The Influence of Lower-Body Training, Upper-Body Training and a Combination of Both on Pain, Functionality and Quality of Life in Knee Osteoarthritis Patients

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Authors’ contributions

This work was carried out in collaboration among all authors. Author KB designed the study, wrote the protocol and the first draft of the manuscript. Author UH performed the statistical analysis. Author FB managed the questionnaire searches. All authors read and approved the final manuscript.

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ABSTRACT

Purpose: Regular physical activities are a keystone in the nonmedical and nonsurgical treatment of knee-osteoarthritis. However, the underlying mechanisms are still regarded as a black-box and a matter of debate. As potential candidates, two groups can be distinguished: First, joint-specific influences such as better biomechanical functioning and improvements in the quality of cartilage. Secondly, more unspecific effectors like anti-inflammatory cytokines and a central modulation of pain perception. In order to distinguish between these two groups the present study compared the training effects of knee-joint surrounding muscles (LBT), upper body muscles (UBT), and the combination of both (WBT).

Methods: 372 physically inactive, adult knee-osteoarthritic patients of both sexes were enrolled in the multi-centered, controlled, and randomized training intervention. All three exercise groups fulfilled an 8-week circle-training intervention two times per week with a subjective intensity of 4 - 5 for the first five sessions (on a 0 = no effort to 10 = extreme effort scale). From the 6th to the 10th session, intensity was adjusted to 6 – 7 and thereafter to 7 – 8. The single training sessions were

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1. INTRODUCTION

With respect to the reduction of pain and the enhancement of functionality in osteoarthritis (OA), a huge number of international guidelines recommend regular training as a keystone among the non-pharmaceutical and non-surgical options [1,2,3,4,5,6,7]. For example, the German S2k guideline on gonarthrosis [7], published in 2018, provides 100% consensus for the implementation of “exercise therapy” in the form of strength, endurance, and flexibility training for primary treatment (recommendation 5.1). The evidence for physical training has become so overwhelming that Uthman et al. [8] concluded that in (knee) osteoarthritis further studies are hardly needed to compare the effects of training versus non-training. Rather, the focus should be on optimizing training modes.

Until recently, mechanical factors such as an enhanced joint stability following strength training of joint-surrounding muscles were primarily regarded as the origin of pain reduction [9,10,11,12]. In contrast, strength training interventions evaluating pain and forces/torques within the arthrotic knee joint yielded reduced pain intensities after training but unchanged characteristics of joint loads [13,14,15]. Obviously, a purely mechanical explanation for the observable pain reductions following training appears to be at least incomplete. During the last decades, three further candidates came into play: An increased cartilage content of proteoglycans inducing a biochemically improved cartilage quality [16,17,18], an exercise-induced analgesia (EIA) [19], and anti-inflammatory cytokines released from exercising skeletal muscles [20,21]. Although no evidence exists that cartilage thickness can be increased by exercise, the buffer properties of cartilage adapt to the load. According to the training intervention of Van Ginckel et al. [27] a significant increase of proteoglycans can already be obtained within few weeks. EIA means an increase in pain thresholds to mechanical, thermal or electrical stimuli, which is already induced by a single bout of physical exercise [22,23,24]. Burrows et al. [19] found normal EIA in patients with knee osteoarthritis after training of the upper body while training of leg muscles did not induce a systemic EIA. There is some evidence that the influence of muscular activity on the sensation of pain is not exclusively limited to the acute phase. Both a systematic training [25] and an increase in normal daily activities [26] led to a chronically reduced pain sensitivity in healthy subjects. Landmark et al. [27] found in the adult population of a Norwegian county associations between volume and intensity of recreational exercise and a lower occurrence of chronic pain. In patients with painful peripheral arterial disease both upper- and lower limb aerobic exercise led to significantly increased maximum walking distances of nearly identical amounts [28]. Due to unchanged pain thresholds the authors concluded that both a generalized elevated pain tolerance and physiologic adaptations contribute to the obtained improvement in walking. All in all, exercise appears to result in a general suppression of pain sensation.

