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CENTRO UNIVERSITÁRIO DE LISBOA

FACULDADE DE MEDICINA VETERINÁRIA

MESTRADO INTEGRADO EM MEDICINA VETERINÁRIA

Evaluation of two anesthetic protocols in elective reproductive surgery in coatis (*Nasua nasua*)

Dissertação apresentada a provas públicas para a obtenção do grau de mestre em Medicina Veterinária, orientada por a Professora Doutora Sónia Patrícia Seabra Campos e co-orientador Professor Rui Filipe Galinho Patrício.

Laura Inês Mendes Nunes da Costa, n.º 21702571

2024

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Comparison of two different analgesic drugs for elective procedures in Coatis (*Nasua nasua*)

Versão final

Dissertação defendida em provas públicas na Universidade Lusófona, Centro Universitário de Lisboa, no dia 22/10/2024, perante o júri, nomeado pelo Despacho de Nomeação Nº 967/2024 de 30 de setembro de 2024 com a seguinte composição:

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Este trabalho também foi orientado por Prof. Dr. Rui Patrício

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Resumo

A elaboração de protocolos anestésicos apropriados é essencial para o bem-estar de animais selvagens durante um determinado procedimento, assim como para a segurança de todos os intervenientes. Existem dados limitados sobre anestesia em quatis. Este estudo tem como objetivo avaliar a eficácia do butorfanol e da metadona como fármacos analgésicos durante orquiectomia e ovariohisterectomia em quatis. Três machos e quatro fêmeas (*Nasua nasua*) com idades entre 1 a 3 anos, foram divididos aleatoriamente em dois grupos (G1, G2) e pré-medicados por via intramuscular com: 0,5 mg/kg de midazolam, 5 mg/kg de ketamina, 0,3 mg/kg de metadona e alfaxalona *ad affectum* (G1) ou 0,5 mg/kg de midazolam, 5 mg/kg de ketamina, 0,3 mg/kg de butorfanol e alfaxalona *ad affectum* (G2). Após a instrumentação, os animais foram induzidos com alfaxalona *ad affectum* para permitir a intubação endotraqueal. A anestesia foi mantida com 1% de isoflurano em oxigénio. Parâmetros clínicos, incluindo frequência cardíaca (FC), frequência respiratória (FR), pressão arterial sistólica (PAS), pressão arterial média (PAM), saturação de oxigénio (SpO_2) e dióxido de carbono ao final da expiração ($EtCO_2$) foram recolhidos em pontos de tempo específicos (T0: valor basal, T1: colocação pinças cirúrgicas, T2: incisão da pele, T3: túnicas/incisão abdominal, T4: primeiro pedículo/incisão do testículo, T5: segundo pedículo/testículo, T6: sutura subcutânea, T7: sutura da pele). Os tempos perianestésicos também foram registados e incluem: tempo desde a pré-medicação até à perda do reflexo de postura (P1), tempo de indução e intubação (P2), tempo de cirurgia (P3), tempo total de anestesia (P4), tempo de extubação (P5) e tempo de recuperação (P6). Foi realizada uma análise distributiva dos dados através do cálculo da média e desvio padrão. O tempo necessário para a sedação foi menor no Grupo 2 (15,33±1,24 minutos) em comparação ao Grupo 1 (19,75±0,82 minutos). Não foram necessários resgates analgésicos durante a cirurgia. Nas dosagens utilizadas, ambos os fármacos demonstraram eficácia analgésica intraoperatória, o que apoia a sua inclusão nos protocolos anestésicos para procedimentos eletivos em quatis. No entanto, devido ao pequeno tamanho da amostra, os resultados devem ser interpretados com cautela.

Palavras-chave: Anestesia, Quatis, Metadona, Butorfanol, Cirurgia

Abstract

Appropriate anaesthetic protocols are essential for the welfare of wildlife animals during a given procedure and for the safety of all subjects. There is limited data about anaesthesia in coatis. This study aims to evaluate the efficacy of butorphanol and methadone as analgesic drugs during orchiectomy and ovariohysterectomy in coatis. Three males and 4 females (*Nasua Nasua*) aged between 1 and 3 years old, were randomly divided into two groups (G1, G2) and premedicated intramuscularly with: 0.5mg/kg midazolam, 5mg/kg ketamine, 0.3mg/kg methadone and alfaxalone *ad affectum* (G1) or 0.5mg/kg midazolam, 5mg/kg ketamine, 0.3mg/kg butorphanol and alfaxalone *ad affectum* (G2). After instrumentation, the animals were induced with alfaxalone *ad affectum* to allow endotracheal intubation. Anaesthesia was maintained using 1% isoflurane in oxygen. Clinical parameters including heart rate (RR), respiratory rate (RR), systolic arterial pressure (SAP), mean arterial pressure (MAP), oxygen saturation (SpO_2) and end-tidal carbon dioxide ($EtCO_2$) were collected at specific timepoints (T0: baseline, T1: surgical clamps, T2: skin incision: T3: tunics/ abdominal incision, T4: 1^{st} pedicule/ testicule incision, T5: 2^{nd} pedicule/ testicule, T6: subcutaneous suture, T7: skin suture). The perianesthetic times were recorded as well and include: time from premedication to loss of standing reflex (P1), time of induction and intubation (P2), surgery time (P3), total time of anesthesia (P4), extubation time (P5) and recovery time (P6). A distributive analysis of the data was performed by calculating the mean and standard deviation. Time required for sedation was shorter in G2 (15,33±1,24min) than G1 (19,75±0,82min). No analgesic rescues were required during surgery. At the used dosage, both drugs showed intra- operative analgesic efficacy, advocating their inclusion in anaesthetic protocols for elective procedures in coatis. Nevertheless, due to the small sample size, results should be interpreted with caution.

Keywords: Anesthesia, Coatis, Methadone, Butorphanol, Surgery

List of Abbreviations

%: percentage

μ- the mu receptor

ABCDE: Airway, Breathing, Circulation, Disability, Exposure approach

ASA: *American Society of Anesthesiologists classification of risk*

cm- centimetre

C_{max}: maximal plasma concentration

CRTZ: chemoreceptor trigger zone

DOR: delta opioid receptors

Et al. – and others, latin for "*et al*li"

$ETCO_2$: end-tidal carbon dioxide

G: gauge

G1: group 1

G2: group 2

GABA: gamma-aminobutyric acid

h: hour

HR: heart rate

IM: intramuscular

IV: intravenous

κ- the kappa receptor Kg:

kilogram

KOR: kappa opioid receptors

L: litre

L: litre per minute

MAC: minimum alveolar concentration

Mg/kg: milligram per kilogram

Mg: milligram

Ml: millilitre

mm- millimetre

MOR: morphine opioid receptors

ng/ml: nanogram per millilitre

ng: nanogram

NMDA: N-methyl-D-aspartate

OP1: the delta receptor

OP2: the kappa receptor

OP3: the mu receptor

PAD: diastolic arterial pressure

PAM: mean arterial pressure

PAS: systolic arterial pressure

PO: latin for "*per os*"

RR: respiratory rate

SC: subcutaneous

SPO_2: oxygen saturation

TLC: tender, love and care

δ- the delta receptor

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Internship Overview

The internship was conducted in two different veterinary clinics and had a total duration of 6 months. The first 4 months were carried out at the Vetexóticos Veterinary Clinic, while the remaining two months were conducted at All Pets - Tires Veterinary Clinic.

Vetexóticos – Clinica veterinária

The Vetexóticos – Clinica veterinária is located in Feijó, Almada, and is exclusively dedicated to exotic animals medicine. The internship had a total duration of 4 months, from October 1st to January 31st. The proposed schedule consisted of weekly shifts lasting 7 hours. Additionally, the student would work a 4-hour shift on two Saturdays per month. During the internship, the student had the opportunity to observe consultations across different areas of internal medicine, as well as surgeries, diagnostic imaging and giving assistance in the treatment and care of hospitalized animals.

All Pets – Clínica veterinária de Tires

The All Pets - Clinica veterinária de Tires is situated in Tires, in São Domingos de Rana. This clinic is dedicated consultations, surgery and hospitalization of companion and exotic animals. The internship took place from March 1st to April 30th and the proposed schedule consisted of approximately 6-hour shifts per week. Additionally, every 3 weeks, the student performed a 7-hour shift on Saturdays. Every Thursday afternoon or Tuesday's morning the student had the opportunity to accompany in consultations and surgeries at the Hospital Veterinário Universidade Lusófona. This internship allowed the integration and dynamics across different medical specialties applied to exotic species, through observing consultations, surgeries, imaging exams, and care of hospitalized animals.

Internships' description

The consultations allowed exposure to various areas of medicine, notably internal medicine, preventive medicine, emergencies, and imaging.

In internal medicine, there was the opportunity to observe and perform the anamnesis, physical restraint of the animal, physical examination, blood and other samples collection, wound cleaning etc, as well as engaging in brainstorming sessions with the veterinarian regarding potential differential diagnoses and treatments.

In preventive medicine, prophylactic procedures were carried out, including vaccinations and deworming. Additionally, physical examinations and laboratory analyses (such as hemograms, biochemical profiles, and fecal analyses) were conducted, always from a preventive perspective.

During emergency consultations, it was possible to observe the actions of the veterinarians in critical situations, as well as the implementation of the triage system, rapid anamnesis, and the primary approach (ABCDE protocol) for patient stabilization.

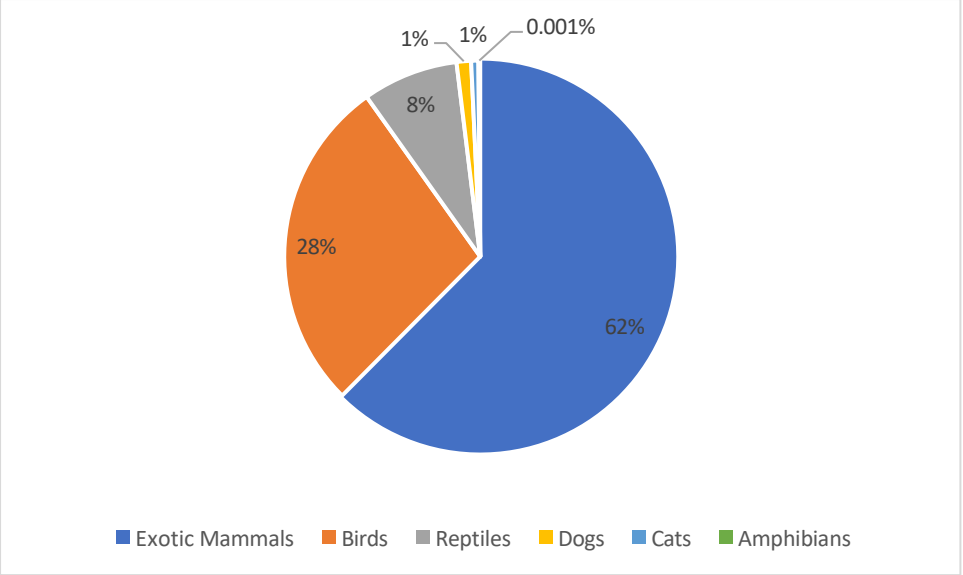
In the field of imaging, there was the opportunity to observe and perform radiological examinations, as well as ultrasounds and electrocardiograms.

On a laboratory level, the student was able to participate in the execution and subsequent analysis of some complementary diagnostic tests, such as biochemical analyses, blood smears, faecal smears, fungal tests, tape test, scrapings, etc.

Regarding hospitalization, there was the opportunity to monitor the hospitalized animals by performing physical examinations, pain assessments, collecting samples for laboratory analysis, measuring blood glucose, and performing wound care. Additionally, the student had the chance to administer medications, provide fluid therapy, insert catheters, offer feeding assistance, and provide TLC (tender, love, and care).

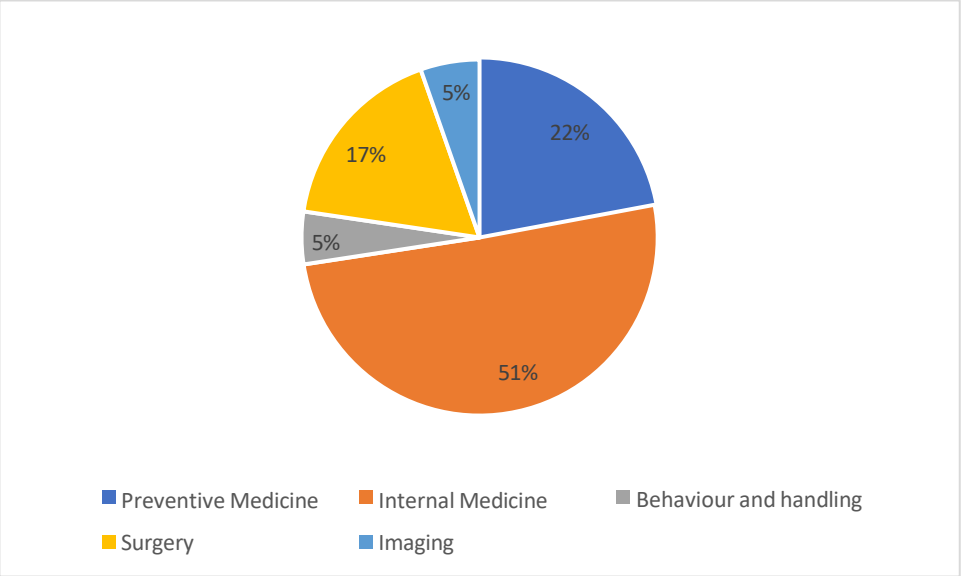
Surgery allowed the student to participate in patient's monitoring and care from the pre-surgical phase to the post-surgical phase. In the pre-surgical phase, there was the opportunity to perform the physical examination and collect blood samples for pre-anesthetic evaluation and interpretation. Sometimes, the student was also responsible for the sterilization of surgical equipment, preparing the operating room, preparing and administering anaesthetic drugs, trichotomy, and ensuring surgical site asepsis. During the surgery, various roles were undertaken, including that of an anesthetist, circulator, instrument handler, and surgical assistant. Lastly, in the post-surgical phase, the animal was closely monitored during its stay, ensuring a successful surgical recovery. This phase involved meticulous monitoring of the animal's condition, including parameters such as temperature, blood pressure and pain assessment.

