Comparison of the Efficacy of Traditional Chinese Veterinary Medicine Versus Conservative Management for Treatment of Cranial Cruciate Ligament Injury in 40 Companion Dogs

Bogdan Ciolanescu DVM, MS

ABSTRACT

This study compared the efficacy of traditional Chinese veterinary medicine (TCVM) and conservative management (CMT) for treatment of canine cranial cruciate ligament (CCL) injury. Forty dogs diagnosed with CCL injury were equally assigned to either CMT or TCVM study groups for a 24-week treatment period. The CMT Group received treatment consisting of joint supplements, laser therapy, pain medication and strength training, whereas the TCVM Group received acupuncture, Chinese herbal medicine, *Tui-na*, and food therapy. Pain severity and activity interference were scored based on the Canine Brief Pain Inventory form by owners (Days 0, 14, 30, 60, Week 24). The mean TCVM pain score was significantly reduced when compared to CMT at all study time points after study start and became increasingly more significant as the study progressed (i.e. Day 14, p=0.046 and Week 24, p=0.0003). For the TCVM group, the mean improvement was significant at Days 14, 30 and 60. The mean activities interference from pain score, which was more difficult for owners to grade consistently, attained statistical significance for TCVM (compared to CMT) at Week 24. The within group comparison (mean pain score, mean activity interference and mean improvement) was significant at all time points in both study groups. The study concluded that both treatments significantly improve pain in dogs with CCL injury by Week 24, however, TCVM treatment attained quicker results. These findings suggest that when surgery is not an option, both treatment approaches are effective with TCVM resulting in more rapid pain relief.

Key words: traditional Chinese veterinary medicine, conservative management treatment, cranial cruciate ligament rupture, acupuncture, herbal medicine, *Tui-na*, food therapy, canine musculoskeletal disease

*Address correspondence to Dr. Bogdan Ciolanescu (bogdan@fairvalevet.com).

ABBREVIATIONS

AROM	Active range of motion
CBPI	Canine Brief Pain Inventory
CCL	Cranial cruciate ligament
CCLR	Cranial cruciate ligament rupture
CMT	Conservative management treatment
DNAP	Dry needle acupuncture
EAP	Electro-acupuncture
GABA	Gamma-aminobutyric acid
IVDD	Intervertebral disc disease
KOA	Knee osteoarthritis
NSAID	Non-steroidal anti-inflammatory drug
OA	Osteoarthritis
PROM	Passive range of motion
ROM	Range of motion
TCVM	Traditional Chinese veterinary medicine
WM	Western medicine/conventional medicine

From: Fairvale Animal Hospital, Rothesay, New Brunswick, Canada (Ciolanescu)

Damaged or ruptured cranial cruciate ligament (CCL) in one or both hind legs is the most frequent condition causing hind limb lameness in dogs.[1] The lameness is a characteristic "toe-touching" gait or chronic lameness (improved with rest, worse with activity). When left untreated, injury to the other stifle may occur and/or additional structures in the affected stifle may become injured such as the meniscus or collateral ligaments, which could lead to long-term osteoarthritis (OA).[2] Reviews and research studies on this topic have been published in veterinary literature since 1963.[3]

Multiple etiologies have been investigated for CCL rupture (CCLR) with the most common etiopathogenesis classified as degenerative disease followed by acute trauma. Other causes include obesity, collagen degradation, immune-mediated disease, patellar luxation or undetermined etiology.[4] Diagnosis includes a thorough orthopedic exam to identify instability in the joint (cranial drawer sign, tibial compression test), signs of trauma, joint effusion/heat or chronicity (quadriceps atrophy, medial buttress formation).[5] In addition, surgeons and

sports medicine specialists in a number of institutions incorporate diagnostic imaging such as CT/MRI (computerized tomography/magnetic resonance imaging) along with radiographs in the routine diagnostic work-up to confirm physical examination findings and document bony changes in the joint.[5-6]

Currently there are two primary methods for approaching CCL injuries: surgical repair and conservative management treatment (CMT). Surgery repair includes several techniques dependent on surgeon preference and joint changes and is recommended in most cases. Studies have shown an 85% to 92% success rate for dogs larger than 15 kg body weight.[7,8] When surgery repair is not an option for patients (due to age, financial consideration, health status, etc.), CMT is often recommended. It may include strict rest for 8 or more weeks, a weight loss program, joint supplements, pain medications/nonsteroidal anti-inflammatory medication (NSAID), and rehabilitation therapy such as passive range motion and hydrotherapy.[9,10] Studies have reported an 87.5% success rate for CMT in CCL-injured dogs with body weight under 15 kg and poorer success with larger and overweight dogs.[7,8,11] Limitations/disadvantages of CMT include: patients not following a strict rest program; continued weight gain even while on a weight management diet, and owners lack of compliance with home exercises suggested by the rehabilitation therapist. These along with variable response of each dog to treatment yields outcomes that can be inconsistent and less predictable.

Traditional Chinese veterinary medicine (TCVM), based on bringing balance back to disharmonic health patterns, designs treatment for the needs of the individual as opposed to Western (conventional) medicine (WM) where treatment is disease specific and all individuals are treated in a similar fashion. There are 4 modalities that are primarily used in TCVM when designing a treatment plan: acupuncture, Chinese herbal medicine, food therapy and *Tui-na* (Chinese therapeutic massage).

In TCVM, tendons and ligaments (*Jin*) are nourished by Liver Blood and *Yin* and normal contraction/relaxation of tendons/ligaments (*Jin*) are dependent on this. Deficiency, therefore, results in abnormal function and inability of tendons/ligaments to remain healthy resulting in muscular cramps/spasm, tremors, Tendon *Bi* (pain) and weakness (partial or full tears of tendon/ligament).[12-16] The TCVM Pattern diagnosis for CCL injury is Liver Blood/*Yin* Deficiency, and if pain is present, diagnosis will include local *Qi*/Blood Stagnation in the tendon. TCVM clinical signs can include a red/dry tongue (Liver *Yin* Deficiency) or pale/dry tongue (Liver Blood Deficiency) and usually a weak/thin pulse.[13-16]

Table 1: Conservative management treatment (CMT) protocol for study dogs

CMT Group	Joint Supplement	Pain Medication	Laser Therapy
Products	Glucosamine and MSM Omega 3 Vitamins E & C	Meloxicam Deracoxib	Class IV Laser[h] Wavelength: 980/870nm Power: 0.5-15 watt (W), Continuous Wave (CW) / Pulse wave Treatment Area (cm^2) = length (cm) x width (cm) Typical dose range = 6-12 joules (J) per square centimeter
Dose	Glucosamine +MSM (500 mg /24 lbs) per day Omega 3+Vit E (1000mg+400UI/25lbs) per day	Meloxicam – 0.1 mg/kg Deracoxib - 1 to 2 mg/kg/day	Dependent on dog size Power used: Small dogs (<10 kg): 6W, CW, 1200 J for 5 min Dogs 30kg: 8W, CW, 2104J for 6 min Dog>50 Kg: 12W, CW, 4044J 7 min
Frequency	Daily	Daily	3 times per week (Dog pain score > 7) 2 times per week (Dog pain score 5) 1 time per week (Dogs with pain score 3) Decreased frequency: Last 2.5 month of study. Once every 2 to 3 weeks.