Unfortunately, to our best knowledge no findings exist concerning the effects of knee-specific exercises of the lower limbs and unspecified exercises of the upper body on pain sensation in OA-patients. Therefore, to differentiate the local and general influences of regular training, the present study deals with the training effects of knee-surrounding muscle groups, a training
modality not including the lower body, and a combination of both.

2. METHODS

The study was conducted in accordance to all the relevant national regulations and the tenets of the Declaration of Helsinki and was approved by the ethical committee of the German Sport University Cologne.

2.1 General Overview

The investigation was designed as a prospective, single-blind, multicenter, and cluster randomized controlled trial. Initially, all 149 facilities of the German Physio Aktiv Group were invited to participate in the study. 59 facilities declared their interest and were randomly assigned in a 1:1:1 order to one of the following training forms: Lower body training (LBT), upper body training (UBT), whole body training (WBT). In preparation of the investigation, all participating staffs were thoroughly instructed about procedures, contents, and endpoints of the investigation. Subjects were consecutively included from the 1st of July to the 15th of October 2019. Due to the individual eight-week training period, data collection was finished on the 10th of December 2019. Three different strength-endurance circles (Chap. 2.3) were applied two times a week resulting in a total maximum amount of 16 sessions per subject. For final examination at least 13 session had to be performed. Before (T0), after 4 weeks of training (T4) and at the end of the intervention period (T8) online questionnaires (chap. 2.4) were applied. Patients could quit the study without mentioning any reason.

2.2 Patients

Patients with diagnosed (MRI or X-ray imaging) painful knee osteoarthritis were recruited through orthopedic surgeons, general practitioners and media announcements. Subjects who met the inclusion- and exclusion criteria (see below) and agreed to participate were included after verbal and written informed consent.

Inclusion criteria

Women and men aged 30 to 80 years.

Diagnosed knee osteoarthritis (Kellgren-Lawrence Grade 1 to 4).

Mastery of German language (due to the questionnaires).

Exclusion criteria

Other knee-joint diseases than osteoarthritis.

Neurologic disorders

Stroke

Heart attack. Heart failure.

Pregnancy.

More than a week absence during the study period.

Regular training during the last 3 months.

Initially 372 patients were enrolled in the study with 241 females (65%) and 131 males (35%). The highest school-leaving qualification was 20% basic school qualification (Hauptschulabschluss), 61% intermediate secondary school certificate (Mittlere Reife) and 19% general qualification for university entrance (Abitur).

A drop-out of 96 patients (26%) led to a final examination of 276 subjects. Among drop-outs, 13 subjects originated from LBT, 33 subjects from UBT, and 50 subjects from WBT corresponding to 14%, 30%, and 29% of the corresponding group, respectively. None of the anthropometric, educational, or medical parameters investigated could be evaluated as a prognostic item of adherence / non-adherence.

2.3 Training

2.3.1 General aspects

Both LBT, UBT, and WBT were performed as a circuit training with 1 minute of exercise for the strength devices, 4 minutes for the endurance devices, and 0.5 minutes of rest between each station. All participating centers of a given training mode used identical devices (milon industries ltd., Emersacker, Germany). In a familiarization session, each device was individually adjusted to the size and leverage conditions of the subject and the correct device settings transferred to an individual chip card. So, before training sessions the setting could be made automatically.
The strength devices (chest press, back extension, abdominal crunch, seated rowing, leg extension, leg curl) operate concentrically and eccentrically with a duration of 1.5 seconds each. Intensities were set in a familiarization session by the patient corresponding to “4” to “5” on a scale from “0” (= no effort) to “10” (= maximum effort). If this intensity evoked knee pain, it was stepwise reduced to a well tolerable state. As with the biomechanical data, device settings were stored on the individual chip card. They were kept constant for the first five training sessions (TS). In the 6th to 10th TS, intensities were increased to “6” to “7” and from the 11th TS to “7” to “8”.

The load of two endurance devices (cross trainer, stationary bike) was set by means of heart rate using the following formula.

\[ HR_{\text{exercise}} = (220 - \text{age}) \times 0.65 \]

2.3.2 Lower body training

4 devices were used for the LBT circle (two circuits per session) in a sequence as follows: 1 min. leg extension - 0.5 min. rest - 4 min stationary bike - 0.5 min. rest - 1 min. leg curl - 0.5 min. rest - 4 min. cross trainer - 0.5 min. rest. The exercise net time per session (ENT) amounted to 20 min.

