1 Abdominal pain assessment in rabbits: using the CANCRS to 2 recognize pain and testing its internal validity over time

3 Penelope Banchi¹, Giuseppe Quaranta¹, Alessandro Ricci², Mitzy Mauthe von Degerfeld^{1*}

4 ¹ C.A.N.C. (Centro Animali Non Convenzionali), Dipartimento di Scienze Veterinarie, Università
5 degli Studi di Torino, Grugliasco, Turin, Italy,

6 ² Dipartimento di Scienze Veterinarie, Università degli Studi di Torino, Grugliasco, Turin, Italy

7 *Corresponding author

8 Email: mitzy.mauthe@unito.it (MMvD)

9

10

11 Abstract

12 A composite scale for pain assessment in rabbits has been previously designed and tested
 13 (CANCERS). The present study describes the refinement of the scale and the evaluation of its ability
 14 to detect pain variations over time. Furthermore, a comparison between the CANCRS and the
 15 Visual Analogue Scale (VAS) has been performed, to underline the differences between an
 16 objective (CANCERS) and a subjective (VAS) assessment of abdominal pain. In the first part of the
 17 study, 86 rabbits (n=47 healthy patients and n=39 patients with gastrointestinal stasis syndrome)
 18 underwent pain assessments with the VAS and the CANCRS. Thirty-two patients with
 19 gastrointestinal stasis syndrome participated to the second part of the study. These patients
 20 underwent four pain assessments with the CANCRS. The first assessment took place before
 21 meloxicam administration and the others after 30, 60 and 90 minutes. The CANCRS showed
 22 differences between healthy and diseased rabbits ($P = 0.0001$), median scores were 5 (IQR 4 - 6)
 23 and 9 (IQR 7 - 11) respectively. The VAS showed differences between healthy and diseased rabbits
 24 ($P = 0.02$), the median scores were 4 (IQR 2 - 5.35) and 5.3 (IQR 2.65 - 6.45) respectively. The cut-
 25 off scores for the CANCRS and for the VAS for differentiation between healthy and diseased
 26 patients were 7 (Sp 89%, Se 79%) and 4.4 (Sp 59%, Se 69%) respectively. Sensitivity and
 27 specificity for each parameter of the CANCRS were calculated, in order to obtain weighting factors.
 28 Accordingly, the evaluation of respiratory pattern and vocalizations should be excluded from the
 29 CANCRS, since their performances in pain evaluation are poor. Internal validity of the CANCRS
 30 was tested assessing pain before and after the analgesic treatment and the results showed
 31 significance at each time point. The CANCRS showed better performances than the VAS and its
 32 responsiveness to pain variations has been verified.

33

34 Introduction

As rabbit popularity as companion animal increases, veterinarians' confidence in revealing rabbit pain has improved in the last decade (1). However, most of veterinarians (64%) declare to be just "Fairly confident" and 29% declare to be "Not very confident" in revealing rabbit pain (2). A survey by Benato et al. (2020) showed how the majority of respondents relies on behavioral changes when assessing pain. On the contrary, changes in physiological parameters are considered less reliable as they can be altered in any stressful situation (3). Behavioral and physiological parameters can be included in composite pain scales (4-7), in order to point out the multidimensional aspect of pain. It has been previously showed that composite pain scales are more reliable than simple one-dimensional pain scales like the Visual Analogue Scale (VAS) (8). The VAS is a subjective tool (9) and the rater is asked to make an estimate of the pain of the patient placing a mark on a 10 cm-line. The VAS is an effective tool in human medicine (10), when a self-assessment is performed, whereas its use in veterinary medicine comes with limitations, since the assessment is performed on another individual belonging to another species. Therefore, one-dimensional scales are considered suboptimal tools for pain evaluation in veterinary medicine (11). Nevertheless, they are sometimes used in domestic animals (8, 12), but their performances have never been previously evaluated in rabbits. Testing a subjective tool like the VAS could be useful to point out the advantages and the limitations of a subjective assessment of pain. Finding a tool with high validity, reliability and feasibility is a key point in the pain management of the rabbit, in order to support the veterinarian in clinical decisions concerning analgesia and in order to monitor the patient during the hospitalization. In our previous study (4) a composite pain scale for the assessment of pain in pet rabbits was developed and its construct validity and reliability were assessed. However, internal validity should be assessed, and a refinement of the scale should be performed in order to have a useful tool (13).

