Good short- to medium-term results after osteochondral autograft transplantation (OAT) in middle-aged patients with focal, non-traumatic osteochondral lesions of the knee

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Abstract

Background: Osteochondral autograft transplantation (OAT) offers the opportunity to repair cartilaginous defects by restoring hyaline cartilage anatomy. Encouraging results have been reported in patients suffering from acute knee trauma or osteochondritis dissecans. Patients with focal chronic, non-traumatic osteochondral (FCNO) lesions of the knee, however, have rarely been the subject of investigation. Some authors even consider higher age as contraindications to OAT.

Objectives: To assess the short- to medium-term outcomes of OAT in middle-aged patients with FCNO lesions of the knee and to identify predictors of clinical outcome.

Hypothesis: Filling FCNO defects with autologous osteochondral grafts should restore the congruency of the middle-aged knee joint and thereby reduce pain and loss of function on the one hand, and increase quality of life on the other hand.

Methods: One hundred and twelve patients (48.01 ± 1.12 yrs) with FCNO of the knee were assessed before OAT and 26.2 ± 0.24 months after surgery. Clinical outcome was measured by WOMAC Index and the Visual Analogue Scale (VAS) for pain.

Results: Pain (pre-OAT VAS vs. post-OAT VAS: 7.14 ± 0.19 vs. 3.74 ± 0.26, P<0.001) was reduced and quality of life (pre-OAT WOMAC vs. post-OAT WOMAC: 134.88 ± 5.84 vs. 65.92 ± 5.34, P<0.001) improved. Retropatellar defects were associated with poor outcome, while overall surface and number of cylinders were not.

Discussion: Middle-aged patients with FCNO of the knee also profit from OAT at a short follow-up.

Level of evidence: IV. Mono-centric, prospective clinical series.

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1. Introduction

Osteoarthritis (OA) reduces patients’ quality of life and ability to work due to pain and loss of function [1,2]. For a long time, therapy was restricted to the symptomatic use of non-steroidal anti-inflammatory drugs, intra-articular injections of steroids and – eventually – knee arthroplasty as a final treatment. As in OA the destruction of hyaline cartilage constitutes the central pathological mechanism, biological substances aiming at the regeneration of the cartilaginous function, such as hyaluronic acid or autologous conditioned serum, have recently gained importance in the treatment of OA [1–4]. Full-thickness cartilage defects, however, have a poor regenerative capacity [5,6]. In the last decades, several approaches to address this difficulty have been suggested, e.g. subchondral drilling, abrasion, microfracture, autologous chondrocyte implantation (ACI), and osteochondral autograft transplantation (OAT)[5,7]. Currently, the two latter techniques are considered most promising: in ACI, cultured autologous chondrocytes are placed in the articular cartilage defect site with the help of different scaffolds [8]. In OAT, cartilage defects are filled with osteochondral autografts from minimal weight-bearing portions of the distal femur [5–14]. Compared with ACI, OAT fills the defect with a higher amount of hyaline (instead of fibrous)
cartilage and OAT can be performed in only one surgical stage [5,6,9,15]. Despite these merits, in terms of clinical outcome, OAT has not proved superior to ACI yet, it has, however, been studied less extensively so far [5,7,16,17].

Traditionally, cartilage defects resulting from acute knee injuries and osteochondritis dissecans are regarded as the typical indications of OAT and ACI [8,18]. Chronic cartilage defects, by contrast, have rarely been considered an indication: according to some authors, knee OA and patients’ age over 50yrs even constitute contraindications [12,19], whereas other authors consistently tried to extend the indications of OAT by including certain focal forms of chronic non-traumatic osteochondral lesions [6,10,14].

To the best of our knowledge, the clinical outcome of OAT has not yet been investigated in a larger population of patients with chronic osteochondral lesions. The aim of the present study was therefore to assess the short to medium-term outcomes of OAT in middle-aged patients with focal, chronic non-traumatic osteochondral lesions (FCNO) of the knee and to identify predictors of clinical outcome. We hypothesized that filling FCNO with autologous osteochondral grafts would restore the congruency of the knee joint and thereby reduce patients’ pain and loss of function on the one hand, and increase quality of life on the other hand.