2.3.3 Upper body training

4 devices were used for the UBT circle (three circuits per session) in a sequence as follows: 1 min. abdominal crunch - 0.5 min. rest - 1 min. back extension - 0.5 min. rest - 1 min. seated rowing - 0.5 min. rest - 1 min. chest press - 0.5 min. rest. ENT was 12 min.

2.3.4 Whole body training

All eight devices from LBT and UBT were used (two circuits per session). ENT was 28 min.

2.4 Questionnaires

The questionnaires (Tab. 1) were applied online and technically constructed by means of a commercially available internet-based survey software (Survio). In order to minimize the influence of local stuffs on answering the questions, patients filled out the surveys without any supervision. Therefore, all data were exclusively accessible to the authors. The identity number of patients was build by postal code of the center, the sequential number of patients within the center, and the training group. Sex, age, height, and weight were asked as antropometric values. The educational qualification asked for the highest level of education in school.

The Kellgren-Lawrence grade was taken separately for the left and right knee. Further knee osteoarthritis specific questions related to the frequency of doctor’s visits during the past six months, the consumption of pain killers, and the history of treatment with hyaluronic acid.

Comorbidities, resulting doctor visits, and concomitant drug consumption were evaluated for diabetes mellitus type 1 and 2, arterial hypertension, diseases of lipid metabolism, thyroid diseases, and others.

The knee and hip specific Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used to evaluate pain, stiffness, and physical functioning of the joints [29]. WOMAC data are presented as normalized values from 0 (best situation) to 100 (worst situation).

The Veterans Rand 12 item health survey (VR-12) was taken to access general health related physical (PQL) and mental quality of life (MQL) [30].

The believes of patients about the influence of the training with respect to general fitness, upper and lower body fitness, and knee pain reduction were asked with a numeric scale from 0 = no effect to 10 = extremely strong effect at T4 and T8.

2.5 Statistics

If not otherwise stated data are presented as mean ± standard deviation (SD). The comparisons between the three groups (UBT, LBT, WBT) and between finisher and non-finisher for anthropometric data, educational qualification, comorbidities, regular drug consumption and physician visits were investigated with a Mann-Whitney-U-Test.

The two-way ANOVA with factors time (T0, T4, T8; as repeated factor) and group followed by Bonferroni test for multiple comparisons were used for pain, stiffness, physical function, physical and mental quality of live.
Correlations were analyzed applying a Spearman Rank coefficient. Statistical significance was set to an alpha level of 0.05. All statistical analyses have been performed with IBM SPSS statistics 25.

3. RESULTS
3.1 Anthropometry

The anthropometric data of patients are presented in Table 2. No significant differences between groups could be detected.

3.2 Medical History of Patients

The T0 questionnaire yielded a medical history as follows: During the last six months, 81% had at least one orthopedic visit related to knee problems. More detailed, 39% of participants had 1 to 2 contacts, 16% 3 to 4 contacts, 5% 5 to 6 contacts and 11% more than 6 contacts to a physician. Pain-killers were used regularly from 20% of patients for at least one times per week, 48% occasionally and 32% reported no intake. Within the last year, hyaluronic acid had been injected intra-articular to 21% of patients. As comorbidities, 43% reported arterial hypertension, 17% thyroid disease, 5% a fat metabolism disorder, 5% diabetes type 2 and 27% other diseases. 32% indicated no co-morbidity.

3.3 WOMAC-Scores

The initial WOMAC-Scores did not significantly differ between groups (Table 3).

The two-way ANOVA yielded for all WOMAC-scores (pain, function, stiffness, total) a highly significant influence of time (p < 0.0001) but no significant effect of the training mode. Fig. 1 shows in all three training regimens a decline from T0 to T4 and from T4 to T8 except the stiffness-score in the LBT group. For the total WOMAC score, the differences from T0 to T8 amounted to 4.1 ± 15.9, 5.5 ± 14.3, and 8.4 ± 15.0 for LBT, UBT, and WBT, respectively. Detailed ANOVA probabilities for differences in pain, stiffness, function, physical quality of life, and mental quality of life are presented in Table 4.