One of the most common presentations for rabbits is gastrointestinal stasis (RGIS) (14, 15). It is a syndrome characterized by decreased appetite or anorexia, decreased or absent fecal output, abdominal discomfort and lethargy (15, 16). It has a multifactorial etiology (17) and it can result

61 from dental diseases, dietary changes, stressful events, environmental changes, dysbiosis, pain,
 62 infection, neoplasia, drug effect (anesthetic agents, anticholinergics, opioids, and antibiotics),
 63 obstruction. The reduced food intake leads to retarded colonic transit, dehydration of the *digesta*
 64 and impairment of the enteric microflora. If the patient is left untreated, this process can lead to
 65 obstruction and accumulation of gas within the gastrointestinal tract, leading to severe
 66 consequences, such as dyspnea and hypovolemic shock (15).

67 Managing pain during gastrointestinal stasis syndrome is essential to promote food intake in rabbits.
 68 However, analgesia can have risks associated with the chosen drug. The use of opioids is
 69 discouraged due to their effects on gastrointestinal motility, that is furtherly reduced (3, 18). Non-
 70 steroidal anti-inflammatory drugs (NSAIDs), such as meloxicam, show adverse effects in dogs and
 71 cats and should be cautiously administered in rabbits because patients presenting with
 72 gastrointestinal stasis syndrome are likely to have or to develop gastric ulcerations (15, 17). A
 73 dosage of 1 mg/kg is considered safe for rabbits when administered orally with no clinical,
 74 biochemical or postmortem abnormalities reported (19). When a gastrointestinal syndrome is
 75 ongoing, oral therapy is discouraged in some cases (i.e. obstruction, altered mentation), and all the
 76 drugs should be administered parenterally (15).

77 Being gastrointestinal stasis is a common syndrome causing abdominal pain in domestic rabbits
 78 (16), patients presenting with the syndrome were the chosen subject of the present study.

79 Furthermore, the majority of the respondents to the survey of Benato et al. (2020) declares to make
 80 subjective assessments for pain in rabbits. This led to the decision of testing the VAS, which is a
 81 tool that allows a subjective assessment of pain, with numerical results. Specifically, the objectives
 82 were:

- 83 (I) To define cut-off scores for the CANCRS and the VAS between healthy animals and
- 84 rabbits experiencing pain and to estimate their sensibility and specificity in pain
- 85 detection.

- (II) To evaluate each parameter included in the CANCRS for its sensibility and specificity in detecting pain, for future refinement of the scale by attributing a lower weight to parameters that lacks in specificity or sensibility.
- (III) To assess the responsiveness of the CANCRS to changes in pain levels associate with the administration of the analgesic drug (meloxicam 1 mg/kg SQ q24) by evaluating the internal validity of the CANCRS.

Materials and methods

Eighty-six rabbits admitted to the C.A.N.C. (the exotics and wild animals Veterinary Teaching Hospital of the Veterinary Science DPT. Of University of Torino) were enrolled in the study, between January and August 2020. No restrictions were placed on breed, sex, age or weight of the rabbits. Thirty-nine patients were admitted due to gastrointestinal stasis syndrome (RGIS), whereas 47 patients were admitted for checkups or vaccination and were deemed as healthy according to the clinical examination (HEALTHY).

The owners of 7 of the 39 patients belonging to the RGIS group refused hospitalization. Therefore, only 32 rabbits of the RGIS group were included in the second part of the study. Furthermore, rabbits requiring nasogastric tube were excluded from the study because of its interference with the use of facial expression for pain evaluation.

The first part of the study took place at admission: all the rabbits underwent a pain assessment with both the CANCRS and the VAS. Regardless of the attending clinician, the same veterinarian performed all the assessments using the VAS and the CANCRS at the end of the clinical examination. The VAS score was recorded prior to the assessment of the patients with the CANCRS, in order to avoid bias deriving from clinical data collection.

Pain assessments for the first part of the study always happened in the clinical examination room. The patients were taken out from the carrier and positioned on a table for clinical examination and pain assessment.