During the 6-month internship, a total of 671 clinical cases were observed. Most of the observed animals were exotic mammals, followed by birds, reptiles, dogs, cats, and finally amphibians, with only a single case observed. In the record of observed animals, those that appeared more than once in consultations were considered. Graph 1 depicts this distribution.



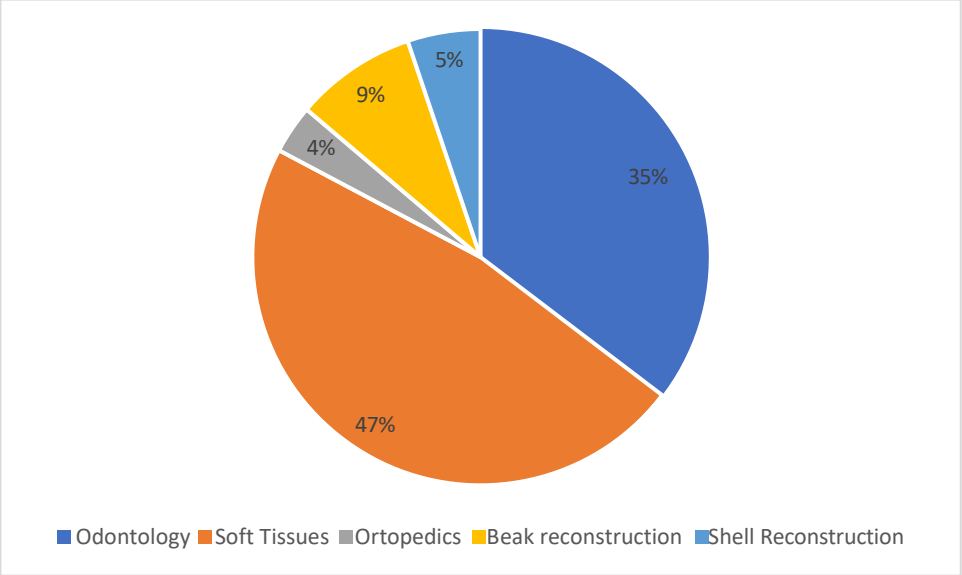
Graph 1 - Graphic distribution of the animals observed throughout the entire internship period

In Graph 2, the distribution of the cases observed during the curricular internship can be visualized. The cases were sorted into internal medicine consultations, preventive medicine, behaviour and management consultations, imaging or surgery.



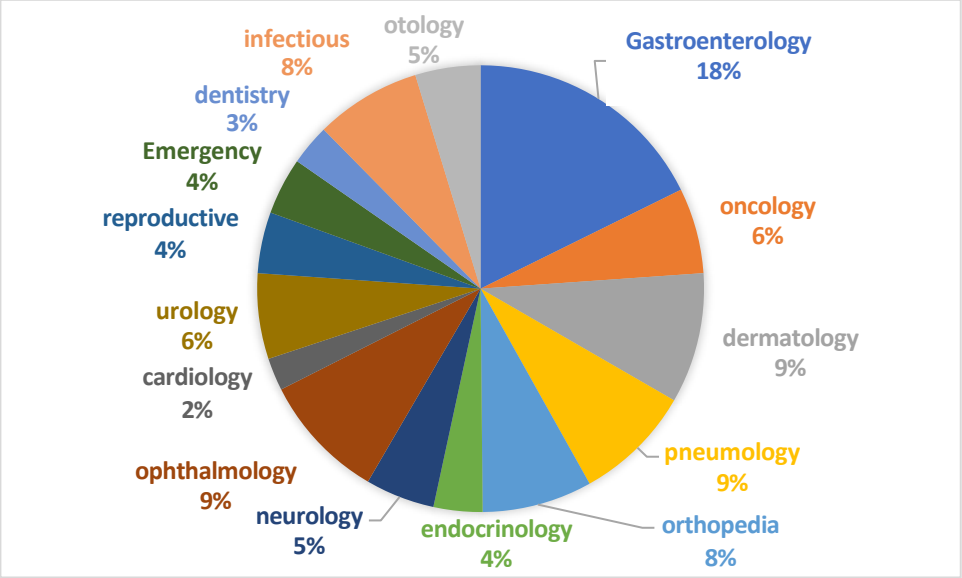
Graph 2 - Distribution of the different types of cases observed during the internship.

Regarding surgeries, soft tissue surgeries were the most observed, followed by odontologic surgeries, beak reconstruction surgeries in birds, turtle shell' reconstruction surgeries, and orthopedic surgeries, as depicted in Graph 3.



Graph 3 - Distribution of the different surgery types observed during the internship period.

Throughout the internship, the student had the opportunity to contact with a diverse range of internal medicine areas. The majority of the observed consultations were in gastroenterology, dermatology, and oncology, while cardiology and dentistry consultations were the least frequent.



Graph 4 - Different areas of internal medicine observed during the internship.

Chapter I- Bibliographic Revision

1- Coatis

1.1- Coatis' biology

Coatis are arboreal mammals native to the American continent (Silva *et al*. 2018). They belong to the order *Carnivora*, the family *Procyonidae*, and to two genera, *Nasua* or *Nasuella* (González-Maya *et al*, 2015). The genus *Nasua* includes the ring-tailed coatis (*Nasua nasua*) and white-nosed coatis (*Nasua narica*), while the genus *Nasuella* includes mountain coatis (*Nasuella olivacea*) (Salómon & Ramírez, 2011). White-nosed coatis (*Nasua narica*) are characterized by their abundant geographical distribution in Central America, particularly in countries such as Mexico and Costa Rica. However, their presence in South or North America is rare, with only a few records of their presence in the northern region of Colombia and the southern United States of America (González-Maya *et al*., 2011; Salcedo-Rivera *et al*., 2022).The ring-tailed coatis (*Nasua nasua*), on the other hand, are widely distributed throughout almost all of South America, with records of their presence from Venezuela to Uruguay and the northern region of Argentina (Fonseca *et al*., 2017). Mountain coatis (*Nasuella olivacea*), as their name suggests, inhabit mountainous regions and are typically found at high altitudes, usually above 2000 meters. This makes their geographical distribution limited to the Andes Mountain region, with records of their presence in countries such as Peru, Colombia, and Ecuador (González-Maya *et al*., 2015, Helgen *et al*, 2009;; Hyde *et al*, 2021). Both genera are quite similar (Salómon & Ramírez, 2011). They are characterized by their dark brown fur with a yellowish-white ventral region and a tail with light bands (Geraldene, 2012; Helgen *et al*., 2009;). Their faces have a lighter tone compared to their bodies, and Nasua coatis also have white markings around the orbital region (Helgen *et al*., 2009; Geraldene, 2012). Their snouts are highly developed and have a darker color, as do their limbs, paws, and orbital region (Geraldene, 2012; Helgen *et al*., 2009). The main difference between the two genera is their size, with Nasuella coatis being smaller. They weigh an average of 1 to 1.5 kg and have a body length of about 80 cm, including the tail (Medrano-Vizcaíno, 2018). Nasua coatis, on the other hand, are larger, weighing 3 to 6 kg, with a total length of 80 to 130 cm (Geraldene, 2012). Unlike other members of their family, coatis are characterized by their diurnal, gregarious, and social habits (Ferreira, 2013). They live in groups consisting of females and their offspring, while males only joining during the breeding season (Geraldene, 2012). Regarding their diet, they are omnivores, primarily feeding on invertebrates but also consuming fruits and vertebrates (Beisiegel, 2001; Silva *et al*., 2018). In the wild, this species typically lives for about seven years. However, in captivity, their lifespan significantly increases, with records of coatis (*Nasua narica*) living up to 17 years of age (Romero &

Aureli, 2008).

According to the Decreto-Lei n. º 92/2019, in Portugal all individuals of the *Procyonidae* family, are considered invasive exotic species, with the potential to cause negative impacts on ecosystems and threaten the existing biological diversity. As such, the commercialization, possession, breeding, transportation, or use of these species as pets is prohibited (Decreto-Lei n. º 92/2019).

1.2-Reproductive characteristics

Regarding their reproductive system, male coatis have two horizontal and ovoid testicles, located within the scrotal sac (Queiroz *et al*, 2010). The scrotum hangs between the perineal and inguinal regions and is pendulous. The testicles are enveloped by the tunica albuginea. Proximally, are located the spermatic cord and all its constituents, including the pampiniform plexus, vas deferens, vaginal tunics, and testicular artery and vein. The penis is suspended between the hind limbs and is composed of the penile bone and penile urethra. The spongy body surrounds the penile urethra, while the cavernous body comprises the rest of the penis. Penile vascularization is ensured by the dorsal artery and vein of the penis. Coatis have only two accessory glands of the reproductive system, the ampulla of the vas deferens and the prostate, while the bulbourethral and vesicular glands are absent in this species. The prostate surrounds the urethra and it is globular. It is important to note that sexually immature male individuals exhibit some differences. In these animals, the penis adheres to the skin of the abdominal region instead of being suspended, and the scrotum is not pendulous (Franciolli *et al*, 2007).

Regarding females, they possess a bicornuate uterus, consisting of two uterine horns, and macroscopically it presents a pinkish colour. Additionally, the uterus is composed by the uterine body, which is small in this species, and the cervix, which is highly muscular. The two ovaries are surrounded by the ovarian bursa. The uterine tube is responsible for transporting the oocyte from the ovary to the uterus and is composed of three portions: the infundibulum, ampulla, and isthmus (Mayor *et al*, 2013).

1.3- Parameters

1.3.1- Physiological parameters

Coatis are wild species, and as so, there are few reports regarding the normal values of certain physiological parameters. The few data available demonstrates significant variations between values.

In the table below (Table 1), a compilation of some clinical parameters [heart rate (HR), respiratory rate (RR), non-invasive blood pressure (SAP, MAP and DAP), end-tidal carbon dioxide ($ETCO_2$), oximetry (SPO_2)] in coatis (*Nasua nasua*), retrieved from various references can be observed. These data are regarding animals previously sedated with one of the protocols present in the table. Within some papers, clinical data are described in two study groups.

Table 1 - Clinical Parameters of coatis (Nasua nasua), previously sedated, retrieved from different references (source: Vinyals, 2015; Conforti et al, 2017; Fonseca et al, 2017; Nascimento et al., 2021; Thomas et al, 2021; Kunz et al, 2021).

Reference	Groups	Anesthetic Protocol	HR (bpm)	SAP (mmHg)	MAP (mmHg)	DAP (mmHg)	$ETCO_2$ (mmHg)	SPO_2 (%)	RR (mpm)
Nascimento *et al*, 2021	Group 1	10µ/kg Dexmedethomidine, 0,2 mg/kg Butorphanol, 8 mg/kg Ketamine (IM)	155.2	111.4	*n. i.**	*n. i.**	*n. i.**	*n. i.**	67.4
	Group 2	Xylazine 0,1 mg/kg, Butorphanol 0,2 mg/kg, ketamine 8 mg/kg (IM)	173.4	*n. i.**	*n. i.**	*n. i.**	*n. i.**	*n. i.**	99.4
Thomas *et al*, 2021		10 mg/kg ketamine, 0.3 mg/kg midazolam, 0.2 mg/kg methadone (IM); propofol 4 mg/kg for induction	180	138	*n. i.**	*n. i.**	32	*n. i.**	15
Conforti *et al*, 2017		10 mg/kg Tiletamine and Zolazepam (Zoletil)	223	*n. i.**	*n. i.**	*n. i.**	*n. i.**	*n. i.**	53
Kunz *et al*, 2021		0.25mL of 1.0% atropine sulphate; 0.265mL of Detomidine (Dormiun-V®), 2.2mL of distilled water to a bottle of Zoletil / 50®)	161	*n. i.**	*n. i.**	*n. i.**	*n. i.**	87	56
Fonseca *et al*, 2017	Group 1	15 mg/kg Ketamine, a 0,2 mg/kg midazolam, 5 mg/kg pethidine (IM); propofol 5 mg/kg for induction	217	147	*n. i.**	*n. i.**	*n. i.**	*n. i.**	22
	Group 2	15 mg/kg Ketamine, a 0,2 mg/kg midazolam, 5 mg/kg pethidine (IM),	229	151	*n. i.**	*n. i.**	*n. i.**	*n. i.**	28

		continuous infusion propofol 4 mg/kg							
Vinyals, 2015		5mg/kg ketamine, 50 µg/kg medetomidine,0,3mg/ kg methadone (IM)	91	98	79	70	32	92	25

*n. i.**- no information

1.3.2- Hematologic parameters

Currently, there is no data showing the normal range of haematological values in *Nasua nasua* animals. However, data can be extrapolated from related species such as the white-nosed coati. Rovirosa-Hernandez *et al*., 2012 conducted a study with the purpose of obtaining baseline data on the blood chemistry and hematological values of white-nosed coatis (*Nasua narica)*. For this purpose, 44 coatis in semi-free conditions (animals can roam freely while being confined in zoological gardens or parks) were utilized. They were captured using anesthetic darts composed of 3x32mm needles and 3mL syringe each with 10-15 mg/kg of ketamine hydrochloride (Inoketam®).