Acupuncture, perhaps the best known of these 4 treatment modalities, has been used with success to relieve pain/inflammation, optimize healing, and improve knee function in humans with knee dysfunction. A clinical human-based study investigated improvement of knee osteoarthritis (KOA) using electro-acupuncture (EAP) as the method of treatment. The EAP protocol used the following acupoints on the affected knee: ST-34, ST-35a, ST-35b, ST-36, SP-9, GB-33, and GB-34.[17] It was concluded that EAP was able to relieve pain and stiffness with improved joint function for all 77 participants in the study.[17]

The successful use of Chinese herbal medicine for integrative treatment of tendon/ligament disease has been documented in several species of animals as well as humans.[18-20] The herbal formulas used in these studies accent combinations of nourishing Liver *Yin* and Blood, invigorating Blood and *Qi*, unblocking Meridians/ Channels and resolving Stagnation. Although there is literature in human medicine supporting the use of both *Tui-na* and food therapy to address tendon/ligament disease, at this time there are no clinical studies supporting their use in veterinary medicine.[18,21-23]

The objective of this clinical study was to compare the efficacy of TCVM versus conservative management for treatment of canine cranial cruciate ligament injury. The hypothesis was that the proposed TCVM approach, using a combination of acupuncture, Chinese herbal medicine, food therapy, and *Tui-na* would be a more effective non-surgical CCL injury treatment than conventional conservative management.

MATERIALS AND METHODS

Dogs recruited for this study were patients from the investigator's Rehab Veterinary Hospital in Rothesay, New Brunswick, Canada, along with referrals by other veterinarians in nearby areas. Subject recruitments were achieved through distributing flyers in Kennebecasis Valley (Saint John, Rothesay, NB, Canada). Inclusion criteria for the study were dogs of any age, breed or sex with CCL injury confirmed by clinical signs, history, physical examination and imaging (radiography). Exclusion criteria included: (1) dogs scheduled to undergo surgery; (2) dogs with other conditions such as neurological disease or neoplasia; and (3) dogs already on pain medication (2 weeks) prior to the initial evaluation. Owners gave permission for use of their animals in the study and dogs were handled and housed in a variety of husbandry methods consistent with owner preferences.

Partial randomization was used to assign enrolled dogs to study groups. Owners were presented with the pros and cons of the CMT and TCVM approaches and were informed that there was no scientific evidence as to which approach would have better treatment outcome for their dogs. For owners who could not decide which approach to choose, the patients were randomly assigned to either treatment group.

At study start (Day 0), owners were asked to score their dog's pain based on the Canine Brief Pain Inventory (CBPI).[24] The CBPI grades two aspects: pain severity and

Table 2: Rehabilitation therapy protocol for the conservative management treatment group[9,10]

Rehabilitation Therapy Protocol for Conservative Management of CCL injury in Dogs	
Phase I: Protection (weeks 1-4)	• Increase ROM: PROM flexion and extension leg affected • Increase muscle function using movement synergies and motor learning transfer (toe pinches, leash walking 5 minutes, and increase time per week by 3-5 minutes, weight shifting exercises, walking in circles or figure eight patterns). • Increase proprioception – joint compression • Decrease pain and effusion: icing, PROM and AROM, joint compression • Decrease pain and effusion: icing, PROM and AROM, joint compression.
Phase II: Early strength training (weeks 2-8)	• Full ROM: PROM flexion and extension, may add extension on the stairs • Normal gait: obstacle walking • Increase motor control and strength: underwater treadmill or swimming exercise, side stepping, walking backwards, hill walking, NMES or manual tapping on quadriceps or gluteals with 3 leg standing. • Load 50% – 60% of uninjured limb: increase time and duration of exercise.
Phase III: Intense strength training (weeks 9-12)	• Increased strength and motor control: more exercises like above, walking on uneven surface • Increase load 70% - 80% of uninjured limb: more exercise, increase time and duration
Phase IV: Intensive strength training	• Increased strength: add jumping exercise • Increased coordination: some agility type training • Increased ability in sport specific activities: ball retrieves • Avoid play with other dogs (6 months)

ROM-range of motion; PROM-passive range of motion; AROM-active range of motion; NMES-neuromuscular electric stimulation.

interference with daily functions. Pain severity contains 4 questions about severity of the patient pain and is assessed as: "worst, least, and no current pain".[24] The first four questions are graded on a scale from 0 to 10, with 0 representing no pain and 10 equals extreme pain.[24] Interference with daily function measured how pain interfered with the dog's daily activities and included six questions on general activity, enjoyment of life, rise to standing, walking, running, and climbing.[24] Similarly, it is scored from 0 to 10; 0 = no interference and 10 = complete interference.[24] The responses of these questions are averaged to deliver a pain severity score or pain interference score. The CBPI was completed by the same owner (or person very familiar with the study dog) each time to keep scoring consistent within each study dog.

Each subject in the CMT group received daily joint supplements and pain medication (dependent on the CBPI assessment) along with laser therapy (Table 1). In addition, the animals followed a rehabilitation therapy program that was organized into 4 phases: protection (week 1-4), early strength training (weeks 5-8), intense strength training (weeks 9-12) and finally intensive strength training (Table 2).[9-10]

The TCVM group was treated with acupuncture, Chinese herbal medicine, *Tui-na*, and had their diet modified to address TCVM patterns. The acupuncture protocol (dry needle, electro-acupuncture, aqua-acupuncture) consisted of 3 weekly sessions, which were then decreased to every 3-4 weeks for the remainder of the study. Dry needle acupuncture (DNAP) technique was used to stimulate distal acupoints including: LIV-3, KID-3, BL-60, LI-4, SP-6, GB-39 (0.30 x 25 mm stainless steel needles for large and giant breeds; 0.25 x 25 mm stainless steel needles for medium to large breeds, and 0.22 x 25 mm needles stainless steel needles were used for small breeds).