The second part of the study included thirty-two of the patients included in the RGIS group. These patients underwent four pain evaluation with the CANCRS during the hospitalization. A pain assessment was performed just before the administration of the anti-inflammatory drug (meloxicam 1 mg/kg SQ q24). Afterwards, three assessment were performed 30 (T30), 60 (T60), and 90 (T90) minutes after the administration of the anti-inflammatory drug. Pain assessments for the second part of the study always happened in the hospitalization room. The patients were taken out from the cage and positioned on a table for clinical examination and pain assessment. Environmental conditions, including light, noise, and temperature were stable through the process.

Pain assessment tools

The VAS consisted of a 10-cm line representing no pain at the left end and severe pain at the right end. The rater placed a mark on the line that corresponded to the degree of pain for the patient (20, 21).

As for what concern the CANCRS, the scores were given as stated in our previous study (4) and the scale is presented in *Table 1*. It includes five facial action units (orbital tightening, cheek flattening, nostril shape, whisker position, and ear position) and each one was scored according to whether it was not present (score 0), moderately present (score 1) and obviously present (score 2).

Furthermore, it includes some clinical parameters. Pupillary dilation was scored as 1 if present or scored as 0 if not present. For heart rate, increases lower than 20% of the physiological value (250 bpm)(16) were given the score of 0, increases higher than 20% were given the score of 1, and increases higher than 50% were given the score of 2. Heart rate was measured with a stethoscope for 15 seconds and the result was multiplied by four, in order to obtain beats per minute.

The average respiratory rate varies from 30 to 60 bpm (16); for rates of 60 bpm or less a score 0 was given, for rates between 61 and 72 a score 1 was given, for rates between 73 and 90 a score of 2 was given, and for rates higher than 90 bpm a score of 3 was given.

Respiratory pattern was considered as eupneic (score 0) or dyspneic (score 1).

140 Since the palpation of the suspected painful area is a parameter included in the CANCRS,
 141 abdominal palpation was delicately performed and the reaction of the patient was classified as no
 142 reaction (score 0), reaction during the palpation (score 1) and reaction before the palpation (score
 143 2).
 144 Absence of vocalization was scored as 0, vocalization when touched was scored as 1, intermittent
 145 vocalization without any contact with the operator was scored as 2, whereas continuous
 146 vocalization was scored as 3.
 147 Finally, the mental status was classified as ‘normal’ (score 0), ‘depression’ (score 1) and
 148 ‘obtundation’ (score 2).
 149
 150 In accordance with the Dipartimento di Scienze Veterinarie of Università degli Studi di Torino
 151 policy, this research does not require the approval of the ethical committee, for our assessment tool
 152 does not interfere with the clinical development of the included cases and rabbits were manipulated
 153 for routine diagnostic purposes only. Proper informed consent was collected from the owner prior to
 154 each clinical examination.
 155

Table 1. Score sheet for the CANCRS (Centro Animali Non Convenzionali Rabbit Scale).

Orbital tightening	Not present	0
	Moderately present	1
	Obviously present	2
Cheek flattening	Not present	0
	Moderately present	1
	Obviously present	2
Nostril shape	Not present	0
	Moderately present	1
	Obviously present	2
Whisker position	Not present	0
	Moderately present	1
	Obviously present	2
Ear position	Not present	0
	Moderately present	1
	Obviously present	2
Pupil dilation	Not present	0
	Present	1
Heart rate	Increases $\leq 20\%$ of the physiological value (250 bpm)	0

156		Increases between 20% and 50% of the physiological value (250 bpm)	1
		Increases >50% of the physiological value (250 bpm)	2
157	Respiratory rate	≤60 bpm	0
		61-72 bpm	1
158		73-90	2
		>90	3
159	Respiratory pattern	Eupneic	0
		Dyspneic	1
160	Palpation of the painful area	No reaction	0
		Reaction during the palpation	1
161		Reaction before the palpation	2
162	Vocalization	Absent	0
		When touched	1
		Intermittent vocalization without any contact	2
163		Continuous vocalization without any contact	3
	Mental status	Normal	0
164		Depression	1
		Obtundation	2
165	Total .../24		

