

Manual Acupuncture at LI11, Local Points and Both for Knee Osteoarthritis: A Pilot Randomized Controlled Trial

Aijun Zheng¹, Fangfang Zheng¹, Kai Jin¹, Ming Chi¹, Jiajia Mu¹, Hongxia Wei², Jian Lei², Chao Xu³

¹Department of Acupuncture and Moxibustion, Peking University Third Hospital Yanqing Hospital, Beijing, 102100, People's Republic of China;

²Department of Traditional Chinese Medicine, Nancaiyan Community Hospital, Beijing, 102100, People's Republic of China; ³Department of Pharmacy, Peking University Third Hospital Yanqing Hospital, Beijing, 102100, People's Republic of China

Correspondence: Aijun Zheng, Email zaji1970@163.com

Objective: Knee osteoarthritis (KOA) is a common chronic degenerative joint disease, and acupuncture is an alternative therapy for KOA. This study aims to detect the effectiveness of acupuncture at LI11 in improving pain and function for KOA patients.

Methods: A total of 108 patients with KOA were randomly allocated to Control Group (local points), Treatment Group A (LI11), and Treatment Group B (local points and LI11) with a treatment phase of 4 weeks and a follow-up phase of 4 weeks. Primary outcome was response rate. Secondary outcomes included Visual Analogue Scale (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and recurrence rate. Study was registered on Chinese Clinical Trial Registry (Registered number: ChiCTR2000034926).

Results: The response rate in Treatment Group A, Treatment Group B, and Control Group was 71.43%, 85.29%, and 51.53%, respectively, at Week 4, and Treatment Group B was significantly higher than Control Group (difference[98.3% CI]: 33.86 [0.135,0.543], $P = 0.003$). Although no significant difference was found, Treatment Group A had a better response rate compared with Control Group (difference[98.3% CI]: 20.00 [-0.072, 0.472], $P = 0.086$). For VAS and WOMAC, there were significant differences within 3 groups at Week 4 compared with the baseline. There was a significant improvement in VAS scores and WOMAC function and pain subscales at Week 4 in Treatment Group B compared with Control Group and Treatment Group A.

Conclusion: LI11 is an effective point for patients with KOA, and it could be a selection for young acupuncturists and acupuncturists who work in rural areas; however, large-sample studies are necessary to further verify results in the future.

Keywords: knee osteoarthritis, manual acupuncture, Quchi, LI11, pilot randomized controlled trial

Introduction

Knee osteoarthritis (KOA) is one of the most common chronic degenerative joint diseases, characterized by pain and dysfunction of the affected joint. Globally, the population of patients with KOA increased in the past 20 years, up to 2019, more than 350 million patients have been affected by KOA,¹ leading to a great burden on health system. China has a large population of KOA, according to Global Burden of Disease (GBD) 2019, the incidence of KOA increased by 128.7% in 2019 compared with 1990, which was 84.258/100,000.² Moreover, several studies have demonstrated that the prevalence of KOA in rural areas of China was significantly higher than that in urban regions (16.9% vs 11.1% in one study).^{3,4} The different prevalence could be associated with the different lifestyles (more manual labor in rural areas) and medical systems (low level of healthcare in rural areas). Therefore, we need to pay more attention to patients with KOA in rural areas.

Pain and dysfunction disturb mostly patients with KOA, and non-steroidal anti-inflammatory drugs (NSAIDs) are the most common prescription for KOA to relieve pain;⁵ however, NSAIDs cause adverse events in gastrointestinal and cardiovascular systems, which limits the usage among patients with KOA.⁶ Non-pharmacological treatments include education, weight loss, and exercise. The structured program of diet and exercise helps patients lose weight (for those who are overweight) and strengthen lower extremity muscles. However, inappropriate exercise may exacerbate the knee and increase the burden on elderly patients; therefore, a professional physical therapist is necessary for producing a personal program.⁷ Other treatments such as knee arthroscopy and knee replacement are suitable for patients with severe clinical manifestations, and they are costly, which might not be first chosen for patients who live in rural areas.⁵

Acupuncture has been widely used and studied as an alternative therapy for KOA in clinical practice, a study has demonstrated that three sessions per week of manual acupuncture for KOA were effective and safe.⁸ Another study has suggested that compared with sham acupuncture, intensive electroacupuncture had a better effect in relieving pain and improving function among patients with KOA.⁹ However, the selected acupuncture points in these two studies were all located in the local regions around the knee. According to the meridian theory, certain distal points are effective for KOA, LI11 (Quchi) is one of the points. Moreover, studies have indicated that certain regions of upper limbs and lower limbs are derived from the same primitive body segment, which still has an association with the development of human body.¹⁰ Also, several studies have confirmed the effect of LI11 in treating KOA.¹¹ Therefore, LI11 is an ideal selection for acupuncturists working in community hospitals in rural areas or young acupuncturists due to the effectiveness, safety, and convenience, as well as for patients with KOA in rural areas due to the minimal invasion and low cost.

However, there is no study comparing the effect of LI11 and local acupuncture points for patients with KOA; thus, we aimed to conduct a pilot randomized controlled trial (RCT) in rural areas of Beijing to detect the effect of LI11 for pain relief and function improvement in patients with KOA.

