Damage to the cranial cruciate ligament (CCL) in dogs causes rapid histologic, radiographic, and biochemical changes in the stifle joint consistent with naturally occurring osteoarthritis (OA). Experimental transection of the CCL is a widely accepted model for the evaluation of morphologic, biomechanical, and biochemical alterations associated with naturally occurring OA of the stifle joint. This model has been studied in an attempt to elucidate pathways of joint destruction. Additionally, use of this model has increased in an effort to prove efficacy of compounds referred to as sign-modifying or structure-modifying agents of OA.

Researchers have used multiple outcome measures to assess alterations in joint deterioration. One objective outcome measurement is the determination of forces transferred across the joint. The progression of OA is related to dynamic loading during movement. Determination of ground reaction forces (GRF) has been used to evaluate lameness and, in dogs, it is well established as a primary outcome measurement. In addition, measurement of vertical GRF has been widely used as a primary outcome measurement. However, to assess long-term changes of any disease process, information must be available on the progression and variability of the outcome measurements chosen. This knowledge is vital to establish effective test-group sizes and to determine appropriate sampling periods within the course of the disease.

In dogs with OA of the stifle joint induced by transection of the CCL, there is a period of pronounced lameness followed by an ill-defined period of gait improvement. The time frame at which this improvement stops and a persistent lameness remains is not yet defined. The nature of the chronic lameness in terms of variability and severity over periods of months to years is also not clearly understood. The objective of the study reported here was to document changes in vertical GRF (e.g., vertical peak force and vertical impulse) over a 48-month period in dogs with a transected CCL. Specific aims were to determine variability and severity over periods of months.

Materials and Methods

Objective—To describe changes in vertical ground reaction forces (GRF) over 48 months in dogs with osteoarthritis (OA) of the stifle joint induced by transection of a cranial cruciate ligament (CCL).

Animals—12 clinically normal adult dogs.

Procedure—Vertical GRF (eg, peak force and impulse) were determined prior to and 1, 2, 3, 6, 10, and 12 months after transection of the right CCL. In 7 dogs, data were also collected 24, 32, 38, 42, and 48 months after transection.

Results—Vertical peak force and impulse were significantly decreased in the right hind limb at all times after transection, compared with baseline values. From 10 through 48 months after transection, vertical GRF remained essentially static. Ground reaction forces in the unoperated (left) hind limb also changed significantly during the study. Left vertical impulse significantly increased 3 months after transection, whereas at 24, 38, 42, and 48 months after transection, left vertical peak force was significantly decreased, compared with the baseline value. Mean intradog coefficients of variation (CV) for peak vertical force and impulse ranged from 738 and 9.32, respectively, 1 month after transection to 1.96 and 2.76, respectively, at 42 months.

Conclusions and Clinical Relevance—Vertical GRF in the affected hind limb equilibrated approximately 10 months after CCL transection. Prior to this, force transmission across the affected stifle joint changed significantly over time. Intradog CV were small, indicating that GRF may be an appropriate outcome measurement for evaluation of OA development induced by CCL transection in dogs.

Statistical analyses—A repeated measures ANOVA was used to compare each vertical peak force and impulse over time. If significant changes were found, means were compared by use of a least-squared differences test. Significance was set at P < 0.05. At each measurement time, coefficients of variation (CV) were calculated for each dog for each vari-
able. Again, a repeated measures ANOVA was used to compare changes in CV over time.

**Results**

Vertical peak force and associated impulse were significantly decreased in the right hind limb at all times after CCL transection, compared with baseline (pretransection) values (Fig 1). At no time did vertical peak force or impulse return to baseline values. Vertical peak force and impulse were significantly increased from 6 through 48 months after transection, compared with values measured from 1 to 3 months. Peak force and impulse at 10 months were increased, but not significantly ($P = 0.09$) so, over those at 6 months. From 10 through 48 months, vertical force and impulse remained relatively static.

Following transection of the right CCL, vertical peak force was significantly different between limbs at all times except at 48 months. For the first 12 months after transection, vertical peak force in the unoperated (ie, left) hind limb did not differ significantly from the baseline value (Fig 1). However at 24, 38, 42, and 48 months, left vertical peak force decreased significantly. Vertical impulse in the left hind limb was increased slightly but not significantly ($P = 0.07$) 2 months after CCL transection, compared with the baseline value. However, left vertical impulse determined 3 months after transection was significantly increased, compared with the baseline value. Vertical force peak and impulse in the unoperated limb were significantly greater 2 and 3 months after transection, compared with all values measured after 24 months except those measured at 32 months.