166 Statistical analysis

167 Differences in scores between healthy animals and rabbits with RGIS were analyzed using the
168 Mann–Whitney *U* test. Cut-off values for CANCRS and VAS were determined to obtain maximal
169 differentiation between HEALTHY and RGIS. The same cut-off values were used to determine
170 internal sensitivity, specificity, and positive and negative predictive values for both CANCRS and
171 VAS. Sensitivity and specificity for individual parameters of the CANCRS were also determined.
172 Based on these values, weighting factors for future adjustments of the scale, were determined
173 retrospectively. When sensitivity or specificity was ≤25%, a weighting factor of 0 was applied;
174 between 25% and 50% the weighting factor was 1; between 50% and 75% the weighting factor was
175 2; and when both sensitivity and specificity were ≥75% a weighting factor of 3 was applied. The
176 effect of the analgesic drug over time for the CANCRS in RGIS patients was assessed by means of
177 the repeated measures ANOVA followed by Bonferroni's post hoc test.

178 Statistical analysis was performed using R 3.2.2. Statistical significance was accepted for $P \leq 0.05$.

179

180 Results

181 Differences between healthy patients and rabbits with RGIS

182 The CANCRS showed extremely significant differences between HEALTHY and RGIS rabbits ($P =$
183 0.0001), the median score was 5 for HEALTHY rabbits (IQR 4 to 6) and 9 for RGIS rabbits (IQR 7
184 to 11).

185 The VAS showed statistically significant differences between HEALTHY and RGIS rabbits ($P =$
186 0.02), the median score was 4 (IQR 2 to 5.35) and 5.3 for RGIS rabbits (IQR 2.65 to 6.45).

187 Cut-off values between healthy patients and rabbits with RGIS

188 The cut-off value for the CANCRS for differentiation between HEALTHY and RGIS rabbits was 7.
189 Sensitivity and specificity were 89% and 79% respectively. The AUC was 0.88 (CI 0.80-0.97).
190 Positive predictive value was 86% and negative predictive value was 84% with accuracy of 85%.
191 The cut-off value for the VAS for differentiation between HEALTHY and RGIS rabbits was 4.4.
192 Sensitivity and specificity were 69% and 59% respectively, as represented in *Figure 1*. The AUC
193 was 0.64 (CI 0.52-0.76). Positive predictive value was 49% and negative predictive value was 61%
194 with accuracy of 53.5%.
195 Cut-off values for individual parameters of the CANCRS for differentiation between HEALTHY
196 and RGIS rabbits are resumed in *Table 2*.

197 Internal validity of the CANCRS

198 Patients experienced a strongly significant reduction in pain at each time point following
199 meloxicam administration ($P \leq 0.001$ between T0-T30, T0-T60, T0-T90, T30-T60, T30-T90, T60-
200 T90). Means ($\pm$ DS) of the CANCRS scores for each time point are resumed in *Table 3* and the
201 variation of pain scores over time is presented in *Figure 2*.

Table 2. Sensitivity, specificity, area under the curve (AUC) with confidence intervals (CI), cut-off values and weighting factors for individual parameters of the CANCRS.

Parameters	HEALTHY - RGIS		Cut-off values	AUC	CI	Weighting factor ^a
	Sensitivity	Specificity				

Orbital tightening	66%	85%	1	0.77	0.68-0.86	2
Cheek flattening	56%	80%	1	0.7	0.60-0.80	2
Nostril shape	82%	66%	1	0.77	0.68-0.86	2
Whisker position	77%	76%	1	0.79	0.7-0.87	2
Ear position	51%	57%	1	0.53	0.41-0.64	2
Pupil dilation	77%	68%	1	0.72	0.63-0.82	2
Heart rate	64%	70%	2	0.66	0.55-0.77	2
Respiratory rate	100%	61%	2	0.76	0.66-0.86	2
Respiratory pattern	21%	98%	1	0.59	0.52-0.66	0
Palpation of the painful area	28%	91%	1	0.6	0.51-0.68	1
Vocalization	7%	100%	1	0.49	0.49-0.58	0
Mental status	53%	91%	1	0.73	0.64-0.82	2

^aSensitivity or specificity is $\leq 25\%$, weighting factor = 0; 25-50%, weighting factor = 1; 50-75%, weighting factor = 2; sensitivity and specificity are $\geq 75\%$, weighting factor = 3.