Methods

Study Design and Setting

Our multi-center, three-arm randomized controlled trial (RCT) was conducted according to the Declaration of Helsinki and was approved by the research ethic committee of Peking University Third Hospital Yanqing Hospital (No 202000102). The intervention included 4 weeks of manual acupuncture therapy and 4 weeks of follow-up. Our study was registered on Chinese Clinical Trial Registry (Registered number: ChiCTR2000034926). Our study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline.¹²

Participants

Participants were recruited from the outpatient units of acupuncture and moxibustion department at Peking University Third Hospital Yanqing Hospital and Nancai Yuan Community Hospital. The enrollment started in June 2020 and ended in May 2023.

Diagnosis Criteria

Our study used the “consensus of four-step ladder program of knee osteoarthritis (2018)” to diagnose KOA. Participants were diagnosed with KOA if they met the following first situation and any two of the second, third, fourth or fifth situations.

1. Chronic knee pain for the last 1 month
2. X-ray confirmation of narrowing of articular space, sclerosis and/or cystic degeneration of subchondral bone, and osteophyte formation at articular margin
3. Age ≥ 50 years
4. Morning stiffness ≤ 30 min
5. Bone friction sound (sensation) on movement

Inclusion Criteria

1. Aged 50–70 years, male or female
2. Diagnosed with KOA based on the abovementioned diagnosis criteria
3. X-ray confirmation of Kellgren-Lawrence grade I, II and III within 6 months¹³
4. Agreed to refrain from the routine use of analgesics; If participants needed rescue medication, they were provided ibuprofen (SK&F Co, Ltd, Tianjin, China; 0.4 g/8 hours).
5. Written informed consent

Exclusion Criteria

1. Had knee surgery or waiting for surgery
2. Knee pain caused by other diseases (eg, tumor, autoimmune disease, trauma, and infection)
3. Had arthroscopy within 1 year or intra-articular injection within 4 months
4. Had acupuncture therapy within 3 months
5. Had serious acute or chronic organic or mental disorders
6. Pregnant or breastfeeding women
7. Coagulation diseases (such as hemophilia)
8. Had participated in other clinical trials within 3 months

Randomization and Allocation Concealment

Eligible participants were randomly allocated to the local point group (Control Group), LI11 (Quchi) group (Treatment Group A), or a combination of local point and LI11 point group (Treatment Group B) in a ratio of 1:1:1. The randomization sequence was generated with the R software (4.2.1), and we used minimization to minimize the total imbalance between treatments over multiple baseline covariates. We defined age, Body Mass Index (BMI), Kellgren-Lawrence grade, and center as baseline covariates with weight of 1, 2, 3, 1, respectively, and the allocation probability of Control, Treatment Group A, and Treatment Group B was 0.6, 0.3, 0.1. All processes were done by an independent statistician who was not involved in the later implementation or statistical analysis.

Blinding

The participants and acupuncturists in our study were not blinded because of the nature of the intervention. Data analysts and outcome assessors were blinded to group assignments.

Interventions

Manual acupuncture was performed with sterile disposable needles (Hwato Needles, Sino-foreign Joint Venture Suzhou Hwato Medical Instruments, China, size 0.25mm*40mm). The needles were inserted into a depth of 15 to 30mm at the acupuncture points and were stimulated manually (lifting and thrusting combined with twirling and rotating) for at least 10s to achieve “Deqi” (a compositional sensation of soreness, numbness, distention, and heaviness). The needles were manually stimulated every 10 min and were retained for 30 min. Participants received acupuncture therapy 6 times per week (Monday to Saturday) for 4 weeks.

Participants were allowed to use Ibuprofen sustained-release capsules (0.3g/T, Tianjin Smith Kline & French Laboratories Ltd., Tianjin, China) as a rescue medication, and the dose should not exceed 1200mg per day. The details of usage were recorded in the case report form (CRF).

Control Group (Local Point)

The selection of acupuncture points in Control Group was based on traditional Chinese medicine meridian theory of Bi syndrome. Nine selected points were ST34 (Liangqiu), ST36 (Zusanli) EX-LE5 (Neixiyan), ST35 (Dubi), SP9 (Yinlingquan) SP10 (Xuehai), GB34 (Yanglingquan), BL40 (Weizhong) and Ahshi point. If one knee was affected, nine points were selected on the affected side, and bilateral nine points were selected if both knees were affected.

Treatment Group a (LI11)

The acupuncture point in Group B was LI11 (Quchi), based on the Yellow Emperor's Classic of Internal Medicine, contralateral LI11 was selected based on the affected knee, for example, if left knee was affected, the right LI11 was selected, but if two knees were affected, bilateral LI11 was selected.

Treatment Group B (Local Point & LI11)

The acupuncture points in Treatment Group B were the combination of the acupuncture points in Control Group and Treatment Group A (Figure 1).

Outcomes

Primary Outcome Measurement

Participants used Visual Analogue Scale (VAS) to evaluate the average pain intensity and McMaster Universities Osteoarthritis Index (WOMAC) function subscale to assess daily ability. The primary outcome was response rate¹⁴ which is defined as the proportion of participants whose average VAS scores decrease ≥ 2 points and the WOMAC function subscale scores decrease ≥ 6 points at Week 4 compared with baseline. If one knee was affected, the assessment was based on that knee, if both knees were affected, the assessment was based on the worse one (Figure 2).