Blood work information obtained by Rovirosa-Hernandez *et al*., 2012 in white-nosed coatis is summarized in Table 2.

Table 2 - Hematological values from the White-nosed coati (Nasua narica) (source: Rovirosa-Hernandez et al., 2012).

Parameters	Males	Females
Hemoglobin (g/dL)	10.71 ± .43	9.21 ± .18
Hematocrit (%)	31.84 ± 1.48	27.86 ± .61
Red Blood Cell count (× 106/uL)	6.54 ± .27	5.81 ± .13
Mean Corpuscular Volume (fl)	48.64 ± .72	48.03 ± .36
Mean Corpuscular Hemoglobin (pg)	16.42 ± .31	15.87 ± .11
Mean Corpuscular Hemoglobin Concentration (g/dl)	33.79 ± .34	33.13 ± .17
Platelet (× 103/uL)	512.71 ± 19.55	595.43 ± 22.07
White blood cell (× 103/uL)	9.48 ±.84	8.61 ± .43
Monocyte (× 103/uL)	2.42 ± .27	2.13 ± .10
Lymphocyte (× 103/uL)	3.37 ± .33	2.72 ± .15
Garanulocytes (× 103/uL)	3.69 ± .39	3.76 ± .30

1.3.3- Biochemical parameters

Regarding biochemical values, Júnior *et al*, 2017, conducted a clinical study with 10 *Nasua nasua* individuals aiming to analyse differences in blood parameters in coatis, either with or without direct exposure to humans to humans.

Biochemistry values obtained from this study are summarized in Table 3. In the respective table, group 1 corresponds to animals used to human contact, and group 2 to animals with no direct exposure to humans.

Table 3 - Biochemical values for ring-tailed coatis in which Group 1 correspond to the coatis used to human contact and Group 2 to the ones without human contact. (Source: Júnior et al, 2017.)

Parameters	Group 1	Group 2
Glucose (mg/dL)	106,60 ± 8,65a	63,80 ± 2,40
Triglyceride (mg/dL)	52,40 ± 16,86	32,00 ± 3,97
Cholesterol (mg/dL)	121,00 ± 30,98	144,60 ± 23,42
Urea (mg/dL)	25,50 ± 5,30a	44,80 ± 6,24b
Ureic Acid (mg/dL)	1,20 ± 0,20	1,62 ± 0,13
Creatinine (mg/dL)	1,09 ± 0,06	0,60 ± 0,25
Total Protein (g/dL)	7,36 ± 0,11a	9,42 ± 0,34b
Albumin g/dL	2,94 ± 0,32	3,14 ± 0,17
Globulin g/dL	4,42 ± 0,27a	6,27 ± 0,17b
Albumin/Globulin relation (mg/dL)	0,69 ± 0,12	0,50 ± 0,02
AST UI/L	200,60 ± 45,38	210,80 ± 20,86
ALT IU/L	87,80 ± 20,14	98,60 ± 9,61
Gama GT U/L	11,00 ± 2,88	16,60 ± 4,83
Alkaline Phosphatase (U/L)	29,40 ± 3,93	33,40 ± 3,59
Calcium (mg/dL)	9,52 ± 0,59	8,83 ± 0,39
Phosphorous (mg/dL)	6,30 ± 0,98	5,44 ± 0,99
Seric iron µg/DL	122,76 ± 34,91	135,82 ± 15,24

2- Anesthesia

2.1- Importance of Anesthesia in Wild animals

As it happens with other species, increasing our knowledge about anesthesia in wild species, is becoming increasingly relevant, as they are also subjected to procedures and interventions, for which sedation or anesthesia might be required (Fowler, 2008; Kunz *et al*, 2021). These procedures can be varied, from blood sample collection, transportation, treatment of an injury or illness, collecting physiological parameters for scientific research or monitorization purposes, or even surgical procedures (Fowler, 2008; Martini *et al*., 2017). The presence of wild species in zoos or sanctuaries is increasingly common. Specifically, regarding coatis, in 2017, there were records of 1,277 coatis living in captivity, with 936 of them in Europe (Shora *et al*., 2018).

It is also important to consider the growing popularity of exotic species as pets, making it relevant to increase our knowledge about them (Grant *et al*., 2017). The elaboration of adequate anesthetic protocols is essential to guarantee the safety of all intervenients, as well as the well-being of the animal during a given procedure (Thomas *et al*. 2021). Despite safety, it should also be taken in account that the protocol chosen must be the most suitable for the procedure performed (Fowler, 2008). This becomes even more pertinent since coatis, regardless of being pets or being in the wild, have a greater potential for aggression compared to other animals.

2.2- Anesthetic Drugs

2.2.1- Midazolam

Midazolam is a drug belonging to the class of benzodiazepines and is among the most commonly utilized in veterinary medicine (Liao *et al*, 2017; Rankin, 2015).

In addition to being used in various species, administration can be both by intravenous (IV) and intramuscular (IM) vias (Rankin, 2015). The IM administration constitutes a significant advantage as it facilitates administration in animals without a catheter or those that are aggressive (Rankin, 2015). When administered IM, midazolam exhibits high absorption and rapid onset of action (Hopkins *et al*, 2014). In canines, its bioavailability exceeds 90%, and a peak plasma concentration occurs within a 15-minut interval (Rankin, 2015).

Midazolam acts at the level of the neurotransmitter gamma-aminobutyric acid receptor (GABA receptor), acting as an agonist and bringing diverse benefits at the anesthetic level (Drees *et al*, 2015; Kropf *et al*, 2018). Despite its role as a potent sedative and muscle relaxant, it also has anxiolytic and hypnotic effects and causes amnesia (Kropf *et al*, 2018). Midazolam, as a pre-anesthetic agent, allows for the reduction of other anesthetic drugs' doses while also decreasing the minimal alveolar concentration (MAC) (Seddighi *et al*, 2011). Moreover, it also presents a synergistic effect when co-administered with propofol or alfaxalone, and its sedation effect can be amplified when paired with certain drugs such as opioids (Rankin, 2015; Zapata *et al*, 2018). In cases of a *status epilepticus*, midazolam can be used as a first-line drug due to its anticonvulsant properties (Kropf *et al*, 2018).

As such, midazolam is deemed a safe drug with no significant cardiovascular side effects (Drees *et al*, 2015; Hopkins *et al*, 2014). Occasionally, upon administration, a slight tachycardia and cardiac output decrease may occur (Drees *et al*, 2015). Nevertheless, these effects are usually minimal and often associated with higher doses (Drees *et al*, 2015; Rankin, 2015) Additionally, due to its action on vasomotor centres, a decrease in blood pressure may occur post-administration (Rankin, 2015). Furthermore, midazolam can induce ataxia, hypersalivation, and profound weakness (Hopkins *et al*, 2014; Zapata *et al*, 2018)

When used as a sole anesthetic agent, it can lead to the onset of an excitatory state in dogs during the induction period. The most common reactions include agitation, noise sensitivity, restlessness, aggression, drooling, licking and vocalization (Simon *et al*, 2014). Hence it should be administered in combination with other drugs, thus favouring a multimodal approach. (Hopkins *et al* 2014; Zapata *et al*, 2018). An example of this is the association of midazolam and ketamine. This association of drugs is frequently administered as it results in a decrease in excitatory effects (Allerton, 2020). Midazolam, in cats has a much less potent effect, potentially causing ataxia or excitement, especially at higher doses (Kanda & Hikasa, 2008; Rankin, 2015).

In dogs and cats, the recommended dose range for Midazolam is 0.2–0.3 mg/kg IV for sedation (Allerton, 2020).

Reference doses of midazolam used in coatis range from 0.2 to 0.5 mg/kg IM (Fonseca *et al*, 2017; Martini *et al*, 2017; Minto *et al*, 2017; Thomas *et al*, 2021).

2.2.2- Alfaxalone

Alfaxalone is a neurosteroid, which use as an anesthetic induction agent has been increasing in veterinary medicine (Liao *et al*, 2017; Zapata *et al*, 2018). It is characterized by providing good anesthetic induction leading to muscle relaxation and neurological depression without causing significant cardiovascular effects (Tamura *et al*, 2015; Zapata *et al*, 2018). Alfaxalone primarily acts by binding to the type A GABA receptors on the cell surface. This leads to the modulation of chloride transport across neuronal cell membranes, inducing cell hyperpolarization and decreasing the propagation of neuronal impulses (Ahmad *et al*, 2019; Tamura *et al*, 2015).

Its use has already been reported in various species, including cats and dogs but also exotic animals such as marmosets, goldfish, Yellow-Bellied Sliders, guinea pigs, black-tailed prairie dogs, and others (Álvarez *et al*, 2022; Castañer *et al*, 2023; Hiebert *et al*, 2022; Leonardi *et al*, 2019; Morici *et al*, 2021; Thomas *et al*, 2012). It can be administered both intravenously and intramuscularly (Benedetti *et al*, 2018). However, IM route is not authorized in all countries (Marín *et al*, 2020).

The sole use of alfaxalone in anesthetic protocols has been reported, however, its use in combination with other drugs such as opioids or benzodiazepines is proven to be more effective and beneficial (Allerton, 2020; Seo *et al*, 2015; Tamura *et al*, 2015). The use of multiple drugs allows a reduction in the dose of alfaxalone during induction, which contributes to decreasing the incidence of potential side effects caused by it, both during the anesthetic period and in the recovery phase (Seo *et al*, 2015; Tamura *et al*, 2015).

Ribas *et al*. (2014), reported that the use of alfaxalone, along with butorphanol in cats, led to deep sedation and rapid anesthesic induction, without clinically relevant cardiovascular changes (Ribas *et al*, 2014). However, despite causing fewer cardiovascular effects compared to propofol, it still might still lead to a slight tachycardia and hypotension in supraclinical doses. (Casoria *et al*, 2023; Castañer *et al*, 2023). Alfaxalone, also might cause respiratory depression, that may progress to apnea and lead to hypoxia (Muir *et al*, 2008; Seo *et al*, 2015). It is suspected rapid IV administrations of alfaxalone might increase the prevalence of respiratory depression and apneas (Benedetti *et al*, 2018). During the recovery period, alfaxalone can also cause some adverse effects, including limb paddling, noise sensitivity, or excitement (Zapata *et al*. 2018). According to Zapata *et al*. (2018), these effects can be reduced, and sedation can be enhanced during the anesthetic period if alfaxalone is administered prior to midazolam (Zapata *et al*, 2018).

Regarding dosage, this drug has a wide safety margin (Castañer *et al*, 2023). In dogs, to induce deep sedation, the dose of alfaxalone should be 3 to 4 mg/kg IV. However, if used in combination with other drugs, the dose can be reduced up to 2 mg/kg. (Allerton, 2020; Castañer *et al*, 2023). In cats, the dose range is from 2 to 5 mg/kg IV (Allerton, 2020).

To the author's knowledge, there are no references about alfaxalone use in coatis for anesthetic purposes. However, in a study conducted by Ahmad *et al*., the use of a of 5 mg/kg dose was reported in common palm civets (Paradoxurus musangus) (Ahmad *et al*, 2019).

2.2.3- Ketamine

Ketamine is a drug derived from phencyclidine (Arenilla *et al*, 2021). It is frequently utilized in anesthetic protocols due to its properties as an anesthetic agent, providing dissociation, sedation and analgesia (Arenilla *et al*, 2021). It comprises two isomers, R (-) and S (+), with the latter demonstrating greater analgesic efficacy (Posner *et al*, 2018). Formulations containing solely the S (+) isomer are also available for veterinary medicine use (Casoni *et al*, 2015; Larenza *et al*, 2009).

Its mode of action occurs at the level of N-methyl D-aspartate (NMDA) receptors, which are related to nociception (Khaleghi *et al*, 2023; Solano *et al*, 2006). Ketamine exerts a non-competitive antagonistic action on these receptors, preventing the amino acid glutamate from binding to them (Ko *et al*, 2023; Saberfard *et al*, 2022). This inhibition of NMDA receptors located in the cortex, subcortical regions, thalamus, and brainstem leads to a decrease in the hippocampus and thalamocortical pathway activity, causing a state of general anesthesia (Ko *et al*, 2023). On the other hand, the administration of low doses of ketamine results in reduced activity in the hippocampus but increased thalamocortical pathway activity, as it only inhibits NMDA receptors in the cortex and subcortical regions (Ko *et al*, 2023). This results not only in a dissociative state but also excitation (Ko *et al*, 2023).