Table 3 – Means and standard deviations of the CANCRS scores at each time point. Assessments were performed just before the meloxicam administration (T0) and 30 (T30), 60 (T60), 90 (T90), and 120 (T120) minutes after the administration.

	Mean	DS
T0	9.37	1.71
T30	8.43	1.99
T60	7.12	2.07
T90	5.18	1.82

Fig 1. Receiving operating characteristic (ROC) curve assessing the cut-off point for the CANCRS and the VAS to evaluate the presence of abdominal pain in rabbits.

The cut-off score for differentiation between healthy rabbits and patients with gastrointestinal stasis syndrome is 7 (sensitivity 89%, specificity 79%). The cut-off score for differentiation between healthy rabbits and patients with gastrointestinal stasis syndrome is 4.4 (sensitivity 69%, specificity 59%).

Fig 2. Variation of CANCRS pain scores over time.

The mean scores ($\pm$ DS) of the scores of the CANCRS from T0 to T90 is represented in the figure. It can be observed that patients experienced a significant reduction in pain at each time point following meloxicam administration ($P < 0.05$ between T0-T30, T0-T60, T0-T90, T30-T60, T30-T90, T60-T90).

Discussion

The present study describes the use of the CANCRS and the use of the VAS to detect pain in rabbits with gastrointestinal stasis syndrome, the responsiveness of the CANCRS to analgesic treatment,

220 and it takes another step towards the refinement of the scale. Difference in pain levels between
 221 healthy rabbits and patients with abdominal pain can be detected with both tools. The CANCRS
 222 scale shows a cut-off score of 7 to differentiate between healthy animals and rabbits with abdominal
 223 pain with good sensitivity and specificity and it can detect pain variation over time according to
 224 analgesia administration. Even if pain variation over time were not investigated for the VAS, the
 225 scale showed very low sensibility and specificity in rabbits. No previous study concerning the VAS
 226 in rabbits had been performed previously, however the limitations of the VAS were previously
 227 discussed for other veterinary species (8, 12, 22-24). The VAS is a subjective, simple and poorly
 228 reliable tool and it is not aimed to consider the multidimensional aspect of pain (25), whereas
 229 composite pain scales are objective tools and are intended to capture the behavioral and
 230 physiological changes associated with pain. According to Benato et al. (2020), the majority of
 231 veterinary surgeons is fairly confident in recognizing pain in rabbits, although it is mostly a
 232 subjective evaluation. This led to the decision to test the VAS for pain detection and quantification
 233 in rabbits, for it allows a subjective assessment too. However, the confidence in revealing pain
 234 improves with objective pain scale use and experience (2, 25). Accordingly, being a subjective tool,
 235 the ability to use the VAS to detect pain could improve with experience. This aspect was not
 236 considered in the present study, since the same experienced clinician performed all the assessments.
 237 The reliability of the VAS and its responsiveness to pain level variations were not tested, because of
 238 the risk of bias associated with the serial assessment carried out by the same individual after the
 239 diagnosis, and this represent a limitation of the present study. On the other hand, the VAS scale is
 240 fast to use, and this is its main advantage compared to more complete pain scales, such as the
 241 composite ones. The average time for a pain assessment using the CANCRS is 3 minutes. In order
 242 to limit the number of the parameters included in the scale, sensitivity and specificity were
 243 determined for each parameter of the CANCRS and they were used to determine weighting factors.
 244 Weighting factors are useful in order to refine the scale by eliminating parameters with low
 245 sensibility or specificity for pain detection (8). This improves the overall sensitivity, specificity, and

246 positive and negative predictive values of the scale. Accordingly, parameters with weighting factors
 247 equal to 0 should be excluded, therefore the parameter ‘vocalization’ and the parameter ‘respiratory
 248 pattern’ should not be considered in the future when assessing rabbits for abdominal pain. However,
 249 their inclusion in the scale should be furtherly investigated for diseases other than gastrointestinal
 250 stasis syndrome. All the other parameters have weighting factors equal to 2, except for the
 251 parameter ‘palpation of the painful area’ (weighting factor = 1). However, no weighting factor
 252 resulted to be equal to 3, pointing out that none of the included parameters has both sensitivity and
 253 specificity $\geq 75\%$. This might be due to the fact that rabbits tend to mask any signs of pain and it is
 254 generally accepted that it is more challenging to assess pain in rabbits than in predatory species
 255 (such as cats and dogs) (18). According to Benato et al. (2020), veterinary surgeons state to
 256 recognize pain through changes in appetite and abnormal body posture. These parameters could
 257 certainly be investigated for future inclusion in a composite pain scale, possibly considering
 258 patients with conditions different from gastrointestinal stasis syndrome, which implies changes in
 259 appetite by definition.