Secondary Outcome Measurement

The secondary outcomes were VAS and WOMAC. VAS is an 11-point self-administrated tool, ranging from 0 (no pain at all) to 10 (worst pain)¹⁵ to evaluate the average pain intensity. WOMAC is a self-administered questionnaire consisting of 3 subscales with a total of 24 items. Pain subscale evaluates the intensity of pain in 5 different conditions, stiffness subscale

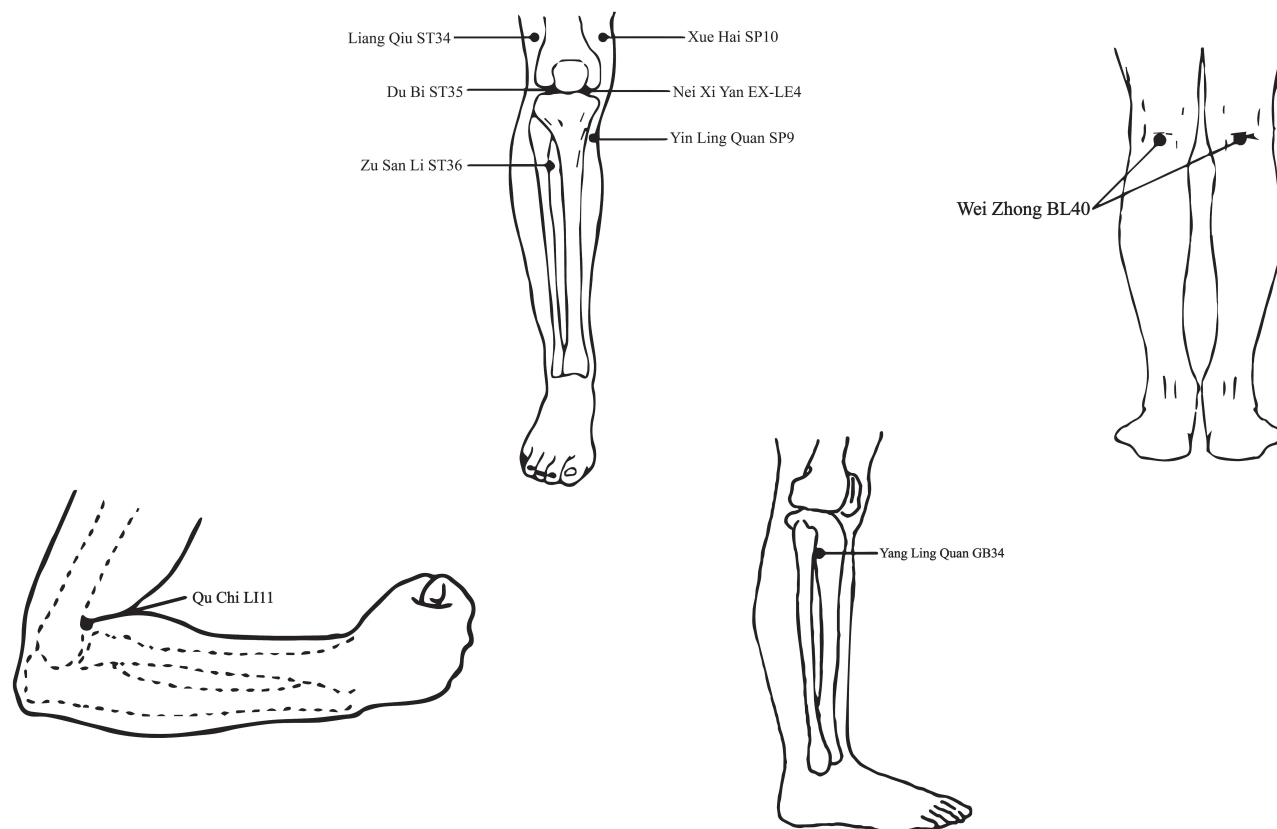


Figure 1 Selected acupuncture points used in the study.

| | Study Period | | | |
|------------------------------|--------------|-----------------|---------|-----------------|
| | Baseline | Treatment Phase | | Follow-up Phase |
| | -1 week | 0 day | 4 weeks | 4 weeks |
| Enrolment | | | | |
| Informed consent | × | | | |
| Inclusion/Exclusion criteria | × | | | |
| Basic information | × | | | |
| Medical history | × | | | |
| Physical examination | × | | | |
| Pain diary | × | | | |
| Randomization | | × | | |
| Interventions | | | | |
| Treatment Group A (n=35) | | × | ← → × | |
| Treatment Group B (n=34) | | × | ← → × | |
| Control Group (n=35) | | × | ← → × | |
| Assessments | | | | |
| Response rate | | | | |
| VAS | | × | × | |
| WOMAC | | × | × | |
| Compliance of participants | | | × | |
| Recurrence rate | | | | × |
| Adverse events | | × | ← → × | × |

Figure 2 Schedule for data collection of this trial. Treatment Group: A LIII, Treatment Group: A LIII & local points, Control Group: local points.

Abbreviations: VAS: Visual Analogue Scale, WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

evaluates the stiffness of the affected knee, and function subscale evaluates the ability to move and daily activities. The total score of WOMAC is 68, higher scores indicate worse pain, stiffness, and function¹⁶ (Figure 2).

Compliance assessment was assessed at Week 4, participants with scores lower than 80 were considered as poor compliance.

$$\text{Compliance score} = \frac{\text{Actual treatment sessions}}{\text{Required treatment sessions}} \times 100$$

The recurrence rate at follow-up phase was defined as VAS scores increased ≥ 2 points and WOMAC function scores increased ≥ 6 points (Figure 2).

Adverse Events

Adverse Events (AEs) were evaluated and recorded by researchers after the end of weekly treatment and during the follow-up phase. Serious adverse events were reported and handled based on regulations. Common acupuncture-related adverse events include dizziness, subcutaneous hematoma, infection, etc.