Ketamine can be administered both via IV and IM (Posner 2018). Its administration extends beyond dogs and cats and can be given to various species (Posner 2018). There are reports of its administration in exotic animals, including coatis (Fonseca *et al*, 2017; Martini *et al*, 2017; Minto *et al*, 2017; Silva *et al*, 2018; Thomaz *et al*, 2021)

The use of this drug in anesthetic protocols offers several benefits. One of them is, providing good analgesia, which effect may last longer than its anesthetic effect (Saberfard *et*

al, 2022; Ko *et al*, 2023). It is also a good option for chemical restraint when administering to wild or refractory animals (Posner *et al*, 2018).

One of the most notable side effects of ketamine is muscular rigidity and the possible onset of spontaneous movements (Arenillas *et al*, 2021; Khaleghi *et al*, 2023; Pascoe & Steffey, 2018). Additionally, the use of ketamine does not inhibit cranial and swallow reflexes, which not only complicates endotracheal intubation but can also lead to laryngospasm and cough (Imboden *et al*, 2023; Posner *et al*, 2018). To mitigate these effects, ketamine should be co- administered with other drugs capable of muscle relaxation, such as benzodiazepines or α2 - agonists (Khaleghi *et al*, 2023; Posner *et al*, 2018). Ketamine also leads to a decrease in the reuptake of norepinephrine in presynaptic nerves due to stimulation of the sympathomimetic system, which might result into the appearance of tachycardia and hypertension (Imboden *et al*, 2023; Khaleghi *et al*, 2023; Ko *et al*, 2023).

On top of that, it can also cause respiratory depression or an apneustic pattern of breathing (Posner *et al*, 2018). These respiratory effects are commonly associated with high doses or rapid IV administrations (Posner *et al*, 2018). The respiratory depression might also be exacerbated when ketamine is combined with other respiratory depressant drugs (Posner *et al*, 2018). Other side effects include hypersalivation, vomiting, vocalizations, and hypertonicity (Arenillas *et al*, 2021; Khaleghi *et al*, 2023; Posner *et al*, 2018). In certain species, it can also lead to excitement and dysphoria, as in the case of horses (Arenillas *et al*, 2021; Ko *et al*, 2023; Pascoe & Steffey, 2018).

Its use is contraindicated in patients with glaucoma, cardiac pathologies where increased myocardial function may cause decompensation, severe hypertension, or increased intracranial pressure (Posner *et al*, 2018).

In dogs, ketamine doses range from 2 to 5 mg/kg IV and 5 to 10 mg/kg IM. For cats, the dosage range is from 5 to 10 mg/kg, both IV and IM (Posner *et al*, 2018). These doses are established for multimodal protocols where ketamine is co-administered with other drugs, namely benzodiazepines or α2 -agonists (Posner *et al* 2018). Various doses have been reported in coatis, ranging from 8 to 20 mg/kg IM, according to (Fonseca *et al*, 2017; Martini *et al*, 2017; Minto *et al*, 2017; Nascimento *et al*, 2021; Thomaz *et al*, 2021).

2.3-Opioids

2.3.1- Opioid Receptors

Opioid receptors are G-protein-coupled receptors. They are present not only in the central nervous system but also in other tissues such as the *vas deferens*, gastrointestinal tract and heart, although in smaller quantities (Pathan & Williams, 2012). These opioid receptors interact with specific peptides naturally found in the body, known as endogenous opioids. The combined interaction of these receptors and peptides triggers a natural physiological response, including pain modulation (Kukanich & Papich, 2018). There are three distinct types of opioid receptors: mu (μ), kappa (κ), and delta (δ). They may also have other designations, as the μ receptors are also referred to as OP3 or MOR receptors, while κ and δ receptors are known as OP1 or KOR and OP2 or DOR receptors, respectively (Trescot *et al*, 2008). Different endogenous opioids have specific affinities for particular receptor types. μ Receptors have a higher affinity for β-endorphin, κ receptors for Dynorphin A, and δ receptors exhibit a strong affinity for Leucine- and methionine-enkephalin (Kukanich & Papich, 2018). Recent studies suggest the possible existence of subtypes of opioid receptors, although this requires further scientific research, as a consensus on this topic has not yet been reached (Pathan & Williams, 2012; Kukanich & Papich, 2018).

2.3.2- Opioids' pharmacology

Opioids are drugs that bind to opioid receptors and can be classified based on their interactions with these receptors (Pathan & Williams, 2012). They can be categorized as agonists, partial agonists, agonist-antagonists, or antagonists (Quintavalla *et al*, 2022). Full agonist opioids bind to opioid receptors, stimulating them and causing a full effect. Partial agonists work similarly to full agonists but produce a milder effect compared to full agonist opioids. Additionally, they often exhibit a ceiling effect, which means that after a certain dose, increasing the dosage further will not yield additional effects (Kukanich & Wiese, 2015). Agonist-antagonist opioids are characterized by their antagonistic effect on the μ receptor but a strong agonistic effect on the κ receptor (Trescot *et al*., 2008). On the other hand, antagonist opioids have a strong affinity for receptors but do not produce any effects. However, because the antagonist is binding to the receptor, it prevents the binding of other drugs, inhibiting their effects (Kukanich & Wiese, 2015). Full agonist μ opioids provide deep and strong analgesia. Partial μ agonists, on the other hand, due to their weaker effect, are more suitable for treating

moderate pain or in cases where full agonist opioids might cause dysphoria or excitement (Kukanich & Papich, 2018).

It's important to note that the potency of an opioid is not synonymous with effectiveness. A potent opioid is one that can achieve the desired effect with the lowest dose. However, this consideration doesn't consider the duration of the effect and potential adverse effects or reactions. This means that a less potent drug might be a better choice if it presents a longer duration of action and fewer adverse effects (Kukanich & Wiese, 2015).

The opioids can be administered through various routes, with the most common ones being intramuscular, subcutaneous (SC), and intravenous (Simon and Steagall, 2016). Other routes, such as oral or rectal, are also a possibility, however, they are less effective. This is because, through these routes, bioavailability and plasma concentrations are lower due to hepatic first-pass metabolism. Nasal or oral transmucosal routes can bypass first-pass hepatic metabolism but have other disadvantages, such as the amount of drug that can be administered, the frequency of administration, and irritation of the mucous membranes (Kukanich & Papich, 2018).

The main advantages of opioid usage include strong analgesia, sedation, minimal vascular effects, and antitussive properties (Kukanich & Papich, 2018; Mwangi *et al*, 2018). They can also be reversed, which is a significant benefit (Kukanich & Papich, 2018). These characteristics contribute to these opioids being considered relatively safe drugs (Simon & Steagall, 2016). On the other hand, opioids are associated with adverse effects, especially during recovery or in the post-operative phase (Mwangi *et al*, 2018). This includes hypoventilation, urinary retention and emesis (Peterson *et al*, 2014). Hypoventilation is a consequence of respiratory depression due to the depression of medullary ventilatory control centres, resulting in a reduced response to increased partial pressures of carbon dioxide. Emesis, on the other hand, its more common when morphine or hydromorphone is used (Koh *et al*, 2014). This can occur due to activation of the chemoreceptor trigger zone (CRTZ) and central dopamine receptors, that stimulate the vomiting centre, as well as gastrointestinal hypomotility and increasement of vestibular sensitivity (Koh *et al*, 2014). Some opioids however, such as butorphanol and methadone, may have antiemetic effects by inhibiting the vomiting centre (Kukanich & Wiese, 2015). Even so, the potential antiemetic effect of these opioids, depend on its type, dose, and administration route (Kukanich & Wiese, 2015). Sometimes, bradycardia may be a side effect of opioid usage in dogs, due to a secondary vagotonic effect. Dogs however can compensate for this, in a way that doesn’t decrease the cardiac output, and anticholinergic drugs are usually not necessary. Bradycardia’s occurrence

varies depending on factors, such as the animal species, the specific opioid agent used, and the dose administered (Kukanich & Papich, 2018).

All these diverse systemic effects are justified due to opioid receptors wide distribution and location throughout the body (Pathan & Williams, 2012). When performing surgical procedures, opioids alone are not sufficient to provide an adequate anesthesia, and a diverse protocol is always required. This is because Aδ nociceptors, responsible for acute and localized pain, are not effectively affected by appropriate opioid doses. Opioids primarily act on C fiber nociceptors, which are characterized by slower conduction and are responsible for diffuse and dull aching pain (Kukanich & Papich, 2018).

2.3.3- Methadone

Methadone is a drug belonging to the opioid group, being classified as a synthetic pure opioid agonist (Kukanich & Wiese, 2015). It acts as an μ opiod agonist and N-methyl-D-aspartate (NMDA) receptor antagonist (Warne *et al*., 2013). It's methadone's action in this last receptor, that decreases tolerance from developing opiate related effects (KuKanich & Papick, 2018). Its composition consists of two enantiomers, S-methadone (d-isomer) and R-methadone (l-isomer) (Bortolami *et al*., 2012; Kapur *et al*., 2011). The d-isomer acts on the NMDA receptor antagonizing it. The l-isomer in turn has an agonist action on opioid receptors, being the principal responsible for the analgesic effect (Bortolami *et al*., 2012; Fishman, 2002). Methadone also promotes blockade of nicotinic cholinergic receptors α3β4 (Warne *et al*., 2013). It's the combination of all these action mechanisms that make this drug have such a strong analgesic effect, being therefore indicated in the treatment of chronic or severe pain (Warne *et al*., 2013). In addition to its strong analgesic effect, methadone also presents antitussic properties, as well as dose dependent sedation (Kukanich & Wiese, 2015; Trimble *et al*., 2018). Consequently, methadone's integration as part of pre-anesthetic protocols, in association with other anesthetic drugs, has become increasingly prevalent (Slingsby *et al*., 2015). An advantage of methadone compared to other opioids, such as morphine, is that it presents less neurotoxicity (Fishman. S, 2002). This is due to the fact that, it does not lead to the production of metabolites (Cardozo, 2014; Monteiro *et a*l., 2008). However, being methadone an opioid, it still presents some adverse effects (Amon *et al*., 2021). These are characterized by bradycardia, sedation and hypothermia (Amon *et al*., 2021). A dose dependent respiratory depression might occur as well, however often can be avoided if the appropriated dosages are respected (Cardozo *et al*, 2014; Kukanich *et al*, 2018). Less frequently, it also might cause, dysphoria, panting, hypotension, decreased cardiac output and

increased systemic and coronary vascular resistance (Monteiro. E *et al*l., 2008). Contrary to what happens with other opioids, vomiting and nausea do not seem to be side effects, following methadone administration. (kukanich *et al*., 2005; Monteiro *et al*l., 2008). This might be due to its effect in inhibiting the vomiting center (Kukanich & Wiese, 2015).

Contrary with what happens in humans, methadone in canine species presents high clearance rate, being therefore eliminated from the body faster (Maiante *et al*, 2009). Scientific studies conducted in dogs, indicate also that the elimination half-life in this species is short, varying between 1.75 and 4.33 hours when administered IV ou SC, in the dosage of 0.5 mg/kg (Kukanich *et al*., 2005). However, this is still a longer elimination half-life time, compared to what is observed when the same dosage of morphine is administered IV (Credie *et al*., 2010).

Since methadone has a high oral bioavailability in humans, the oral route is one of the most commonly used (Alinejad *et al*, 2015). In dogs and cats however, methadone exhibits a lower oral bioavailability, making the IM, IV and SC administration routes the best administration options (Kukanich & Papich, 2018). In a study carried out by Ingvast-Larsson *et al*, (2010) it was observed that IV methadone administration, has a smaller terminal half-life (3.9 ± 1.0 hours) compared with the SC administration (10.7 ± 4.5 hours). Additionally, was noted that SC administration, despite having a longer terminal half-life, less plasma fluctuations and a higher bioavailability, presented a smaller maximal plasma concentration (C_{max}) in comparison with IV administration (Ingvast-Larsson *et al*, 2010). In another study, conducted by Ferreira *et al*, (2011) the oral transmucosal efficiency was evaluated in cats (Ferreira *et al*. 2011). It was concluded that administration by this route at a dose of 0.6 mg/kg results in a lower C_{max} peak, but a lasting antinociceptive effect, of 4 hours, making this route a considerable option for perianesthesic administration in cats (Ferreira *et al*. 2011).

Regarding dosages, methadone should be administered in the dose of 0.1-0.5 mg/kg IM or 0.1-0.3 mg/kg IV., both for dogs and cats, to provide adequate analgesia (Allerton, 2023).

In coatis (*Nasua nasua*), to the author's knowledge, there are two report of methadone usage in which the doses used were of 0,2 mg/kg and 0.3 mg/kg IM (Thomas *et al*, 2021; Vinyals *et al*, 2015).

2.3.4- Butorphanol

Butorphanol is a drug classified as an opioid, more specifically a mixed antagonist/agonist opioid, due to its agonist action in the κ receptors, and antagonist action in

the μ receptors (Murdock *et al*, 2020). It has an onset of action of 10 to 15 minutes, yet a small antinociception duration of about 1 to 3h (Warne *et al*., 2013) (Johnson *et al*. 2007). Butorphanol possesses sedative, analgesic, and antitussive properties (Kukanich & Papich, 2018). It can be administered by the oral (PO), intravenous, subcutaneous, and intramuscular routes, with the latter being the most commonly used (Wells *et al*., 2008). Oral administration, although less common due to its reduced bioavailability and consequently lower analgesic efficacy, is the preferred method when seeking antitussive action (Kukanich & Papich, 2018). Similar to methadone, butorphanol also demonstrates a Ceiling Effect, where higher doses do not result in further antinociceptive effects (Leppänen *et al*., 2006; Wells *et al*., 2008).