Improvements in WOMAC-subscores pain and stiffness were comparable for patients showing maximal Kellgren-Lawrence grades 1 to 2 as compared to grades 3 to 4 with a mean amplitude all above MCID. For WOMAC-subscore function, the minimum clinical important difference of WBT was exceeded by a factor of 2 in patients with KLG 3 and 4 but was not reached for UBT and LBT (Fig. 2).

The difference between T8 and T0 in WOMAC total score showed a distribution of 53% clinical important improvement, 28% no clinical important effect and 19% worsening. This proportion was similar for LBT, UBT, and WBT with a small and insignificant advantage for WBT (Fig. 3).

3.4 Correlations between WOMAC scores and imaging

A strong correlation between Kellgren-Lawrence grade and WOMAC-subscore pain (Pearson’s R = 0.81) is shown in Fig. 4. Within WOMAC-subscores, a significant correlation also exists concerning the subscores pain and function (Fig. 5). In contrast, stiffness was not related to any other parameter.

| survey | T0 | T4 | T8 |
|--------|----|----|----|
| identity number | 1 | 1 | 1 |
| anthropometric data | 4 | | |
| educational qualification | | | |
| Kellgren-Lawrence Grade | 2 | | |
| physician visits | 2 | | |
| Medications due to knee pain | 2 | | |
| regular drug consumption due to comorbidities | 7 | | |
| VR-12 | 12 | 12 | 12 |
| WOMAC | 24 | 24 | 24 |
| patient’s believe in the influence of training | 5 | 5 | |
| number of training sessions | 1 | 1 | |
| total number of items | 55 | 42 | 42 |

Numbers indicate number of subitems, T0 = survey before training, T4 = survey after 4 weeks training, T8 = final survey after 8 weeks training, VR-12 = Veterans Rand 12 item health survey, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.
Fig. 1. Total WOMAC score (left top) and its subscores function (right top), pain (left bottom), and stiffness (right bottom) before (T0), after 4 weeks (T4), and after 8 weeks training intervention. LBT = lower body training, UBT = upper body training, WBT = whole body training. * = significant different from T0, § = significant different from T4. Mean ± standard error

Table 2. Anthropometric data of subjects

| Group | Number | Age (years) | Height (cm) | Mass (kg) | BMI (kg/m²) | Female Total | Female % | Male Total | Male % |
|-------|--------|-------------|-------------|-----------|-------------|--------------|---------|------------|-------|
| All   | 372    | 58.9 ± 9.5  | 172 ± 9.0   | 87.1 ± 17.8 | 29.4 ± 5.7  | 241 ± 65    | 131 ± 35 |
| LBT   | 91     | 61.1 ± 9.0  | 173 ± 8.7   | 86.1 ± 18.7 | 29.1 ± 5.8  | 53 ± 58     | 38 ± 42  |
| UBT   | 111    | 57.7 ± 10.3 | 172 ± 8.9   | 88.7 ± 17.4 | 30.0 ± 6.0  | 72 ± 65     | 39 ± 35  |
| WBT   | 170    | 58.4 ± 9.0  | 172 ± 9.5   | 86.7 ± 17.5 | 29.3 ± 5.4  | 116 ± 68    | 54 ± 32  |

LBT = lower body training, UBT = upper body training, WBT = whole body training. Mean ± SD

Table 3. Initial WOMAC scores

| Group | WOMAC – Score (0 – 100) |
|-------|-------------------------|
|       | Total | Pain | Stiffness | Function |
| All   | 33 ± 17 | 32 ± 18 | 46 ± 25 | 31 ± 18 |
| LBT   | 31 ± 15 | 30 ± 17 | 45 ± 24 | 29 ± 16 |
| UBT   | 34 ± 15 | 33 ± 17 | 49 ± 26 | 32 ± 15 |
| WBT   | 33 ± 9  | 31 ± 19 | 46 ± 20 | 32 ± 20 |