Sample Size Calculations

No effective response rate of manual acupuncture on LIII was found in previous studies, while we found one study indicated that a reasonable minimum number of participants from the population of interest is 30.^{17,18} Thus, a total of 90 participants were needed in our study, considering 15% of dropouts, we decided to recruit 108 participants (36 for each group) to achieve the practical purpose of the trial based on clinical experience.

Statistical Analysis

All data were assessed using R software (4.2.1). Continuous data were described using mean (standard deviation) or median (interquartile range) and the paired *t*-test (normal distribution) and Wilcoxon rank sum test (abnormal

distribution) were used for comparison within groups. Categorical data were described using number and percentage, and the Wilcoxon rank sum test was used for comparison within the group. The chi-squared test was used to compare the response rate, VAS, and WOMAC between 3 groups. α was adjusted using Bonferroni and set at 0.017 for multiple comparisons of response rate and recurrence rate, while α was not adjusted for other outcomes. Adverse events were described using the chi-squared test. All test indicators were analyzed using Intention-To-Treat (ITT), and missing data were obtained using the last observation carried forward (LOCF) method.

Results

Participant Characteristics

We screened 150 participants in total, of them, 42 participants were excluded after screening. A total of 108 participants (36 in each group) were randomized, and 4 participants did not receive allocated intervention due to the pandemic, which was eliminated from analysis, thus 35 participants in Treatment Group A, 34 participants in Treatment Group B, and 35 participants in Control Group were included in the ITT analysis and safety analysis. Among these, 34 participants in Treatment Group A, 31 participants in Treatment Group B, and 28 participants in Control Group completed all treatment at Week 4 (Figure 3).

There was no significant difference in demographic, clinical characteristics or outcome measurements at baseline. The mean (SD) of age and BMI was 60 (5.73) years and 26.35 (3.65) kg/m². Eighty-four (80.77%) participants were female in our study, and mean (SD) duration of KOA was 5.5 (5.96) years. Almost half of participants (49[47.12%]) were at Grade II of Kellgren-Lawrence grade. The mean (SD) of VAS and WOMAC was 5.48 (1.52) and 34.96 (14.34), respectively (Table 1).

Primary Outcome

In our study, the response rate in Treatment Group A, Treatment Group B, and Control Group was 71.43%, 85.29%, and 51.53%, respectively, at Week 4. The pairwise comparison showed that the response rate of Treatment Group B was significantly higher than that of Control Group (difference[98.3% CI]: 33.86[0.135,0.543], P = 0.003). While there was no significant difference between Treatment Group A and Control Group (difference[98.3% CI]: 20.00 [-0.072, 0.472],

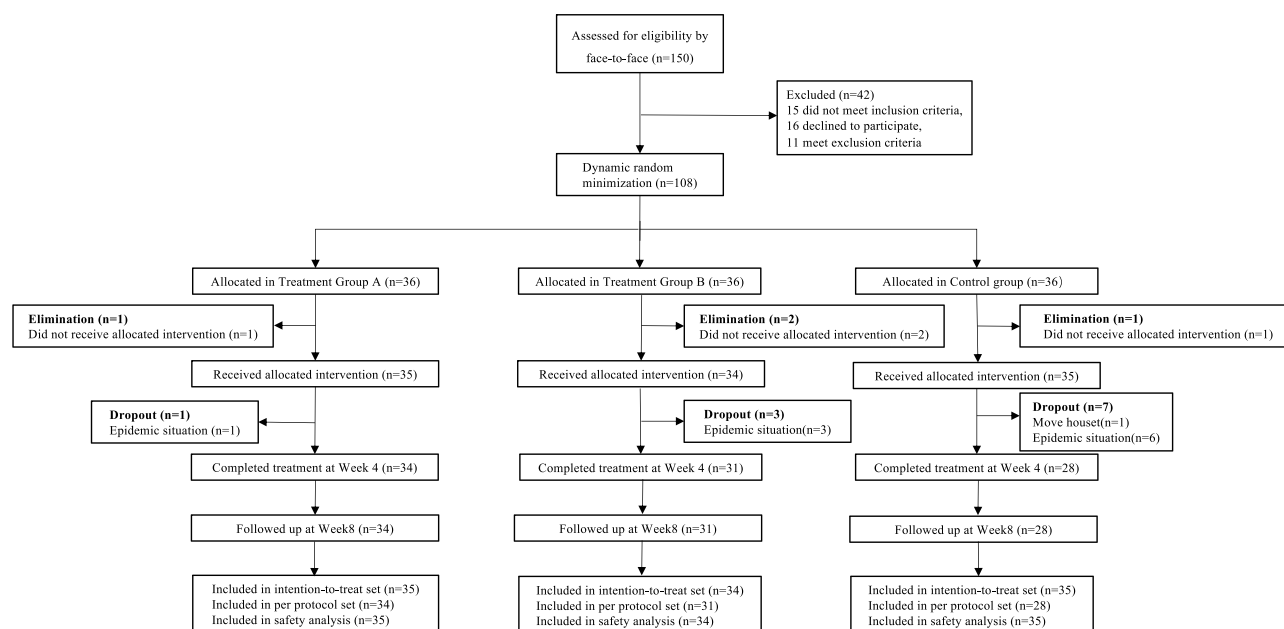


Figure 3 Trial flow chart. Treatment Group: A LIII, Treatment Group: A LIII & local points, Control Group: local points.

