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Patients with focal full-thickness cartilage lesions benefit less from ACL reconstruction at 2–5 years follow-up

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Abstract
Purpose To investigate differences in patient-reported outcome after anterior cruciate ligament (ACL) reconstruction between patients with and without a concomitant full-thickness cartilage lesion.
Methods 30 primary ACL-reconstructed patients with an isolated concomitant full-thickness cartilage lesion and 59 matched controls without cartilage lesions were identified in the Norwegian National Knee Ligament Registry and included in the present study. The Knee Injury and Osteoarthritis Outcome Score (KOOS) was used as the outcome measure. At a median follow-up of 2.1 years (range, 2–5 years) after ACL reconstruction, 80 (90%) of the patients completed the KOOS.
Results Preoperatively, there were no differences in KOOS between the study group and the control group. At follow-up, patients with full-thickness cartilage lesions reported significantly decreased scores compared to patients without cartilage lesions in the KOOS subscales pain (mean difference, 8.1; 95% confidence interval [CI], 0.8–15.3), activities in daily living (mean difference, 5.8; 95% CI, 0.3–11.2), sport/recreation (mean difference, 19.8; 95% CI, 5.3–34.3) and quality of life (mean difference, 17.2; 95% CI, 4.2–30.1). Patients with full-thickness cartilage lesions reported significantly less improvement from preoperative to follow-up than patients without cartilage lesions for the KOOS subscales pain (mean difference, 11.6; 95% CI, 3.2–19.9), sport/recreation (mean difference, 20.6; 95% CI, 8.1–33.1) and quality of life (mean difference, 16.3; 95% CI, 3.8–28.7).
Conclusions ACL-injured patients with full-thickness cartilage lesions reported worse outcomes and less improvement after ACL reconstruction than those without cartilage lesions at 2–5 years follow-up.
Level of evidence Prognostic; prospective cohort study, Level I.

Keywords Anterior cruciate ligament · Cartilage lesion · Outcome · KOOS

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Introduction

The combination of anterior cruciate ligament (ACL)-injury and an articular cartilage lesion is a common finding in arthroscopic knee surgery. A cartilage lesion is detected in 16–46% of ACL-injured patients [5], but the impact of these cartilage lesions on the outcome after ACL reconstruction is not clear. Studies on the presence of a cartilage lesion at the time of primary ACL reconstruction have indicated an increased risk of later development of knee

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osteoarthritis (OA) [7, 11]. However, previous studies [18, 19, 21] have found no clinically relevant differences in patient-reported outcomes after ACL reconstruction between patients with and without cartilage lesions, and the benefits from surgical treatment of concomitant cartilage lesions in ACL-injured knees have been debated. A recent review on the surgical treatment of these combined injuries, concluded based upon only 5 case series studies that simultaneous cartilage surgery and ACL reconstruction can result in reasonable short-term outcome [5].

There is a lack of knowledge on the prognosis for individuals with cartilage lesions in ACL-injured knees. Thus, decision-making regarding different treatment options is difficult and more knowledge is needed regarding any differences in knee function in ACL-reconstructed individuals with and without cartilage lesions.

The current study is a longitudinal follow-up of an initial cohort of ACL-injured patients with full-thickness cartilage lesions (International Cartilage Repair Society [ICRS] grade 3–4) [4] and a matched control group without cartilage lesions previously described by Hjermundrud et al. [10]. In the index study, no differences in patient-reported outcome between patients with and without cartilage lesions were found prior to the ACL reconstruction. In the current study, these patients were then followed for 2–5 years after ACL reconstruction, with the primary objective to investigate if there at follow-up were differences in patient-reported outcome between patients with a concomitant full-thickness cartilage lesion and patients without any cartilage lesions. The null hypothesis was that ACL-injured patients with a concomitant full-thickness articular cartilage lesion will report equal outcome by the Knee Injury and Osteoarthritis Outcome Score (KOOS) compared to patients without cartilage lesions at 2–5 years after primary ACL reconstruction.