Electro-acupuncture (EAP) technique was utilized to stimulate local acupoints and balance/Back-*Shu* points. The acupunctoscope[a] was set first at low-frequency stimulation (1-40 Hz) to release ß-endophins and enkephalins, for 20 minutes.[25] It was then changed to high frequency stimulation (80-120 Hz) to release dynorphins for 10 more minutes.[25] Acupoints were paired in the following manner: BL-11 to BL-23 bilateral (or BL-17, BL-19), BL-19 and BL-23 bilateral, ST-35a or ST35b to BL-40, ST-36 to ST-34, GB-33 to GB-34, SP-9 to SP-10 or SP-10 to GB-32 (Table 3).[13-16]

In addition, aqua-acupuncture was utilized to stimulate local and Back-*Shu* acupoints, using 0.5 ml of vitamin B_{12} per acupoint (3 ml syringe, 27G ½ inch needle): BL-11, BL-17, BL-18, BL-19, BL 23, ST-35a, ST-35b, ST-36, GB-33, GB-34, SP-9, SP-10, KID-7, BL-40.[14-16] Not all of the acupoints listed above were used in every acupuncture session. A few acupoints were selected from the previous list from each category: respective local points, distal points, Back-*Shu* / balance points. Also

Table 3: Acupoints used to treat CCL injury with anatomic location, indications and actions for each acupoint[14]

Acupoint	Anatomic Location	Attributes, Indications and Actions
ST-34	Craniolateral aspect of the thigh, 2 *cun* proximal and caudolateral to the patella, in the vastus lateralis muscle.	Stifle pain/swelling and Local *Qi* and Blood Stagnation Expels Wind-Damp
ST-35a	Located in depression distal to the patella, lateral to the patellar ligament	Stifle pain and local *Qi* and Blood Stagnation Ligamentous disorder
ST-35b	Located in depression distal to the patella, medial to the patellar ligament	Stifle pain and local *Qi* and Blood Stagnation Ligamentous disorder
ST-36	Located on the cranial aspect of the proximal crus, into tibialis cranialis muscle, 0.5 *cun* lateral to the tibial crest.	Local *Qi* and Blood Stagnation Stifle disorder
GB-32	Localized on lateral aspect of thigh, in a depression, 3 *cun* proximal to the lateral epicondyle of the femur	Local point, pelvic limb pain
GB-33	Located on the lateral aspect of the stifle, into large depression, just proximal to the lateral epicondyle of the femur between the insertion of the biceps femoris tendon and the femur bone.	Pain and swelling of the stifle Relaxes the sinews
GB-34	Located on the lateral aspect of the stifle in a depression cranial and distal to the head of the fibula	Tendon and ligament disorder Stifle pain
BL-40	Located in the center of popliteal fossa, mid-point, between the biceps femoris and semitendinosus muscle	Stifle disorder Local *Qi* and Blood Stagnation in the back of stifle Relieves Blood Stagnation
BL-54	Located in depression dorsal to the greater trochanter of femur, third of the line between the coxal tuber and the ischial tuberosity	*Qi* and Blood Stagnation on the hip and pelvic limb
SP-9	Located in a depression, ventral to the medial condyle of tibia, between the caudal aspect of tibia and gastrocnemius muscle	Stifle pain and arthritis

Table 3 cont.

Acupoint	Anatomic Location	Attributes, Indications and Actions
SP-10	Located, with the stifle flexed, 2 *cun* above the craniomedial edge of patella, in a depression, into the belly of the cranial aspect of the sartorius muscle, on the cranial aspect of femur, on the tip of the vastus medialis muscle	Stifle disorder Blood Stagnation and Stasis
LIV-3	Located in the skin webbing between the second and third metatarsal bone, proximal to the metatarsophalangeal joint	General pain alleviation Muscular spasm Tonifies Liver Blood and *Yin*
LIV-10	Located on the medial aspect of thigh, on the caudal border of abductor muscle, 3 *cun* distal to ST-30, which is localized ventrolateral abdomen, at the level of pubis, 2 *cun* lateral midline	Local point for pain and swelling
KID-3	In a depression between the medial malleolus and Achilles tendon, at the height of the tip of medial malleolus	Local point for the ankle joint, pain in the lower back
KID-7	Located on the caudomedial aspect of the tibia	Local point
KID-10	Medial side of the popliteal fossa, just cranial to BL-40, between the semi-membranous and semi-tendinous muscles	Knee pain
BL-17	Localized on the dorsolateral aspect of spine 1.5 *cun* lateral to caudal edge of the spinous process of the seventh thoracic vertebra	Blood Deficiency Blood Stagnation *Yin* Deficiency
BL-18	Localized on the dorsolateral aspect of spine 1.5 *cun* lateral to caudal edge of the spinous process of the tenth thoracic vertebra	Muscle and tendon disorder Liver Blood and *Yin* Deficiency Tonify Liver *Yin* and Blood
BL-23	Localized on the dorsolateral aspect of spine 1.5 *cun* lateral to caudal edge of the spinous process of the second lumbar vertebra	Stifle disorder Bony *Bi* Syndrome
BL-11	Localized between the medial edge of scapula, and dorsolateral aspect of spine, 1.5 *cun* lateral to caudal edge of the spinous process of the first thoracic vertebra	Osteoarthritis Bony *Bi* Syndrome Soothes the sinews Benefits the bones and joints
Bai-hui	Localized on dorsal midline, between L7 and S1 (lumbosacral space)	Calming point, tonifies Blood

Table 4: Ingredients of the Chinese herbal medicine *Bu Gan Qiang Jin San* (Tendon/Ligament Formula[b]) and their actions [32]

English Name	Chinese *Pin-Yin*	Actions
Lycium	*Gou Qi Zi*	Nourishes Liver *Yin* and Blood
Ligusticum	*Chuan Xiong*	Moves Blood, resolves Stagnation
Paeonia	*Bai Shao Yao*	Nourishes Blood and *Yin*, smooths Liver *Yang*
Cornus	*Shan Zhu Yu*	Nourishes Liver *Yin*
Acanthopanax	*Wu Jia Pi*	Strengthens ligaments and tendons
Cyathula	*Chuan Niu Xi*	Strengthens Kidney and benefits the knees
Rehmannia	*Shu Di Huang*	Nourishes Blood and *Yin*
Psoralea	*Bu Gu Zhi*	Nourishes Kidney *Yang* and *Yin*
Epimedium	*Yin Yang Huo*	Nourishes Kidney *Yang* and *Yin*
Angelica	*Dang Gui*	Nourishes Blood
Morus	*Sang Zhi*	Soothes limbs
Cinnamon	*Gui Zhi*	Activates the Channels and limbs

acupuncture techniques (dry needle, aqua-acupuncture, EAP) were alternated and rotated with each session of acupuncture.

