

The Challenge of Evaluating Pain and a Pre-incisional Local Anesthetic Block

Background: Our objective was to test the effectiveness of a local anesthetic line block administered before surgery in reducing postoperative pain scores in dogs undergoing ovariohysterectomy (OVHX). Methods: This study is a prospective, randomized, blinded, clinical trial involving 59 healthy female dogs. An algometric pressure-measuring device was used to determine nociceptive threshold, and compared to three subjective pain scales. Group L/B received a line block of lidocaine (4 mg/kg) and bupivacaine (1 mg/kg) subcutaneously in the area of the incision site and saline subcutaneously as premedication; group L/BM (positive control) received a similar block and morphine (0.5 mg/kg) subcutaneously for premedication; and group SS (negative control) received a saline line block and saline premedication. Criteria for rescue analgesia were defined before the study. Dogs were assessed prior to surgery, at extubation (time 0) and at 2, 4, 6, 8 and 24 hours post-recovery. The data were analyzed with one-way ANOVA, and a Split Plot Repeated Measures ANOVA with one grouping factor and one repeat factor (time). $P < 0.05$ was considered statistically significant. Results: Approximately 33% of dogs required rescue analgesia at some point during the study, with no significant difference between groups. There was no significant difference between treatment groups with any assessment method. Conclusions: As there were no statistically significant differences between positive and negative controls, the outcome of this technique cannot be proven.

1 Challenges in evaluation of pain and a pre-incisional line block

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14 Abstract

15 Background: Our objective was to test the effectiveness of a local anesthetic line block
16 administered before surgery in reducing postoperative pain scores in dogs undergoing
17 ovariohysterectomy (OVHX). This study was a prospective, randomized, blinded, clinical trial
18 involving 59 healthy female dogs. An algometric pressure-measuring device was used to
19 determine nociceptive threshold, and compared to three subjective pain scales. Group L/B
20 received a line block of lidocaine (4 mg/kg) and bupivacaine (1 mg/kg) subcutaneously in the
21 area of the proposed incision and saline subcutaneously as premedication; group L/BM (positive
22 control) received a similar block and morphine (0.5 mg/kg) subcutaneously for premedication;
23 and group SS (negative control) received a saline line block and saline premedication. Criteria for
24 rescue analgesia were defined before the study. Dogs were assessed prior to surgery, at extubation
25 (time 0) and at 2, 4, 6, 8 and 24 hours post-recovery. The data were analyzed with one-way
26 ANOVA, and a repeated measures ANOVA with one grouping factor and one repeat factor (time).
27 $P < 0.05$ was considered statistically significant.

28 Results: Pain was so subtle that there were no significant differences between treatment groups
29 with any assessment method, and no significant difference between positive and negative
30 controls.

31 Conclusions: Pain in non-verbal responders is subtle, even in animals with a known stimulus that
32 results in pain. Pre-emptive, intraoperative and post-operative analgesia is necessary regardless of
33 pain score within the first 24 hours. None of the pain scales evaluated were sensitive enough to
34 determine pain in all animals in this study.

35 Key words: Dog, lidocaine, bupivacaine, local anesthetic, pain assessment

36 Introduction

37 As any verbal responder who has experienced pain may attest to, pain decreases quality of
38 life (1). Therefore, pain management in patients experiencing pain is crucial for improving
39 quality of life. Pain management of non-verbal patients is uniquely challenging because the
40 ability to effectively diagnose and treat pain becomes very subjective. Pain assessment in non-
41 verbal species has been investigated along three principal lines: a) objective measures of
42 physiologic responses to experimental pain, b) subjective or semi-objective assessment of
43 behavior postoperatively, and c) quantitative measures of postoperative behavior and physiology.
44 While studies using objective physiological data (i.e. variables such as heart rate, respiratory rate
45 and blood pressure) are easy to perform and analyze statistically, there is minimal evidence that
46 these measures are reliable indicators of pain (2, 3). Most peer-reviewed research studies in
47 veterinary medicine use subjective or semi-objective assessments of postoperative pain or
48 sensitivity of an anatomical site to assess outcomes.

49 Algometers are devices used to quantitate pressure required to elicit a response from a
50 subject; this is termed “nociceptive threshold”. Algometers provide a (partially) objective
51 measurement of incisional sensitivity. The “threshold” reading is numeric and objective, but the
52 factor determining the threshold (behavioral response) is subjective. Various mechanical
53 threshold devices are validated to assess somatosensory processing changes (4).

54 Multimodal analgesia is the combination of analgesic drugs with different methods of
55 action, with the goal of reducing or preventing nociceptive stimulation at multiple receptors and
56 pathways. In humans, multimodal analgesia has been shown to decrease post-operative morbidity
57 and mortality, improve quality of life and patient satisfaction, and decrease the associated costs to
58 hospitals and insurance companies (5). In addition to the general agreement of a clinical benefit
59 to this approach (6), there are also an increasing number of research studies in non-verbal species
60 supporting multimodal analgesia (7-9). One simple way to include multimodal analgesia is the

61 incorporation of a local anesthetic to desensitize a specific region, in combination with systemic
62 analgesic administration.

63 This study was designed to assess the effect of pre-incisional administration of a
64 combination of local anesthetics on post-operative pain, measured by subjective and objective
65 pain scores after canine ovariohysterectomy (OVHX). We hypothesized that pre-incisional
66 infiltration of the incision area with local anesthetic agents (group L/B) would result in similar
67 post-surgical pain levels compared to animals receiving local anesthetic and an opioid (group
68 L/BM), and decreased post-surgical pain compared to animals not receiving any pre-operative
69 analgesics (group SS).

70 **Materials and methods**

71 This study examined 59 healthy intact female dogs admitted to a local animal shelter
72 (Sacramento Society for Prevention of Cruelty to Animals [SPCA], Sacramento, CA, USA),
73 ranging in age from six months to eight years old with weights ranging from 3.4–35.5 kg. A
74 physical examination was performed, and temperature, heart rate, and respiratory rate were
75 recorded prior to sedation for anesthesia and surgery. Each dog had a packed cell volume (PCV),
76 total protein (TP), and blood urea nitrogen (Azostick, Bayer Corporation, Elkhart, IN, USA)
77 checked prior to surgery. Please see Table 1 for a summary of baseline data. No dogs with
78 abnormal physiologic parameters, abnormal blood tests, evidence of a previous OVHX, or
79 requiring extension of the incision beyond the blocked area were used in this study. All protocols
80 were approved by the University of California, Davis, Institutional Animal Care and Use
81 Committee, as well as by administrative study reviewers at the Sacramento Society for
82 Prevention of Cruelty to Animals (SSPCA).

