# Correlation of pain assessment parameters in dogs with cranial cruciate surgery

Dražen Matičić<sup>1\*</sup>, Marko Stejskal<sup>1</sup>, Marko Pećin<sup>1</sup>, Mario Kreszinger<sup>1</sup>, Boris Pirkić<sup>1</sup>, Dražen Vnuk<sup>1</sup>, Ozren Smolec<sup>1</sup>, and Vlatko Rumenjak<sup>2</sup>

<sup>1</sup>Clinic for Surgery, Orthopaedics and Ophthalmology, Faculty of Veterinary Medicine, University of Zagreb, Croatia

<sup>2</sup>Department for Clinical Laboratory Diagnostics, General Hospital "Sveti Duh", Zagreb, Croatia

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#### ABSTRACT

The objective of this study was to compare postoperative pain, as assessed by multiple objective and subjective methods, after Tibial Tuberosity Advancement and Modified Retinacular Imbrication Technique, procedures that differ significantly in the extent of the operative trauma. We compared the preoperative, 2, 6, 10, 20, 44 and 68-hour postoperative results of the University of Melbourne Pain Scale and visual analogue scale with the dynamics of the physiologic, biochemical and behavioural parameters. The integration of various parameters increases the objectivity of pain assessment. The invasiveness of the surgical technique does not necessarily correlate with the level of postoperative pain.

Key words: pain assessment, cranial cruciate surgery, dog

## Introduction

Pain is an unpleasant sensory or emotional experience most commonly associated with actual or potential tissue damage (HELLYER et al., 2007; MERSKEY, 1979). The sensation of pain is a consequence of the activation of specialized receptors and neurological pathways after such nocuous stimulus. Physiological and behavioural changes show that pain is also the awareness of acute or chronic discomfort of various degrees after trauma, disease or suffering, thus always subjective. Pain is accompanied by emotions of fear, anxiety and panic. Pain elicits protective motor actions, results in learned avoidance, and may modify species-specific behaviour (KITCHELL, 1987). Acute pain is a symptom of disease, while chronic pain itself is a disease (FOX, 2002; THURMON et al., 1996). Studies of acute clinical

Prof. dr. sc. Dražen Matičić, Clinic for Surgery, Orthopaedics and Ophthalmology, Faculty of Veterinary Medicine, University of Zagreb, Heinzelova 55, 10000 Zagreb, Croatia, Phone: +385 91 2390 121; Fax: +385 1 2390 380; E-mail: drmaticic@vef.hr

<sup>\*</sup>Corresponding author:

pain have most often evaluated the effects of surgical trauma on animals (HANSEN, 2003), while prevention and pain management are the key issues within anaesthesia. Because of the lack of verbal communication, the level of postoperative pain in dogs is hard to assess. Therefore the assessment of pain in veterinary medicine relies on vocalization, activity level, lameness, reaction to palpation, and to manipulation. All those criteria are subjective and prone to numerous external factors. The objective indicators of pain are physiological and biochemical response and pain threshold. The purpose of multimodal assessment of pain is to achieve objectiveness and credibility of results.

Due to a difference in the extent of operative trauma between the two surgical techniques, we compared the stifle pain, the dynamics of heart rate, respiration rate and temperature, creatin phosphokinase (CK), glucose and cortisol in plasma during the first three postoperative days. The pain response was assessed by one observer only, but there was no intention to determine the repeatability of the method.

## Materials and methods

The study was conducted on twenty dogs of various breeds, different sexes, age, weight, affected hind-limb and, the duration of lameness, with diagnosed cranial cruciate ligament rupture. According to the surgical technique, Tibial Tuberosity Advancement - TTA (TEPIĆ et al., 2002; MONTAVON et al., 2002) or Modified Retinacular Imbrication Technique - MRIT (FLO, 1975), the dogs were divided into two groups of ten.

In order to assess the level of pain, just before the surgery and 2, 6, 10, 20, 44 and 68 hours postoperatively, the physiological parameters - temperature, heart rate and respiration rate and behavioural indicators - University of Melbourne Pain Scale (UMPS; FIRTH and HALDANE, 1999) and Visual Analogue Scale (VAS) score were recorded. The blood samples for the biochemical parameters analysis were collected from the cephalic vein at the same time. The biochemical parameters used in this study were cortisol, glucose and CK.