LBT = lower body training, UBT = upper body training, WBT = whole body training. Mean ± SD
Fig. 2. Improvement in WOMAC subscores between T8 and T0 for maximal Kellgren-Lawrence grades 1 to 2 (left) and 3 to 4 (right). LBT = lower body training, UBT = upper body training, WBT = whole body training. Mean ± standard error

Table 4. ANOVA p-values

| Group | Times  | ANOVA p-values |
|-------|--------|----------------|
|       |        | Pain | Stiffness | Function | PQL | MQL |
| WBT   | T0–T4  | 0.037 | 0.004 | 0.013 | 0.0001 | 0.037 |
|       | T0–T8  | 0.0001 | 0.0001 | 0.0001 | 0.0001 | 0.013 |
|       | T4–T8  | 0.002 | 0.004 | 0.007 | 0.236 | 1 |
| UBT   | T0–T4  | 0.736 | 0.009 | 1 | 0.0001 | 1 |
|       | T0–T8  | 0.004 | 0.0001 | 0.092 | 0.0001 | 1 |
|       | T4–T8  | 0.052 | 0.124 | 0.026 | 0.286 | 1 |
| LBT   | T0–T4  | 0.125 | 0.0001 | 0.739 | 0.078 | 1 |
|       | T0–T8  | 0.013 | 0.004 | 0.171 | 0.003 | 1 |
|       | T4–T8  | 0.819 | 0.986 | 0.768 | 0.532 | 1 |

LBT = lower body training, UBT = upper body training, WBT = whole body training. PQL = Physical quality of life, MQL = Mental quality of life

Fig. 3. Distribution of clinical important effects in WOMAC total score. LBT = lower body training, UBT = upper body training, WBT = whole body training. White bars = clinical important improvement, gray bars = no clinical important effect, black bars = clinical important worsening
3.5 Health related quality of life

The initial physical quality of life was 36.7 ± 8.0 (LBT), 32.4 ± 8.1 (UBT), and 34.4 ± 8.2 (WBT). At the end of the intervention, PQL increased by 2.8 ± 6.6 (LBT), 5.0 ± 8.0 (UBT), and 4.9 ± 7.0 (WBT), which was significant in all cases. In general, higher initial values of the mental quality of life corresponded to nearly no changes during the intervention phase except for WBT, were MQL at T4 and T8 were significantly higher than at T0 (Fig. 6).

3.6 Patient’s Beliefs about the Effects of Training

Fig. 7 depicts the believes of patients about the influence of the 8 weeks training with respect to their personal physical improvements in general, upper and lower body fitness, and knee pain
reduction. The three training modalities were considered equivalent in terms of improving general fitness. For all 4 parameters, a nearly identical pattern occurred already at T4.

Fig. 6. Physical (left diagram) and mental (right diagram) health related quality of life. LBT = lower body training, UBT = upper body training, WBT = whole body training. * = significant different from T0. Mean ± standard error

Fig. 7. Box-plots concerning patients believes in the influence of their training on improvements in general fitness (left top), lower body fitness (right top), general physical fitness (left bottom), and reduction of knee pain (right bottom). LBT = lower body training, UBT = upper body training, WBT = whole body training
4. DISCUSSION

4.1 Functionality and Pain

The main findings of the present study are a significantly better functionality and a pain reduction in knee osteoarthritis patients in all three training modalities, i.e. an upper body training, a lower body training, and a combination of both. The statistical analysis, however, could not prove significant differences between training modalities. Since any morphological or biomechanical influence of the upper body training on leg muscles and knee surrounding tissues can be excluded, other factor(s) should be responsible for the obtained pain reduction. A simple placebo effect appears unlikely to be responsible since the belief of subjects in an exercise induced knee pain improvement was lowest in the UBT group. The step-by-step improvements from T0 to T4 and from T4 to T8 also does hardly match with a placebo effect.

A central pain sensitization is a common phenomenon in knee osteoarthritic patients [31] and its reduction by means of regular exercise may play a major role for the pain relief achieved. In support of this theory, Henriksen and coworkers [32] found in knee osteoarthritic patients a reduced pressure-pain sensitivity after a systematic and progressive twelve-week circuit training focusing on strength and coordination of the trunk and legs. A second candidate may be a systemic anti-inflammatory effect of muscular activity as initially suggested by Petersen and Pedersen [20]. In a recent meta-analysis, the beneficial effect of skeletal muscle derived cytokines could be confirmed [21].