83 **Anesthesia**

84 Dogs were allocated into one of three groups using a computer generated randomized
85 block design. All three groups were sedated with acepromazine (Acepromazine maleate, Vedro,

86 St. Joseph, MO, USA) (0.03 mg/kg, subcutaneously [SC]) administered prior to catheter
87 placement. An 18-22-gauge (depending on the animal's weight) over the needle IV catheter was
88 placed in a cephalic vein for drug and fluid administration. Anesthesia was induced with propofol
89 (Diprivan, AstraZeneca LP, Wilmington, DE, USA) to effect and maintained with isoflurane
90 (Isoflurane, Abbot Laboratories, North Chicago, IL, USA) in oxygen to effect. Lactated Ringer's
91 solution was administered at 10 mL/kg/hour until recovery. Heart rate, respiratory rate, and
92 systolic blood pressure were monitored throughout the procedure.

93 Dogs in group L/B received a line block prior to surgery in the incision area, consisting of 4
94 mg/kg lidocaine (Lidocaine, Hospira Inc., Lake Forest, IL, USA) and 1.0 mg/kg bupivacaine
95 (Bupivacaine, Hospira Inc., Lake Forest, IL, USA). These dogs also received 0.05 mg/kg of
96 saline SC at the same time as acepromazine administration. Group L/B were test subject dogs, to
97 compare to positive and negative control groups. Dogs in the group L/BM received a line block
98 prior to surgery, using 4.0 mg/kg lidocaine and 1.0 mg/kg bupivacaine. These dogs also received
99 0.5 mg/kg of morphine (Morphine sulfate, Baxter Health Care Corporation, Deerfield, IL, USA)
100 SC at the same time as acepromazine administration. Group L/BM was the positive control group
101 (i.e. dogs anticipated to have minimal pain). Group SS was the negative control group (i.e. dog
102 anticipated to have pain). Dogs in group SS received 0.275 mL/kg of normal saline prior to
103 surgery in the incisional area. These dogs also received 0.05 mg/kg of saline SC at the same time
104 as acepromazine administration. Because we anticipated animals with pain, criteria for rescue
105 analgesia were defined prior to the study's commencement and strictly adhered to. The line block
106 or saline (depending on the group) was administered after induction of anesthesia and initial
107 surgical preparation of the field, approximately five minutes prior to surgical incision.

108 Line block procedure

109 Appendix 1 shows the line block in schematic form. Local anesthetic or saline (depending
110 on the group) was infused with a 2.5 inch, 22-gauge spinal needle in three separate lines to form

111 an inverted double “L” administration site. One third of the volume of drug or saline was
112 administered at each site, as volume allowed. The level of the first line (Appendix 1, “1”) was
113 roughly halfway between the umbilicus and the first set of nipples below the umbilicus;
114 placement was guided by consultation with the surgeon prior to incision to ensure coverage of the
115 area to be incised (Appendix 1, “A”). The width of this first line ran mediolaterally for
116 approximately 1.25 cm on either side of midline. The second line (Appendix 1, “2”) began at the
117 left-most lateral point of the first line, and ran craniocaudally for the length of the spinal needle
118 on the left side of midline. The third line (Appendix 1, “3”) paralleled the second on the right side
119 of the umbilicus. In Appendix 1, “B” denotes the pubis. These blocks were administered in the
120 subcutaneous and fascial planes. Aspiration prior to administration of the block was performed to
121 ensure the drugs were not given intravenously.

122 Surgical procedure

123 The hair was clipped from the xiphoid process to the pubis and three cm laterally to the
124 nipple on both sides of the abdomen. The skin was scrubbed with chlorhexidine and rinsed with
125 water three times. The line block was applied after initial preparation; additional preparation
126 followed until the area was aseptically prepared. An incision was made extending below the
127 umbilicus to one-third the distance from the umbilicus to the pubis. An OVHX was performed in
128 a standard fashion (10) by one of three experienced, shelter veterinary surgeons. The skin was
129 closed in a routine manner.

130 Assessment

131 Four pain scoring assessments were used; initial values for each were recorded prior to
132 the sedation of the animal for anesthesia and surgery (time negative one). Assessments were then
133 made at zero (time of extubation), two, four, six, eight, and 24 hours postoperatively by one
134 veterinarian (CMM) who was blinded to which treatment group each animal was in. Caretakers

135 made additional assessments during the day when animals were handled, to ensure any animal
136 that needed additional analgesia would receive it.

137 The first pain scoring assessment was a visual analog scale (VAS) score. This assessment
138 was made prior to any manipulation or handling of the animal. A mark on a ten centimeter (cm)
139 line corresponded to the assessor's visual assessment of the animal's pain, ranging from zero ("no
140 pain") to ten cm ("the most pain an animal could possibly be in"), measured in mm using a
141 standard ruler at each scoring assessment, and recorded after each measurement was taken.

142 The next two pain scoring assessments were done sequentially. One of these pain scales
143 was based on a previously validated scoring system, the Glasgow Composite Pain Scale (GCPS,
144 [http://www.gla.ac.uk/faculties/vet/smallanimalhospital/ourservices/painmanagementandacupunct](http://www.gla.ac.uk/faculties/vet/smallanimalhospital/ourservices/painmanagementandacupuncture)
145 [ure](http://www.gla.ac.uk/faculties/vet/smallanimalhospital/ourservices/painmanagementandacupuncture), subheading: Short form pain questionnaire). The primary variables included vocalization
146 (quiet, crying, groaning, screaming), attention to painful area (ignoring, looking, licking, rubbing,
147 or chewing), mobility (normal, lame, slow or reluctant, stiff, or refusal to move), response to
148 touch (none, looking around, flinch, growl, snap, or cry), demeanor (happy and content, bouncy,
149 quiet, non-responsive or indifferent to surroundings, nervous or anxious or fearful, or depressed
150 or non-responsive to stimulation), and posture (comfortable, unsettled, restless, hunched or tense,
151 or rigid). Additional assessment was made using the University of Melbourne Pain Scale (UMPS)
152 (11). The primary variables included physiologic data (dilated pupils, percentage increase in heart
153 rate, percentage increase in respiratory rate, rectal temperature, salivation), response to palpation
154 (no change, guards/reacts when touched, guards/reacts before touched), activity (at rest [sleeping
155 or semiconscious, awake], eating, restless [pacing, getting up and down], or rolling/thrashing),
156 mental status (submissive, overtly friendly, wary, or aggressive), posture (guarding or protecting
157 affected area, recumbency, standing or sitting with head up, standing with head down, moving, or
158 abnormal body posture [prayer/hunched]), and vocalization (none, vocalizing when touched,
159 intermittent vocalization, or continuous vocalization).

