15-week treatment period was lower in the tapentadol ER group (22.7%) than in the oxycodone CR group (36.8%).

**Conclusions:** Treatment over 1 year with tapentadol ER (100–250 mg bid) for the relief of moderate to severe chronic pain was associated with a longer period of dose stability than oxycodone HCl CR (20–50 mg bid). This may have been because of a numerically lower rate of discontinuations early in the study and a numerically lower rate of overall AE-related discontinuations throughout the trial in the tapentadol ER group compared with the oxycodone CR group.

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THE EFFECTS OF SHOCKWAVE ON BONE HEALING AND SYSTEMIC CONCENTRATIONS OF NITRIC OXIDE (NO), TGF-β1, VEGF AND BMP-2 IN LONG BONE NON-UNIONS

C.-J. Wang

**Purpose:** We hypothesized that the elevations of systemic concentrations of nitric oxide level and osteogenic factors may reflect a local stimulation of shockwave in bone healing in long bone non-unions. This study investigated the effects of extracorporeal shockwave treatment (ESWT) on bone healing and the systemic concentrations of NO (nitric oxide) level, TGF-β1 (transforming growth factor-β1), VEGF (vessel endothelial growth factor) and BMP-2 (bone morphogenic protein-2) in long bone non-unions.

**Methods:** Non-union was defined when the fracture failed to heal in six months from the initial treatment. The inclusion criteria comprised of patients with non-unions of diaphyseal fractures of femur and tibia. Patients must be skeletally matured and are mentally competent and agree to the follow-up examinations. The exclusion criteria included patients with underlying pathological fracture, fracture in the epiphyseal region or active bone infection, patients with fracture near major neurovascular structures such as spine and skull or chest wall, patients with cardiac pacemaker and cardiac arrhythmia, patients receiving immunosuppressive drugs or anti-coagulation therapy and pregnancy. Forty-two patients with 42 established non-unions of the femur and tibia were enrolled in this study. Each long bone non-union was treated with 6000 impulses of shockwave at 28 Kv (=0.62 mJ/mm² energy flux density) in a single session. Ten milliliters of peripheral blood were obtained for measurements of serum NO level and osteogenic growth factors including TGF-β1, VEGF and BMP-2; serum levels of calcium, alkaline phosphatase, calcitonin and parathyroid hormone before treatment and at 1 day, 1, 3 and 6 months after treatment. The evaluations for bone healing included clinical assessments and serial radiographic examinations.

**Results:** At six months, bony union was radiographically confirmed in 78.6%, and persistent non-union in 21.4%. Patients with bony union showed significantly higher serum NO level, TGF-β1, VEGF and BMP-2 at one month after treatment as compared to patients with persistent non-union (Table 1).

**Table 1**
The results of NO Level, TGF-β1, VEGF and BMP-2 at one month after treatment

<table>
<thead>
<tr>
<th>NO and osteogenic markers</th>
<th>Normal Control (N=16)</th>
<th>Ununion (N=33)</th>
<th>Non-union (N=9)</th>
<th>P-value²</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>53.2±6.4</td>
<td>99.0±52.3</td>
<td>68.1±26.9</td>
<td>0.003</td>
</tr>
<tr>
<td>P-value²</td>
<td></td>
<td></td>
<td></td>
<td>0.017</td>
</tr>
<tr>
<td>TGF-β1</td>
<td>4274±4000</td>
<td>6098±13961</td>
<td>49337±8132</td>
<td>0.002</td>
</tr>
<tr>
<td>P-value²</td>
<td></td>
<td></td>
<td></td>
<td>0.034</td>
</tr>
<tr>
<td>VEGF</td>
<td>330±351</td>
<td>532±318,3</td>
<td>290±190,2</td>
<td>0.012</td>
</tr>
<tr>
<td>P-value²</td>
<td></td>
<td></td>
<td></td>
<td>0.028</td>
</tr>
<tr>
<td>BMP-2</td>
<td>72.4±6.4</td>
<td>86.4±29.5</td>
<td>68.6±5.5</td>
<td>0.035</td>
</tr>
<tr>
<td>P-value²</td>
<td></td>
<td></td>
<td></td>
<td>0.003</td>
</tr>
</tbody>
</table>

**Conclusions:** Shockwave-promoted bone healing was associated with significant increases in serum NO level and osteogenic growth factors. The elevations of systemic concentration of NO level and the osteogenic factors may reflect a local stimulation of shockwave in bone healing in long bone non-unions. Clinical relevance: The measurements of serum NO level and the osteogenic factors may be used as the predictors in bone healing in long bone fractures.

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FACTORS RELATED TO DISEASE SPECIFIC DISABILITY AND GENERAL HEALTH PHYSICAL DISABILITY IN PATIENTS WITH KNEE OSTEOARTHRITIS

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**Purpose:** Many studies have shown relationships between BMI and knee osteoarthritis. The purpose of this study was to determine other factors that may be related to knee osteoarthritis. This will be measured as disease specific disability and general health physical disability.

**Methods:** Demographic, objective and radiographic data were collected on 325 patients who presented to a referral clinic for treatment of osteoarthritis of the knee. Data collected included gender, age, BMI, Kellgren Lawrence Grade (KL), shift in mechanical axis of the knee, knee extension and flexion, WOMAC, and the SF-12 physical component and mental component. The WOMAC score was converted to a percentage score with 100% equal to perfect WOMAC and 0% equal to worst WOMAC. The WOMAC was considered the disease specific measure of disability and the physical component score (PCS) of the SF-12 was considered the general health measure of disability.