Materials and methods

Norwegian Knee Ligament Registry

The Norwegian Knee Ligament Registry was established in June 2004 as the world's first national knee ligament registry, with the main aim to prospectively monitor the outcome of knee ligament surgery [8]. Surgical procedures on the anterior cruciate ligament (ACL), posterior cruciate ligament (PCL), medial collateral ligament (MCL), lateral collateral ligament (LCL) and posterolateral corner (PLC) are reported to the registry, including reconstructions, revisions and any type of reoperation. The registry is approved by the Norwegian Data Inspectorate as a national health registry. At the time of primary ACL reconstruction, the patients are asked to participate in the Norwegian Knee Ligament Registry. If accepted, they sign an informed consent form allowing the data assembly and later use of their registry data for follow-ups at 2, 5 and 10 years, postoperatively. Preoperatively, the patients complete the KOOS questionnaire, and postoperatively the surgeons complete a form including specific variables for the patient, knee and surgical procedure. Concurrent focal cartilage lesions are graded according to the ICRS guidelines [4]. The national compliance rates of reported primary ACL reconstructions and completed preoperative KOOS questionnaires are considered satisfactory with 97 and 88%, respectively [9]. At 2, 5 and in the future 10 years postoperatively, the patients receive the KOOS questionnaires by postal mail and return the completed questionnaires to the registry.

Knee Injury and Osteoarthritis Outcome Score

The KOOS is considered as a valid, reliable and responsive self-administered questionnaire for patients with several types of knee injury and knee OA [15]. It has been validated for ACL and cartilage injury, as well as other knee injuries [1, 16], and age- and gender-specific population-based reference data of the KOOS have been established [14]. It consists of 42 questions distributed between 5 subscales: pain (9 questions), other symptoms (7 questions), activities in daily living (ADL) (17 questions), function in sport and recreation (sport/rec) (5 questions) and knee-related quality of life (QoL) (4 questions). Each subscale ranges from 0 (worst) to 100 (best) and it is recommended to use each subscale independently in outcome evaluations [16]. Calculation of the score of each subscale and treatment of missing data were done according to the guidelines given by ROOS et al. [16]. KOOS QoL was defined as the primary outcome measure, as this subscale is considered to be the most sensitive for ACL-injured patients [16]. A difference or change of 10 points or more in either of the KOOS subscales was considered as clinically relevant [15].

Inclusion

All patients were included from the Norwegian Knee Ligament Registry. At the time of inclusion in December 2007, a search among the 4849 primary ACL reconstructions in the registry's database was performed [10]. Approximately 6% had a full-thickness cartilage lesion [17], and of these, a cohort of 30 patients met all of the following inclusion criteria: A full-thickness cartilage lesion (ICRS grade 3 or 4), age less than 40 years, no associated ligament or meniscus injury, no previous knee surgery and less than 1 year from the ACL-injury to reconstructive surgery. In addition, the preoperative KOOS

questionnaire had to be completed. For each of these 30 patients in the study group, two control patients with an isolated ACL-injury and no cartilage lesion present were included. Except for having no cartilage lesion of any grade (ICRS 1–4), the control patients had to fulfil the same inclusion criteria and were matched to the patients in the study group according to age, gender, days from injury to surgery and type of graft. Of the original 60 patients in the control group, one of the patients was excluded from the index data because of an incomplete preoperative KOOS questionnaire.

The strict inclusion criteria were set in order to isolate the cartilage lesion as the only factor distinguishing the two groups, and to minimize the impact of other possible factors influencing on knee function and degenerative development such as age, meniscus injury, chronic instability and previous knee surgery/injury.

The full-thickness cartilage lesions of the patients included in the study group were located within the knee as follows: 20 (67%) in the medial tibiofemoral compartment, 6 (20%) in the lateral tibiofemoral compartment and 4 (13%) in the patellofemoral compartment. 22 (73%) were ≤ 2 cm^2 and 8 (27%) were >2 cm^2. Of the 30 patients with a cartilage lesion, 7 patients were treated with a cartilage procedure simultaneously with the ACL reconstruction. Of these 7, 4 patients had a debridement procedure with removal of unstable cartilage and 3 patients underwent a microfracture procedure.

