): 3 – 9.

8. Presentations

National presentations

17.10.2020. End-range Maitland mobilization effecting immediately pressure pain threshold in knee osteoarthritis, MedPECS2020 Conference, Pécs (online presentation)

27.11.2020. Véghelyzeti Maitland mobilizáció hatása a perifériás és centrális szenzitizációra térdartrózis esetén, Hungarian Rehabilitation Society XXXIX. Convention, Budapest (online presentation)

08.10.2021. A véghelyzeti Maitland mobilizáció kiegészítő hatása térdartrózis esetén, FizioPéntek 11, Budapest (online presentation)

09.10.2021. Egyszeri véghelyzeti Maitland mobilizáció időbeli hatásának vizsgálata a fájdalomnyomás-küszöbértékre térdartrózis esetén, Hungarian Rehabilitation Society XL. Convention, Szeged

22.10.2021. A véghelyzeti Maitland mobilizáció hatása a lokális és távoli fájdalomnyomás-küszöbértékre térdartrózisos betegek körében – összefoglaló az eddig elért eredményeinkről, MMGYFE Self-training meeting, Budapest

22.11.2021. A komplex fizikoterápia és az ízületi manuálterápia együttes hatása a térdartrózis funkcionális állapotára, Hungarian Balneological Society 2021. year Convention, Harkány

International presentations

04.27.-04.28.2018. The beneficial effect of Maitland's manual therapy on muscle mechanic and knee function during the treatment of knee osteoarthritis, World Congress On Osteoarthritis, OARSI 2018, Liverpool, poster presentation

04.30-05.03.2020. The immediate effect of end-range Maitland mobilization on pain pressure threshold in patients with knee osteoarthritis, World Congress On Osteoarthritis, OARSI 2020, Vienna, poster presentation

04.29-05.01.2021. The time curve of a single end-range Maitland mobilization on pressure pain threshold and functional outcomes in knee osteoarthritis, World Congress On Osteoarthritis, OARSI 2021, Denver, poster presentation (virtual congress)