Algometric examination consisted of palpation of the incision site and the passive range of motion of the stifle. Vocalization was according to the Colorado State University Canine Acute Pain Scale regarded as half the highest possible intensity of pain.

For plasma cortisol, the blood was taken in the EDTA tubes and immediately centrifuged 10 minutes at 3500 rpms. The plasma was kept at -20 °C until analysis. The samples were analyzed by a Immunoanalyser Cobas® e 411 S/N 071227, Roche Diagnostics, Mannheim, Germany.

For glucose and CK analysis, blood was taken in 1.5 mL microvettes (Microvette, Sarstedt, Nümbrecht, Germany) and immediately centrifuged for one minute at 15800 rpms (Idexx StatSpin, Westbrook, Maine, USA). The samples were tested on an Idexx VetLab Station, Idexx VetTest 8008, Westbrook, Maine, USA.

Every surgery was performed under general inhalation anaesthesia. The same anaesthetic protocol was applied to both groups, taking the individual patient requirements (breed, age) regarding sedative and induction dose into account. The analgesia protocols were the same in both groups.

Premedication consisted of acetylpromazine (PromAce®, Fort Dodge Animal Health, Fort Dodge, Iowa, USA) at 0.05 mg/kg i/m and methadone (Heptanon®, Pliva Hrvatska d.o.o., Zagreb, Croatia) at 0.5 mg/kg i/m. Induction was performed by diazepam (Apaurin®, Krka Tovarna zdravil d.d., Novo Mesto, Slovenia) at 0.25 mg/kg i/v and ketamine (Narketan 10®, Vétoquinol AG, Belp Bern, Switzerland) at 8 mg/kg i/v. Additional analgesia was provided by epidural application of lidokaine (Lidokain 2%, Belupo d.o.o., Koprivnica, Croatia) at 4 mg/kg. All the dogs were intubated and maintained by 1.5-2.5% isoflurane (Forane®, Abbott Laboratories Ltd, Queenborough, UK) in oxygen. At the end of the procedure carprofen (Rimadyl®, Pfizer AH, Zawantem, Belgium) was administered at a dose of 2 mg/kg s/c. The patients were monitored using Ultraview 1030 monitor, Model 90367 (SpaceLabs Medical Inc., Redmond, Washington, USA). The patients were sent home the day after surgery on oral antibiotics (bid, seven days) and carprofen (bid, fourteen days). The application of coldpacks to the affected stifle was also encouraged. If the UMPS score exceeded 10 at any time, the patient was given additional methadone (0.25 mg/kg i/m).

Statistical analysis of collected data was done using the Statistica 6.0 program. The minimum level of significance was defined as P<0.05.

## Results

Two hours postoperatively a statistically significant difference was found for the CK, concentrations, which were double in the TTA group. That ratio continued until 44 hours postoperatively. Six hours postoperatively significantly higher values for UMPS, VAS and temperature were found in the MRIT group, while CK remained significantly higher in the TTA group. At hours 10 and 20 the only statistically significant parameter was the CK concentration, still higher in the TTA group. At 44 hours postoperatively, the temperature was slightly higher in the TTA group. The 68th hour showed measurements for most parameters very close to the preoperative values. Comparative results of recorded UMPS scores are displayed in Fig. 1. Comparative results of recorded VAS scores are displayed in Fig. 2. Comparative results of recorded temperature are displayed in Fig. 3. Comparative results of recorded heart rate are displayed in Fig. 4. Comparative results of recorded plasma glucose levels are displayed in Fig. 5. Comparative results of recorded plasma creatin phosphokinase levels are displayed in Fig. 7. Comparative results of recorded plasma cortisol levels are displayed in Fig. 8.

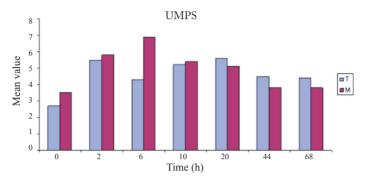


Fig. 1. Comparative results of recorded UMPS scores. T = tibial tuberosity advancement, M = modified retinacular imbrication technique.