160 The final assessment method used a digital von Frey apparatus (IITC 2390 Series
161 Electronic Von Frey Anesthesiometer, Woodland Hills, CA, USA) (12). The tip of the von Frey
162 apparatus was placed one cm adjacent to the center of the incision. It was pressed with a slow,
163 continuous pressure until a response was noted, with a maximal force of 1000 g. A response was
164 considered an acknowledgement that the stimulus was noxious; this included behaviors such as
165 withdrawing from the stimulus, a cry, active head turn to the stimulus, attempt to bite, etc. This
166 measurement was repeated three times at five-minute intervals, and each value was recorded as
167 force in grams. The average value of these three readings was used in the data analysis. At each
168 time point, algometer measurements were also taken from the lateral thoracic wall in the same
169 manner. These measurements, as well as pre-sedation measurements, acted as controls for
170 analysis.

171 Rescue analgesia protocol

172 All animals were assessed by the observing veterinarian (CMM), and rescue analgesia
173 (0.5 mg/kg morphine IM) was administered to any animal that achieved a maximum score in any
174 one category of the GCPS, any animal with a pain score of 8 or greater on the GCPS or who did
175 not improve over time as compared to pre-sedation GCPS score, any animal developing
176 aggression, or a combination of these previous factors. Animal handlers at the SPCA also had the
177 opportunity to declare an animal as being in pain, based on their observation, and these animals
178 also received rescue analgesia. Administration of rescue analgesia and the reason for
179 administration was recorded, and these animals were included in assessments; see “Blinding,
180 exclusion criteria and statistical analysis”. Any animal receiving rescue analgesia was reassessed
181 30 minutes later to ensure efficacy of the rescue analgesia administration.

182 Blinding, exclusion criteria, and statistical analysis

183 The evaluator (CMM) was blinded to which dog was in which group (i.e. L/B, L/BM or
184 SS) as well as to whether a placebo or a study drug was contained in a particular group. The

185 statistician who performed the data analysis remained blinded to which study drug was contained
186 in each group until the analyses were completed.

187 Initial power calculations were performed prior to commencing the study. An alpha error
188 level was set at 5%. Standard deviation was set at 1.8 Glasgow Composite Pain Scale units (13).
189 A beta error level was set at 20%. These calculations indicated the need for approximately 19
190 dogs in each group to find significant differences in our study populations, assuming a difference
191 of 2.6 on the Glasgow Composite Pain Scale as being significant (13). The groups were analyzed
192 for differences in age, weight, preoperative temperature, heart rate, respiratory rate, BUN,
193 PCV/TS, propofol dose [mg/kg], and time negative one algometric values, by means of one-way
194 ANOVA. Normality of the errors was assessed by visual inspection of a histogram of the errors
195 and a normal probability plot. Errors were considered normal if the histogram was unimodal and
196 approximately symmetrical (14), and the normal probability plot was an upwardly sloping,
197 approximately straight line. Homogeneity of variance was tested by means of a studentized
198 residual vs. means plot. The response variable of treatment groups was analyzed by means of a
199 repeated measures ANOVA with one grouping factor and one repeat factor (time). Those dogs
200 receiving rescue analgesia were analyzed in a similar fashion in two separate analyses: within
201 their collective treatment group and as a separate subgroup. $P < 0.05$ was considered statistically
202 significant.

203 **Results**

204 There were 20, 19 and 20 dogs in Groups L/B, L/BM, and SS, respectively, for a total of
205 59 dogs. Twenty of the 59 dogs initially enrolled, required rescue analgesia (seven, three and ten
206 dogs in groups L/B, L/BM, and SS, respectively, with no significant differences in the proportion
207 requiring rescue analgesia between groups). Of all the predetermined rescue analgesia criteria,
208 the only criteria triggering administration of rescue analgesia were animals that achieved a
209 maximum score in any one category (mobility: refusal to move) of the GCPS and animals

210 developing aggression. The majority of the dogs requiring rescue analgesia required it at time 0
211 (extubation; 18 of 20 dogs) for refusal to move. All fifty-nine dogs were included in the analysis;
212 additional analysis of the separate subgroup of dogs who received rescue analgesia showed
213 similar results to the analysis of all 59 dogs, but the low numbers of dogs remaining in the groups
214 after removal of those requiring rescue analgesia brought into question the validity and precision
215 of the statistical analyses (therefore, data not shown).

216 VAS, GCPS, and UMPS analyses showed no significant difference in pain scores between
217 treatment groups, and there was a significant effect of time (i.e. a decrease in pain scores over
218 time; Figures 1, 2, and 3). Algometric values were compared to one of two controls. Regardless
219 of whether the value obtained at the wound was compared to the thoracic measurement obtained
220 at the same time or compared to the pre-incisional control reading (i.e. measurement at abdomen /
221 control measure), there was no significant difference in values obtained between treatment
222 groups, and there was a significant effect of time (i.e. a decrease in pain scores over time; Figures
223 4 and 5).

224 **Discussion**

225 We chose three different groups to test the efficacy of our line block to improve
226 postoperative pain scores and algometric values. One group of animals (L/BM) was selected to
227 receive morphine premedication to serve as the positive control group (i.e. the group anticipated
228 to have the best analgesia). The group of animals that did not receive analgesia (SS) served as
229 the negative control (i.e. the group anticipated as having pain). The treatment group of interest,
230 L/B, was evaluated in comparison to these positive and negative controls. The most profound
231 result of our study was the lack of statistically significant differences between our positive and
232 negative control at any given time point; that is, there was no statistically significant difference
233 between an animal that received no pre-emptive analgesia and an animal receiving a full mu
234 opioid receptor agonist to provide analgesia, using any of the assessment methods. This result

235 was surprising, not only from the perspective of rendering the effects of treatment only
236 speculative, but also in the implications this possesses for investigators researching pain in non-
237 verbal species.