All TCVM Group dogs received Chinese herbal therapy which included the concentrated formulas of Tendon/Ligament[b] (*Zhuang Jin Jian Fang*, modified *Bu Gan Qiang Jian San*) and Body Sore[c] (*Shen Tong Fang*, modified *Shen Tong Zhu Yu Tang*), dosed orally at 0.1 – 0.25g per 10-20lbs body weight twice daily (Tables 4 and 5). For subjects whose radiographs showed significant arthritic changes, *Di Gu Pi San*[d] (classical antecedent *Di Gu Pi* San) was included at a dose of 0.5g per 10-20lbs body weight twice daily (Table 6).[12]

Tui-na was applied by the author to relieve stifle pain and continued daily by the dog's owner or caregiver (Table 7).[23] In addition, food therapy was instituted to help resolve *Qi*/Blood Stagnation, address *Yin* Deficiency and nourish Blood. Cooler, neutral food was recommended such as beef, beef liver, beef heart, bison, bone marrow, pork, pork lung, turkey, rabbit, sardines, white fish, crab, egg, barley, rice, carrots, kelp, radish, oyster, mushroom, bee pollen, leafy vegetable.[22] The recipe consisted of 30%-40% protein (including meat and internal organs), 10%-20% carbohydrate and 40%-60% vegetables and fruits. Flax seed or hemp oil was given at 1 to 2 tablespoon per day, depending on dog size.

To determine the success of pain relief and return of normal joint function, outcome measurements were based on the CBPI form completed by the owners at Days 0, 14, 30, 60 and Week 24.[24] The pain interference score was only used in outcome measurements when pain interfered with all six activities noted by the person who completed the CBPI (general activity, enjoyment of life, rising to standing, walking, running, climbing). This was done to eliminate erroneous scoring of an activity that might not be associated with pain. The final pain interference score was the average of all scores that interfered with daily activities.[24] Scores from Day 0, 14, 30, 60 and week 24 were collected for each study subject.

Statistical hypotheses were formulated for comparisons within group pre- vs. post-treatment scores; between group score improvements; and within group score improvements among different post-treatment assessment times. Wilcoxon Signed Rank test, Rank Sum test, and Repeated Measure ANOVA test were applied for testing these three types of hypotheses, respectively. All tests were two-sided and significance level was set to be 0.05. A sample size of 20 subjects in each group was planned, which was anticipated to have a power over 90% to detect a difference at least 1.2s (s = sample standard deviation) for both Wilcoxon Rank Sum and Sign rank tests as well as the Repeated Measure analysis of variance (ANOVA) test with a 0.05 significance level.

RESULTS

A total of 50 dogs with CCL disease were enrolled in the study, among which 10 dogs were excluded due to a variety of reasons (meniscal tear, opted for surgery, moving into other provinces of Canada). The partial-random treatment group assignments resulted in 20 dogs in each of the CMT and TCVM groups. There were a variety of breeds in each subject group. In the CMT group,

Table 5: Ingredients of the Chinese herbal medicine *Shen Tong Zhu Yu Tang* (Body Sore Formula[c]) and its actions [32]

English Name	Chinese *Pin-Yin*	Actions
Ligusticum	*Chuan Xiong*	Relieves pain and activates Blood
Notopterygiun	*Qiang Huo*	Relieves pain and activates Blood
Angelica	*Dang Gui*	Activates Blood, resolves Stagnation, relieves pain
Epimedium	*Yin Yang Huo*	Tonifies Kidney *Yang* and *Yin*
Cyathula	*Chuan Niu Xi*	Strengthens bones and limbs
Angelica	*Du Huo*	Relieves pain and eliminates Wind-Damp
Cuscuta	*Tu Si Zi*	Nourishes Kidney and Liver
Corydalis	*Yan Hu Suo*	Moves *Qi*/Blood, resolves Stagnation, relieves pain
Paeonia	*Chi Shao*	Relieves pain and cools Blood
Eucommia	*Du Zhong*	Strengthens back and tonifies *Yang*
Psoralea	*Bu Gu Zhi*	Strengthens bone and tonifies *Yang*
Myrrh	*Mo Yao*	Moves Blood, relieves pain
Olibanum	*Ru Xiang*	Moves Blood, relieves pain
Millettia	*Ji Xue Teng*	Nourishes Blood
Persica	*Tao Ren*	Breaks down Blood Stasis, relieves pain
Carthamus	*Hong Hua*	Breaks down Blood Stasis, relieves pain

there were 11 breeds with no more than 3 dogs of the same breed, and 13 different breeds in the TCVM Group with no more than 4 dogs of the same breed.

All 40 dogs in the study were altered (castrated/spayed) at approximately 6 months old. The distribution of sex in the CMT group was 60% (12/20) female versus 40% (8/20) males. In the TCVM group, 55% (11/20) were female and 45% (9/20) were male. Based on the Exact Binomial test, the sex of a study dog (male or female) in the CMT or TCVM groups was not significantly greater than 0.5 (p= 0.50 or p=0.824 respectively). Between the two treatment groups, the proportions of female (or male) were not significantly different (p = 1.00) based on Fisher's Exact test.

The mean ± SD body weight among subjects in the CMT group was 30.94 ±12.4 kg (range 7.8 ~ 55; median = 33) and was 30.76 ±16.4 kg (range 2.6 - 75; median = 32.5) among those in the TCVM group. The difference in mean weight between the two groups was not statistically significant (p = 0.969) based on the Two-sample t test. Mean ± SD age in the CMT Group was 5.93 ±3.1 years (range 2-13; median = 5.5) and was 6.83 ±3.5 years for the TCVM Group (range 2-14; median = 7.0). Based on the Two-sample t test, the difference in subject's age was not statistically significant (p = 0.382). Both groups were assumed to be normally distributed based on the results of the Shaprio-Wilke normality test.

There were no adverse effects from any of the treatments administered to the TCVM or CMT groups throughout the 24-week duration of the study. During the study, only 1 dog (Dog #4, CMT Group) did not respond to treatment which was considered related to age and overweight status. A total of 9 dogs in the TCVM Group and 2 dogs in the CMT Group scored a pain severity score of 0 (no pain) during the study while the activities interference score had 8 TCVM dogs and 4 CMT dogs that achieved a 0 score (normal). There were several dogs that injured the opposite stifle during the study in both groups (TCVM Dogs #2, #3, #13; CMT Dogs #1, #10, #13). Only dog #3 (TCVM Group) continued in the study, as it was the only dog that could still be treated according to the study treatment protocol as it was using the leg again by the third evaluation. Dogs #2, #13 (TCVM group) #1, #10, and #13 (CMT Group) were removed from the study as these dogs could no longer follow the study treatment protocol. These dogs were replaced (to maintain 20 dogs/group) with dogs close to the same body weight and gender (Week 3 for CMT Group, Week 5/6 for TCVM Group). Reinjury to the affected stifle occurred in 7 TCVM dogs and 6 CMT dogs (Table 8). These dogs remained in the study and followed the study treatment protocol.