In comparison to other pure μ agonist opioids, butorphanol exhibits less respiratory depression, bradycardia, as well as cardiovascular effects (Cho *et al*., 2023; Gultiken *et al*., 2022). However, some possible adverse effects of butorphanol administration include sedation, dysphoria, decreased gastrointestinal motility, constipation, and mydriasis (only in cats). These effects are more common when the appropriated dosages are not respected, or animals present some preexisting health condition (Kukanich & Papich, 2018).

Wells *et al*, (2008), conducted a study on the pharmacodynamics of butorphanol, when administered intramuscularly in cats. This study revealed that butorphanol is rapidly absorbed, taking approximately 0.35 ± 0.14 hours to reach peak concentration. The mean peak concentrations were 132.02 ± 87.35 ng/mL, and the terminal half-life was 6.28 ± 2.77 hours (Wells *et al*., 2008).

For both dogs and cats, the recommended dosage is 0.2-0.5 mg/kg IV/IM/SC to provide analgesia (Allerton, 2023). Due to the ceiling effect, dosages above 0.8 mg/kg, don´t produce any further effects (Kukanich & Papich, 2018). Additionally in dogs, butorphanol can be administered in the dose of 0.05-0.1 mg/kg IV/IM/SC for its antitussic properties (Allerton, 2023).

Regarding coatis (*Nasua nasua*), three studies were found describing buthorphanol administration. The doses used ranged from 0,1 to 0,35 mg/kg IM (Fehr *et al*, 2018; Georoff *et al*, 2004; Nascimento *et al*, 2021).

2.4- Anesthesia in Coatis

Regarding venous accesses in this species, the cephalic and saphenous veins are the most commonly used for catheterization (Fonseca *et al*., 2017; Minto *et al*., 2017; Thomas

et al., 2021). Fonseca *et al*. (2017) reported the use of a 22G catheter for cephalic vein cannulation in coatis, while Vinyals *et al*. (2015) documented the use of a 24G catheter (Fonseca *et al*., 2017; Vinyals *et al*., 2015). As for endotracheal intubation, Vinyals *et al*. (2015) reported using a 4.5 mm endotracheal tube (Vinyals *et al*., 2015). However, there are few records of this procedure being performed in this species, and there are no reports regarding specific challenges or difficulties that may arise.

Concerning anesthetic protocols for coatis, there is a significant lack of information. This is due to the fact that keeping coatis as pets is prohibited in many countries, and the majority of studies conducted on this topic involve animals from the wild (Vinyals *et al*, 2015).

Given that there is no single drug capable of ensuring a good anesthetic plan, combinations of various drugs that act synergistically are commonly used (Kunz *et al*., 2021). This approach allows for the reduction of the dose of each drug and, consequently, their adverse effects, while benefiting from the advantages of each (Pascoe and Steffey, 2018). This becomes even more relevant since the use of a single drug may induce a state of unconsciousness and immobility without altering nociception capacity, potentially leading to increased pain and longer recovery time (Pascoe and Steffey, 2018).

In anesthetic protocols for coatis, the drug classes most frequently administered in pre-medication include alpha-2 adrenergic agonists, benzodiazepines, dissociative agents, and opioids (Fonseca *et al*., 2017). Alpha-2 adrenergic agonists provide muscle relaxation and good sedation and analgesia, while opioids offer a superior analgesic effect and some sedation (Kunz *et al*., 2021). Dissociative agents, in turn, lead to a change of awareness and in some species sedation as well as analgesia (Tranquilli & Grimm, 2015). They also have a wide safety margin, and their use is particularly beneficial in the case of fractious animals (Pascoe and Steffey, 2018).

Among the alpha-2 adrenergic agonists, xylazine is very commonly described in coatis. Although its use has been decreasing, there are several records of its use in coatis (Barros *et al*, 2009; Freitas *et al*, 2008; Nascimento *et al*, 2021; Martini *et al*, 2017; Queiroz *et al*, 2010; Silva *et al*, 2018). Its administration is often combined with opioids or dissociative agents to generate a neuroleptanalgesic effect (Tranquilli and Grimm, 2015). It is frequently administered in conjunction with ketamine (Barros *et al*, 2009). Xylazine has some advantages as it produces muscle relaxation and sedative and analgesic effects (Nascimento *et al*., 2021). However, the use of this drug is associated with an increase in certain undesirable effects such as bradycardia, hyperglycemia, transient hypertension followed by hypotension, and increased urine volume (Nascimento *et al*., 2021).

In a study conducted by Martini *et al*. 2017, where different anesthetic protocols were compared in coatis, it was found that groups receiving xylazine exhibited cardiac instability with an increased incidence of sinus arrhythmias as well as bradycardia, compared to other groups (Martini *et al*., 2017). In this study, xylazine was administered in combination with ketamine at doses of 2 mg/kg and 10 mg/kg, respectively (Martini *et al*., 2017). Another article by Nascimento *et al*. compares the use of dexmedetomidine and xylazine in association with butorphanol and ketamine in coatis (Nascimento *et al*., 2021). It was concluded that despite both protocols being safe, the use of dexmedetomidine is more effective compared to xylazine, as it provides a longer sedation time, better anesthetic quality, and good anesthetic recovery (Nascimento *et al*., 2021).

At times, instead of alpha-2 adrenergic agonists, the administration of benzodiazepines is chosen as they provide greater cardiovascular stability (Fonseca *et al*., 2017). In coatis, the most commonly used benzodiazepines are midazolam and zolazepam.

Midazolam is commonly used in anesthetic pre-medication since, it can be administrated intravenously, but is also rapidly absorbed via intramuscular administration. It has minimal cardiovascular effects, potentially causing only slight bradycardia and a decrease in blood pressure (Rankin, 2015).

Zolazepam, in turn, is also a common choice as part of anesthetic protocols. However, its commercial formulations are already combined with the dissociative agent tiletamine, making individual administration not possible (Pascoe and Steffey, 2018). The fact that these two drugs exist only in combination allows to reduce the dose of each one, while still benefiting of the sedative effects of each (Pascoe and Steffey, 2018). It may result, however, in a longer duration of effect than the desired (Pascoe and Steffey, 2018). Also, in case an anesthetic reversal is needed, this combination of drugs presents another disadvantage (Posner, 2018). This is because it is only possible to reverse zolazepam, so if significant amounts of tiletamine are still present in the blood plasma, it may result in a poor recovery (Posner, 2018). It is important to note that in cats, tiletamine's duration of action is shorter than of zolazepam, whereas in dogs, the opposite is true (Pascoe and Steffey, 2018). To date, there is no information available for coatis regarding which drug exhibits a longer duration of effect. Regarding its efficacy as an anesthetic in coatis, this drug combination leads to a reduced induction time and low incidence of vomiting or nausea (Conforti *et al*., 2017). However, it may result in hypersalivation and hypothermia, as well as a prolonged recovery time (Conforti *et al*., 2017; Martini *et al*., 2017).

Regarding dissociative agents, ketamine is the most commonly used in coatis (Kunz *et al*., 2021). It has a wide safety margin in healthy animals and its usage is recommended for animals in which restraint and control are limited (Posner, 2018). This is attributed to its rapid induction of a general anesthetic state, leading to a fast and safe chemical restraint of the animal (Nascimento *et al*, 2021; Pascoe and Steffey, 2018). As coatis are considered a wild species with limited tolerance for manipulation, the use of dissociative agents becomes an important component of anesthetic protocols (Pascoe and Steffey, 2018). However, a disadvantage of this drug class, is that in certain species, it may lead to central nervous system excitement and, in more extreme cases, seizures (Pascoe and Steffey, 2018). It can also result in muscle rigidity, necessitating administration alongside benzodiazepines or alpha-2 adrenergic agonists (Barros *et al*., 2009, Nascimento *et al*., 2021).

Finally, regarding opioid usage in coatis, there is little information available. There are a few mentions to the usage of butorphanol, morphine, methadone and fentanyl, mainly as part of anaesthetic pre-medication or an analgesic rescue during surgical procedures (Mintos *et al*, 2017; Thomaz *et al*, 2021). Although, its usage appears safe and might benefit the anaesthetic protocols more information is needed.

Concerning drug's dosages, little information exists regarding coatis. There is a scarcity of specific data, being often necessary the extrapolation of doses from other species (Kunz *et al*, 2021). The raccoon, being in the same family as coatis and more commonly kept as a pet, is a frequently used species for such extrapolations, providing valuable insights into anesthesia (Vinyals, 2015). Additionally, dogs serve as another model for dose extrapolation (Fonseca *et al*, 2017; Kunz *et al*, 2021).

3- Objectives

The aim of this study was to understand the analgesic efficacy of the opioids butorphanol and methadone at various anesthetic moments in elective surgeries in coatis, by answering to the following questions:

- What’s the influence of these drugs on cardiopulmunary parameters during elective reproductive procedures?
- How long do anaesthetic and surgical last when these drugs are administered?

This study aimed to demonstrate that these two drugs, besides being safe in this species, also provide good analgesia, thus making them a suitable option for invasive procedures. To the author's knowledge, there is no literature regarding the efficacy and effects of these two drugs as part of anesthetic protocols in this species.

Chapter II

1- Materials and methods

This study was submitted to the Ethics Committee of the Lusófona University (FMV-ULHT) for appreciation under the process n. 89/2018. Besides internal validation, there was also an informed consent signed by the responsible of the sanctuary where the animals belonged. All procedures were conducted in accordance with the Standard Operating Procedures and ethical guidelines for animal welfare outlined in the Deontological Code of FMV-ULHT. The reason behind the procedure was behavioural and control of the exotic species in agreement with the European Law for exotics species control and conservation (Regulation (EU) Nº 1143/2014).

1.1- Study Population

For this study, seven adult coatis (*Nasua nasua*) were used, of which four were females and three males. These animals came from sanctuaries and ranged in age from 1 to 3 years old. For this study, the animals were randomly distributed into two groups, Group 1 (G1) or Group 2 (G2) and were submitted to the elective procedures of ovariohysterectomy and orchiectomy. G1 and G2 differed only in the opioid used in pre-medication, being that animals in G1 received methadone and the ones in G2 received butorphanol.

1.2- Inclusion and exclusion criteria

This study focused exclusively on animals belonging to the *Nasua nasua* species, as so, only animals belonging to this specie were included. All the candidates had to be eligible for orchiectomy or ovariohysterectomy, thus, only sexually mature animals over 1 year of age were included. Upon arrival at the veterinary hospital and prior to the surgical procedure, all animals underwent a physical examination and hematological and biochemical analyses. Only animals with normal results in these examinations, and classified according to the American Society of Anesthesiologists (ASA), as ASA I in terms of anesthetic risk, were included in the study.

Any animals showing clinical signs or diagnosed with chronic or ongoing diseases were excluded, as well as, if presenting any abnormalities in pre-anesthetic bloodwork.

1.3- Clinical Protocol

All the animals were distributed into two groups (G1 or G2). G1 consists of two females and two males, while G2 consists of two females and one male. Animals in G1 received methadone and the ones in G2 received butorphanol. Different parameters including heart rate, respiratory rate, systolic arterial pressure, mean arterial pressure, diastolic arterial pressure, oxygen saturation and end-tidal carbon dioxide, were collected at specific timepoints during the procedures. The time points used for data collection were: surgical clamps (T1), skin incision (T2), tunics/ abdominal incision (T3), 1st pedicule/ testicule incision (T4), 2nd pedicule/ testicule (T5), subcutaneous suture (T6), skin suture (T7). The perianesthetic times were recorded as well, and include: time from premedication to loss of standing reflex (P1), time of induction and intubation (P2), surgery time (P3), total time of anesthesia (P4), extubation time (P5) and recovery time (P6). The following diagram represents all the steps carried out during the clinical protocol.

