



What parameters affect knee function in patients with untreated cartilage defects: baseline data from the German Cartilage Registry

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Abstract

Purpose To evaluate the factors influencing the baseline Knee Injury and Osteoarthritis Outcome Score (KOOS) in patients with knee cartilage defects and planned cartilage repair surgery and to provide baseline KOOS data from a large patient population.

Material and methods Between October 2013 and April 2017, a total of 2815 patients assigned for cartilage repair surgery were included into the German Cartilage Registry (KnorpelRegister DGOU) and their data were analyzed for the present study. Multivariate regression model and ANOVA were used to detect patient- and defect-specific factors with an influence on baseline KOOS. In addition, KOOS baseline data was calculated and compared according to these parameters.

Results Sex, age, body mass index (BMI), and smoking status were revealed as patient-specific factors, and defect location and the number of previous knee and cartilage operations were revealed as defect-specific factors with a significant influence on baseline KOOS. Most subscores were affected in accordance with the total KOOS. Interestingly, defect ICRS grade, defect size, and symptom duration had no significant influence. The mean baseline KOOS was 56.7 (± 17.9). Men had significantly higher mean overall KOOS (60 ± 17.3 vs. 51.8 ± 17.6 , $p < 0.001$) than women, and patients with a BMI over 30 and smokers scored significantly lower (58.07 ± 17.67 vs. 50.32 ± 17.29 , $p < 0.001$; 57.64 ± 17.86 vs. 53.59 ± 18.06 , $p < 0.001$). Patients with two or more previous knee operations as well as patients with more than one previous cartilage procedure also showed significantly lower overall KOOS (57.19 ± 17.89 vs. 54.56 ± 17.58 , $p < 0.001$; 57.68 ± 18.01 vs. 52.72 ± 17.58 , $p < 0.001$).

Conclusion Several factors influencing baseline KOOS data in patients with knee cartilage defects assigned for cartilage repair surgery could be detected. Their individual influence in the multivariate linear regression model was not very strong. Baseline data according to these criteria is presented in this paper.

Keywords Cartilage · KOOS · Baseline data · German Cartilage Registry · Patient-reported outcome

Introduction

Cartilage defects of the knee joint represent a common pathology, which is found in up to 60% of patients who undergo arthroscopy independent of the initial diagnosis [1, 2]. Distribution and morphology of those defects have been described in detail reporting the medial femoral condyle being affected most frequently followed by the patella and treatment algorithms have been established [3–5].

A significant effect of focal cartilage defects on quality of life and everyday activity has been described and was found comparable to patients with severe osteoarthritis [6]. Nevertheless, also in asymptomatic patients, cartilage defects are frequently found even in highly active subgroups

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and the underlying mechanisms in the development of pain are not completely understood [7]. Inflammation on the one hand side and mechanical exposure of the subchondral bone or subchondral bone reaction which can be detected in early osteoarthritis before cartilage breakdown is observed are discussed.

Accordingly, a wide variety of treatment options for chondral and osteochondral lesions have been developed, many of which could be shown to improve functional, objective, and patient-reported outcome parameters. Examples are matrix-based autologous chondrocyte implantations (MACI) [8], autologous matrix-induced chondrogenesis (AMIC®) [9], and various cell-free graft options [10, 11]. Data (including baseline data) concerning all treatment options for cartilage defects are collected in the German Cartilage Registry (KnorpelRegister DGOU).

The Knee Injury and Osteoarthritis Outcome Score (KOOS) is a patient-reported questionnaire, developed as an extension to the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) to evaluate the patient's opinion about their knee and possible dysfunction. Long- and short-term consequences of knee injuries and primary osteoarthritis can be assessed. It comprises 42 items divided into five subscales: KOOS pain, KOOS symptoms, function in daily living (KOOS ADL), function in sport and recreation (KOOS Sport/Rec), and knee-related quality of life (KOOS QOL) [12]. It has been validated as reliable and responsive for patients with articular cartilage defects [13, 14].

The present study was initiated aiming on two different questions:

The first aim was to evaluate patient-specific parameters as well as morphological aspects of cartilage defects around the knee joint including location of the defect, grade and size of the defect, and further parameters and their influence on knee function in a large cohort of patients assigned for surgical cartilage treatment using data from the German Cartilage Registry (KnorpelRegister DGOU).

Furthermore, the second aim of the present study was to provide baseline data for the KOOS based upon a large patient population dependent of patient-specific and defect-specific parameters, which seems important for further interpretation of scientific studies in this field.