2. Material and methods

2.1. Study patients and design

Data collection and treatment took place at a university clinic for orthopaedics and orthopaedic surgery between 2001 and 2005. The study was a mono-centric, prospective clinical series. Data is reported as Mean ± Standard Error of Mean (M ± SE).

A total of 163 patients initially participated in the study, 51 patients dropped out resulting in 112 patients (48.01 ± 1.12 yrs) of whom 59 were female. Inclusion criteria were chronic clinical symptoms (such as knee pain, swelling, restriction of motion), Outerbridge grade IV focal cartilage defects of the femoral condyles, i.e. erosion of cartilage down to the bone [20], diagnosed pre-operatively by magnetic resonance imaging (MRI; Fig. 1) and/or by a previous diagnostic arthroscopy as well as at least 2yrs of unsuccessful conservative treatment, such as non-steroidal anti-inflammatory drugs (NSAR’s), physical therapy, orthoses, acupuncture and/or intra-articular injections of corticosteroids or hyaluronic acid.

Patients with acute knee injuries, osteochondritis dissecans, associated Outerbridge grade IV cartilage defects of the tibia, femoral defects larger than half the femoral condyle – assessed pre-operatively via MRI or diagnostic arthroscopy, radiologically confirmed generalized osteoarthritic changes (Kellgren/Lawrence grades 3–4) [21], osteophytes in the intercondylar notch, severe mechanical axis malalignment (hip-knee-ankle [HKA] angle ≥ 5° varus or valgus), active infection, clinically relevant haematologic or abnormal clinical chemistry values, bone cancer, metastasis or tumor like lesions in immediate proximity to the treated knee, and poor general health were excluded.

All investigations were conducted in conformity with the ethical standards laid down in the 1975 Declaration of Helsinki, the ethics review board of the conducting institution approved the study and its subsequent publication. Participation was voluntary and informed consent for participation in the study was obtained.

Of the 112 patients, 45 were classified as Kellgren/Lawrence grades 1 and 67 as grade 2, i.e. joint narrowing was maximum 2 mm [22], 97 patients had accompanying degenerative meniscal lesions of either the medial (n = 61), the lateral meniscus (n = 30), or both menisci (n = 6). Forty-eight patients had already undergone a previous arthroscopic partial meniscectomy which was conducted by other surgeons independently and before the onset of the present study.

All patients completed the Visual Analogue Scale (VAS) for pain [23] and a German version of the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) Index [24] before surgery and 26.2 ± 0.24 months after surgery (range = 7–45 months); higher WOMAC-scores indicate worse conditions. Both the VAS and the WOMAC have repeatedly been shown to be reliable and valid research instruments [25].

Apart from pre-operative and periodic post-operative clinical examinations, all patients underwent radiological examinations pre-OAT (X-ray: full-length lower limb, anterior-posterior and lateral view of the knee as well as aerial view of the patella in patients with retropatellar symptoms; schuss view was not performed; Fig. 2), 6 weeks post-OAT (X-ray) and 10–16 weeks (MRI) post-OAT. In addition, all patients underwent an MRI examination and/or a diagnostic knee arthroscopy before surgery. Patients were examined by physicians not involved in surgery.

Upon clinical and radiological examination, no severe complications such as prolonged pain at the donor site, plug migration or long-term swelling/haematoma were reported.

2.2. Osteochondral Autograft Transplantation (OAT)

All patients underwent an OAT involving the transplantation of cylindrical osteochondral grafts from minimal weight-bearing cartilaginous zones to the cartilaginous weight-bearing defect zone. Patients were operated by one of three different, experienced surgeons. In the present study, all surgeries were carried out as an open miniarthroscopy. Mild mechanical axis malalignments, i.e. HKA angle < 5° varus or valgus, were accepted and no concomitant osteotomies were conducted. Further, potential associated lesions of the menisci, the collateral or cruciate ligament(s) were assessed, but not treated in the same surgery because of the different rehabilitation protocols and surgical techniques.