Follow-up

At a median follow-up of 2.1 years (range, 2–5), KOOS data were received from the Norwegian Knee Ligament Registry on 80 (90%) patients. 30 patients (100%) in the study group and 50 (85%) in the control group responded. Among the 9 patients with missing KOOS data at follow-up, 8 patients were considered as lost to follow-up, as they did not respond to reminders by postal mail from the registry or telephone, and one patient was of medical reasons not able to complete the KOOS questionnaire. In addition to the KOOS questionnaire, the patients answered questions about any additional surgical procedures and/or new traumas to the knee which had occurred during the follow-up period. Scores on the Tegner activity scale [3, 20] ($n = 70$), height and weight ($n = 57$) and smoking status ($n = 54$) were also collected at follow-up. As shown in Table 1, the study group and the control group were comparable regarding age, time from injury to surgery, follow-up period, Tegner activity score, body mass index (BMI), gender distribution, type of ACL graft and smoking status at follow-up. During follow-up, 5 patients in the study group and 6 patients in the control group underwent additional surgical procedures, of which the type of surgery and distribution within the groups are shown in Table 2.

Statistical analysis

All analyses were performed in SPSS (Statistical Package of Social Sciences) version 16.0. Paired samples t test was used to compare the patients with full-thickness cartilage lesions (study group) to those without cartilage lesions (control group). In cases where the KOOS were available for both control patients, the data were considered as clustered and the average KOOS scores of the two controls were used in the analysis [12]. Level of significance was defined as $p \leq 0.05$. All mean changes and mean differences measured by the KOOS are given with 95% confidence intervals (CIs). Furthermore, an effect size, the standardized response mean (SRM) was estimated to evaluate whether the changes in KOOS scores from preoperative to follow-up were regarded as clinically relevant. SRM was calculated as a ratio of the observed change ($\bar{D}$) and the standard deviation (SD) of the observed change [SD(D)], $SRM = \bar{D}/SD(D)$, for all the subscales of KOOS.

Table 1 Characteristics of the study group and the control group at follow-up

	Study group	Control group
Age, years[a] ($n = 80$)	30.4 (7.0)	30.9 (6.9)
Time from injury to surgery, months[a] ($n = 80$)	5.4 (2.5)	5.6 (2.3)
Follow-up, years[a] ($n = 80$)	2.7 (1.1)	2.7 (1.1)
Body mass index[a] ($n = 57$)	25.3 (2.9)	25.4 (3.8)
Tegner activity score[b] ($n = 70$)	6 (1–10)	6 (1–9)
Gender[c] ($n = 80$)		
Females	30	30
Graft type[c] ($n = 80$)		
Hamstring tendons	57	56
Patella tendon/other	43	44
Smoking status[c] ($n = 54$)		
Nonsmokers	57	54

[a] Mean and (standard deviation); [b] median and (range); [c] percentages

Table 2 Distribution of surgical procedures during the follow-up period

Patients	Procedures
Study	Diagnostic arthroscopy: findings unknown
Study	Removal of cyclops formation
Study	Microfracture, meniscus surgery
Study	Cartilage debridement, meniscus surgery, ACL revision reconstruction
Study	Microfracture, meniscus surgery, ACL revision reconstruction
Control	Diagnostic arthroscopy: rupture of ACL graft
Control	Removal of scar tissue
Control	Synovectomi
Control	Meniscus surgery
Control	ACL revision reconstruction
Control	ACL revision reconstruction

SRM was regarded as small between 0.20 and 0.50, moderate between 0.50 and 0.80, and large above 0.80 [2, 6]. Power analysis revealed that 26 pairs of patients were needed at follow-up to detect a change or difference in KOOS QoL of 10 points with a power of 0.80, a significance level of 0.05 and a SD of the difference between the study patients and the control patients of 17.2, which was the SD of the difference in KOOS QoL between the two patient groups prior to ACL reconstruction.

Results

The KOOS profiles with the mean scores at preoperative and follow-up for the study group ($n = 30$) (ACL-injured patients with a concomitant full-thickness cartilage lesion) and the control group ($n = 50$) (ACL-injured patients without cartilage lesions) are shown in Fig. 1. Those with missing KOOS scores at follow-up ($n = 9$) were excluded from the preoperative KOOS data. As previously demonstrated, there were no significant differences between the groups regarding the preoperative KOOS [10]. This was true also when excluding the patients with missing KOOS scores at follow-up (Table 3).