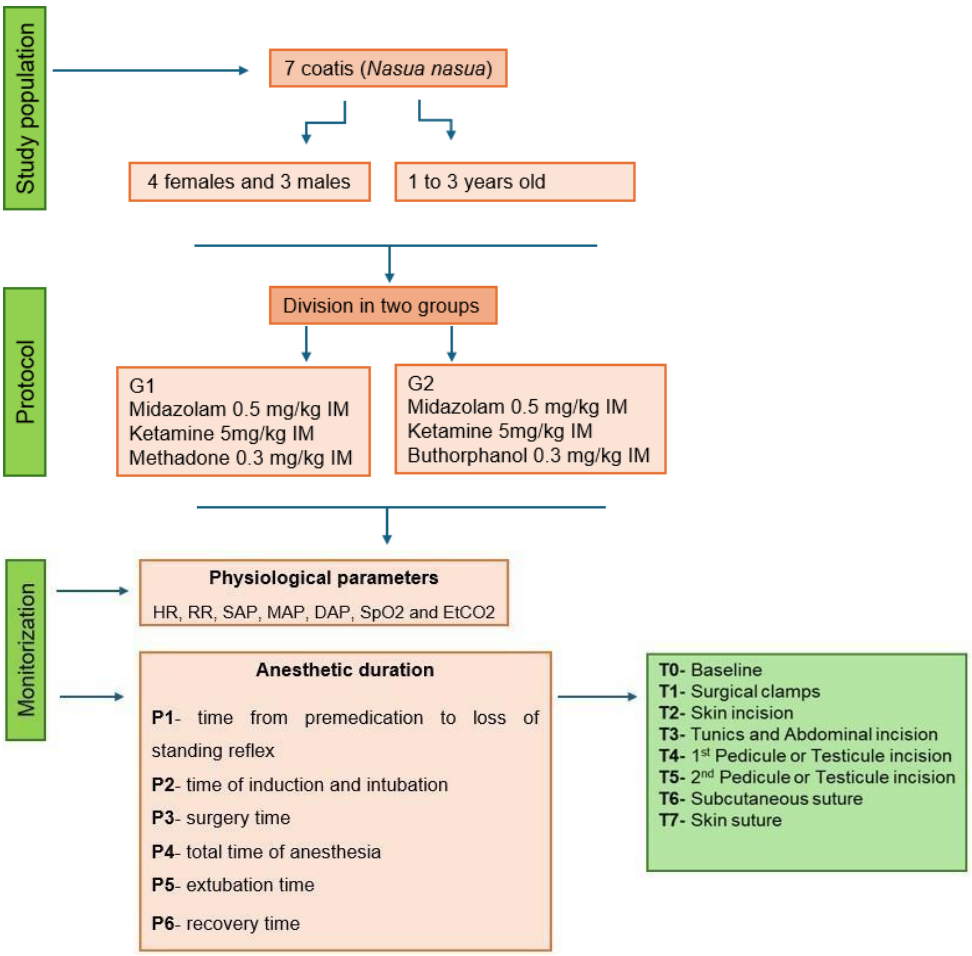


Figure 1 - Diagram representing the clinical protocol. HR- heart rate; RR- respiratory rate; SAP- Systolic arterial pressure; MAP- Mean arterial pressure; DAP- Diastolic arterial pressure; ETCO2- end-tidal carbon dioxide; SPO2-oxygen saturation.

1.4- Pre-anaesthetic preparation

Food was withheld 8h prior to surgery. Blood analyses (complete blood count and biochemical profile) and physical examination were performed after pre-medication due to the feral nature of the animals. Baseline values (HR, SPO_2, $ETCO_2$, MAP, SAP, DAP and RR) were taken right after the loss of standing position, after pre-medication. These baseline values served as references to assess changes in the parameters during the different phases of the surgery. After confirming the health status, the animals were prepared for surgery. Paramentation started with pre-oxygenation with 100% oxygen using a face mask and flowmeter settings at 4L/min. A pulse-oxymeter was constantly used to check the pulse rate and SpO_2. First, the fur was clipped on the front left limb for vascular access and after proper aseptic technique, a 22G cannula (Introcan ®, BBraun,, Germany) was inserted in the cephalic vein. This venous access allowed the injection of induction agents and crystalloids (Lactated Ringers [BBraun, Portugal) for fluid therapy (5 mL/Kg/h). The fur on the ventral abdomen was also clipped, followed by skin cleaning and asepsis.

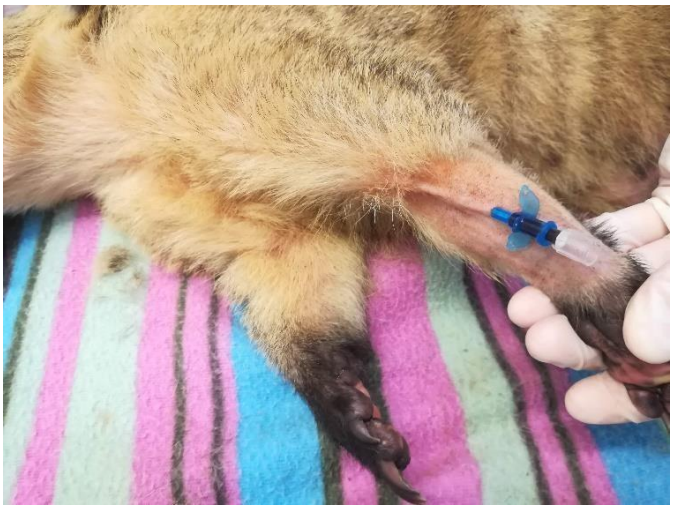


Figure 2 - Illustrative figure of the catheterization of one of the coatis of this study, in the cephalic vein. Photographs provided by Dr. Rui Patrício.

1.5- Anesthetic protocol

Each group received a different anesthetic protocol. G1 received IM methadone (Semfortan ® 10mg/ml, Dechra, The Netherlands) (0.3 mg/kg) as part of the anaesthetic protocol, while G2 received IM butorphanol (0.3 mg/kg, Tuborgesic, Zoetis, Spain). The rest of

the protocol was identical for both groups. Pre-medication included the administration of midazolam (Dormazolam® 5 mg/ml, Dechra, The Netherlands) (0.5 mg/kg), ketamine (Nimatek®, Dechra, Bladel, The Netherlands) (5 mg/kg), and either metadone or butorphanol, all given via IM. Induction was performed using alfaxalone (Alfaxan® 10mg/ml, Jurox, Ireland) (1-2 mg/kg) intravenously (IV) *ad effectum* to allow loss of mandibular tonus and swallow reflex and allow endotracheal intubation. The larynx was visualized using a Macintosh laryngoscope and 45 seconds after 1 puff of lidocaine spray (Xilonibsa, xylocaine spray 100 mg/ml, Sintra, Portugal), the trachea was intubated using a 5 to 5.5 ID tracheal tube (tubo PVC, Kruuse, Denmark). Anesthesia was then maintained with isoflurane (Isoflurin®, Vetpharma animal health, S.L., Barcelona, Spain) (1-1.5% vaporizer settings) delivered in 100% oxygen (oxygen flow: 200 ml/kg/min). The anesthesia protocol is summarized in Table 4 and Table 5.

Table 4 - Group 1 anesthetic protocol with methadone.

Group 1 (G1)		
Pre-medication	Induction	Maintenance
Midazolam(0.5 mg/kg) IM	Alfaxalone (1-2 mg/kg) IV	Isoflurane (1-1.5%) in 100% oxygen
Ketamine (5 mg/kg) IM		
Methadone (0.3 mg/kg) IM		

Table 5 - Group 2 anesthetic protocol with buthorphanol.

Group 2 (G2)		
Pre-medication	Induction	Maintenance
Midazolam (0.5 mg/kg) IM	Alfaxalone (1-2 mg/kg) IV	Isoflurane (1-1.5%) in 100% oxygen
4Ketamine (5 mg/kg) IM		
Butorphanol (0.3 mg/kg) IM		

After the implementation of the anesthetic protocol, the animals were transported to the surgical room where the surgical site was aseptically prepared one last time before surgery.

In the surgery room, each animal was connected to a T-piece anesthetic circuit and anesthesia was maintained with 1-1.5% isoflurane vaporized in 100% oxygen (O_2 flow= 1.8L/min) in order to maintain a correct anesthetic depth of anesthesia for the surgical procedure (orchydectomy or ovariohytecrectomy). The depth of anesthesia was intra-operatively assessed according to Guedel's (1937) [Signs and Stages of Anesthesia based on 'Ether' anesthesia in cats.] and kept between the light and medium stages. Admixture of oxygen and medical air was not performed as the FiO_2 was maintained between 70 and 50% and the surgical procedures implied small duration. The multiparametric monitoring was attached to the animal and continuous ECG (electrocardiogram), HR, pulse rate, RR, SpO_2, $ETCO_2$, non-invasive blood pressure (cuff placed in the right arm, mid antebrachium) and esophageal temperature were continuously monitored. Temperature was maintained with a heated pad (Carbon vet, BBraun, Spain) and oscillated between 36.1 and 37.5ºC. No adverse events occurred during or after the surgical procedures in any group. All animals recovered well and were discharged the day after the procedure, after feeding re-start.

1.6 – Surgical Technique

1.6.1 -Ovariohysterectomy

The technique used was an ovariohysterectomy, through a midline incision. Thus, an incision of about 4 to 8 cm was made, both at the skin and subcutaneous levels, until the *linea alba's* visualization was possible. Subsequently, an incision was made with a scalpel on the *linea alba* to access the abdominal cavity and locate the uterus. Once found, the left uterine horn was pulled caudally and medially, and the suspensory ligament of the ovary and the left ovary were identified. The ovary was then exteriorized, and two hemostatic clamps were placed, one on the ovarian pedicle, and another on the proper ligament of the ovary. A ligature was then placed caudally to the two hemostatic clamps on the ovarian pedicle, and the most caudal clamp was removed. A second ligature was then made below the first, and a hemostatic clamp was placed on the suspensory ligament of the ovary. The ligatures were made using an absorbable 2/0 suture material (Monosyn®, Braun, Melsungen, Germany). Subsequently, the pedicle was transected between the clamp and the ovary. The same exact procedure was carried out for the right ovary. After each pedicle transection, it is essential to confirm if it was completely removed and check for the presence of hemorrhage. The broad ligament was then separated from the uterine horn. This involved an opening in the ligament, adjacent to the uterine body and the uterine artery and vein, and the placement of a clamp, on each side of the broad ligament before cutting. Then, cranial traction was applied to the uterus, and a figure-

eight suture was placed on the uterine body, with another ligature cranially to the cervix. A hemostatic clamp was placed cranially to the ligatures, and the section was made between the clamp and the proximal ligature. The absence of hemorrhage was then confirmed, and since none was present, the uterine stump was repositioned in the abdominal cavity. Finally, a three-layer closure with intradermal skin sutures was performed. Since descriptions of this technique in Coatis are limited, dogs guidelines were used. (McPhail, 2013)

1.6.2- Orchiectomy

For the orchiectomies of male coatis, a pre-scrotal open technique was employed. Initially, the animals were positioned in dorsal recumbency, and the presence of cryptorchidism was ruled out. Scrotal pressure was applied to push one of the testicles into the pre-scrotal area, and an incision at the cutaneous and subcutaneous levels was made, as well as another, at the level of the spermatic fascia. The testicle was then exteriorized, and an incision was made in the parietal vaginal tunic without incising the *tunica albuginea*. A hemostatic clamp was placed across the vaginal tunic at the point where it attaches to the epididymis, and the ligament of the tail of the epididymis was manually separated from the tunica. Subsequently, the spermatic cord was identified, and ligatures were placed around the vascular cord and ductus deferens, followed by an encircling ligature around both, using absorbable 2/0 suture material (Monosyn®, Braun, Melsungen, Germany). A hemostatic clamp was then placed on the spermatic cord, and both the ductus deferens and the vascular cord were transected between the hemostat and the ligatures. Hemorrhage was then checked for, and the cord was returned to the inside of the tunic. Finally, one last ligature was applied to encircle the cremaster muscle and the tunic. For the second testicle, the same technique was employed, using the already existing incision. After the removal of both testicles, the fascia was closed with a continuous suture, and the skin was closed with an intradermal suture. Since descriptions of this technique in Coatis are limited, dogs guidelines were used. (McPhail, 2013)

1.7 - Statistical Analysis

In this study, values of clinical parameters were collected over different anesthetic moments (Baseline, surgical clamps, skin incision, Tunics/ abdominal incision, 1st pedicule/ testicle incision, 2nd pedicule/ testicle incision, subcutaneous suture, skin suture). These parameters included RR, HR, SAP, MAP, DAP, SpO_2, and $EtCO_2$. Furthermore, the time of each anesthetic phase (P1: time to loss of standing reflex, P2: induction and intubation, P3:

surgery time, P4: total time of anesthesia, P5: time to extubation, P6: recovery time) was recorded for each study animal.

All data was initially registered in the anesthetic records and then transposed to Excel spreadsheet Software®, that was also used for basic calculation and graphics. A distributive analysis of the data was performed by calculating the mean and standard deviation. This allowed a better understanding of the central tendency and variability within the data set.