Mean intradog CV for vertical peak force ranged
from 7.38 one month after transection to 1.96 at 42 months, whereas intradog CV for vertical impulse ranged from 9.32 at 1 month to 2.76 at 42 months (Fig 2). Compared with baseline CV for vertical peak force and impulse, CV significantly increased 1 and 2 months after transection, then decreased and were not significantly different from baseline until 42 months, at which time CV were significantly less than baseline values for the remainder of the study.

**Discussion**

A longitudinal (repeated measures) experimental design offers several advantages to a cross-sectional design for the evaluation of potential treatments for OA. The major difficulty in a longitudinal design lies in establishing outcome measurements that are valid, reliable, and repeatable. In short-term studies evaluating the canine stifle joint, vertical gait analysis has been shown to provide valid, reliable, and repeatable data. Authors of 1 study attempted to provide additional long-term data but compared results obtained for different dogs at different time periods; data were not obtained repeatedly from the same dogs. To be considered as a possible outcome measurement in long-term studies evaluating OA in dogs by use of the model described in this report, knowledge of the inherent variability of vertical GRF is essential. Data reported here established 2 important points. First, vertical force transmission changes over time as a result of development of OA. Vertical gait (ie, vertical GRF) equilibrated approximately 10 months after CCL transection. Prior to that, significant changes were evident in force transmission across the stifle joint. Causes of the initial decrease and subsequent increase in force transmission were likely multifactorial. The initial surgical insult, induced mechanical joint instability, and subsequent cartilage and meniscal injuries probably all accounted in part for the decrease in force transmission during the first few months after surgery. Increases in force transmission between 3 and 10 months were most likely attributable to healing of the surgical wound and the production of periarticular fibrosis in response to stifle joint instability.

The second point established by results of this study was that CV were small for each variable at each measurement point. Given the small CV and the documented repeatability of GRF measurements in dogs, some assumptions can be made regarding the sample size necessary to measure outcomes over time. Coefficients of variation < 10% indicate that this model (eg, experimental transection of the CCL) may be useful for assessing compounds for which even a small magnitude of effect can be expected, given the proper sample size. Coefficients of variation initially increased after CCL transection, which was expected, given the variable return to function in individual dogs after surgical intervention. However, CV decreased during the final 6 months of the study, and this result was less expected. It is unlikely that the dogs suddenly became more accustomed to the measurement techniques after 40 months. The other possibility for the decrease in CV is that the dogs used both hind limbs more consistently, either because the affected stifle joint became more stable and less painful or the neuromuscular system reprogrammed over time to minimize energy loss attributable to limb use. Given that vertical peak force or vertical impulse did not increase during this same period, the latter explanation is more likely.

A point of potential concern in this study was the intermittent use of nonsteroidal anti-inflammatory drugs and the effect that these drugs may have on progression of OA or periarticular remodeling. However, drugs were given for only brief periods. In addition, only etodolac was given during the first year after CCL transection; the other drugs were given at least 2 years following transection. It is doubtful that these drugs
administered for such brief durations affected the progression of OA.

The GRF measured in the present study over time point to a potential drawback of this model that must be avoided when planning future studies. If a study were designed to use this model to assess a treatment for preexisting OA, and treatment was not initiated for 4 to 8 months after CCL transection, it may be difficult to discern a positive treatment effect, using GRF as an outcome measurement, because of expected improvements in the nontreated controls. Thus, a treatment may have a positive effect on preexisting OA, but unless the effect is of sufficient magnitude, it will not be discernable.

Although both vertical peak force and vertical impulse increased in the unoperated hind limb during the first few months after transection, compared with baseline values, only the change in impulse was significant. This result supports 2 conclusions from previous studies. First, in addition to vertical peak force, vertical impulse should also be assessed in dogs, because important data about total force applied during a stance phase may be missed by simply measuring peak magnitude of that force. Secondly, this result indicates that after damage to 1 hind limb, force is redistributed to the contralateral limb, supporting the assertion that, in this model of OA, the use of the contralateral limb as a control is inappropriate. A final finding of the present study was that vertical peak force in the left hind limb significantly decreased, compared with the baseline value, at several measurement times 2 years after transection of the right CCL. Although vertical impulse did not significantly increase in the unoperated limb at these same times, this result does suggest reprogramming of compensatory loading over time. Overall, these data provide further evidence of neurologic modification of quadruped locomotion as a result of chronic unilateral stifle joint instability. However, caution must be used when interpreting these data, because GRF were measured by use of a single force platform; such measurements may not allow for accurate simultaneous evaluation of compensatory loading by other limbs.

References