Table I Characteristics of the Patients at Baseline

| Characteristics | Treatment Group A (N=35) | Treatment Group B (N=34) | Control Group (N=35) | All(N=104) | P |
|---------------------------------|-----------------------------|-----------------------------|-------------------------|--------------|--------------------|
| Age, mean(SD) years | 60.43(5.81) | 59.65(5.92) | 59.91(5.61) | 60.00(5.73) | 0.849 ^a |
| Gender, No.(%) | | | | | |
| Female | 28(80.00%) | 27(79.41%) | 29(82.86%) | 84(80.77%) | 0.957 ^b |
| Male | 7(20.00%) | 7(20.59%) | 6(17.14%) | 20(19.23%) | |
| BMI, mean(SD) kg/m ² | 26.36(3.18) | 26.25(4.34) | 26.44(6.00) | 26.35(3.65) | 0.978 ^a |
| Duration, mean(SD) years | 6.49(6.75) | 4.85(4.55) | 5.15(6.36) | 5.5(5.96) | 0.254 ^a |
| Radiological grade, No.(%) | | | | | 0.940 ^b |
| Grade I | 11(31.43%) | 10(29.41%) | 11(31.43%) | 32(30.77%) | |
| Grade II | 15(42.86%) | 17(50.00%) | 17(48.57%) | 49(47.12%) | |
| Grade III | 9(25.71%) | 7(20.59%) | 7(20.00%) | 23(22.11%) | |
| VAS, mean(SD) | 5.63(1.59) | 5.50(1.52) | 5.31(1.47) | 5.48(1.52) | 0.728 ^a |
| WOMAC, mean(SD) | 35.49(14.79) | 32.71(13.49) | 36.63(14.81) | 34.96(14.34) | 0.511 ^a |
| Function subscale | 25.49(11.66) | 24.09(9.89) | 26.34(11.1) | 25.32(10.85) | 0.689 ^a |
| Pain subscale | 7.40(3.11) | 6.65(3.44) | 7.43(3.10) | 7.16(3.21) | 0.523 ^a |
| Stiffness subscale | 2.60(1.80) | 1.97(1.62) | 2.86(1.94) | 2.48(1.82) | 0.093 ^a |

Notes: ^aAnalyzed using ANOVA. ^bAnalyzed using chi-squared test.

Abbreviations: BMI, Body Mass Index; VAS, Visual Analogue Scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

P = 0.086), Treatment Group A had a better response rate. Although Treatment Group B had a better response rate compared with Treatment A, no significant difference was found (difference[98.3% CI]: -13.86 [-0.372, 0.094], P = 0.163) (Table 2).

Secondary Outcomes

For VAS and WOMAC, there were significant differences within 3 groups at Week 4 compared with baseline. There was a significant improvement in VAS scores at Week 4 in Treatment Group B compared with Control Group (difference [95% CI]: -1.65 [1.000 to 2.000], P = 0.001) and Treatment Group A (difference[95% CI]: 1.08 [0.000 to 2.000], P = 0.006). Moreover, a statistically significant difference was found in Treatment Group A (difference[95% CI]: 4.39 [1.000 to 6.000], P = 0.006) and Control Group (difference[95% CI]: -7.07 [3.000 to 10.000], P = 0.000) compared with Treatment Group B for WOMAC function subscale at Week 4, and similar results were found in WOMAC pain subscale, and Treatment Group B had significantly better pain relief compared with Treatment Group A (difference[95% CI]: 1.08 [0.000 to 2.000], P = 0.012) and Control Group (difference[95% CI]: -1.65 [1.000 to 2.000], P = 0.001). However, merely Treatment Group B vs Control Group (difference[95% CI]: -0.64 [0.000 to 1.000], P = 0.012) had statistical significance in WOMAC stiffness subscale (Table 2).

The compliance of participants in each group was $\geq 80\%$, which was considered good compliance (Table 3). The number of participants who used rescue medication (Ibuprofen) was 6, 5, and 5 in Treatment Group A, Treatment Group B, and Control Group, respectively (Table 3). The recurrence rate was highest in Control Group (34.29%), and there was no significant difference in pairwise comparison. We also performed sensitivity analysis using Per-Protocol analysis (PP analysis), the results were similar with ITT analysis (Table 4).

Safety

No severe adverse events were found among all three groups. A total of 8 adverse events (8/104) occurred in our study (Table 3), 4 participants had subcutaneous hematoma, and 4 had subcutaneous hemorrhage, all participants healed completely within one week. There was no significant difference among three groups.

Table 2 Primary and Secondary Outcomes (ITT)