260 The responsiveness of the CANCRS to meloxicam administration confirms the internal validity of
 261 the scale and makes the scale a valid tool for the monitoring of rabbit with gastrointestinal stasis
 262 syndrome. Furthermore, the scale could be used in the future for evaluating other analgesic drugs.
 263 However, it should be pointed out that studies concerning pharmacology of analgesic drugs in
 264 rabbits other than meloxicam are very limited in the literature (26).

265 In conclusion, the assessment of internal validity by testing and confirming its responsiveness to
 266 analgesia administration, the refinement of the scale by determining weighting factors for each
 267 parameter, the determination of a cut-off point for the recognition of pain in rabbits with
 268 gastrointestinal stasis syndrome, together with the previously established construct validity and
 269 reliability, make the CANCRS a useful tool for pain evaluation. Further studies should focus on the
 270 reliability of the VAS and on the responsiveness of the VAS to changes in pain level. A refined

271 version of the CANCRS could be useful to determine cut-off values for pain level detection for
272 conditions other than gastrointestinal stasis syndrome.

273

274 **References**

- 275 1. Keown AJ, Farnworth MJ, Adams NJ. Attitudes towards perception and management of
276 pain in rabbits and guinea pigs by a sample of veterinarians in New Zealand. N Z Vet J.
277 2011;59(6):305-10.
- 278 2. Benato L, Murrell JC, Blackwell EJ, Saunders R, Rooney N. Analgesia in pet rabbits: a
279 survey study on how pain is assessed and ameliorated by veterinary surgeons. Vet Rec.
280 2020;186(18):603.
- 281 3. Barter LS. Rabbit analgesia. Vet Clin North Am Exot Anim Pract. 2011;14(1):93-104.
- 282 4. Banchi P, Quaranta G, Ricci A, Mauthe von Degerfeld M. Reliability and construct validity
283 of a composite pain scale for rabbit (CANCRS) in a clinical environment. PLoS One.
284 2020;15(4):e0221377.
- 285 5. Shipley H, Guedes A, Graham L, Goudie-DeAngelis E, Wendt-Hornickle E. Preliminary
286 appraisal of the reliability and validity of the Colorado State University Feline Acute Pain Scale. J
287 Feline Med Surg. 2019;21(4):335-9.
- 288 6. Reid J, Scott EM, Calvo G, Nolan AM. Definitive Glasgow acute pain scale for cats:
289 validation and intervention level. Vet Rec. 2017;180(18):449.
- 290 7. Reid J HJ, Lascelles D, Pawson P, Scott EM. Development of the short-form Glasgow
291 Composite Measure Pain Scale (CMPS-SF) and derivation of an analgesic intervention score.
292 Animal Welfare. 2007(16):97-104.
- 293 8. van Loon JP, Van Dierendonck MC. Monitoring acute equine visceral pain with the Equine
294 Utrecht University Scale for Composite Pain Assessment (EQUUS-COMPASS) and the Equine