The cranio-lateral or medial femoral condyle and the intercondylar notch were used as the favored minimal weight-bearing donor sites. The Osteochondral Autograft Transfer System (OATS®) Arthrex Inc., Naples, FL) were used. After preparing the defect site, i.e. debonding and measuring it afterwards, and harvesting the donor cylinder (diameter = 1 cm), the donor cylinder was placed in the lesion site via press-fit-technique. When complete filling
informative – especially when samples are very small or large – we followed Cohen’s advice to additionally determine effect sizes [28] using G’Power 3 [29]. According to Cohen’s criteria for the interpretation of effect sizes, in ANOVAs $\eta^2 \geq 0.10$ indicates a large effect, $\eta^2 \geq 0.06$ a moderate one, and $\eta^2 \geq 0.01$ a small effect. In $\chi^2$-tests, the measure of effect size is $\omega$, with $\omega \geq 0.50$ a large, $\omega \geq 0.30$ a moderate, and $\omega \geq 0.10$ a small effect. The correlation coefficient $r$ itself is a measure of effect size, with $r \geq 0.50$ a large, $r \geq 0.30$ a moderate, and $r \geq 0.10$ a small effect. In regression analysis, $R^2 \geq 0.10$ is considered satisfactory.

3. Results

3.1. Patient characteristics

Patients were middle-aged (48.01 ± 1.12 yrs) and gender was equally distributed (52.7% female) in the sample. In contrast, the defects were not equally distributed with medial femoral (50.0%) and retropatellar defects (25.9%) dominating (Table 1).

3.2. Properties of self-report measures

Both WOMAC subscales (pre-/post-operative pain: $\alpha = 0.87/0.94$ – stiffness: $\alpha = 0.86/0.90$ – physical function: $\alpha = 0.97/0.98$) and WOMAC overall score ($\alpha = 0.98/0.98$) showed high internal consistency. VAS and WOMAC-scores correlated highly positively and significantly (pre-operative: $r = 0.78$, $P < 0.001$ – post-operative: $r = 0.88$, $P < 0.001$).

3.3. Overall clinical outcome

Both the post-operative WOMAC-scores and VAS-scores were significantly lower than pre-OAT. The effects were very large (Table 1). Clinical improvement was not restricted to the younger patients ($< 49$ yrs, $n = 50$), the effects were large and significant in older patients ($49$ yrs and older, $n = 62$) as well–both regarding WOMAC and VAS (Table 2).

3.4. Predictors of clinical outcome

Only retropatellar defect localization turned out as a somewhat relevant risk factor for poor clinical outcome, whereas age, gender, number of transplanted cylinders, overall defect surface and the remaining defect localizations showed no association with the outcome whatsoever (Tables 3 and 4).