238 There are a number of potential reasons for the results obtained. Study design is critical
239 to successfully identifying targeted outcome. One potential reason no significant difference
240 between pain scores for any treatment group was evident was the number of dogs included in the
241 study, thus limiting statistical power of our study. Our initial sample size calculations potentially
242 hindered the study in two ways. Firstly, we applied sample size calculations meant for two groups
243 to three groups. In retrospect, in order to correctly calculate our initial sample size, we would
244 modify alpha ($P=0.05$), with three groups and the number of potential comparisons (3), and
245 therefore use an alpha value of 0.017 ($0.05/3$); this was not done. Secondly, our initial sample
246 size calculations used a difference in the GCPS of 2.6, based on previous work (13). This was
247 regarded as the minimum difference that would be clinically relevant. |The differences in pain
248 scores in our study were smaller than this (Figure 2) and while increasing the number of animals
249 treated may possibly have reached statistical significance it would still have had little relevance
250 for the clinician. Additionally, because we cannot account for Type II error, our statistical analysis
251 is not conclusive.

252 The other aspect of study design was the intent to maximize the potential for successful
253 pain identification, and thus the inclusion of one group that did not receive any preemptive
254 analgesic medication (negative control). This decision was not made lightly, and the criteria were
255 very strict for the use of rescue analgesia because of this. Even in light of this group that
256 intentionally included, albeit aggressively managed for, pain, there was still no significant
257 difference between the negative and positive control groups.

258 It may be that the dogs in this study were experiencing little discomfort, making it
259 difficult to distinguish between the treatment groups. While this may seem unreasonable in

260 regards to an intra-abdominal procedure, pain scores on the only validated scoring system
261 (GCPS) were very low, never achieving a score of greater than five out of a maximal value of 24
262 at any one time point. A study evaluating intervention levels using the GCPS suggested
263 intervening if a score of greater than seven out of 24 was obtained; the GCPSs values obtained in
264 the present study were below this threshold (15). With such low pain scores, it was difficult to
265 establish differences between the treatment groups. The low pain scores may have been due to the
266 highly experienced veterinarians who were performing the OVHX creating minimal tissue trauma
267 during surgery (and thus minimal pain associated with the surgery). In this study, the three
268 surgeons were shelter veterinarians who performed up to 40 surgeries on any given day with over
269 30 years of combined experience between them; surgery time ranged from 11 to 47 minutes, with
270 an average surgery time of 21 minutes. This is considerably less than the average time of 140
271 minutes for a veterinary student to spay a dog (16). If a group of less experienced surgeons—for
272 example, veterinary student surgeons—performed the procedures, more detectable differences
273 may have arisen. There is extensive debate about this subject, further complicated by a lack of
274 reporting surgeon experience level in well-performed pain studies. At least one study specifically
275 examining surgeon experience level suggested experience level of the surgeon was not correlated
276 with a change in postoperative pain score (17). However, recent basic science evidence
277 underscores the importance of deep tissue trauma to the experience of pain (18). Basic science
278 work also supports this on a receptor level: surgical tissue injuries enhanced the membrane
279 translocation of receptors important in post-operative hypersensitivity (19, 20). Surgery
280 performed by experienced surgeons, as was the case in this study, may reduce post-operative pain
281 (21, 22) to levels below the sensitivity of current pain assessment scales.

282 Another reason for low pain scores on various scales may be due to inherent insensitivity
283 of the measurement techniques, preventing a significant difference between positive and negative
284 controls. Surprisingly little work has been performed to produce validated assessment systems for

285 acute pain, with the Glasgow Composite Pain Scale standing out as the most validated scale in
286 this regard (13). However, this scoring system was validated using a variety of surgical
287 procedures, including orthopedic procedures. Additionally, the GCPS has not undergone criterion
288 validation testing. It is possible that a dog undergoing OVHX by an experienced veterinarian may
289 have signs of pain more subtle than this assessment instrument can detect. The von Frey
290 apparatus was sensitive to changes in threshold testing with dogs given 1 mg/kg morphine (12),
291 and appears reliable in clinically normal dogs (4). However, data gathered by one of the authors
292 (BDXL) found no difference in von Frey thresholds when it was used to assess wounds being
293 infused with saline or with local anesthetic (23). This suggests that the von Frey may not be the
294 appropriate instrument for assessing sensitivity of clinical wounds. Testing site could make a
295 difference in the reliability of the algometer, as previous reports suggest that the canine carpal
296 pad may be the most satisfactory site for testing (12, 24). Because this location was considered
297 unusual for testing sensitivity of an abdominal wound, it was not used for either the control or the
298 test site, which may contribute to the difficulty of using the algometer for assessment. This topic
299 needs further research to understand why the results appear counterintuitive, and to understand
300 appropriate means to assess wound sensitivity.

301 There is no doubt that expertise of the assessor in regards to pain assessment plays a
302 major role, as evidenced by a single experienced anesthesiologist finding a statistically significant
303 improvement after an incisional block with bupivacaine in dogs undergoing a celiotomy (25). As
304 involved as veterinarians are in the care of animals on a daily basis, it is still possible to
305 misclassify an animal as not in pain for many reasons — including temperament, breed, type of
306 surgery, and surgeon experience. In a study comparing staff observations versus a self-report of
307 pain in young children, staff observations of pain were generally lower than the self-reports (26).
308 However, for animals there is little alternative to an observer for pain assessment. The negative
309 aspects of such a misclassification are obvious. The inclusion of multiple pain assessment tools

310 with very defined criteria was intended to counter potential inexperience, but cannot negate the
311 possibility altogether. Although the differences in the three reduced-size groups that received
312 rescue analgesia failed to reach statistical significance, the difference between the L/BM group
313 and the SS group (16% vs. 50% treated), if real, is clinically important and suggests that the
314 clinical judgment of when to administer rescue analgesia includes factors that are not captured in
315 the scoring systems that were used. We elected to give rescue analgesia to any patient with a
316 maximum value in any one GCPS category (27-29), as a means to favor generous administration
317 of rescue analgesia for any patient who might need it. Our decision to give rescue analgesia to
318 patients with a maximum value in any one GCPS category may have biased our results, as 18 of
319 20 dogs received rescue analgesia for a maximum value in the category of refusing to move post-
320 surgery. However, given the large number of patients in group SS that received rescue analgesia
321 (almost half of the animals in that group), it is possible that refusal to move may be a sensitive
322 indicator of patient discomfort in the patient with pain secondary to an OVHX.

323 The effect of time present (i.e. a decrease in pain scores over time) in this study suggests
324 that we do see changes in pain scale scores and von Frey readings over the course of a 24-hour
325 period. Using subjective pain scores, all values returned to baseline or near baseline by 24 hours,
326 suggesting that we could no longer detect pain effectively at that point. When assessing
327 algometric scores, there was an initial decrease from baseline after extubation, and while values
328 tended to move back towards baseline between eight and 24 hours, the values never returned to
329 baseline. This suggests wound sensitivity may still be present when subjective assessments do not
330 detect pain. An alternative explanation is that the dogs had become behaviorally sensitized to the
331 testing device. Ideally, testing of dogs that were not operated on would have been performed to
332 evaluate the effect of time on threshold readings. Data (30) suggest there is a learned response
333 that decreases thresholds over time in normal dogs, but the data were generated using a more
334 blunt device than the von Frey used in the present study.