At follow-up, the study group reported significantly lower scores (poorer results) than the control group in the KOOS subscales pain, ADL, sport/rec and QoL (Table 3). The largest difference in scores between the groups at follow-up was observed in the KOOS subscale sport/rec (mean difference 19.8; 95% CI 34.4–5.3).

When comparing the change over time in scores from preoperative to follow-up between the two groups, the study group showed significantly less improvement than the control group in the KOOS subscales pain, sport/rec and QoL (Table 3). The largest difference in change over time between the groups was observed in the KOOS subscale sport/rec (mean difference, 20.6; 95% CI, 8.1–33.1).

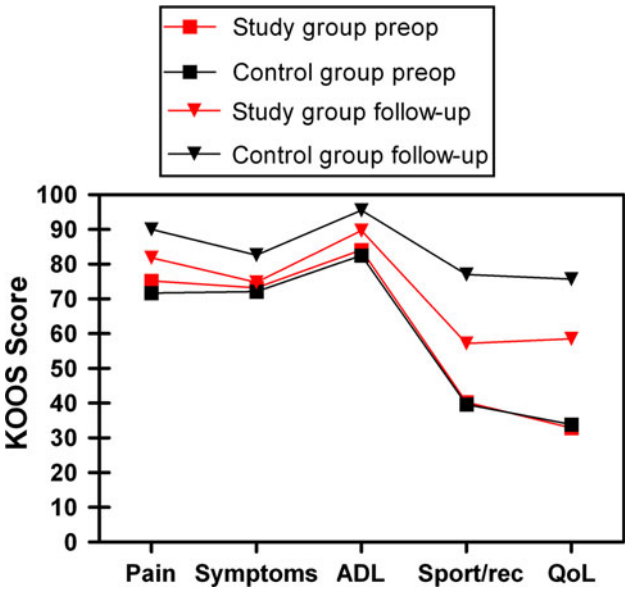

Fig. 1 Knee Injury and Osteoarthritis Outcome Score (KOOS) profiles with mean scores at preoperative and follow-up of the study group and the control group

The mean changes in KOOS scores from preoperative to follow-up for both groups are shown in Table 4, together with the effect sizes (SRM). The control group reported significant improvements during follow-up in all subscales. The study group also showed statistically significant changes over time for all the KOOS subscales, except for the subscale symptoms. The largest change over time for both groups was observed in the primary outcome measure, KOOS QoL, with the study group reporting a mean increase of 25.6 (95% CI, 15.8–35.5) between preoperative and follow-up and the control group reporting a mean increase of 41.9 (95% CI, 34.9–48.9). However, the magnitude of the observed change over time for the two groups, the SRM values, showed that the study group revealed only low effect sizes for the KOOS subscales pain (0.42), symptoms (0.08), and ADL (0.39), moderate effect sizes for the subscale sport/rec (0.66), and

Table 3 Mean difference between the study group and the control group in Knee Injury and Osteoarthritis Outcome Score (KOOS): at preoperative, follow-up and change over time

KOOS subscales	Preoperative		Follow-up		Change over time	
	Mean difference (95% CI)	p	Mean difference (95% CI)	p	Mean difference (95% CI)	p
Pain	3.5 (−4.8 to 11.8)	0.392 (n.s.)	−8.1 (−15.3 to −0.8)	0.031	−11.6 (−19.9 to −3.2)	0.008
Symptoms	1.1 (−6.6 to 8.7)	0.776 (n.s.)	−7.8 (−16.8 to 1.2)	0.086 (n.s.)	−8.9 (−20.2 to 2.5)	0.122 (n.s.)
ADL	1.6 (−6.9 to 10.1)	0.703 (n.s.)	−5.8 (−11.2 to −0.3)	0.038	−7.4 (−15.6 to 0.9)	0.077 (n.s.)
Sport/recreation	0.8 (−10.7 to 12.2)	0.895 (n.s.)	−19.8 (−34.3 to −5.3)	0.009	−20.6 (−33.1 to −8.1)	0.002
QoL	−0.9 (−7.4 to 5.5)	0.768 (n.s.)	−17.2 (−30.1 to −4.2)	0.011	−16.3 (−28.7 to −3.8)	0.012