The CMT Group received NSAIDS for a 2-4-week period during the study. Laser treatment was prescribed 3 times/week for dogs with a pain score greater than 7. As CMT dogs improved, laser use 2 times/week for a pain score of 5 was adequate and then once weekly for dogs with a pain score of 3. The frequency of laser use decreased markedly in the last 2.5 months of the study where it was only used once every 2-3 weeks (Table 1).

Statistical evaluation of study results was based on pain severity and activity interference scores which were derived from a dog's CBPI assessment. Baseline scores were assigned at study start (Day 0) and repeated on Days 14, 30, 60 and Week 24 to measure treatment effect (score improvement from Day 0) over time. At study start (Day 0), there was no statistically significant difference of the pain severity score between study groups (p=0.196). Statistical comparisons were made both within a group and between groups for mean pain score, mean activity interference and mean improvement. The mean pain score was significantly reduced (between group comparison) in

Table 6: Ingredients of the Chinese herbal medicine *Di Gu Pi* [d] and its actions [32]

English Name	Chinese *Pin-Yin*	Actions
Lycium	*Di Gu Pi*	Nourishes *Yin* and clears deficient Heat
Moutan	*Mu Dan Pi*	Cools Blood, clears Heat, resolves Stagnation
Rehmannia	*Shu Di Huang*	Nourishes Blood and *Yin*
Rehmannia	*Sheng Di Huang*	Clears Heat, nourishes *Yin*
Gentiana	*Qin Jiao*	Clears Wind-Damp, nourishes *Yin*
Psoralea	*Bu Gu Zhi*	Tonifies Kidney *Yang* and *Yin*
Drynaria	*Gu Sui Bu*	Tonifies Kidney *Yang* and strengthens bones
Eucommia	*Du Zhong*	Strengthens the back
Alisma	*Ze Xie*	Drains Damp and benefits urination
Salvia	*Dan Shen*	Invigorates Blood and resolves Stagnation
Angelica	*Du Huo*	Dispels Wind, Cold and Dampness, relieves pain
Angelica	*Dang Gui*	Nourishes Blood and relieves pain
Phellodendron	*Huang Bai*	Nourishes *Yin* and Clears Heat

the TCVM Group at all study time points after study start (Day 0) with statistical significance increasing to very significant by Week 24 (i.e. Day 14, $p = 0.046$ to Week 24, $p = 0.0003$) (Table 9, Figure 1). Comparisons between the groups revealed that mean improvement was significantly larger in the TCVM group at Day 14 ($p = 0.018$), 30 ($p = 0.004$), and 60 ($p= 0.025$), respectively, whereas the difference at Week 24 was not statistically significant ($p = 0.176$) (Table 10, Figure 2). The within group comparison (mean pain score, mean improvement) was significant at all time points in both study groups ($p < 0.001$) (Tables 9 and 10). Post hoc

Table 7: Daily *Tui-na* protocol used to relieve stifle pain in the TCVM Group study dogs [23]

***Tui-na* Technique**	**Application**	**Actions**
Moo-fa (massaging)	Stifle and hip area for 3 minutes	Introduction and relaxation, calming effect
An-fa (pressing) *Rou-fa* (rotary-kneading)	Hip to stifle 12 times clockwise and 12 times counter-clockwise.	*An-fa* - invigorates the Blood and *Qi* and unblocks obstructions. *Rou-fa* - unblocks the *Qi* and Blood Stagnation, and relieves pain
An-fa (pressing) *Tui-fa* (pushing)	GB-34, GB-32, ST-36, ST-35a, ST-35b, and ST-34 12-20 times	*An-fa* - invigorates the Blood and *Qi* and unblocks obstructions. *Tui-fa* - relaxes the tendons, resolves local Stagnation, excites the muscles, and invigorates Blood
Yi-zhi-chan (single thumb) and *Rou-fa* (rotary-kneading)	BL-40, SP-9, SP-10, GB-33, and LIV-3 5-10 minutes	Regulates the *Zang-fu* organs, promotes the flow of *Qi*, and smooths the tendons
Na-fa (pressing and pulling)	Stifle area 6-12 times	Expels Wind and Cold, relaxes the tendons, invigorates the Channels
Ca-fa (rubbing)	At the rear paws for 2 minutes and pulling each digit once daily	Warms Channels, unblocks the collaterals, tonifies *Zang-fu* organs

Table 8: Study dogs which had reinjury to the affected stifle in both the TCVM Group and CMT Group during the study

TCVM Group

Patient	**Number of reinjuries during study**
Dog 1	1
Dog 3	2
Dog 4	1
Dog 6	3
Dog 11	1
Dog 15	1
Dog 18	1

CMT Group

Patient	**Number of reinjuries during study**
Dog 1	1
Dog 3	2
Dog 7	2
Dog 8	1
Dog 10	1
Dog 14	1

Table 9: Pain severity score statistics (mean / median ±SD) at each assessment time with between-group and within-group comparisons

	CMT (mean/median ± SD)	**TCVM (mean/median ± SD)**	***p*-value (between groups)**
Day 0	7.33 / 7.13 ± 1.11	6.65 / 6.75 ± 1.66	0.196
Day 14	5.93 / 6.13 ± 1.41	4.85 / 4.88 ± 1.76	0.046*
Day 30	4.10 / 4.25 ± 1.45	2.71 / 2.63 ± 1.48	0.005**
Day 60	2.71 / 3.00 ± 1.15	1.40 / 1.13 ± 1.26	0.002**
Week 24	1.93 / 2.00 ± 1.03	0.75 / 0.88 ± 0.82	0.0003**
p-value (within group)	< 0.001^	< 0.001^	

^= The *p*-value of repeated measure ANOVA test within each group among all assessment times is $< 2x10^{-16}$ (*p*-values smaller than the precision of R software); *statistically significant $p < 0.05$; ** statistically significant $p < 0.01$

Table 10: Pain severity score improvement statistics (mean / median ± SD) at each assessment time with between-group and within-group comparisons

	CMT (mean/median ± SD)	TCVM (mean/median ± SD)	*p*-value (between groups)
Day 14	1.40 / 1.38 ± 0.42	1.80 / 1.89 ± 0.58	0.018*
Day 30	3.23 / 3.25 ± 0.61	3.94 / 3.88 ± 0.76	0.004**
Day 60	4.61 / 4.75 ± 0.71	5.25 / 5.25 ± 1.04	0.025*
Week 24	5.40 / 5.25 ± 0.65	5.90 / 6.00 ± 1.31	0.176
p-value (within group)	< 0.001^	< 0.001^	