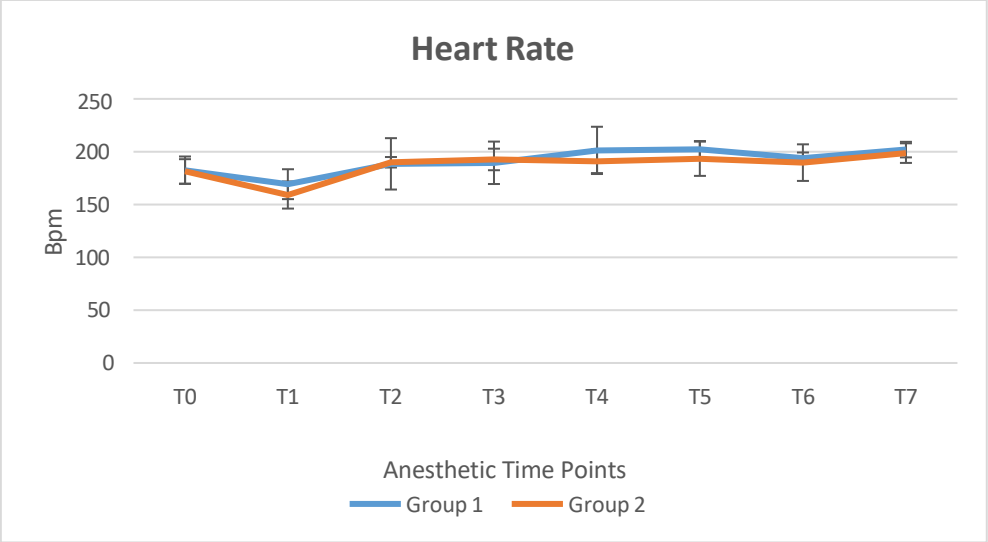
Chapter III

1- Results

1.1.-Physiological parameters

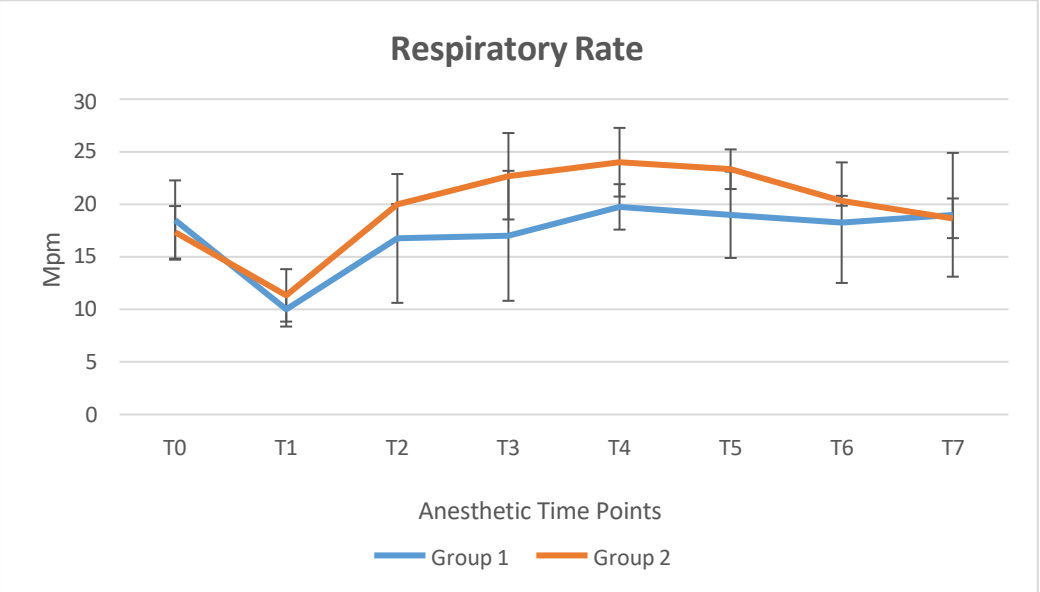
The coati population (*Nasua nasua*) under study was composed by 4 females (4.75± 0.36kg) and 3 males (5.3 kg ± 0.58kg). No changes were observed on the hematological and biochemistry profile of each animal. Data from white nosed coatis **(**Rovirosa-Hernandez *et al*., 2012) was used as reference for hematological values. No adverse events were seen during the implementation of the anesthetic protocol.

Information about the physiological parameters obtained in coatis of both groups under study can be observed in the following Figures of this chapter, that show the variation of all the studied clinical signs (HR, SAP, MAP, DAP, $ETCO_2$, SPO_2 and, RR), collected at the defined time points during surgery. Some data are missing due to monitor malfunction.



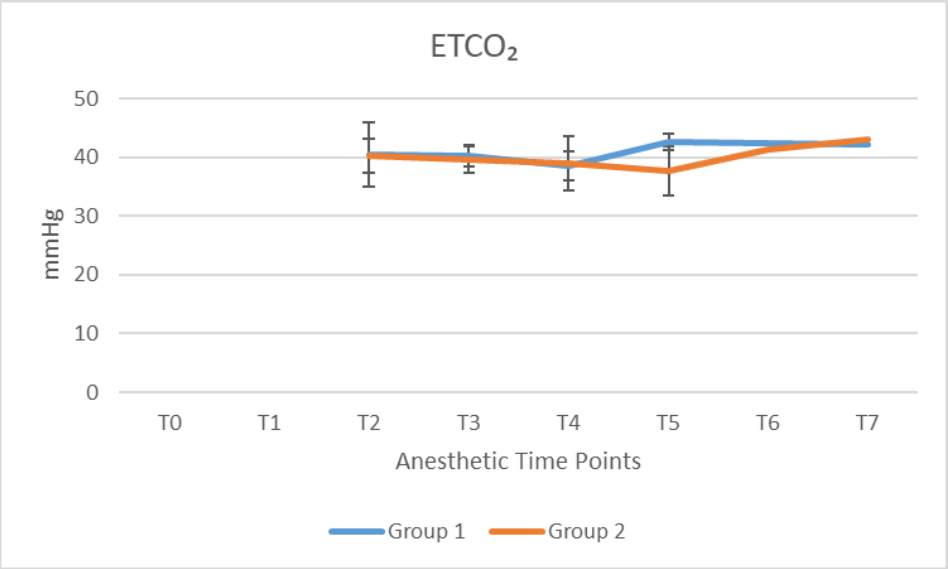
Graph 5 - Mean and standard deviation of HR throughout the anesthetic moments in Group 1 and Group 2.

Regarding HR, as can be seen in graph 5, both groups exhibit a minor decline at timepoint T1, followed by a slight and progressive rise from T2 to T7.



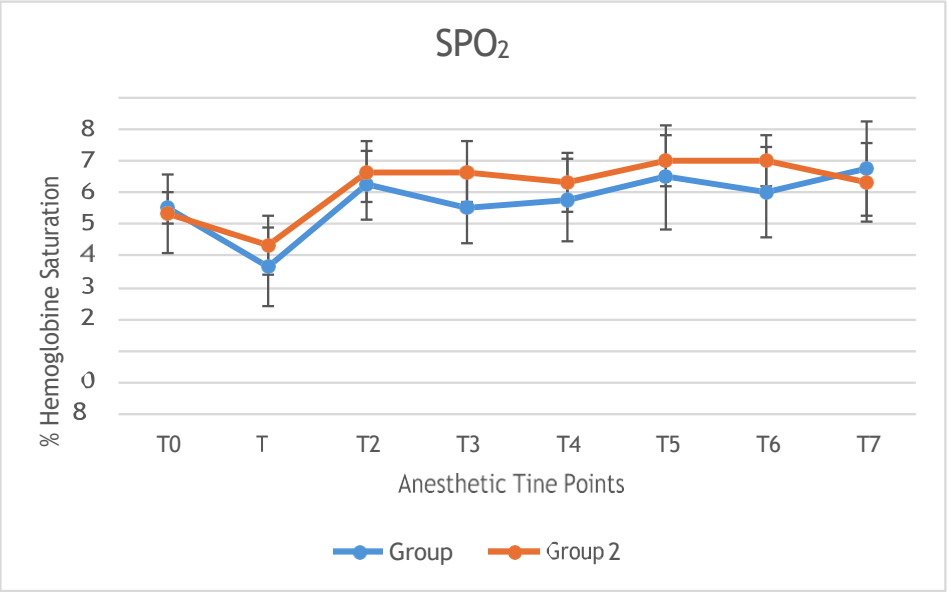
Graph 6 - Mean and standard deviation of RR throughout the anesthetic moments in Group 1 and Group2.

Both groups experienced a pronounced decrease in RR at T1, followed by an increase from T2 to T4, returning to baseline values by the end of the procedure. Apart from T1 and T7, G2 exhibits, slightly higher, respiratory values, compared to G1. All this is depicted in Graph 6.



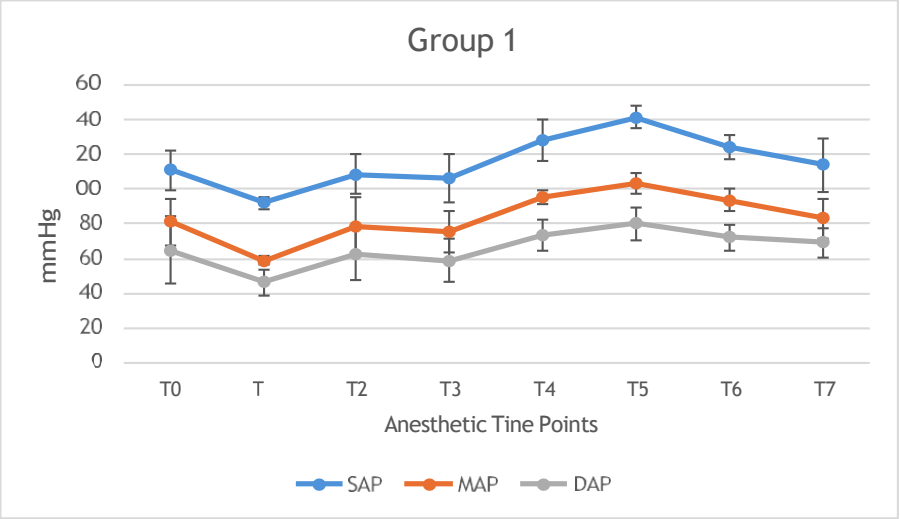
Graph 7 - Mean and standard deviation of ETCO2 throughout the anesthetic moments in Group 1 and Group 2.

The $ETCO_2$ parameter was only obtained after endotracheal intubation. As Graph 7 shows, this parameter was only recorded from T2 forward due to a monitor malfunction. In the recorded times, it remained consistently stable for both groups, although with slightly variances. From T4 onward, in G1, a slight increase can be observed. In G2, there is a small decrease in T5, but it is then followed by a slightly increase till T7.

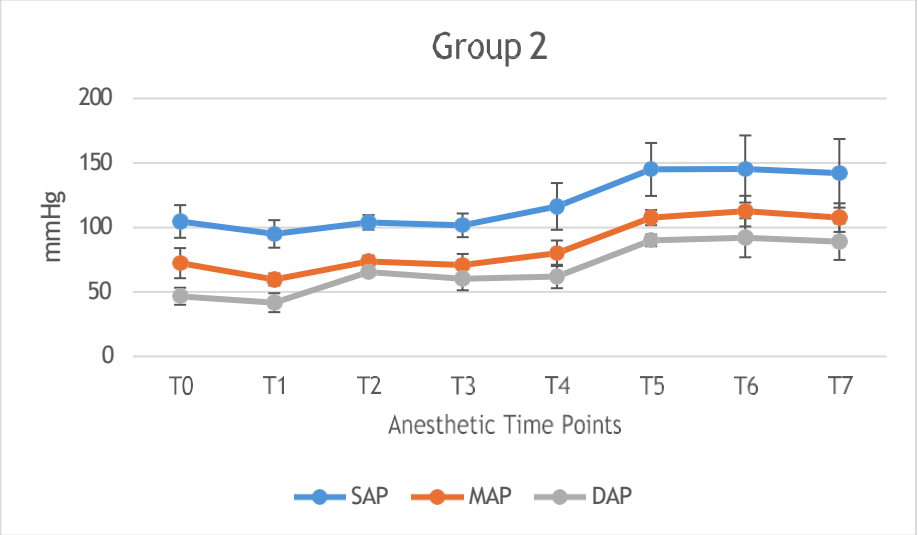


Graph 8 - Mean and standard deviation of SPO2 throughout the anesthetic moments of Group 1 and Group 2.

Regarding SPO_2, there is a decrease in this parameter in T1, for both groups, followed by an increase in T2, and remaining stable for the rest of the procedure, as can be seen in Graph 8.



Graph 9 - Average SAP, MAP and DAP throughout the anesthetic moments of Group 1.



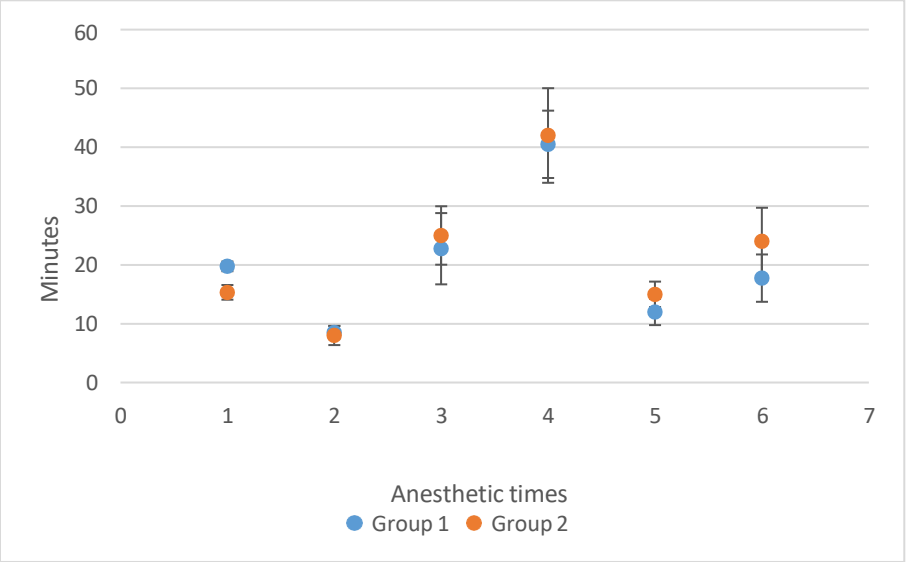
Graph 10 - Average SAP, MAP and DAP throughout the anesthetic moments of Group 2.

The SAP, MAP, and DAP parameters, for G1, demonstrate a pronounced decrease during T1, followed by an increase from T2 until T5 followed by a return to baseline values at T7. As for the G2, these parameters, also display a decrease in T1. It then is followed by a significant increase from T3 to T5 (probably due to visceral manipulation), subsequently remaining stable until T7 but never returning to baseline values. As intra-operative hypertension wasn't observed, no analgesic rescues were needed in the animals of this study.