Mean difference = study group minus control group

Change over time = follow-up minus preoperative

CI confidence interval, *p* level of significance, *n.s.* non-significant, *ADL* activities in daily living, *QoL* quality of life

Table 4 Mean change over time in Knee Injury and Osteoarthritis Outcome Score (KOOS) and effect size of the study group and the control group

KOOS subscales	Study group		Control group	
	Mean change over time (95% CI)	Effect size SRM	Mean change over time (95% CI)	Effect size SRM
Pain	6.8 (0.8 to 12.7)	0.42	18.3 (12.8 to 23.8)	1.24
Symptoms	1.5 (−5.9 to 9.0)	0.08	10.4 (3.3 to 17.6)	0.54
ADL	5.6 (0.2 to 11.0)	0.39	13.0 (6.8 to 19.3)	0.78
Sport/recreation	16.8 (7.4 to 26.3)	0.66	37.4 (29.5 to 45.4)	1.76
QoL	25.6 (15.8 to 35.5)	0.97	41.9 (34.9 to 48.9)	2.24

Mean change over time = follow-up minus preoperative

CI confidence interval, *SRM* standardized response mean, *ADL* activities in daily living, *QoL* quality of life

large effect size only for the subscale QoL (0.97). In contrast, the magnitude of the observed change, the effect sizes for the control group, revealed no low effect sizes, moderate effect sizes for the KOOS subscales symptoms (0.54) and ADL (0.78), and large effect sizes for the three remaining KOOS subscales, pain (1.24), sport/rec (1.76), and QoL (2.24).

Discussion

The main finding of the present study is that ACL-injured patients with a concomitant full-thickness cartilage lesion report impaired outcomes after ACL reconstruction compared to patients without such lesions. To our knowledge, this is a new finding. Patients with full-thickness lesions reported statistically significant worse KOOS scores (pain, ADL, sport/rec and QoL) at follow-up and less improvement in KOOS scores (pain, sport/rec and QoL) during the follow-up period, than those without cartilage lesions. There was also a trend toward worse outcomes in those who had a cartilage lesion in the remaining subscales both at follow-up and in changes over time.

The magnitude of the change in scores for the control group (SRM values) was higher for all of the KOOS subscales compared to the study group (from 0.08 to 0.97 for the study group and from 0.54 to 2.24 for the control group) [2, 6]. This magnitude of change is also supported by Roos et al. [15], who suggested that a change in score of above 8 to 10 points could be regarded as clinically relevant. The control group revealed a change in score above 10 points for all the KOOS subscales, but the study group achieved a change above 10 points only for the KOOS subscales sport/rec and QoL (as found for the moderate effect size for the study group). These findings support the fact that the magnitude of change which could be considered clinically relevant was higher for the control group compared to the study group. The study group achieved a considerable less improvement in knee function over time compared to the control group without cartilage lesions.

There were no significant differences between the study group and the control group in either of the KOOS subscales at the time of ACL reconstruction, meaning that the observed differences in KOOS scores between the groups must have occurred during the follow-up period. The

results of the study are in disfavor of the null hypothesis, and assuming no significant confounding, the differences in patient-reported outcome between the study group and the control group can be explained by the presence of the full-thickness cartilage lesions. In a cohort study from a clinical setting like this, it is however difficult to have control of all possible confounding factors. However, the two patient groups were strictly matched at inclusion and they were comparable for all reported variables (age, time from injury to surgery, follow-up period, Tegner activity score, BMI, gender, type of graft and smoking status) at follow-up.

Seven of the 30 cartilage lesions were treated surgically at the time of ACL reconstruction. This might have influenced the results of those patients, but most probably by improvement. Furthermore, the majority of the cartilage lesions in the present study were located in the medial tibiofemoral compartment and the majority were also ≤ 2 cm^2. Because of small subgroups, no correlation analysis of localization, lesion size and outcome were conducted. However, the relationship between lesion size and outcome has already been studied by Shelbourne et al. [18] and Widuchowski et al. [21], who found no significant correlation between larger lesion size and low reported knee scores.