Table 1

<table>
<thead>
<tr>
<th>Demographics, surgical characteristics, and clinical outcome.</th>
<th>$n = 112$</th>
<th>$P$</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>48.01 ± 1.12</td>
<td>0.57</td>
<td>0.05 ($\omega$)</td>
</tr>
<tr>
<td>Gender (female), n (%)</td>
<td>59 (52.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of plugs</td>
<td>2.67 ± 0.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall surface (mm²)</td>
<td>25.53 ± 1.46</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Defect localization</td>
<td>56 (50.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medial, n (%)</td>
<td>7 (6.3)</td>
<td>&lt;0.001</td>
<td>1.89 ($\omega$)</td>
</tr>
<tr>
<td>Lateral, n (%)</td>
<td>29 (25.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retropatellar, n (%)</td>
<td>20 (17.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined, n (%)</td>
<td>134.88 ± 5.84</td>
<td>&lt;0.001</td>
<td>0.45 ($\eta^2$)</td>
</tr>
<tr>
<td>Pre-operative WOMAC</td>
<td>65.92 ± 5.34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-operative WOMAC</td>
<td>7.14 ± 0.19</td>
<td>&lt;0.001</td>
<td>0.46 ($\eta^2$)</td>
</tr>
<tr>
<td>Post-operative VAS</td>
<td>3.74 ± 0.26</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VAS: Visual Analogue Scale; WOMAC: Western and McMaster Universities Index. The figures represent either $M \pm SE$ or absolute frequencies (percentages). For continuous variables, $P$-values were calculated by one-way within subjects analyses of variance (ANOVAs) with the effect size $\eta^2$ ($\geq 0.14 = $ large, $\geq 0.06 = $ moderate, $\geq 0.0 = $ small). For nominal variables, $P$-values were calculated by $\chi^2$-tests with the effect size $\omega$ ($\geq 0.50 = $ large, $\geq 0.30 = $ moderate, $\geq 0.10 = $ small).
Table 2
Clinical outcome by age.

<table>
<thead>
<tr>
<th></th>
<th>&lt; 49 yrs (n = 50)</th>
<th>P</th>
<th>Effect size ($\eta^2$)</th>
<th>≥ 49 yrs (n = 62)</th>
<th>P</th>
<th>Effect size ($\eta^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-operative WOMAC</td>
<td>124.48 ± 8.80</td>
<td>&lt;0.001</td>
<td>0.43</td>
<td>143.26 ± 7.00</td>
<td>&lt;0.001</td>
<td>0.46</td>
</tr>
<tr>
<td>Post-operative WOMAC</td>
<td>79.82 ± 7.33</td>
<td>&lt;0.001</td>
<td>0.45</td>
<td>70.84 ± 7.61</td>
<td>&lt;0.001</td>
<td>0.47</td>
</tr>
<tr>
<td>Pre-operative VAS</td>
<td>7.01 ± 0.30</td>
<td></td>
<td></td>
<td>7.24 ± 0.25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-operative VAS</td>
<td>3.83 ± 0.39</td>
<td></td>
<td></td>
<td>3.67 ± 0.35</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VAS: Visual Analogue Scale; WOMAC: Western and McMaster Universities Index. The figures represent M ± SE. For continuous variables, P-values were calculated by one-way within subjects analyses of variance (ANOVAs) with the effect size $\eta^2$ (≥ 0.14 = large, ≥ 0.06 = moderate, ≥ 0.01 = small).

Table 3
Predictors of clinical outcome as measured by pre-operative WOMAC vs. post-operative WOMAC difference (n = 112).

<table>
<thead>
<tr>
<th></th>
<th>Correlation (r)</th>
<th>P</th>
<th>Regression ($R^2 = 0.08, P = 0.25$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (0 = female, 1 = male)</td>
<td>0.09</td>
<td>0.34</td>
<td>0.15</td>
</tr>
<tr>
<td>Age</td>
<td>−0.09</td>
<td>0.36</td>
<td>−0.07</td>
</tr>
<tr>
<td>Number of cylinders</td>
<td>−0.11</td>
<td>0.27</td>
<td>0.06</td>
</tr>
<tr>
<td>Overall surface</td>
<td>−0.10</td>
<td>0.28</td>
<td>−0.16</td>
</tr>
<tr>
<td>Medial localization</td>
<td>−0.09</td>
<td>0.36</td>
<td>−0.05</td>
</tr>
<tr>
<td>Lateral localization</td>
<td>−0.15</td>
<td>0.12</td>
<td>−0.16</td>
</tr>
<tr>
<td>Retropatellar localization</td>
<td>0.20</td>
<td>0.03</td>
<td>0.12</td>
</tr>
<tr>
<td>Combined localization</td>
<td>−0.02</td>
<td>0.83</td>
<td>0.43</td>
</tr>
</tbody>
</table>

* Combined defect localization: reference category in multiple linear regression. Positive correlations and β-coefficients, respectively, indicate predictors of poor outcome, as they are associated with post-operative increase in WOMAC-scores, while negative correlations and β-coefficients, respectively, indicate predictors of good outcome, i.e. post-operative WOMAC decrease. $R^2 ≥ 0.10$ is considered satisfactory.