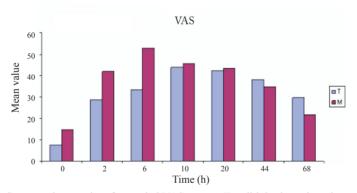


Fig. 2. Comparative results of recorded VAS scores. T = tibial tuberosity advancement, M = modified retinacular imbrication technique.

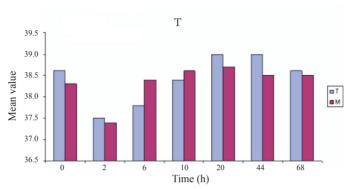


Fig. 3. Comparative results of recorded temperature. T = tibial tuberosity advancement, M = modified retinacular imbrication technique.

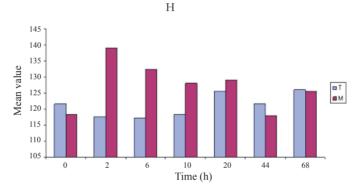


Fig. 4. Comparative results of recorded heart rate. T = tibial tuberosity advancement, M = modified retinacular imbrication technique.

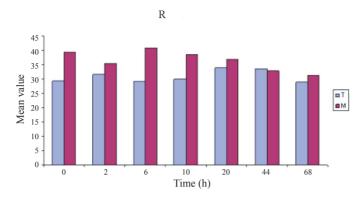


Fig. 5. Comparative results of recorded respiratory rate. T = tibial tuberosity advancement, M = modified retinacular imbrication technique.

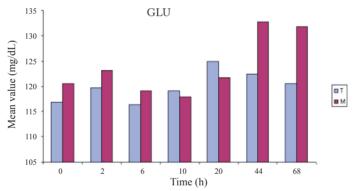


Fig. 6. Comparative results of recorded plasma glucose levels. T = tibial tuberosity advancement, M = modified retinacular imbrication technique.

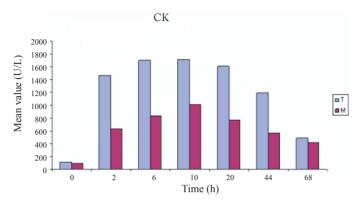


Fig. 7. Comparative results of recorded plasma creatin phosphokinase levels. T = tibial tuberosity advancement, M = modified retinacular imbrication technique.

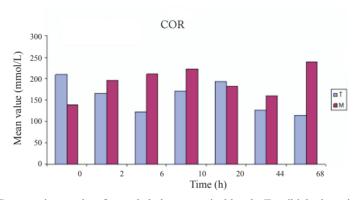


Fig. 8. Comparative results of recorded plasma cortisol levels. T = tibial tuberosity advancement, M = modified retinacular imbrication technique.

## Discussion

The degree of postoperative pain is related to the procedure performed (GAYNOR, 2007). In order to increase sensitivity and decrease bias while measuring the pain parameters, multiple objective and subjective pain assessment methods were used.

The lack of verbal communication with the patient makes pain assessment quite challenging. Various pain scales, like a visual analogue scale, a numerical rating scale, simple descriptive scale, behavioural and physiological response rating scales have been developed in veterinary medicine (FIRTH and HALDANE, 1999; HOLTON et al., 1998;

MATHEWS 2000; MICH and HELLYER, 2008). All these systems rely to a certain extent on subjective assessment of behaviour, but its correlation with other physiological and behavioural parameters has not been proved yet. Therefore, a multimodal approach to pain assessment in animals is generally accepted as the best method so far, multiple methods offering the most accurate results (MATHEWS, 2000; MICH and HELLYER, 2008). Today we still do not have a sufficiently sensitive method that could include all relevant parameters. On the other hand, the changes of physiologic and behavioural parameters can be so subtle or quick that they can be easily overseen by existing methods of assessment. The result is the nonexistence of a standard behavioural pain assessment method in veterinary medicine (MICH and HELLYER, 2008). The University of Melbourne Pain Scale (FIRTH and HALDANE, 1999) is regarded as more sensitive and more accurate than many descriptive and numerical rating scales (GRANT, 2006; MICH and HELLYER, 2008). The UMPS recognizes the importance of specific behavioural patterns, thereby eliminating the observers' bias. The behavioural and physiological parameters are taken into account and divided into six categories: physiologic data, response to palpation, activity, mental status, posture, and vocalization. The application of multiple parameters results in better accuracy and sensibility. The limitations of the system are the incapability of detecting subtle behavioural changes, the exclusive use for postoperative patients and the requirement of broad knowledge of manifestations of pain in animals (MICH and HELLYER, 2008).