| | Treatment Group A(N=35) | Treatment Group B(N=34) | Control Group (N=35) | Treatment Group A vs Control Group | | Treatment Group B vs Control Group | | Treatment Group A vs Treatment Group B | |
|------------------------------------------------|-------------------------|-------------------------|----------------------|------------------------------------------------------------|-------------------------|-----------------------------------------------|-------------------------|----------------------------------------------|-------------------------|
| | | | | Difference (98.3% CI) ^c | P ^b | Difference (98.3% CI) ^c | P ^b | Difference (98.3% CI) ^c | P ^b |
| Primary outcome | | | | | | | | | |
| Response rate ^a , No.(%) Week4 | 25(71.43%) | 29(85.29%) | 18(51.43%) | 20.00(-0.072,0.472) | 0.086 | 33.86(0.090,0.587) | 0.003 | -13.86(-0.372,0.094) | 0.163 |
| Secondary outcomes | | | | Difference(95% CI) | P ^b | Difference(95% CI) | P ^b | Difference(95% CI) | P ^b |
| VAS, mean(SD) | | | | | | | | | |
| Baseline | 5.63(1.59) | 5.50(1.52) | 5.31(1.47) | 0.32(-1.000,0.000) | 0.463 | 0.19(-1.000,0.000) | 0.537 | 0.13(-1.000,0.000) | 0.845 |
| Week4 | 2.57(1.42) | 1.68(1.72) | 3.06(1.81) | -0.49(0.000,1.000) | 0.301 | -1.65(1.000,2.000) | 0.001 | 1.08(0.000,2.000) | 0.006 |
| Z or t | 5.192 | 4.960 | 4.568 | | | | | | |
| P ^d | 0.000 | 0.000 | 0.000 | | | | | | |
| WOMAC function subscale, mean(SD) | | | | | | | | | |
| Baseline | 25.40(11.66) | 24.09(9.89) | 26.34(11.1) | -0.94(-4.574,6.289) | 0.754 | -2.25(-2.804,7.314) | 0.377 | 1.31(-3.807,6.602) | 0.594 |
| Week4 | 9.86(7.94) | 5.47(4.71) | 12.54(8.69) | -2.68(-1.000,6.000) | 0.115 | -7.07(3.000,10.000) | 0.000 | 4.39(1.000,6.000) | 0.006 |
| Z or t | 7.769 | 12.413 | 5.015 | | | | | | |
| P ^d | 0.000 | 0.000 | 0.000 | | | | | | |
| WOMAC pain subscale, mean(SD) | | | | | | | | | |
| Baseline | 7.40(3.11) | 6.65(3.44) | 7.43(3.10) | 0.03(-1.452,1.509) | 0.969 | -0.78(-0.790,2.353) | 0.324 | 0.75(-0.821,2.327) | 0.343 |
| Week4 | 3.17(2.61) | 2.09(2.12) | 3.74(2.56) | -0.57(0.000,2.000) | 0.267 | -1.65(1.000,2.000) | 0.001 | 1.08 (0.000,2.000) | 0.012 |
| Z or t | 8.028 | 8.301 | 4.799 | | | | | | |
| P ^c | 0.000 | 0.000 | 0.000 | | | | | | |
| WOMAC stiffness subscale, mean(SD) | | | | | | | | | |
| Baseline | 2.60(1.80) | 1.97(1.62) | 2.86(1.94) | -0.26(-1.000,1.000) | 0.779 | -0.89(0.000,2.000) | 0.033 | 0.63(0.000,2.000) | 0.108 |
| Week4 | 0.94(1.26) | 0.62(1.16) | 1.26(1.34) | -0.32(0.000,1.000) | 0.238 | -0.64(0.000,1.000) | 0.012 | 0.32(0.000,0.000) | 0.224 |
| Z or t | 4.357 | 5.441 | 4.191 | | | | | | |
| P ^d | 0.000 | 0.000 | 0.000 | | | | | | |
| Recurrence rate ^a , No.(%) Week8 | 8(22.86%) | 4(11.76%) | 12(34.29%) | Difference (98.3% CI) ^c -11.43(-0.370,0.141) | P ^b 0.482 | Difference (98.3% CI) -22.53(-0.458,0.007) | P ^b 0.054 | Difference (98.3% CI) 11.10(-0.104,0.327) | P ^b 0.369 |

Notes:^aThe significance level for response rate and recurrence rate was adjusted at 0.017 for multiple comparisons using the Bonferroni method. Thus, the 98.3% CI were used.^bAnalyzed using chi-squared test.^cAnalyzed using paired t-test.^dAnalyzed using Wilcoxon rank sum test.

Abbreviations: VAS, Visual Analogue Scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Table 3 Compliance Data, safety Assessment and Rescue Medication Usage

| Compliance | Treatment Group A | Treatment Group B | Control Group | P |
|---------------------------------------------------------------------------------------------------------------|-------------------|-------------------|---------------|-------|
| Participants received at least 20-session treatment in Group H (24 sessions in total, compliance rates > 80%) | 34 | 31 | 28 | |
| Compliance data, No.(%) | | | | |
| Low | 1(2.86%) | 3(8.82%) | 7(20.00%) | |
| High | 34(97.14%) | 31(91.18%) | 28(80.00%) | 0.182 |
| Safety assessment, No.(%) | | | | |
| Total adverse events | 2 | 3 | 3 | 1.000 |
| Severe adverse events | 0(0.00%) | 0(0.00%) | 0(0.00%) | |
| Subcutaneous hematoma | 1(50.00%) | 1(33.33%) | 2(66.67%) | |
| Subcutaneous hemorrhage | 1(50.00%) | 2(66.67%) | 1(33.33%) | |
| Rash | 0(0.00%) | 0(0.00%) | 0(0.00%) | |
| Rescue medication usage (Ibuprofen), No.(%) | 6(17.14%) | 5(14.71%) | 5(14.29%) | 1.000 |

Note: Adverse events were analyzed in participants who received treatment at least once.

Discussion

In our study, participants with KOA who received acupuncture at LI11 had a better response rate than those who received acupuncture at local points. Meanwhile, participants improved better regarding pain and dysfunction in LI11 group compared with local point group. Besides, the combination of two selected points showed best in alleviating pain and dysfunction. No severe adverse events were found among all three groups, and participants who had adverse events such as bleeding healed completely within one week. These results indicated that LI11 may be an effective point for patients with KOA, and it could be used as a selection for young acupuncturists and acupuncturists who work in rural areas; however, large-sample studies are required to further verify the results in the future.