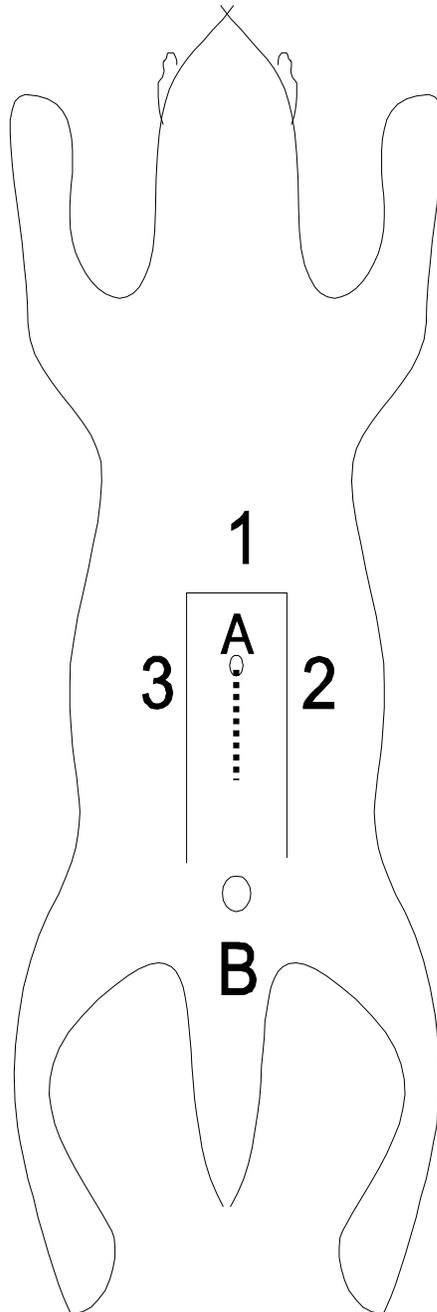
335 No adverse events were documented in this study to suggest that a local anesthetic
336 infiltrative block is harmful to a patient, as opposed to another study examining incisional line
337 block (31). Fitzpatrick et al. (2010) may have seen greater complications because they choose to
338 infiltrate the site of the incision, where as we infiltrated the tissue surrounding the incision. The
339 block took a short time (<2 minutes) to perform. Other studies have found that incisional blocks
340 provide effective analgesia (25, 32).

341 **Conclusions**

342 We believe we cannot make firm conclusions about whether or not this line block is
343 effective due to the lack of statistically significant differences between positive and negative
344 controls. Indeed, the ability to assess pain in non-verbal species even with multiple assessment
345 tools is called into question with the results of this study, necessitating a humble and
346 compassionate approach to pain management in all non-verbal species.

347 The veterinary medical profession must work towards developing more sensitive and
348 specific assessments of pain to evaluate the effectiveness of postulated analgesic interventions,
349 while continuing to provide conscientious therapy knowing such strategies have not yet been
350 developed. If an experienced observer cannot detect a patient with known pain from one that
351 received adequate analgesia using four different techniques, it is relatively easy to miss a patient
352 experiencing pain that cannot self-communicate. If one is inducing something that is likely to
353 result in pain, aggressive pain management is warranted as a moral and ethical obligation.

354 Appendix 1: Site for line block/infiltration of local anesthetic or saline. Please see text for
355 description of labels.



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Figure 1

Figure 1

Visual Analogue Scale (VAS), from 0-10 centimeters, prior to premedication (time -1), extubation (time 0), and 2, 4, 6, 8 and 24 hours post-operatively. Note: L/B received saline premedication and local anesthetic line block, L/BM received morphine premedication and a local anesthetic line block, and SS received a saline premedication and saline line block. Error bars represent standard deviation.