Table 4
Predictors of clinical outcome as measured by pre-operative VAS vs. post-operative VAS difference (n = 112).

<table>
<thead>
<tr>
<th></th>
<th>Correlation (r)</th>
<th>P</th>
<th>Regression ($R^2 = 0.06, P = 0.49$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (0 = female, 1 = male)</td>
<td>0.07</td>
<td>0.49</td>
<td>0.12</td>
</tr>
<tr>
<td>Age</td>
<td>−0.08</td>
<td>0.42</td>
<td>−0.06</td>
</tr>
<tr>
<td>Number of cylinders</td>
<td>−0.10</td>
<td>0.30</td>
<td>0.06</td>
</tr>
<tr>
<td>Overall surface</td>
<td>−0.10</td>
<td>0.31</td>
<td>−0.14</td>
</tr>
<tr>
<td>Medial localization</td>
<td>−0.03</td>
<td>0.72</td>
<td>0.01</td>
</tr>
<tr>
<td>Lateral localization</td>
<td>−0.14</td>
<td>0.13</td>
<td>−0.14</td>
</tr>
<tr>
<td>Retropatellar localization</td>
<td>0.16</td>
<td>0.09</td>
<td>0.12</td>
</tr>
<tr>
<td>Combined localization</td>
<td>−0.05</td>
<td>0.62</td>
<td>0.44</td>
</tr>
</tbody>
</table>

* Combined defect localization: reference category in multiple linear regression. Positive correlations and β-coefficients, respectively, indicate predictors of poor outcome, as they are associated with post-operative increase in VAS-scores, while negative correlations and β-coefficients, respectively, indicate predictors of good outcome, i.e. post-operative VAS decrease. $R^2 ≥ 0.10$ is considered satisfactory.

4. Discussion

The present study demonstrates the short- to medium-term efficacy of OAT in a large population of middle-aged patients with FCNO of the knee. It seems noteworthy that the positive effects were not restricted to younger patients (<49 yrs) and that overall defect surface was not associated with a poor outcome. To the best of our knowledge, this information is novel and has not been previously defined.

Some limitations of the study should be acknowledged:

• despite our promising results in patients with chronic osteochondral lesions – even in older patients and patients with FCNO of maximum 76 mm² requiring up to 8 cylinders – the implications should not be prematurely generalized to larger osteoarthritic defects: we did not examine the typical OA patients with high K/L grades (3–4) showing diffuse osteoarthritic defects as in kissing lesions with severe joint narrowing (< 2 mm). Our sample was restricted to patients with focal femoral defects (not larger than half the femoral condyle) and/or retropatellar defects. Patients with Outerbridge grade IV defects of the tibial plateau or severe malalignment (HKA angle ≥ 5° varus or valgus) were excluded. The present condition should therefore rather be referred to as FCNO (Figs. 1 and 2) than general OA. We consider these FCNO’s as an early, quite well treatable stage of OA rather than a primary disease. Future studies should focus on the feasibility of OAT in the typical osteoarthritic joint to define its limits and indications more narrowly;

• our study was explorative in nature, i.e. treatment effects were neither blinded nor placebo-controlled. Nonetheless, we believe that the present results go beyond pure placebo effects: first, clinical improvement was not only significant, the effects were also very large [28], both in younger and in older OA patients. Second, reduction of VAS-scores by approximately 48% exceeded the average placebo effect usually reported in knee OA patients, e.g. 27% pain reduction for the saline placebo group in Baltzer et al. [1]. Third, the reported effect in FCNO of the knee is similar in magnitude – or even slightly better – compared with ACI effects in acute knee trauma. Bartlett et al. [30], for instance, report average pre- to post-surgery reduction of VAS pain scores from 6.0 to 4.3 (difference score = −1.7, ACI group, n = 44) and 6.0 to 4.1 (difference score = −1.9, matrix-induced ACI group, n = 47), respectively.
whereas in the present study, OAT reduced VAS pain scores from pre-surgery = 7.14 to post-surgery = 3.74 on average (difference score = -3.4, n = 112);