- 295 Utrecht University Scale for Facial Assessment of Pain (EQUUS-FAP): A scale-construction study.
296 Vet J. 2015;206(3):356-64.
- 297 9. Srithunyarat T, Höglund OV, Hagman R, Olsson U, Stridsberg M, Lagerstedt AS, et al.
298 Catestatin, vasostatin, cortisol, temperature, heart rate, respiratory rate, scores of the short form of
299 the Glasgow composite measure pain scale and visual analog scale for stress and pain behavior in
300 dogs before and after ovariohysterectomy. BMC Res Notes. 2016;9:381.
- 301 10. Safikhani S, Gries KS, Trudeau JJ, Reasner D, Rüdell K, Coons SJ, et al. Response scale
302 selection in adult pain measures: results from a literature review. J Patient Rep Outcomes.
303 2017;2:40.
- 304 11. Lindegaard C, Thomsen MH, Larsen S, Andersen PH. Analgesic efficacy of intra-articular
305 morphine in experimentally induced radiocarpal synovitis in horses. Vet Anaesth Analg.
306 2010;37(2):171-85.
- 307 12. Nascimento FF, Marques VI, Crociolli GC, Nicácio GM, Nicácio IPAG, Cassu RN.
308 Analgesic efficacy of laser acupuncture and electroacupuncture in cats undergoing
309 ovariohysterectomy. J Vet Med Sci. 2019;81(5):764-70.
- 310 13. McLennan KM MA, Dalla Costa E, Stucke D, Corke MJ, Broom DM, Lach MC.
311 Conceptual and methodological issues relating to pain assessment in mammals: The development
312 and utilisation of pain facial expression scales. Applied Animal Behaviour Science. 2019;217:1-15.
- 313 14. Huynh M, Vilmouth S, Gonzalez MS, Calvo Carrasco D, Di Girolamo N, Forbes NA.
314 Retrospective cohort study of gastrointestinal stasis in pet rabbits. Vet Rec. 2014;175(9):225.
- 315 15. Lichtenberger M, Lennox A. Updates and advanced therapies for gastrointestinal stasis in
316 rabbits. Vet Clin North Am Exot Anim Pract. 2010;13(3):525-41.
- 317 16. Varga M, Harcourt-Brown F. Textbook of rabbit medicine : revised and edited. 2nd ed.
318 Edinburgh ; New York: Elsevier; 2014. 1 online resource. p.
- 319 17. DeCubellis J, Graham J. Gastrointestinal disease in guinea pigs and rabbits. Vet Clin North
320 Am Exot Anim Pract. 2013;16(2):421-35.

- 321 18. Mans C. Insights into pain assessment and management in rabbits. *Vet Rec.*
322 2020;186(18):600-2.
- 323 19. Delk KW, Carpenter JW, KuKanich B, Nietfeld JC, Kohles M. Pharmacokinetics of
324 meloxicam administered orally to rabbits (*Oryctolagus cuniculus*) for 29 days. *Am J Vet Res.*
325 2014;75(2):195-9.
- 326 20. Teixeira RC, Monteiro ER, Campagnol D, Coelho K, Bressan TF, Monteiro BS. Effects of
327 tramadol alone, in combination with meloxicam or dipyrone, on postoperative pain and the
328 analgesic requirement in dogs undergoing unilateral mastectomy with or without
329 ovariohysterectomy. *Vet Anaesth Analg.* 2013;40(6):641-9.
- 330 21. Moran CE, Hofmeister EH. Prevalence of pain in a university veterinary intensive care unit.
331 *J Vet Emerg Crit Care (San Antonio).* 2013;23(1):29-36.
- 332 22. Hofmeister EH, Barletta M, Shepard M, Brainard BM, Trim CM, Quandt J. Agreement
333 among anesthesiologists regarding postoperative pain assessment in dogs. *Vet Anaesth Analg.*
334 2018;45(5):695-702.
- 335 23. Holton LL, Scott EM, Nolan AM, Reid J, Welsh E, Flaherty D. Comparison of three
336 methods used for assessment of pain in dogs. *J Am Vet Med Assoc.* 1998;212(1):61-6.
- 337 24. Morton CM, Reid J, Scott EM, Holton LL, Nolan AM. Application of a scaling model to
338 establish and validate an interval level pain scale for assessment of acute pain in dogs. *Am J Vet*
339 *Res.* 2005;66(12):2154-66.
- 340 25. Barletta M, Young CN, Quandt JE, Hofmeister EH. Agreement between veterinary students
341 and anesthesiologists regarding postoperative pain assessment in dogs. *Vet Anaesth Analg.*
342 2016;43(1):91-8.
- 343 26. Benato L RN, Murrell JC. Pain and analgesia in pet rabbits within the veterinary
344 environment: a review. *Veterinary Anaesthesia and Analgesia.* 2019;46(2):151-62.

345

346 **Supporting information**

347 S1 Dataset.

348

Figure 1

Figure 2