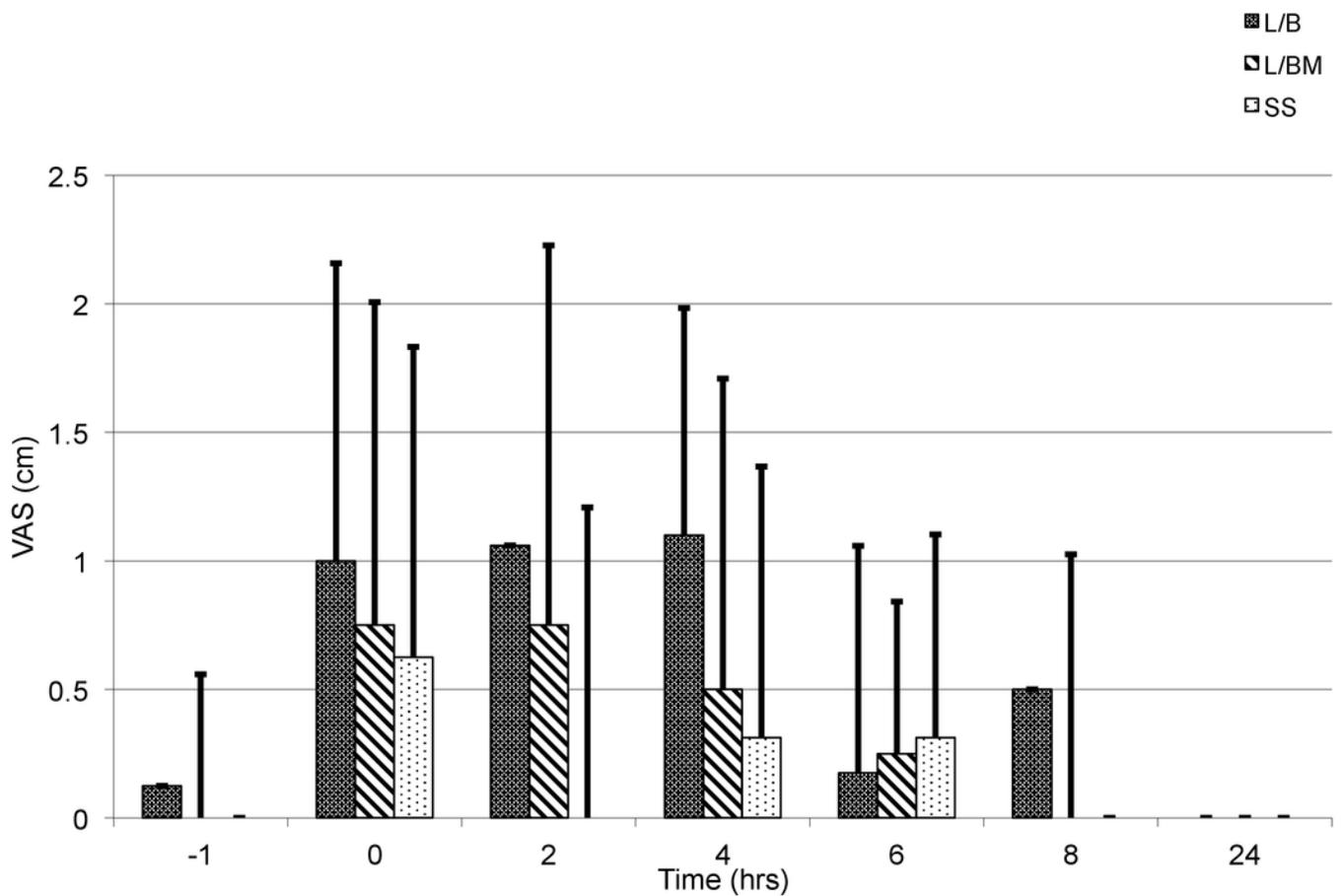


Figure 2

Figure 2

Glasgow composite pain scale (GCPS) scores from 0 to 24 prior to premedication (time -1), at extubation (time 0), and 2, 4, 6, 8 and 24 hours post-operatively. Note: L/B received saline premedication and local anesthetic line block, L/BM received morphine premedication and a local anesthetic line block, and SS received a saline premedication and saline line block. Error bars represent standard deviation.

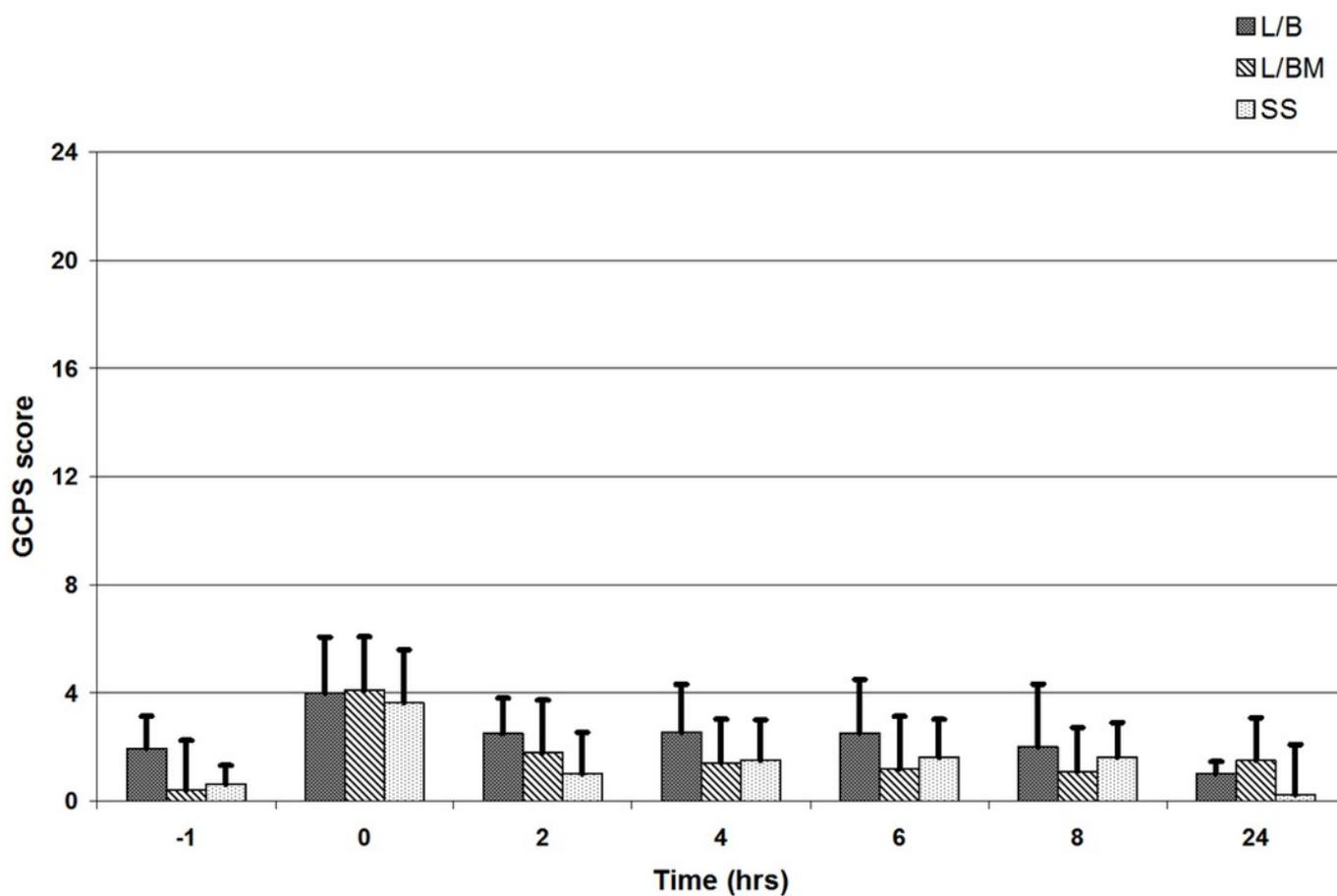


Figure 3

Figure 3

University of Melbourne Pain Scale scores from 0 to 27 prior to premedication (time -1), at extubation (time 0), and 2, 4, 6, 8 and 24 hours post-operatively. Note: L/B received saline premedication and local anesthetic line block, L/BM received morphine premedication and a local anesthetic line block, and SS received a saline premedication and saline line block. Error bars represent standard deviation.