^= The *p*-value of repeated measure ANOVA test within each group among all assessment times is < $2x10^{-16.}$(*p*-values smaller than the precision of R software). *statistically significant $p < 0.05$; ** statistically significant $p < 0.01$

Table 11: Pain interference score statistics (mean / median ± SD) at each assessment time in each treatment group

	CMT (mean/median ± SD)	TCVM (mean/median ± SD)	*p*-value (between groups)
Day 0	7.38 / 7.58 ± 1.64	6.59 / 6.50 ± 1.71	0.159
Day 14	5.71 / 5.75 ± 1.65	5.10 / 4.75 ± 1.64	0.203
Day 30	3.86 / 3.83 ± 1.74	3.35 / 2.92 ± 1.61	0.323
Day 60	2.55 / 2.50 ± 1.85	1.80 / 1.42 ± 1.56	0.207
Week 24	1.51 / 1.25 ± 1.36	0.73 / 0.25 ± 0.85	0.048*
p-value (within group)	< 0.001^	< 0.001^	

^= The *p*-value of repeated measure ANOVA test within each group among all assessment times is < $2x10^{-16.}$ (*p*-values smaller than the precision of R software); *statistically significant $p < 0.05$; ** statistically significant $p < 0.01$

Table 12: Pain interference score improvement statistics (mean / median ± SD) at each assessment time in each treatment group

	CMT (mean/median ±SD)	TCVM (mean/median ± SD)	*p*-value (between groups)
Day 14	1.67 / 1.59 ± 0.61	1.49 / 1.25 ± 0.82	0.193
Day 30	3.52 / 3.25 ± 1.26	3.24 / 3.50 ± 0.93	0.606
Day 60	4.83 / 4.67 ± 1.49	4.79 / 4.59 ± 1.04	0.952
Week 24	5.88 / 5.84 ± 1.41	5.86 / 6.37 ± 1.28	0.753
p-value (within group)	< 0.001^	< 0.001^	

^= The *p*-value of repeated measure ANOVA test within each group among all assessment times is < $2x10^{-16.}$ (*p*-values smaller than the precision of R software)

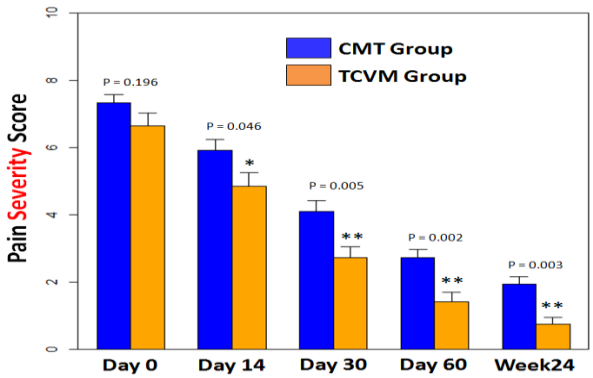

Figure 1: Mean pain severity score at each assessment time in CMT and TCVM groups; * $p < 0.05$ and ** $p < 0.01$ when compared to CMT group

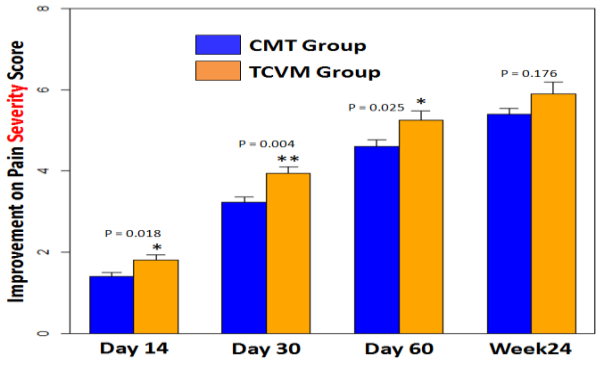

Figure 2: Mean improvement on pain severity score at each post-treatment assessment time in CMT and TCVM groups; * $p < 0.05$ and ** $p < 0.01$ when compared to CMT group

pairwise multiple comparisons (Tukey) indicated that differences were statistically significant ($p < 0.05$) for all pairs of assessment times.

Similar data analyses were conducted on the activity interference score. The statistical comparison between the two groups revealed that the interference score before treatment (Day 0) was not significantly different between the two treatment groups ($p = 0.159$). The mean activity interference score had a statistically significant decrease from baseline (Day 0) through Week 24 in both the CMT and TCVM groups ($p<0.001$). Comparison between groups at study time points demonstrated a statistically significant decrease at Week 24 (study completion) for the TCVM Group when compared to the CMT Group ($p = 0.048$) (Table 11, Figure 3). The mean improvement of activity interference score (within group) had a statistically significant increase from baseline (Day 0) through Week 24 in both the CMT and TCVM groups ($p<0.001$), however, comparison between groups did not demonstrate a statistically significant difference at study time points (Table 12, Figure 4).

DISCUSSION

Cranial cruciate ligament injury is a multifactorial disease and a common cause of hind limb lameness in dogs. Treatment is variable and ranges from surgery to conservative management. In this study, a total of 40 dogs were divided into 2 equal groups with no statistically significant difference between age, sex, breed, body weight or level of pain to compare the efficacy of traditional Chinese veterinary medicine treatment of CCL injury to conservative management. Study results demonstrated that both treatments resulted in statistically significant reduction of pain and activity level interference scores ($p<0.001$) by study termination (Week 24), however, TCVM treatment resulted in more rapid pain relief with statistically significant greater pain reduction scores at all study time points after the Day 0 baseline.

There are a number of studies in the literature reporting successful pain reduction, as in this study, with acupuncture.[11,25,26] At present there have been over 16,080 publications and 2,605 scientific studies regarding acupuncture. The results in human clinical trials have been mirrored by canine studies demonstrating successful use of electro-acupuncture for the reduction of pain in neurological and musculoskeletal conditions.[25] As an example, a recent study on non-surgical treatment for senior dogs with CCLR disease using acupuncture as part of the treatment protocol reported successful therapeutic outcome for dogs included in the study.[26] The reason for successful use of acupuncture for pain relief during rehabilitation of musculoskeletal injury is based on its ability to stimulate both the central and peripheral nervous systems. This is accompanied by release of endogenous substances such as: beta-endorphins, dynorphins, enkephalins, serotonin, epinephrine, GABA (gamma-aminobutyric acid), cortisol, and hormones with the beta-endorphin level elevation in the cerebrospinal fluid documented in 1980 by Clement-Jones.[27] Later Han concluded that, using electro-acupuncture at low-frequency (2Hz) stimulated secretion of beta-endorphins, enkephalins and endorphins, and at a higher-frequency (100Hz) released dynorphins.[28] Additional studies have demonstrated acupuncture stimulation led to the increase of serotonin concentration in blood or increased serotonin in the central nervous system.[29] A standard protocol for selecting acupoints for treatment of canine CCLR disease, although not established, has had some systems recommended in TCVM literature.[14-16]