**Results:** There were 168 males and 157 females. The average age was 61 years (range 40 to 87). The average self-reported BMI was 26 kg/m² (range 18 to 42). 186 were considered overweight (BMI ≥25 kg/m²) and 142 were considered normal (<25 kg/m²). The average knee extension was 3 degrees (range -10 to 43 degrees) and the average flexion was 124 degrees (range 25 to 165). There were 31% grade 4 KL, 40% grade 3, and 29% grade 2. The average shift in mechanical axis was 27% (range 0 to 50).

Gender was not associated with WOMAC, however, males did have a higher PCS (40 vs 38; p=0.019). Grade II KL patients had significantly lower BMI (25 vs 27; p=0.009) and higher WOMAC score (68% vs 63%; p=0.049). Of the grade II KL patients, 50% were overweight, of the grade III KL patients, 59% were overweight, and of the grade IV KL patients 69% were considered overweight (p=0.041). In this patient population, an increase in mechanical axis shift was correlated to a decrease in flexion (r=-0.16; p=0.006). An increase in mechanical axis shift (r=-0.137; p=0.031), loss of extension (r=-0.178; p=0.014), higher BMI (r=0.264; p=0.001) and an increase in age (r=-0.190; p=0.002) were all correlated with an decrease in PCS. An extension loss (r=-0.219; p=0.001) and a increase in BMI (r=-0.214; p=0.001) were correlated with an decreased WOMAC.

One independent predictor of WOMAC was identified. It was loss of extension (r2=0.24; p=0.008). Independent predictors of PCS included age (p=0.002), WOMAC (p=0.0001) and BMI (r2=0.43; p=0.001).

**Conclusions:** Loss of extension predicted disease specific disability (WOMAC). For general health disability, predictors included age, BMI, and WOMAC. General health was more affected by demographic variables, while disease specific was related to knee disability.
range of motion. More research is needed to determine if these factors can be modified through treatment programs in order to decrease disability caused by osteoarthritis of the knee.

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IMPACT OF TOTAL PHYSICAL ACTIVITY IN YOUNGER AGE ON PHYSICAL AND MENTAL HEALTH IN PEOPLE WITH OSTEARTHROSIIS OF THE KNEE

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Purpose: The relationship between physical activity and osteoarthritis remains controversial. The purpose of this study was to determine the effect of total physical activity (TPA) up to middle age and prior to the occurrence of osteoarthritis (OA), on health-related quality of life (HRQoL) in persons with knee OA at the age of 50 or older.

Methods: Data were collected from the Physical Activity and Joint Health (PAJH) online survey conducted across Canada. Participants (age 50+) completed an adaptive lifetime physical activity questionnaire (L-PAQ) to measure total PA, and a new computer adaptive test (CAT-5D-QOL, which contains the following five HRQoL domains: Walking (WALK), Handling Objects (HAND), Daily activity (DAILY), Pain and discomfort (PAIN), and Feelings (FEEL), were included in the study. Total PA, including work-related, domestic, and recreational activities, accumulated between the ages of 20 and 45, was measured by average energy expenditure (METS). Subjects were classified into 5 categories (quintiles) of TPA: very low, low, moderate, high, and very high. The relationships between TPA and CAT-5D-QOL domain scores (50/10 norm-based scores, higher indicating better health) were investigated in multivariate linear regression models, after adjusting for confounding variables age, gender and hip pain.

Results: Among participants with self-reported symptomatic knee OA (n=839), the effect of TPA on CAT-5D-QOL scores was non-linear and showed 3 types of general patterns in the 5 HRQoL domains (Fig. 1). Compared to the least active group (reference), low physical activity (2nd quintile) between ages of 20-45 was associated with improved WALK (1.63 scores above the reference group, 95%CI -0.19, 3.44) and HAND (1.96 above, 95%CI -0.31, 4.23). However, further increase in TPA (3rd to 5th quintile) was associated with a decrease in WALK and HAND scores, with the high and very high activity groups having significantly lower scores than the most inactive group. The progressive increase in TPA was associated with a corresponding decrease in DAILY and increase in PAIN. In contrast, as TPA increased, FEEL scores increased or did not go below the reference group. The highest level of FEEL was reported by those who conducted moderate activity (3rd quintile), which was on average 2.5 scores (95%CI 0.25, 4.76) higher than the most inactive group.

Conclusions: High levels of total physical activity conducted between ages 20 and 45 are associated with more pain and worse physical function in persons age 50+ with self-reported knee OA. Low to moderate activity has little effect on pain or daily activity and correlates with better walking and handling abilities. But, physical activity in young-to-middle age, especially at moderate level, is associated with better subsequent emotional health in persons with OA.

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ASSOCIATION BETWEEN WEIGHT OR BODY MASS INDEX AND HAND OSTEOARTHRITIS: A SYSTEMATIC REVIEW

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Purpose: To investigate the association between weight or Body Mass Index (BMI) and the development of hand osteoarthritis (HOA).

Methods: We searched Medline, Web of Science, Embase and CINAHL databases up to April 2008 and selected studies with data on the association between weight or BMI and HOA. HOA was defined as involvement of at least one hand joint clinically or radiographically. Data extraction were performed and studies were scored using a 19 criteria scoring system. A Forest Plot of studies which presented odds ratio (OR) or relative risk (RR) was generated. No meta-analysis was done since observational studies are in nature heterogenic and data pooling is less appropriate. Instead, a best-evidence synthesis, modified from guidelines on systematic review of Cochrane Back Review Group was performed. This synthesis leads to a level of evidence with possible levels: strong, moderate, limited, conflicting and no evidence. The level was determined on study quality scores and study designs. Studies which scored above the mean score of all studies were deemed