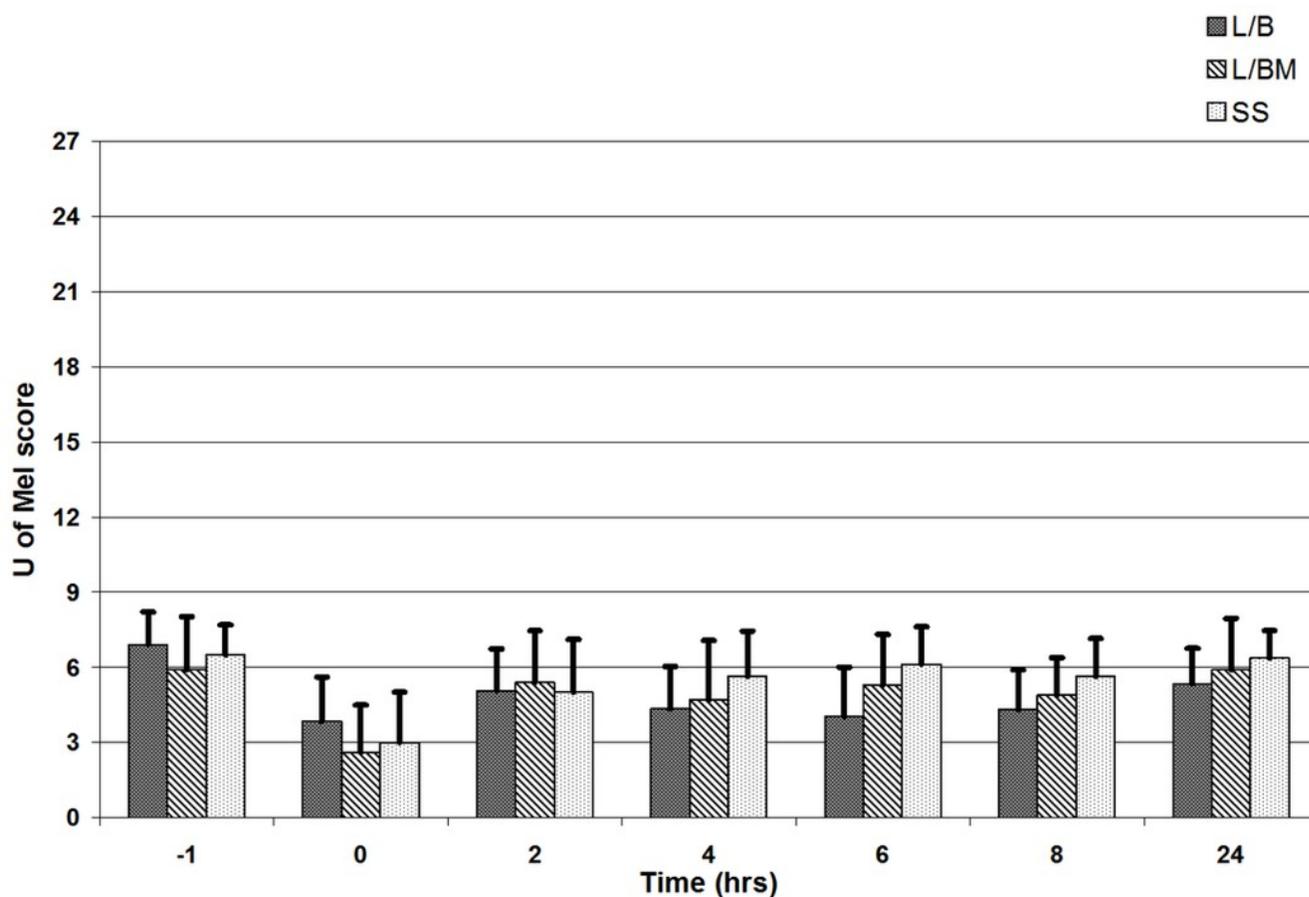


Figure 4

Figure 4

Algometric value, depicted as a ratio compared to the value obtained at the abdomen versus the value obtained at the thorax at the same time points: at premedication (time -1), at extubation (time 0), and at 2, 4, 6, 8 and 24 hours post-operatively. Note: L/B received saline premedication and local anesthetic line block, L/BM received morphine premedication and a local anesthetic line block, and SS received a saline premedication and saline line block. Also note that a ratio of one indicates the animal tolerates the same level of pressure on the abdomen as the thorax. A decreasing ratio indicates the animal tolerates less pressure on the abdomen as compared to the thorax.