The visual analogue scale is widely accepted as a sensitive instrument of behavioural pain assessment (PASCOE, 2000). The VAS was applied in studies of postoperative pain after orthopaedic procedures (BUDSBERG et al. 2002; CONZEMIUS et al., 1997; GRISNEAUX et al., 1999; LASCELLES et al., 1994). It is considered a very sensitive instrument of pain assessment which can appreciate the level of pain as a continuum, instead of in categorical values, and therefore better than simple descriptive scales. The VAS reflects the observers' assessment of pain and that is what makes it variable, but also more sensitive than numerical and simple descriptive scales (JOYCE et al., 1975; OHNHAUS and ADLER, 1975; SCOTT and HUSKISSON, 1976). The method's problem are its subjectivity and differences between observers (GRANT, 2006; HOLTON et al., 1998).

Pain threshold has also been applied in studies of pain in animals. By assigning a number for a specific pressure force (reaction to palpation), algometric studies allow more accurate assessment of pain. The pressure force relates to the conscious reaction. Painful stimuli elicit two types of reaction. Superficial pain is discriminative (A-delta nociceptors), which enables the animal to accurately locate the stimulus. Deep pain is motivational (C nociceptors), meaning behaviour altering. Deep pain originates from the muscles, joints and bones. Both types of pain are included in clinical pain assessment.

The most common sign of pain is change in behaviour (HELLYER et al., 2007). The basic presumption is that pain changes behaviour in a way recognizable to the observer. Furthermore, the intensity of pain relates to the magnitude of behaviour change (HANSEN, 2003). Behavioural response, such as turning the head toward the painful site and vocalization, means conscious perception. It is very important to notice the difference between withdrawal reflex and conscious perception of pain (THOMAS, 2000). Behavioural categories for assessment of pain are conduct, response to people, response to food, posture, mobility, activity, response to touch, attention to the painful area and vocalization (BUFALARI et al., 2007). The animal in pain most often shows decreased activity, depression, mood changes (aggression, withdrawal), resistance to examination, lameness, postural changes, biting or licking the painful area, anorexia and autonomous signs like salivation, tachycardia, perspiration. Behavioural changes can be the direct consequence of loss of function caused by the disease or protective decrease of function. such as in low back pain. Being a matter of experience rather than an objectively quantifiable physiologic category, recognition of pain in animals requires special sensitive methods and the assessment is often difficult. The absence of dramatic behavioural displays in the setting of significant trauma or illness may be a factor in under-treatment (HANSEN and HARDIE, 1993).

Nociceptive stimuli initiate reflex responses of medullar centres for respiration and circulation, centres for endocrine regulation in hypothalamus and limbic system, characterized by hyperventilation, increased sympathetic stimulation and increased secretion of cethecolamines and other endocrine hormones. All this leads to increased minute volume, peripheral resistance and increased blood pressure. Muscle spasm can augment the sensation of pain.

In our study, the physiologic parameters of heart rate and respiratory rate showed no statistically significant differences between the TTA and MRIT groups. Temperature was significantly higher 6 hours postoperatively in the MRIT group, while it was slightly higher in the TTA group at 44 hours. Based on the collected data we could not find any positive correlation between the temperature and the level of postoperative pain.

Physiological parameters used for the assessment of acute pain are heart rate, respiratory rate, temperature, arterial pressure and mydriasis. The first reaction to painful stimulus is the increase of these parameters, but after stabilization of the circulatory system they lose significance (MICH and HELLYER, 2008). Physiological parameters by themselves are not specific enough to differentiate pain from anxiety or fear, but these conditions can influence the circulation. The analgesic agents, like opioids, can decrease the physiological response, even in the case of insufficient analgesia (HANSEN, 2000). The studies show a low correlation between physiological and behavioural parameters of pain in animals (CONZEMIUS et al., 1997).