Patients and methods

In a multicenter nationwide approach including more than 70 centers performing cartilage surgeries on a regular basis, between October 2013 and April 2017, a total of 2815 patients assigned for surgical cartilage treatment were included in the present study. The study was registered at the DRKS website (DRKS Number: DRKS00005617) and approved by the ethical committee (Approval Number 105/13 (Freiburg

University). All patients were included in the present study prior to surgery. Informed consent was given by all patients. Data collection was performed using a web-based remote data entry (RDE) system as described earlier.

All patient-specific and defect-specific parameters evaluated in the present study are presented as reported by the treating surgeon at the time of surgery. Arthroscopic evaluation included defect stage and grade as well as defect location. In addition, patients were asked to report further parameters such as past medical history, previous surgery, sports activity, and duration of symptoms. Knee function at the time of surgery was measured by the means of standardized patient-reported scoring system including KOOS [15] and Tegner scale [16].

Statistical analysis

Descriptive data are presented as mean \pm standard deviation or percentage of the total. A multivariate linear regression analysis was performed to detect ordinal and cardinal variables with influence on the baseline KOOS overall score and its respective subscores. ANOVA was used to analyze nominally scaled parameters. $p \leq 0.05$ was considered significant. Subgroups of significantly influencing factors were compared using the post hoc Tukey test and Student's *t* test.

Results

A total of 2815 patients were included in the present study. Complete data sets for the KOOS were available in 1781 patients representing 63.3%. Detailed patient characteristics are shown in Table 1.

Influencing factors

The factors included into the multivariate regression analysis are listed in Table 2. Body mass index (BMI, $p < 0.001$, $\beta = -0.13$) and age ($p < 0.001$, $\beta = -0.24$) were revealed to have a significant influence on the pre-operative KOOS, so were the number of previous procedures ($p < 0.001$, $\beta = -0.05$) and previous cartilage operations ($p < 0.001$, $\beta = -0.09$) on the affected knee. Interestingly, defect size ($p = 0.656$), symptom duration ($p = 0.755$), defect ICRS grade ($p = 0.186$), and the number of treated defects ($p = 0.334$) had no significant influence on the baseline KOOS. Regarding the respective beta values, though, the influence was not very strong in all cases.

The one-way ANOVA revealed a significant influence of sex ($p < 0.001$), smoking status ($p < 0.001$), and defect location ($p < 0.001$) on the total KOOS and several subscores.

Table 1 Patient characteristics

Patients, <i>n</i> , (% complete data sets)	<i>N</i> = 2815 (63.3%)
Sex, male/female (no data)	1723/1050 (42)
Age (years), mean ± SD	37.42 ± 12.27
BMI (kg/m ²), mean ± SD	26.26 ± 4.015
Smoking status, non-smoker/smoker/ex-smoker/n.a. (%)	70.87/23.23/4.44/1.46
Symptom duration (months), mean ± SD	24.51 ± 39.534
Defect size (mm ²), mean ± SD	357.21 ± 211.019

Baseline data

Mean pre-operative KOOS total was 56.7 (± 17.9). Men showed significantly higher mean KOOS overall scores (60 ± 17.3 vs. 51.8 ± 17.6, $p < 0.001$) than women. This was also reflected in all of the pre-operative KOOS subscores (Table 3). Smokers had significantly lower mean KOOS total scores and subscores than non-smokers except for the QOL and sports subscores (Table 3). Concerning BMI, another factor possibly influencing KOOS ratings, patients with a BMI larger than 30 kg/m² scored significantly lower average total KOOS and subscores except for QOL and symptoms (Table 3). Patients with more than one previous surgery to the affected knee scored less in overall KOOS and all subscores but ADL, and patients with previously treated cartilage defects scored less in all subscores (Table 3). In regard to age, patients older than 40 years showed a mean overall KOOS of 52.26 ± 17.01 compared to 60.61 ± 17.67 ($p < 0.001$). This was reflected accordingly in all subscores. Baseline KOOS data for respective defect locations is shown in Table 4.

Discussion

The present study had two different goals. First, in a large cohort of patients, parameters that affect knee function as

Table 2 Multivariate regression analysis and ANOVA—factors with possible influence on baseline KOOS, respective *p* and beta values

Factor	<i>p</i> value	Beta
Sex	< 0.001	n.a.
Age	< 0.001	− 0.24
BMI	< 0.001	− 0.13
Smoking status	< 0.001	n.a.
Number of previous surgeries	< 0.001	− 0.05
Number of previous cartilage surgeries	< 0.001	− 0.09
Number of defects	0.334	− 0.02
Defect size	0.656	− 0.01
Defect grade	0.186	0.01
Symptom duration	0.755	0.01

assessed by standardized, highly valid, and reliable scoring system [17] such as the KOOS should be evaluated. The second aim was to provide baseline data for a large cohort of patients suffering from cartilage defects and different subgroups of this cohort dependent of gender, defect grade and size, defect location, and others.