The use of Chinese herbal medicine to treat CCL disease has documented successful outcomes in the literature. A novel veterinary specific formula[e] based on modification of *Huo Xue Yang Rong Tang*, in a case series study, reported a success rate of 91.7% for 181 dogs with CCLR.[30] Another clinical trial documented successful therapeutic outcome for 7 geriatric dogs with CCL disease using *Zheng Gu Xu Jin Fang* [f] formula.[26] The 3 herbal formulas used in this study are veterinary specific formulas derived from classical antecedents *Bu Gan Qiang Jin San*, *Shen Tong Zhu Yu Tang* and *Di Gu Pi San*, respectively. In horses, 3 months of oral administration of Tendon/ Ligament Formula (*Bu Gan Qiang Jin San*) in combination with a topical herbal formula[g] applied to the affected tendon resulted in complete tendon healing.[12] A case study describing a poodle with CCLR, reported a successful outcome after eight months of treatment.[19] In human medicine, Body Sore was used successfully to treat sciatica.[12] Other clinical studies with Body Sore (*Shen Tong Zhu Yu Tang*) in human medicine documented successful outcomes for musculoskeletal conditions, including arthritis.[12,21] Studies (both pharmaceutical and clinical) have documented herbal components of *Di Gu Pi* provide anti-inflammatory effects, treat chronic pain disorders, protect against osteoporotic bone loss and modulate bone metabolism.[12, 21]

Two retrospective studies (based on clinic examination) reported that conservative management for CCLR is 85.7% effective for dogs with body weight under 15 kg (36 month follow-up) and 19.3% for dogs over 15 kg (49.1 months).[8] A more recent study by Wuchere et al on overweight dogs with CCLR treated with CMT found disappointing rates of successful outcome after 24 and 52 weeks to be 33.3% and 63.6%, respectively.[11] A similar indication can be concluded from the present study with a treatment time of only 24 weeks. Only 2 out of 20 patients treated with CMT were less than 15 kg. It takes longer (over 24 weeks) for CMT to have a successful outcome for dogs with greater body weight.

Despite encouraging TCVM treatment outcomes for CCL-injured subjects in this study, there were study limitations. Treatment assignments in the present study were not fully randomized due to owners' preferences, which weakened study design. Owner assessment of their dog using the CBPI scoring introduced bias since the owners were the appraisers of improvement. The CBPI is more of an assessment of the impact of pain on daily

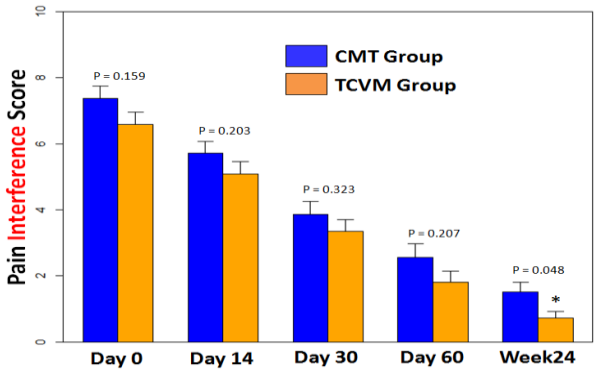

Figure 3: Mean pain interference score at each assessment time in CMT and TCVM groups;
* p <0.05 when compared to CMT group

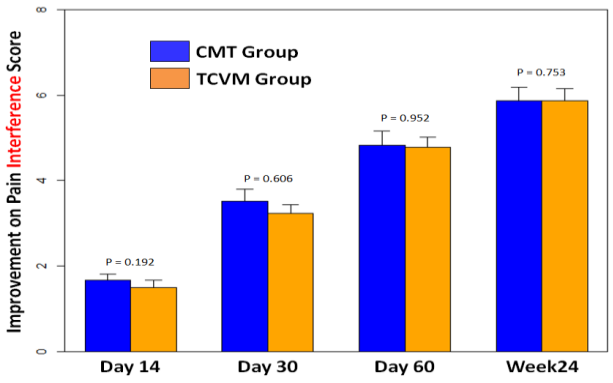

Figure 4: Mean improvement on pain interference score at each post-treatment assessment time in CMT and TCVM groups

living and less of an objective assessment of actual pain or gait analysis. This was particularly evident in the variability of the "interference with activities" scores from owners. This score involved subjective judgment of the "interference" on six daily activities: general activity, enjoyment of life, rising to standing, walking, running and climbing. The score was calculated as the average of pain interference including all six daily activities and most likely was less sensitive for subjects whose pain only interfered with 1 or 2 activities. Finally, both study groups had complicated treatment protocols which introduced variability and would be difficult to exactly emulate in other research studies.

Future studies could use the same lines of investigation as this study but with improvements on its limitations. A full random patient distribution and objective assessment measurements such as blinded evaluation of gait/pain (force plate technology, goniometric measurement) would be superior. If using the CPBI form, calculation of a maximal interference score might be more sensitive than the method used in the current study. An improved future study would also recruit a larger sample size which would allow enough dogs to compare different treatment responses between large and small dogs (>15 kg vs <15 kg) which has been demonstrated in other studies in the literature.[31] Finally other modifications to future studies to advance this area of clinical research could include: conducting the study for a longer period of time to allow more accurate investigation of treatment response for larger dogs which take more time to heal; providing additional time to dogs with bilateral injury to shift to a protocol that allows remaining on study; and investigate increased/decreased OA development depending on the experimental treatment.

In summary, study results demonstrated that both treatments resulted in statistically significant reduction of pain and activity level interference scores ($p<0.001$) by study termination with no adverse effects. By 24 weeks (end of study), most dogs were significantly improved with some dogs (9 TCVM, 2 CMT), registering rating scale scores of "0" (no pain). When comparing the 2 treatments, TCVM stood out as providing more rapid pain relief for study dogs with statistically significant greater pain reduction scores at all study time points after Day 0 baseline: Days 14, 30, 60, Week 24 (p=0.046, p=0.005, p=0.002, p=0.0003, respectively). These findings suggest that when surgery is not an option, both treatment approaches are effective with TCVM resulting in more rapid pain relief.

ACKNOWLEDGEMENTS

The author wishes to thank technical staff from Fairvale Animal Hospital for their assistance in present study, as well all clients and canines who participated in this research, and Dr. Shiau for his advice on data analysis.