To our best, there is no study comparing LI11 with local points for patients with KOA. However, we found two studies comparing distal points with local points for chronic pain, and they have consistent results with ours. Irnich et al¹⁹ found that acupuncture at distal points had better effects in improving flexibility and pain for patients with chronic neck pain compared with dry needling at local myofascial trigger points. Also, Yu et al¹¹ found better pain relief and knee range of motion improvement after acupuncture at distal points than local points in treating KOA. The underlying mechanism of acupuncture at distal points in reducing pain might be related to non-segmental antinociceptive systems, whereas there is limited evidence to demonstrate non-segmental antinociceptive systems, thus more studies need to be done to investigate the mechanisms.

Our study has several limitations. First, we merely used two self-administered outcome measurements to assess the pain and function of patients with KOA. KOA affects the quality of life and mental health as well, thus questionnaires such as SF-36 are necessary. However, the main goal of KOA treatment is to relieve pain and dysfunction, VAS is the most common tool for evaluating pain, and WOMAC is the most common tool for KOA assessment. Secondly, we did not use sham control which is not always the best control in different studies. Our study aimed to detect the effectiveness of acupuncture at LI11 compared with acupuncture at local points which has been proven effective. Moreover, the positive control was more ethical for participants who were seeking relief from their discomfort. Thirdly, the participants and acupuncturists were not blinded in our study, thus it is difficult to exclude the placebo effects. Finally, the sample size in our study was relatively small, thus it is hard to generalize our results. However, this is a pilot study which could provide hints for future studies.

Conclusion

Based on our current results, compared with acupuncture at local points, acupuncture at LI11 had better effects in alleviating pain and dysfunction, indicating that acupuncture at LI11 could be a choice for young acupuncturists and acupuncturists who work in rural areas; however, large-sample studies are necessary to further verify results in the future.

Table 4 Primary and Secondary Outcomes (PP)

| | Treatment Group A(N=34) | Treatment Group B(N=31) | Control Group (N=28) | Treatment Group A vs Control Group | | Treatment Group B vs Control Group | | Treatment Group A vs Treatment Group B | |
|------------------------------------------------|-------------------------|-------------------------|----------------------|------------------------------------------------------------|-------------------------|-----------------------------------------------|-------------------------|----------------------------------------------|-------------------------|
| | Primary outcome | | | Difference (98.3% CI) ^c | P ^b | Difference (98.3% CI) ^c | P ^b | Difference (98.3% CI) ^c | P ^b |
| Response rate ^a , No.(%) Week4 | 25(73.53%) | 29(93.55%) | 18(64.29%) | 9.24(-0.189,0.374) | 0.432 | 29.26(0.052,0.533) | 0.005 | -20.02(-0.409,0.009) | 0.069 |
| | Secondary outcomes | | | Difference(95% CI) | P ^b | Difference(95% CI) | P ^b | Difference(95% CI) | P ^b |
| VAS, mean(SD) | | | | | | | | | |
| Baseline | 5.62(1.61) | 5.45(1.52) | 5.39(1.45) | 0.23(-1.000,1.000) | 0.629 | 0.06(-1.000,1.000) | 0.679 | 0.17(-1.000,1.000) | 0.810 |
| Week4 | 2.50(1.38) | 1.32(1.28) | 2.61(1.55) | -0.11(-1.000,1.000) | 0.833 | -1.29(1.000,2.000) | 0.001 | 1.18(1.000,2.000) | 0.001 |
| Z or t | 5.120 | 4.810 | 4.484 | | | | | | |
| P ^d | 0.000 | 0.000 | 0.000 | | | | | | |
| WOMAC function subscale, mean(SD) | | | | | | | | | |
| Baseline | 25.20(11.74) | 23.55(9.84) | 27.10(11.51) | -1.90(-4.070,7.814) | 0.531 | -3.55(-2.009,9.126) | 0.206 | 1.65(-3.711,7.085) | 0.535 |
| Week4 | 9.15(6.84) | 4.74(4.02) | 10.43(7.48) | -1.28(-2.000,5.000) | 0.371 | -5.69(2.000,8.000) | 0.001 | 4.41(1.000,6.000) | 0.002 |
| Z or t | 5.070 | 12.658 | 4.625 | | | | | | |
| P ^d | 0.000 | 0.000 | 0.000 | | | | | | |
| WOMAC pain subscale, mean(SD) | | | | | | | | | |
| Baseline | 7.41(3.15) | 6.30(3.19) | 7.39(3.22) | 0.02(-1.645,1.607) | 0.982 | -1.09(-0.668,2.680) | 0.234 | 1.11(-0.549,2.598) | 0.198 |
| Week4 | 3.06(2.56) | 1.65(1.40) | 2.93(1.84) | 0.13(-1.000,0.000) | 0.840 | -1.28(1.000,2.000) | 0.002 | 1.41(0.000,2.000) | 0.003 |
| Z or t | 8.258 | 8.162 | 4.558 | | | | | | |
| P ^c | 0.000 | 0.000 | 0.000 | | | | | | |
| WOMAC stiffness subscale, mean(SD) | | | | | | | | | |
| Baseline | 2.56(1.81) | 1.77(1.26) | 2.93(2.12) | -0.37(-1.000,1.000) | 0.646 | -1.16(0.000,2.000) | 0.022 | 0.79(0.000,2.000) | 0.072 |
| Week4 | 0.85(1.16) | 0.39(0.62) | 1.04(1.29) | -0.19(0.000,0.000) | 0.543 | -0.65(0.000,1.000) | 0.034 | 0.46(0.000,1.000) | 0.133 |
| Z or t | 4.357 | 5.686 | 5.943 | | | | | | |
| P ^d | 0.000 | 0.000 | 0.000 | | | | | | |
| Recurrence rate ^a , No.(%) Week8 | 7(20.59%) | 3(9.68%) | 9(32.14%) | Difference (98.3% CI) ^c -11.55(-0.383,0.152) | P ^b 0.564 | Difference (98.3% CI) -22.46(-0.470,0.021) | P ^b 0.094 | Difference (98.3% CI) 10.91(-0.099,0.318) | P ^b 0.382 |

Notes:^aThe significance level for response rate and recurrence rate was adjusted at 0.017 for multiple comparisons using the Bonferroni method. Thus, the 98.3% CI were used.^bAnalyzed using chi-squared test.^cAnalyzed using paired t-test.^dAnalyzed using Wilcoxon rank sum test.