Using multivariate regression analysis and ANOVA, factors with an influence on baseline KOOS total and subscores could be detected. Surprisingly, several factors showed a highly significant influence that was not very strong, though.

Among the patient-specific factors with a significant influence on the KOOS were age, sex, and BMI, as well as smoking status. Defect location and number of previous knee and cartilage surgeries were defect-specific characteristics with a significant influence.

Defect grade and size interestingly showed no significant influence on the KOOS total or subscores except for “Pain” and “Symptoms” subscores, nor did the number of treated defects or symptom duration.

To our knowledge, publications reporting baseline data from a larger patient collective scheduled to receive cartilage repair surgery are scarce. Cameron et al. analyzed KOOS and WOMAC data from a larger collective of young, active subjects entering military service to present normative data [18]. They found significantly lower scores in male and female subjects with a history of knee ligament injury but did not evaluate the influence of sex or age, both of which we found significant. Interestingly, these factors are not commonly evaluated with respect to patient-related outcome measures. Paradowski et al. found women to report more knee-related complaints than age-matched men in “Pain”, “Symptoms”, and “ADL” KOOS subscales in a population-based cohort. Older patients generally scored lower in several subscores [19]. Age veritably had the strongest effect on the baseline KOOS (total and all subscores) in our study.

Most studies, though, focus on outcome data. For example, Rotterud et al. analyzed outcome data from the Norwegian and Swedish National Knee Ligament Registry and showed worse KOOS outcomes in patients receiving ACL reconstruction when full thickness cartilage lesions (ICRS grade 3 or 4) were present. Meniscus lesions, though, had no significant impact [20]. In contrast, analyzing the baseline KOOS, we could only show a significant influence

Table 3 Baseline data—subgroup differences analyzed using post hoc Tukey and Student's *t* test, mean KOOS/subscores (standard deviation), and *p* value

KOOS	Total	ADL	Pain	QOL	Symptoms	Sports/rec
Sex:						
Male (SD)	59.95 (17.30)	70.42 (20.28)	64.09 (19.20)	30.44 (18.55)	64.24 (17.67)	33.51 (25.78)
Female (SD)	51.79 (17.61)	62.42 (21.19)	54.28 (19.72)	25.71 (16.89)	57.03 (18.49)	23.66 (22.96)
	<i>p</i> < 0.001					
Age:						
< 40 (SD)	60.61 (17.67)	72.13 (20.39)	64.19 (19.50)	31.50 (19.20)	63.46 (17.80)	33.33 (26.51)
≥ 40 (SD)	52.26 (17.01)	62.07 (20.37)	55.95 (19.59)	25.41 (16.24)	59.04 (18.62)	25.25 (22.74)
	<i>p</i> < 0.001					
BMI:						
< 30 (SD)	58.07 (17.67)	69.09 (20.08)	61.73 (19.76)	29.24 (18.33)	62.37 (18.22)	31.14 (25.37)
≥ 30 (SD)	50.32 (17.29)	59.41 (20.96)	53.61 (19.56)	25.66 (16.73)	56.76 (18.15)	22.04 (22.44)
	<i>p</i> < 0.001	<i>p</i> < 0.001	<i>p</i> < 0.001	<i>p</i> = 0.001	<i>p</i> < 0.001	<i>p</i> < 0.001
Smoking status:						
Non-smoker (SD)	57.64 (17.86)	68.36 (21.01)	61.15 (20.05)	29.10 (18.35)	62.54 (18.28)	29.87 (25.14)
Smoker (SD)	53.59 (18.06)	63.57 (21.11)	56.88 (20.14)	27.35 (18.08)	57.97 (18.22)	28.54 (25.78)
	<i>p</i> < 0.001	<i>p</i> < 0.001	<i>p</i> < 0.001	<i>p</i> = 0.097	<i>p</i> < 0.001	<i>p</i> = 0.371
No. of previous surgeries:						
< 2 (SD)	57.19 (17.89)	67.51 (21.23)	60.82 (20.01)	29.40 (18.44)	62.26 (18.25)	30.23 (25.29)
≥ 2 (SD)	54.56 (17.58)	66.46 (19.99)	57.89 (19.65)	25.34 (16.30)	57.69 (18.20)	26.56 (24.16)
	<i>p</i> = 0.013	<i>p</i> = 0.379	<i>p</i> = 0.010	<i>p</i> < 0.001	<i>p</i> < 0.001	<i>p</i> = 0.013
No. of previous cartilage surgeries:						
< 1 (SD)	57.68 (18.01)	68.09 (21.15)	61.39 (20.07)	29.62 (18.49)	62.15 (18.47)	30.74 (25.63)
≥ 1 (SD)	52.72 (16.66)	64.19 (20.05)	55.68 (18.93)	24.46 (15.82)	58.15 (17.42)	24.66 (22.36)
	<i>p</i> < 0.001	<i>p</i> = 0.001	<i>p</i> < 0.001	<i>p</i> < 0.001	<i>p</i> < 0.001	<i>p</i> < 0.001