Declaration of Interes

The author declares that there is no conflict of interest that could be perceived as prejudicing the impartiality of this paper.

Funding

The author did not receive any specific grant of funding from any organization in the public, commercial or non-profit sectors.

FOOTNOTES

a. JM -2A Jing Mei Electro-Acupuncture Stimulator, Wuxi Jiajian Medical Instrument, Inc., Wuxi, China
b. Tendon/Ligament Formula (concentrated 90g), Dr. Xie's Jing Tang Herbal, Reddick, FL, USA
c. Body Sore, (concentrated 90g); Dr. Xie's Jing Tang Herbal, Reddick, FL, USA
d. *Di Gu Pi* (200g powder), Dr. Xie's Jing Tang Herbal, Reddick, FL, USA
e. HipGuard, Natural Solutions, Speonk, NY, USA http://www.naturalsolutionsvet.com
f. *Zheng Gu Xu Jin Fang*, Golden Flower, Albuquerque, NM, USA http://www.gfcherbs.com

g. Relief Salve, Dr. Xie's Jing Tang Herbal, Reddick, FL, USA

h. Companion Therapy System (class IV Laser), Companion Therapy Laser Lite Cure LLC, Newark, DE, USA http://www.companiontherapylaser.com

REFERENCES

1. Bennett D, Tennant B. A reappraisal of anterior cruciate ligament disease in the dog. Journal of Small Animal Practice 1988; 29(5): 275.
2. Hegemann N, Wondimu A. Cytokine profile in canine immune-mediated polyarthritis and osteoarthritis. Vet Comp Orthop Traumatol 2005; 18(2): 67-72.
3. Foster W, Imhoff R, Cordell J. "Closed-joint" repair of anterior cruciate ligament rupture in the dog. JAVMA 1963; 143: 281-283.
4. Hayasi K, Frank D. Histologic Changes in Ruptured Canine Cranial Cruciate Ligament. Veterinary Surgery 2003; 32(3): 269-77.
5. Harasen G. Diagnosing rupture of the cranial cruciate ligament. Can Vet J 2002; 43(6): 457-476.
6. Budras K. Anatomy of the dog 5th Edition. Schlutersche 2010: 86-87.
7. Pond M, Campbell J.. The canine stifle joint I. Rupture of the ACL. J Small Anim Pract 1972; 13: 1-10.
8. Vasseur P. Clinical results following non-operative management for rupture of the CCL in dog. Veterinary Surgery 1984; 13:243-6.
9. Edge-Hughes L. Conservative Management of Cruciate Ligament Deficiency with Physical Therapy. Accessed 05/21/19. https://pdfs.semanticscholar.org/8443/f4b4b728d55ab79089ea86bbb61c0c216729.pdf
10. Edge-Hughes L. Updated Conservative Management of Cruciate Deficiency. Accessed 05/21/19. https://www.caninefitness.com/docs/CCL-D-Protocol-2017Update.pdf
11. Wuchere K, Conzemius M, Evans R et al. Short-term and long-term outcomes for overweight dogs with cranial cruciate ligament rupture treated surgically or nonsurgically. JAVMA 2013: 242(10): 1364-1372.
12. Ma A. Clinical Manual of Chinese Veterinary Herbal Medicine. Ancient Art Press 4th Edition 2016:80-82, 142-143.
13. Xie H, Preast V. Traditional Chinese Veterinary Medicine. Fundamental Principles 2nd Edition. Tianjin, China: Chi Institute Press 2013, 364.
14. Xie H, Preast V. Xie's Veterinary Acupuncture. Ames, Iowa: Blackwell Publishing 2007: 256.
15. Xie H, Wedemeyer L. Practical Guide to Traditional Chinese Veterinary Medicine, Emergencies and Five Element Syndromes. Reddick, FL: Chi Institute Press 2014: 61-63.
16. Xie H, Wedemeyer L. Practical Guide to Traditional Chinese Veterinary Medicine, Small Animal Practice. Reddick, FL: Chi Institute Press 2014: 32-33.
17. Ju Z. Electroacupuncture with different current intensity to treat knee osteoarthritis: A single-blinded controlled study. Int J Clin Exp Med 2015; 8(10): 18981-18989.
18. Zippelius K. The integrative TCM treatment of cruciate ligament injury. Journal of Chinese Medicine 2017; 114: 5-14.
19. Schaefer C. Acupuncture and herbal medicine treatment of cruciate tear in poodle. TCVM News 2009; 1(8): 7.
20. Beebe S. Chinese herbal medicine and prolotherapy for treatment of forelimb angular deformity in a juvenile bactrian camel. AJTCVM 2018; 13(1): 57-63.
21. Chen J, Chen T. Chinese Medical Herbology and Pharmacology. City of Industry, CA: Art of Medicine Press 2014: 348, 641,919,932-2.
22. Xie H. Food Therapy Introduction, Veterinary Food Therapy Training Program. Reddick, FL: Chi Institute 2017: 3.
23. Xie H, Ferguson B, Deng X. Application of *Tui-na* in Veterinary Medicine. Reddick, FL: Chi Institute Press 2nd Edition 2013:1-2, 126.
24. Brown C. The Canine Brief Pain Inventory. www.CanineBPI.com. Accessed 05/21/19, http://www.vet.upenn.edu/docs/default-source/VCIC/canine-bpi-user%27s-guide-2017-07
25. Hyashy A. Evaluation of electroacupuncture treatment for thoracolumbar intervertebral disk disease in dogs. JAVMA 2007; 231(6): 913-918.
26. Lee V. Non-surgical treatment for cranial cruciate ligament rupture in senior dogs: A retrospective case series. AJTCVM 2019; 14(1): 49-64.
27. Clement-Jones V. Increased β-endorphin but not met-enkepalin in human cerebrospinal fluid after acupuncture for recurrent pain. Lancet 1980; 2(8201):946-949.
28. Han Z, Han J. Endomorphin-1 mediates 2Hz but not 100Hz electroacupuncture analgesia in the rat. Neurosci Lett 1999; 274: 75-78.
29. Tsai H. Further evidence for possible analgesic mechanism of electroacupuncture: Effect on neuropeptides and serotoninergic neurons in rat spinal cord. Jpn J Pharmacol 1989; 49:181-185.
30. Wen J, Johnston K. Chinese herbal medicine for dogs with complete cranial cruciate ligament rupture: 181 cases. AJTCVM 2016; 11(1): 41-48.
31. Comerford E, Foster K. Management of cranial cruciate ligament rupture in small dogs: A questionnaire study. Vet Comp Orthop Traumatol, Schattauer 2013; 26(6): 493-497.
32. Xie H. Chinese Veterinary Handbook. Reddick, FL: Jing Tang Publishing 2011: 80, 136,187.