Abbreviations: VAS, Visual Analogue Scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Data Sharing Statement

The research team will preserve the original paper-version CRFs in a locked cabinet at Peking University Third Hospital Yanqing Hospital for at least 5 years after publication of study results. The trial database is anonymized, and all data related to the study can be accessible from the corresponding author with appropriate reasons.

Acknowledgments

We would like to give thanks to all the participants.

This work was supported by the capital health research and development of special (No. 2020-3-7161).

Disclosure

The authors have no conflicts of interest to declare.

References

1. Long H, Liu Q, Yin H, et al. Prevalence trends of site-specific osteoarthritis from 1990 to 2019: findings from the global burden of disease study 2019. *Arthritis Rheumatol.* 2022;74(7):1172–1183. doi:10.1002/art.42089
2. Song M, Chen H, Li J, et al. A comparison of the burden of knee osteoarthritis attributable to high body mass index in China and globally from 1990 to 2019. *Front Med.* 2023;10. doi:10.3389/fmed.2023.1200294
3. Kang X, Fransen M, Zhang Y, et al. The high prevalence of knee osteoarthritis in a rural Chinese population: the Wuchuan osteoarthritis study. *Arthritis Rheum.* 2009;61(5):641–647. doi:10.1002/art.24464
4. Li D, Li S, Chen Q, et al. The prevalence of symptomatic knee osteoarthritis in relation to age, sex, area, region, and body mass index in China: a systematic review and meta-analysis. *Front Med Lausanne.* 2020;7:304. doi:10.3389/fmed.2020.00304
5. Sharma L, Solomon CG. Osteoarthritis of the knee. *N Engl J Med.* 2021;384(1):51–59. doi:10.1056/NEJMcp1903768
6. Mandl LA. Osteoarthritis year in review 2018: clinical. *Osteoarthritis Cartilage.* 2019;27(3):359–364. doi:10.1016/j.joca.2018.11.001
7. Katz JN, Arant KR, Loeser RF. Diagnosis and treatment of hip and knee osteoarthritis: a review. *JAMA.* 2021;325(6):568–578. doi:10.1001/jama.2020.22171
8. Lin LL, Li YT, Tu JF, et al. Effectiveness and feasibility of acupuncture for knee osteoarthritis: a pilot randomized controlled trial. *Clin Rehabil.* 2018;32(12):1666–1675. doi:10.1177/0269215518790632
9. Tu J-F, Yang J-W, Shi G-X, et al. Efficacy of intensive acupuncture versus sham acupuncture in knee osteoarthritis: a randomized controlled trial. *Arthritis Rheumatol.* 2021;73(3):448–458. doi:10.1002/art.41584
10. Guo SS, Fu XH, Qin ZH, et al. Preliminary study on influence of neural segmentation effect based on data mining on acupoint selection. *J Chengdu Univ Trad Chin Med.* 2019;42(04):65–69.
11. Yu WZ, Huang C-M, Ng H-P, et al. Distal acupoints outperform proximal acupoints in treating knee osteoarthritis: a randomized controlled trial. *Evid Based Complement Alternat Med.* 2021;2021:4827123. doi:10.1155/2021/4827123
12. Schulz KF, Altman DG, Moher D. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMJ.* 2010;340(1):c332. doi:10.1136/bmj.c332
13. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. *Ann Rheum Dis.* 1957;16(4):494–502. doi:10.1136/ard.16.4.494
14. Tu J-F, Yang JW, Lin LL, et al. Efficacy of electro-acupuncture and manual acupuncture versus sham acupuncture for knee osteoarthritis: study protocol for a randomised controlled trial. *Trials.* 2019;20(1):1.
15. Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). *Arthritis Care Res.* 2011;63(Suppl 11):S240–S252.
16. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the Hip or knee. *J Rheumatol.* 1988;15(12):1833–1840.
17. Julious SA. Sample size of 12 per group rule of thumb for a pilot study. *Pharm Stat.* 2005;4(4):287–291. doi:10.1002/pst.185
18. Johanson GA, Brooks GP. Initial scale development: sample size for pilot studies. *Educ Psychol Meas.* 2010;70(3):394–400. doi:10.1177/0013164409355692
19. Irnich D, Behrens N, Gleditsch JM, et al. Immediate effects of dry needling and acupuncture at distant points in chronic neck pain: results of a randomized, double-blind, sham-controlled crossover trial. *Pain.* 2002;99(1–2):83–89.

Journal of Pain Research

Dovepress

Publish your work in this journal

The Journal of Pain Research is an international, peer reviewed, open access, online journal that welcomes laboratory and clinical findings in the fields of pain research and the prevention and management of pain. Original research, reviews, symposium reports, hypothesis formation and commentaries are all considered for publication. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/journal-of-pain-research-journal>