of defect grade or size on pain and symptoms subscores in our collective. Yet, previous knee and cartilage surgeries had a significantly negative influence on the total score, indicating the relevance of concomitant injuries needing treatment. Cox et al. [21] presented baseline and outcome data in a collective of patients receiving ACL reconstruction and found cartilage lesion grades 3 and 4 to be a significant predictor for inferior outcome in all KOOS subscores, regardless of lesion location. Also, higher BMI and smoking predicted lower KOOS. Jaiswal et al. concurrently showed that smoking had a deleterious effect on preoperative and postoperative modified Cincinnati Knee Score in patients undergoing autologous chondrocyte implantation and suggested respective

pre-operative counseling [22]. Concerning BMI, Jaiswal et al. found a significant influence on the Modified Cincinnati Score [23] after ACI or MACI. Unfortunately, baseline data were not presented here. This seems in line with the data in the present study, showing BMI and smoking status as well as defect location to have a negative influence on baseline scores. A significant influence could not be detected for defect grade or size, supporting Illingworth et al., who found KOOS and WOMAC scores to be poor indicators for femorotibial cartilage loss when they correlated the scores with MRI scans and plain radiographs from 445 patients [24].

Symptom duration was another factor analyzed for influence on baseline KOOS in this study. Michalitsis et al. evaluated

Table 4 Defect location—mean KOOS/subscores (standard deviation) for patients with respective defect locations

Location/score	Total	ADL	Pain	QOL	Symptoms	Sports/rec
Patella	57.29 (18.00)	68.30 (20.61)	60.60 (19.12)	30.14 (19.08)	61.13 (18.10)	30.52 (26.16)
Trochlea	56.18 (17.32)	66.46 (20.69)	60.85 (19.34)	27.48 (17.15)	60.32 (18.51)	28.89 (24.91)
Medial femoral condyle	55.41 (17.68)	65.72 (21.10)	58.74 (20.38)	27.38 (17.42)	61.35 (18.60)	27.72 (24.06)
Lateral femoral condyle	61.84 (18.75)	72.86 (21.56)	65.68 (20.56)	31.69 (19.53)	64.68 (17.81)	35.88 (26.63)
Medial tibial plateau	48.46 (14.60)	57.23 (17.95)	52.20 (19.01)	23.75 (14.02)	57.26 (17.61)	21.97 (20.00)
Lateral tibial plateau	58.74 (16.69)	69.58 (20.72)	60.35 (21.31)	29.32 (15.40)	63.52 (16.57)	33.08 (25.31)
More than one location	51.21 (18.42)	62.50 (22.50)	51.74 (20.77)	22.22 (17.44)	52.50 (20.62)	23.22 (22.93)

KOOS and IKDC scores in patients receiving ACL reconstruction at different time points after injury [25]. No correlation was found between KOOS and intraarticular pathology at any time point after injury. Concurring with these findings, no significant influence of symptom duration on baseline KOOS could be found in the present study either. Nor could we detect a significant influence of the number of treated defects.

Strengths of this study include the large patient population and data collection from multiple study centers using registry data [26]. Knee cartilage defect patients enrolled in randomized controlled trials are suggested not to be representative of patients in an actual orthopaedic practice [27], so the presented data may be more close to reality. Also, the use of a single, multiply-validated [12, 13] patient-reported score to evaluate baseline status enhances comparability.

The study is limited by issues commonly found in register studies. Data is often subject to selection bias [26]. Another problem can be missing data. In this case, a fair 63.3% complete data sets were available. Poor outcome and deprivation have been identified as factors possibly influencing response rates to registry questionnaires [28]. Thus, the German Cartilage Registry uses defined simple email/online questionnaires at a limited amount of time points and actively follows up on non-responders.

Conclusion

There are patient- and defect-specific factors that significantly influence baseline KOOS in patients scheduled to receive cartilage repair surgery. Namely, these are age, sex, BMI, and smoking status, as well as defect location and the number of previous knee and cartilage surgeries.

In this context, possibly, inferior outcome data may need to be put in perspective to possibly inferior baseline data in certain subpopulations.

Compliance with ethical standards

The study was registered at the DRKS website (DRKS Number: DRKS00005617) and approved by the ethical committee (Approval Number 105/13 (Freiburg University)). Informed consent was given by all patients.

Conflict of interest The authors declare that they have no conflict of interest.

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