• comparisons with standard techniques used for the treatment of severe focal osteoarthritis, for instance high tibial osteotomy (HTO) [31–39] or even unicompartmental knee arthroplasty (UKA) [34], would be ethically less troubling and scientifically more interesting than comparisons with genuine placebo groups. Some clinicians combine HTO with cartilage repair techniques [19]. To the best of our knowledge these more invasive approaches, however, have not been directly compared to OAT in patients with FCNO yet. In terms of reduction of pain and increase of quality of life, our present results seem comparable to those achieved with both HTO [33] and UKA [34], but with a short follow-up. Luites et al. [33], for instance, conducted medial opening-wedge HTO and lateral closing-wedge HTO, respectively, in 42 patients with medial knee OA aged 53 yrs on average. At 2-year follow-up, decrease in VAS pain scores was -4.1 points (pre-operative VAS = 5.6, post-operative VAS = 1.5, n = 23, opening-wedge HTO) and -3.6 points (pre-operative VAS = 5.9, post-operative VAS = 2.3, n = 19, closing-wedge HTO), respectively, and thus comparable to the pain reduction of -3.4 VAS points approximately 2 yrs after OAT achieved in our slightly younger patients (pre-operative VAS = 7.14, post-operative VAS = 3.74, n = 112, mean age = 48 yrs). In patients receiving medial UKA, Zuiderbaan et al. [34] report WOMAC total score improvements at a similar follow-up (2.3 yrs on average) of -38 percent points in younger patients (< 65 yrs, n = 56) and -30 percent points in older patients (65 yrs and older, n = 48), respectively, compared to improvements of -27 percent points in our younger patients (< 49 yrs, n = 50) and ~30 percent points in our older patients (49 yrs and older, n = 62), respectively. In cases of early and rather mild osteoarticular degeneration, i.e. Kellgren/Lawrence grade 1 and 2 as in our patients, however, the comparison of OAT with non-invasive, conservative treatments might be of even greater interest than comparisons with HTO or UKA. Several authors demonstrated NSAR’s [35,36], physical therapy [37–39], orthoses and shoe modifications [40–42] as well as intra-articular injections of steroids [43], hyaluronic acid [44] or autologous conditioned serum [1,45] to be effective short-term treatment options especially in the early stages of knee OA in general, and focal knee OA in specific [36,46]. Our patients had already undergone at least 2 yrs of conservative treatment, without enduring success. That is why we considered OAT an adequate and still less invasive treatment option compared to HTO or even UKA;

• we restricted our analyses to effects approximately 2 yrs post-OAT. In addition, radiological examinations were not conducted after more than 16 weeks post-OAT. Notwithstanding the positive clinical results, we can therefore not rule out that cartilage degeneration progressed despite our (successful) surgical procedure. As the average methodological quality of knee articular cartilage studies is still unsatisfactory and OAT has not been sufficiently examined yet [5,16,17], the present promising, yet exploratory, short- to medium-term results in focal, non-traumatic osteochondral lesions of the knee warrant further large-scaled, randomized clinical trials with longer follow-up intervals.

In sum, our results show short-term benefits of OAT in middle-aged patients suffering from focal, non-traumatic osteochondral lesions of the knee resistant to conservative treatment. Due to the limitations of the study such as short follow-up and lack of a placebo/non-surgical control group, more large-scaled randomized controlled trials are necessary before current contraindications to OAT such as degenerative osteochondral lesions in older patients [12] can be revised.

Disclosure of interest

The authors declare that they have no competing interest.

References