Whatever the origin of the training induced pain reduction will be, the phenomenon may contribute to the obtained enhancement in functionality. In a cross-over study, Henriksen et al. [33] showed that in healthy subjects an artificially induced knee pain reduces the maximal isometric quadriceps torque by 15%. The pain was provoked by a 1 ml hypertonic NaCl solution injected into the infrapatellar fat pad while a 1 ml isotonic NaCl control-solution did neither induce pain nor reduce maximal torques. In addition, the intensity of pain correlated with the torque reduction. In a comparable approach the coordination was also negatively affected [34]. In the light of the present results and the findings of Henriksen et al. [33] the causal relationship between training induced leg strength enhancements and pain reductions in knee osteoarthritis patients should be reviewed critically. So far, most of the literature has followed the idea that training initially increases muscle strength and that increasing strength leads to pain reductions. A reverse cause-and-effect mechanism or an interaction of both seems just as possible. Unfortunately, with the present results we cannot draw a conclusion since we did not evaluate the maximal voluntary torques of patients leg muscles. One may argue that a weakness of the present study is the absence of a non-treatment control group. However, our approach focused on the comparison of exercise treatments within different body areas, i.e. pain surrounding tissues and unaffected body regions. Instead of incorporating a third study arm we favored the increase of the relevant informative value since the inclusion of a non-exercising control group would have led to a reduced number of cases in the treatment arms. Moreover, based on the results of other investigations which included a non-exercising control group, it appears unlikely that a non-treatment group would have led to significant improvements in function or pain reductions [35,36,37,38,39,40,41]. In these studies, the missing beneficial effects in a non-treatment control group did not depend on the design of control (attention vs. non attention, different types of attention) and, therefore, the significant improvements in the UBT group of the present study will hardly be explainable with an attention-derived parameter.

Interestingly, the most recent literature concerning the influence of exercise in osteoarthritic patients also does not include a classic no intervention control group [42,43,44, 45,46].

4.2 Quality of Life

According to a representative study of the health related quality of live in Germany, the physical quality of live in the healthy population ranged between 45 (95% confidence interval 44,2 – 45) in the 70-79 years group and 54,3 (ci 53,8 – 54,9) in the 30-39 years group [47]. The mental quality of live amounts to 51,4 (ci 50,7 – 52,1) and 48,7 (ci 48,0 – 49,4), respectively [47]. The patients of the present study, therefore, showed strongly reduced baseline PQL at baseline while MQL was within or even above the norm. That may be a common phenomenon for knee osteoarthritis patients since several other publications from different cultures reported
comparable data [48,49,50,51]. With the training interventions the physical component significantly improved in all three groups while the mental component remained nearly unchanged except an increase in the WBT group from T0 to T4. Obviously, mental and physical quality of live in osteoarthritis patients are affected by different determinants.

4.3 Future Prospects

Due to the study design, the individual training protocol could not be switched within the study period. Although the positive effects were statistically highly significant, in all three study groups about 30% of subjects failed to reach clinically important improvements and about 20% even showed a worsening. Therefore, further training interventions should be encouraged comparing the effects of randomly assigned and patient-chosen training groups as well as an a priori fixed with a changeable training regimen in the case of a non-response after a couple of training weeks.

5. LIMITATIONS

The most striking limitation of the study is the short study period of eight weeks. A second weak point is the comparability of the three training regimen with regard to the duration of a single exercise bout. The net exercise times ranged from 12 min. in UBT to 28 min. in WBT with the LBT time in between. However, the present results suggest that at least in the utilized range this criterion does not play a dominant role in the improvements of physical function and pain reduction.

6. CONCLUSION

A regular training including strength exercises improves the health related physical quality of life, increases functionality and reduces pain in knee osteoarthritis patients. These improvements do not depend on the location of skeletal muscles exposed to the exercise regimen.

CONSENT

Participate were included after verbal and written informed consent.

ETHICAL APPROVAL

All experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards lay down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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