The main finding of the present study is however not in line with existing literature. Prior studies by Shelbourne et al. [18], Spindler et al. [19] and Widuchowski et al. [21] have found that cartilage lesions have no clinically relevant impact on patient-reported outcome after ACL reconstruction. However, different follow-up periods, possible differences in the study populations and the use of other patient-reported outcome measures than the KOOS [18, 21], make it difficult to compare the findings. The follow-ups were done at an average of 2.7 years in the present study, whereas in the other studies they were conducted at 5.4 years [19], 8.7 years [18] and 10 and 15 years [21]. It is of course a possibility that the impaired outcomes of those patients with cartilage lesions in the present study, would adjust over time, and that the outcomes of both patient groups would approach each other with a longer follow-up period. However, the observed differences were quite large and it is unlikely that these differences would disappear until next follow-up at the average of 5 years postoperative. This is supported by the findings of Shelbourne et al. [18], who followed the patients with and without cartilage lesions annually from 1 year postoperatively up to 12 years after ACL reconstruction, and found that the patient-reported outcomes were stable from 1 year postoperatively and throughout follow-up. Regarding study populations, both the studies by Shelbourne et al. [18], Spindler et al. [19] and Widuchowski et al. [21] are most probably recognized as single-institution surveys, while the present study is based on a national registry. Depending on how the institutions or surgeons recruit their patients, both single-institution and single-surgeon surveys might introduce selection bias to the study population. Neither did any of the studies [18, 19, 21] report baseline values of the subjective outcome measures. Such baseline values of the outcome measures are necessary if any differences in change from preoperative to follow-up between patients with and without cartilage lesions are to be detected.

The main strengths of the present study are its prospective design, the high overall follow-up rate (90%) and the strict grade of matching between the two groups. However, there was a difference in the follow-up rate between the study group (100%) and the control group (85%). Even though this difference has a potential of selection bias, this is not likely as the follow-up procedures were similar for both groups and the groups were still matched at follow-up.

The main limitation is the relatively small number of patients in the study group, which could make the findings difficult to generalize to other populations than the study population. However, the small number is a result of the narrow inclusion criteria, which were set in this strict manner to reduce confounding and isolate the cartilage lesion as the only factor distinguishing the two groups. The patients are also included from a population-based national registry with high reporting rates [8, 9], which should contribute in avoiding selection bias. However, we recognize that there is a need to confirm the findings of the present study in larger prospective cohort studies, in order to make firm conclusions about the prognosis related to full-thickness cartilage lesions in ACL-injured knees.

Another limitation is that the KOOS are the only outcome measure. The reasons for choosing the KOOS as the only patient-reported outcome measure in the Norwegian Knee Ligament Registry and its limitations are outlined by Granan et al. [8] and are also discussed in the prior publication of the baseline data from the present study [10]. It might have been beneficial to include radiographic evaluation at follow-up, to evaluate whether the reduced scores in the group with cartilage lesions could be explained by an increased proportion of early onset knee OA. However, by excluding patients with even higher risk of OA through the inclusion criteria and with the follow-up period ranging from 2 to 5 years, it is not likely that there at this stage would be any detectable differences on standard weight-bearing x-rays. Øiestad et al. [13] found that low patient-reported knee function 2 years after ACL reconstruction significantly increased the risk of symptomatic radiographic knee OA at 10–15 years follow-up. In any future follow-up of the present study of at least 10 years, it will therefore be of great interest to include radiographic evaluation.

The findings from the present study indicate that ACL-injured patients with full-thickness cartilage lesions might

have more problems after ACL reconstruction than previously thought, and the discussion about if, when and how to treat cartilage lesions in ACL-injured knees needs to continue. In order to improve the outcome and decide how to treat concomitant cartilage lesions in ACL-injured knees, larger prospective cohort studies and randomized controlled trials are needed. Such studies should include a control group with the cartilage lesions left untreated. To our knowledge, no kind of surgical treatment of cartilage lesions in ACL-injured knees has proven superior to leaving the lesion untreated at the time of ACL reconstruction.

Conclusion

ACL-injured patients with concomitant full-thickness cartilage lesions reported worse outcomes and less improvement after ACL reconstruction than those without cartilage lesions on short to midterm follow-up. This should be considered when informing patients with such combined injuries about the expected outcome of surgery. In order to improve these patients' outcome after ACL reconstruction, there is a need for further studies on the treatment of concomitant cartilage lesions.

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Conflict of interest The authors declare no conflicts of interest.

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