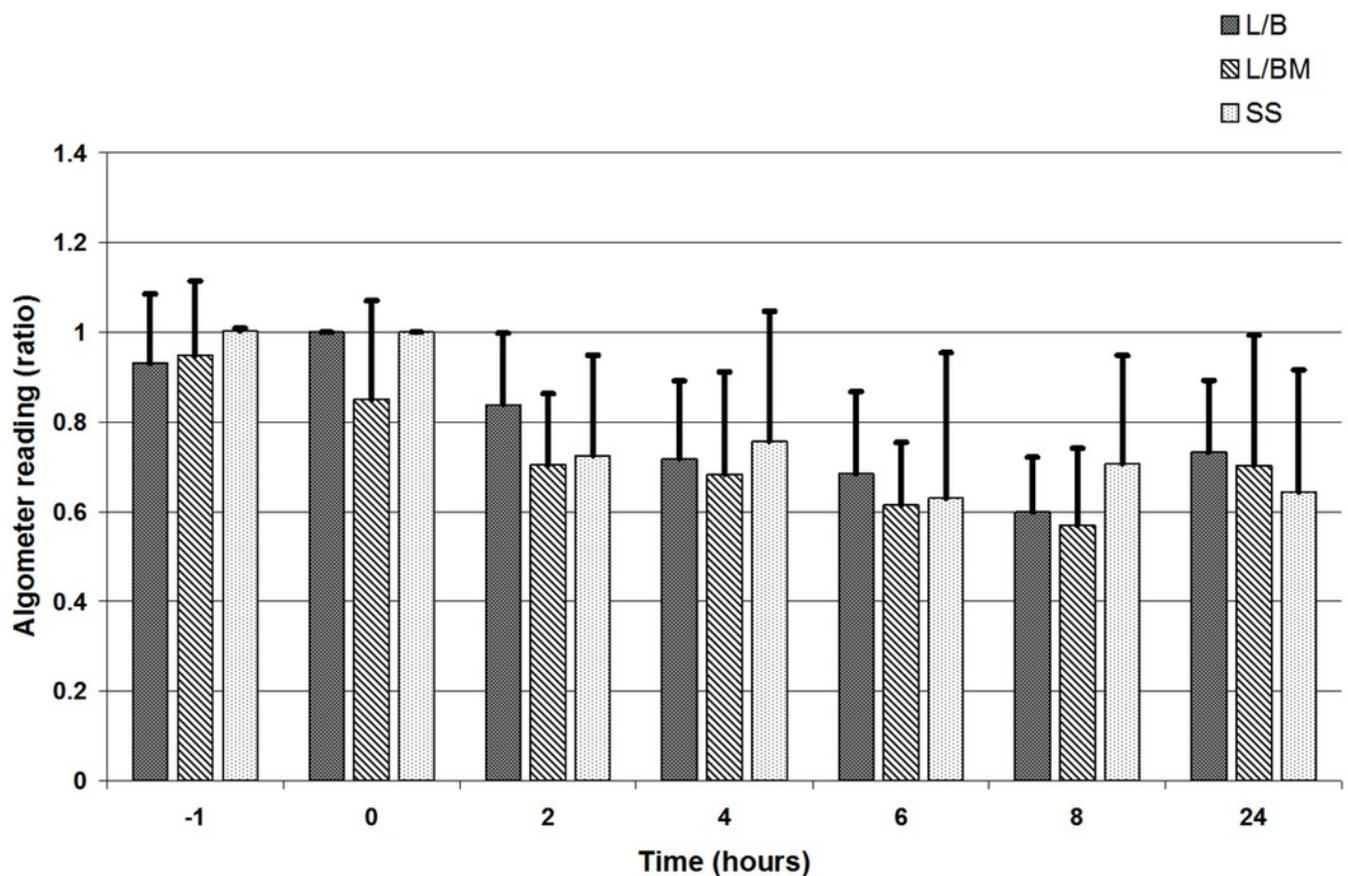


Figure 5

Figure 5

Algomeric value, depicted as a ratio comparing the value obtained at each individual time point to values obtained at the abdomen prior to premedication (i.e. time, but not location, is the dependent variable). Time points for comparison to pre-medication values include pre-medication (time -1), extubation (time 0), and 2, 4, 6, 8 and 24 hours post-operatively. Error bars represent standard deviation. Error bars represent standard deviation. Note: L/B received saline premedication and local anesthetic line block, L/BM received morphine premedication and a local anesthetic line block, and SS received a saline premedication and saline line block. Also note that a ratio of one indicates the animal tolerates the same level of pressure on the abdomen at the time of comparison as it tolerated prior to incision. A decreasing ratio indicates the animal tolerates less pressure on the abdomen at the time of comparison as compared to pressure applied prior to the incision.

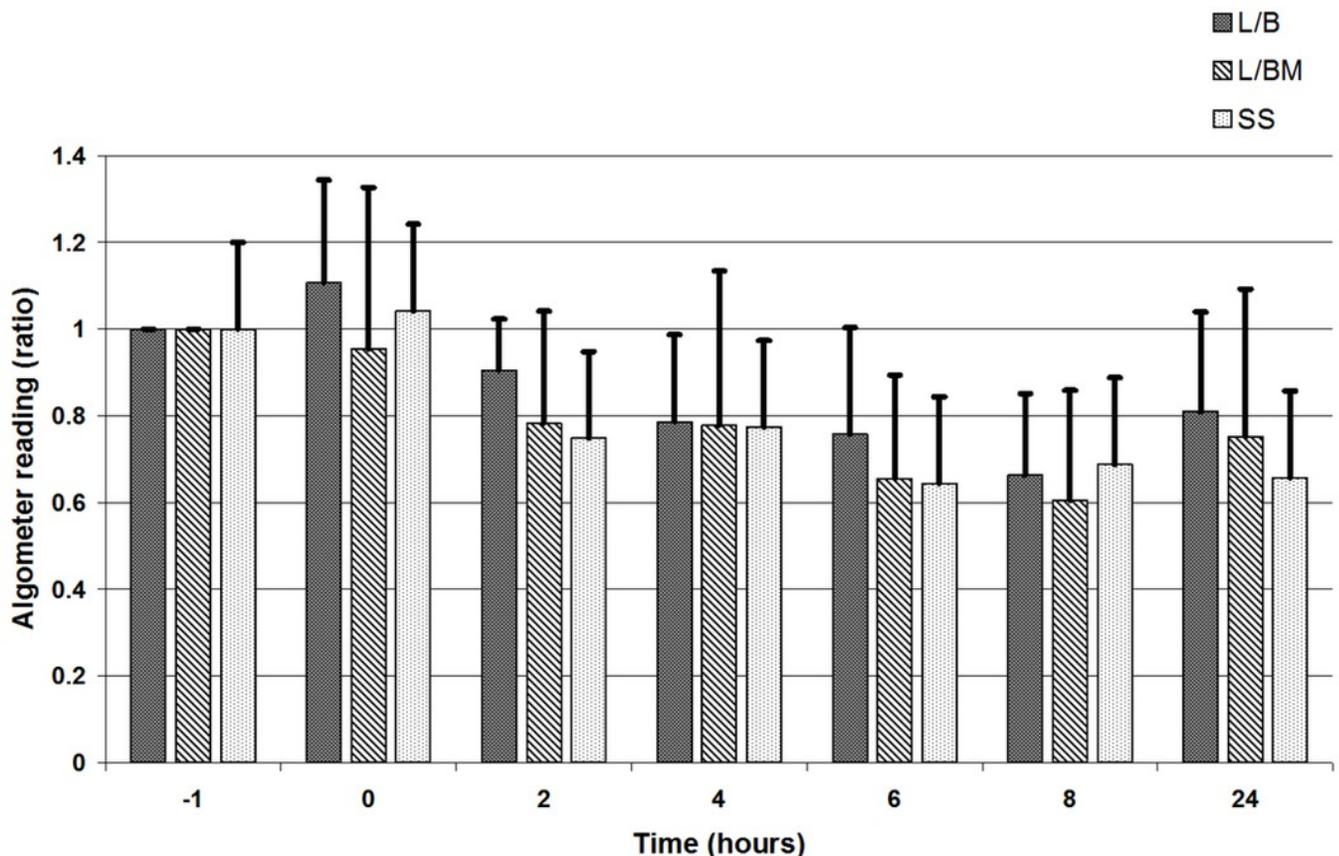


Table 1 (on next page)

Table 1

Baseline data for Groups L/B, L/BM, and SS. Data is presented as average (\pm SD), except for BUN, where average value only is listed. Respiratory rate was not included because a large number of animals were panting.

Group	L/B	L/BM	SS
Number of dogs	20	19	20
Age (years)	1.6±1.7	1.6±1.4	2.3±2.0
Weight (kg)	17±6.8	16.5±1.4	18.2±9.6
Temperature (F)	101.2±1.0	101.1±0.9	101.1±1.0
Heart rate (BPM)	140±22	138±26	138±22
PCV (%)	43±4.0	42±4	42±4
Total protein (g/dL)	6.8±0.6	6.8±0.7	6.5±0.6
BUN (Azostick)	5-15	5-15	5-15
Propofol (mg/kg)	4.6±1.1	4.3±1.6	3.6±1.6