Biochemical parameters have often been used as markers of pain and stress in veterinary medicine. Increase in cortisol plasma level does not necessarily correspond with physiological parameters changes, but it can be related to the duration of the procedure and the extent of operative trauma. Still, the problem is to make a distinction between painful reaction and stress.

Increased secretion of cortisol and other catabolic hormones is typical for stress, together with the increased blood glucose levels. Anxiety and fear are integral parts of the perception of pain. Anxiety itself has a potential to cause stronger secretion of cortisol and cathecolamines than the primary painful stimulus. In patients with extreme posttraumatic or postoperative pain, the neuroendocrine response may cause a state of shock.

The recorded values of creatin phosphokinase at 2 and 44 hours postoperatively were higher in the TTA group, as expected regarding the greater extent of the operative trauma. All postoperative measurements, except the last at 68 hours, showed CK levels almost twice as high in the TTA group compared to the MRIT.

Creatin phosphokinase is a marker of muscle injury (HANCOCK et al., 2005). It is not a common parameter in the assessment of pain in veterinary medicine, but muscle injury may be related to inflammation and pain. Therefore CK might have application in studies of pain, especially of the relationship between the pain and the extent of the operative trauma.

Glucose has been used as an indicator of pain in newborns and animals (SMITH et al., 1996; ANAND, 1987). The recorded plasma glucose levels did not reveal any statistically significant differences between the intervals, nor between the two surgical techniques.

Our study demonstrated concordance of the dynamics of pain measured by the UMPS and VAS. That indicates the reliability of both methods of pain assessment. However, the total VAS mean value was 34% of the scale, while the total mean value of the UMPS was 17,6% of the scale. This may suggest too high criteria in the first case, or too low criteria in the latter. The applied anaesthetic protocol proved to be adequate.

#### Conclusions

The results of our study lead to the conclusion that plasma cortisol level depends more on the patient's condition and environmental circumstances during blood sampling, rather than the invasiveness and duration of the surgical procedure. Since the same anaesthetic protocol was applied to both groups, anaesthesia alone does not explain the changes of cortisol level.

With the same anaesthetic protocol in both groups, the higher levels of creatin phosphokinase do not imply higher intensity of pain, as shown by the UMPS and VAS.

Creatin phosphokinase is an indicator of muscle damage and thus operative trauma, but the assessment of pain in dogs is not possible based on its values alone.

Because the dynamics of glucose in this study do not correlate with the dynamics of other parameters, we consider that plasma glucose level does not reflect the intensity of pain. Glucose is not a reliable indicator of perioperative pain in dogs.

The intensity of pain can be higher than behavioural changes might suggest. The clinical setting can be a setback in the assessment of pain, limiting the expression of behavioural patterns the animal has in its natural environment.

The UMPS is a reliable method of clinical pain assessment. The VAS is a valid, reliable and very sensitive method of pain assessment.

The invasiveness of the surgical technique does not necessarily correlate with the level of postoperative pain. Pain is an individual experience and there is no objective method of measuring pain today. There is no universal or self-sufficient pain assessment system. Although of low intercorrelation, the integration and comparison of physiologic, biochemical and behavioural parameters increase the objectivity of the results and help to explain their relationships, thus making the overall pain response clearer for the observer

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### SAŽETAK

Cilj ovog istraživanja bila je usporedba poslijeoperacijske boli, procijenjene višestrukim objektivnim i subjektivnim metodama, nakon kranijalne transpozicije goljenične kvrge i modificiranog postupka zatezanja retinakula, kirurških zahvata koji se prema opsegu operacijske traume znatno razlikuju. Usporedili smo rezultate bodovnog sustava intenziteta boli Sveučilišta u Melbourneu i vizualne analogne skale s dinamikom fizioloških, biokemijskih i bihevioralnih pokazatelja prije operacije te 2, 6, 10, 20, 44 i 68 sati poslije operacije. Objedinjavanje različitih pokazatelja povećava objektivnost procjene boli. Invazivnost operacijske tehnike ne mora se nužno podudarati sa stupnjem poslijeoperacijske boli.

Ključne riječi: procjena boli, prednji križni ligament, pas