1.2 - Anesthetic Time

Graph 11 contains data regarding the duration of each anesthetic phase. As mentioned earlier, the different anesthetic phases (P1 to P6).

In G1, the average P1 time was longer than G2. P2, in other hand, was very similar between groups. For both P3, P4, P5 and P6, G1 exhibited shorter times than G2. The time from premed to loss of standing reflex' was shorter in G2 than G1.



Graph 11 - Comparison of the anesthetic times for the group 1 and 2

Chapter IV

Discussion

The goal of the present study was to demonstrate the analgesic efficacy of two opioids, butorphanol and methadone, used as part of a pre-medication protocol, and studied during different surgical stages in coatis (*Nasua nasua*). More precisely, this study aimed to show how both opioids influence intra-operative cardiopulmonary variables during specific surgical moments, and how long anesthetic and surgical times last when each drug is administered. To the author's knowledge, there is no literature on the efficacy and effects of these two drugs as part of anesthetic protocols in this species.

The studied population consisted of 7 coatis (*Nasua nasua*) between 1 and 3 years of age, all from sanctuaries. Of this population, four were females and three were males. The average weight of the males was 5.3 kg ± 0.58, while that of the females was 4.75 kg ± 0.36. This weight falls within the normal range for the species (Queiroz *et al*., 2010). Prior to the surgical procedures, all animals underwent blood analyses. All values were within the normal range for the species, according to existing data in white-nosed coatis (Júnior *et al*., 2017; Rovirosa-Hernández *et al*., 2012), however, more studies should be conducted to more precisely determine the values for ring-tailed coati. The existing studies present small samples and can be influenced by various factors, such as diet, stress, and health status (Rovirosa-Hernández *et al*., 2012). For instance, Júnior *et al*. (2017) reported that animals accustomed to human presence had higher glucose and triglyceride levels, as well as lower total protein levels, compared to animals without human contact. The latter, in turn, had higher urea levels. These differences might be related to some of the factors mentioned above, such as diet, since animals with more contact with humans tend to have diets richer in carbohydrates and sugar and poorer in protein, and vice versa (Júnior *et al*., 2017). The coati population under study ranged-free in the sanctuary, ate an omnivorous diet and were used to the human presence.

The surgical procedures performed in this study were orchiectomy and OVH. These are considered elective procedures that cause moderate pain. Since coatis are considered an invasive species in Portugal (Decreto-Lei n. º 92/2019), neutering them becomes even more pertinent, as it ensures they cannot reproduce.

As previously mentioned, the drugs studied were butorphanol and methadone. For canines and felines, the dosage range for analgesia is 0.1 to 1 mg/kg IM / 0.1-05 mg/kg IV for methadone and 0.2 to 0.5 mg/kg IV/IM/SC for butorphanol (Kukanich & Papich, 2018; Allerton, 2023). For coatis (*Nasua nasua*), two references were found regarding the administration of

butorphanol, which used a dose ranging from 0.1-0.2 mg/kg IM (Fehr *et al*, 2018; Nascimento *et al*., 2021). Additionally for white-nosed coati (Nasua narica), a dose of 0.35 mg/kg, was also reported (Georoff *et al*, 2004). For methadone, two doses were reported: 0.2 and 0.3 mg/kg IM (Thomas *et al*., 2021; Vinyals *et al*., 2015). In this study, the doses used were 0.3 mg/kg IM for both drugs. These were administered along with ketamine and midazolam to ensure a balanced anesthetic protocol. To our knowledge, this is also the first study reporting the use of alfaxalone for induction in coatis (*Nasua nasua*). The used ranged from 1 to 2 mg/kg was proven safe and effective, as reported in cats and dogs (Kato *et al*, 2021; Warne *et al*, 2015).

The efficacy of the protocol was assessed by monitoring certain physiological parameters, namely HR, SAP, MAP, DAP, $ETCO_2$, SPO_2, and RR. Since coatis are potentially aggressive animals, there is no information, to the author's knowledge, on the baseline values of these parameters in animals that have not been previously sedated. The few available data come from studies with small populations and are all conducted on previously sedated animals. In the study by Vinyals *et al*. (2015), lower values (HR: 91; SAP: 98; MAP:79; DAP: 70) were reported, at the beginning of anesthesia compared to this and other studies. This difference may be due to factors such as stress and individual response to anesthetic drugs. In this case, the animal undergoing intervention was reared in captivity, and the protocol used consisted of a combination of ketamine, medetomidine, and methadone at the same doses used for wild coatis. The lack of a stress response may have contributed to the lower clinical values observed in the animal under anesthesia. On the other hand, in the study by Conforti *et al*. (2017), a population of 53 individuals was studied. The protocol used consisted of the administration of tiletamine and zolazepam (Zoletil®). These coatis showed a much higher average of some of the clinical values (HR: 223; RR: 53). This might be not only due to the anesthetic combination of drugs, which have a less depressant effect on the cardiovascular system (Pascoe & Steffey, 2018) , but also due to the stress induced by restraint and handling (Fisher & Romero *et al*, 2019), since they lived in a free-ranging regime, accustomed to human presence but not to handling. The study that showed the greatest similarity with the HR and RR parameters, was conducted by Thomas *et al*. (2021), (HR: 180-200 and RR: 12-20). Concerning the parameters PAD, PAM, PAS, and SPO_2, our results are more in line with the ones obtained by Vinyals *et al*. (2015) (PAD: 85-143, PAM: 66-120, PAS: 57-108, and SPO_2: 92-98). These similarities may be due to common points between studies, particularly regarding anesthetic protocols (all including ketamine and methadone), or the fact that the animals were all accustomed to human manipulation and presence.

At baseline (T0), the HR parameter was similar in both groups, with a mean of 182.5 ±12,96 for G1 and 181.33 ±11,58 for G2. Upon placement of surgical clamps (T1), a significant decrease in this parameter was observed in both groups, although it was more pronounced in G2. At the moment of skin incision (T2), HR increased again to values slightly above baseline levels, probably due to the visceral manipulation and associated nociception, and up to T7, this parameter showed a slight and progressive increase for both protocols. Although there was an increase in this clinical value, it remained within the normal range for the specie. The initial increase observed at T2 may be due to the fact that the skin has numerous nerve endings that cause pain, as Rodríguez *et al*. (2016) observed, that during scrotal skin incision in dogs, isoflurane requirements increase due to the presence of a painful stimulus. According to Keating *et al*, (2020), methadone leads to a decrease in HR. In G1, however, this was only observed at time point T1. The addition of ketamine to the protocol may have contributed to the higher HR values, since it presents a sympathomimetic effect that can increase HR and cardiac output (Fonseca *et al*., 2017). In contrast, butorphanol provides greater cardiovascular stability than methadone (Gültiken *et al*., 2022). This was evident with G2 demonstrating a more stable HR compared to G1, except at time point T1 where both groups experienced a pronounced decrease. This decrease in HR, at time point T1, is consistent with Warne *et al*. (2013), who found that in cats, both during the administration of either methadone or butorphanol, transient bradycardia could occur, prior to the surgical incision, and then stabilizing during surgery.

Concerning blood pressures, a marked decrease was observed in both groups at time point T1, which coincided with the decrease in HR. Regarding MAP, an increase between 8% and 11% was observed at moments T2 and T3, for G1 and T3 for G2. These slight increases are consistent with findings by Kukanich & Papich (2018), who reported that after opioid administration, there can be a slight fluctuation of this parameter by approximately 10%. In both groups, an increase in pressure parameters was observed from T3 till T5. According to Maiante *et al*, (2009), methadone's administration in dogs, led to increases in MAP for up to 60 minutes after its injection. These increases were up to 23% above the baseline value at the 0.5 mg/kg dose. Moser *et al*. (2019), also reported that, when butorphanol is used in cats undergoing orchiectomy, no decreases in blood pressures parameters is verified (Moser *et al*, 2019). This time point also corresponds to the initiation of the ligation and removal of the ovarian pedicles, as well as the testicles. A similar observation was made during OVH in dogs, in two different studies by Höglund *et al*, (2011) and Gomes *et al*. (2023), in which during these surgical steps the blood pressures tended to increase significantly. According to Bubalo *et al*. (2008), the stretching of the abdominal muscles and the traction of the suspensory ligament

are among the most critical factors contributing to pain during an ovariohysterectomy. This might also be explanatory of the increase in blood pressure values observed during this period (Bubalo *et al*., 2008). From T5 onward, the blood pressure values decreased, reaching baseline values, in case of G1, in time point T7. The main indicator of intra-operative nociception is defined by hypertension (SAP>160 mmHg or MAP>120mmHg). There was no need for analgesic rescues in our study as SAP and MAP remained within normal range, despite some fluctuations observed in both groups.

In this study, it was not possible to measure $ETCO_2$ values at time points T0 and T1, for both groups, and therefore it is not possible to establish a baseline value for comparison. For the time points where measurements were possible (T2 to T7), $ETCO_2$ remained stable in both anesthetic protocols and within the expected range (35–45 mmHg) (Maiante *et al*., 2009). Butorphanol does not cause significant respiratory depression (Murdock *et al*, 2020), as μ agonist opioids such as methadone do, so the stability of $ETCO_2$ was expected. Regarding methadone, Garofalo *et al*. (2012), mentions that it can lead to the occurrence of panting, which can cause an increase in $ETCO_2$, due to a decrease in alveolar ventilation (Juodzente *et al*, 2018; Maiante *et al*., 2009), though the same was not verified in this study. The G2 presented slightly lower $ETCO_2$ values, compared to G1.

The SPO_2 parameter remained stable throughout the procedure in both groups, experiencing only very slight and clinically unimportant fluctuations. At time point T1, the lowest values were recorded (G1: 93.6 ±1,24 and G2: 94.3 ±0,94). Despite this decrease, it was not pronounced and corresponded to a decrease in RR that was also observed. At time point T2, SPO_2 increased again to values above 95%, and remained as such till T7. This aligns with findings by Burbaitė *et al*. (2024), who, in a comparative study between butorphanol and buprenorphine, in dogs undergoing ovariectomy, did not detect variations in SPO_2 during butorphanol administration, with values remaining within the reference range (>95%) throughout the procedure. Regarding methadone, Cubeddu *et al*. (2023) found that in dogs also undergoing ovariectomy, SPO_2 remained stable and above 95%.

Regarding RR, baseline values were similar between groups, with G1 presenting 18.5 ±3,77 mpm and G2, with 17.33 ±2,49 mpm. At time point T1, a decrease was observed in both groups. G1 experienced a drop to 10 ±2,49 mpm, while G2 saw a decrease to 11.33 ±2,49 mpm. In the remaining time points, RR increased and remained stable, with only minimal

fluctuations. Warne *et al*. (2013) states that in cats, the administration of both methadone and butorphanol kept RR within the normal range without significant respiratory depressive episodes. This is also consistent with Gomes *et al*. (2018), who observed that administering butorphanol in dogs only led to minimal and clinically unimportant RR changes. Although not observed in the present study, several authors report the occurrence of panting following methadone administration (Garofalo *et al*., 2012; Maiante *et al*., 2008; Menegheti *et al*., 2014). This may be associated with high doses of methadone (Menegheti *et al*., 2014) which can lead to alterations in the hypothalamic thermoregulatory center (Kukanich & Papich, 2018).

Regarding anesthetic and surgical times, butorphanol had a faster onset of action compared to methadone. P1 (pre-med to loss of standing reflex) lasted 19.75 ± 0.82 minutes for G1 and 15.33 ± 1.24 minutes for G2. Butorphanol is characterized by its rapid onset of action (Warne *et al*., 2013). According to Gomes *et al*. (2018), cited by Murdock *et al*. (2020), butorphanol might present sedative effects in less than 15 minutes in dogs. P2 (induction and intubation) was very similar between groups, being 8 minutes for both methadone and butorphanol. For P3 (surgery time) and P4 (anesthesia time), methadone presented slightly higher values than butorphanol. In P3, G1 had a duration of 22.75 ± 6.05 minutes, while G2 had a duration of 25 ± 4.96 minutes. In P4, G1 and G2 times were 40.5 ± 5.72 minutes and 42 ± 8.04 minutes, respectively. This is consistent with observations by Warne *et al*. (2013), who reported similar surgical and anesthetic times in ovariohysterectomy in cats. In their study, the surgical time for methadone was 21 ± 3.6 minutes and for butorphanol was 22 ± 5.6 minutes. The anesthetic duration of methadone was 51 ± 8.3 minutes, while butorphanol had a duration of 54 ± 10.13 minutes. As can be seen, despite the similarity in duration with the present study, methadone presents slightly higher values, as well.

According to the results obtained in this study, at the described dosage, both methadone and butorphanol showed intraoperative analgesic efficacy without adverse effects. This is consistent with the findings of Vinyals (2015), where the addition of methadone to the anesthetic protocol proved being effective in providing good sedation and analgesia in a coati undergoing OVH. Thomas *et al*. (2021) also reported the use of methadone in a coati as part of an anesthetic protocol, which provided good analgesia. It is important to note that the animal in their study underwent orthopedic surgery, so a locoregional block was given, to ensure an even more effective analgesia. Regarding butorphanol, Nascimento *et al*.

(2021) reported the use of butorphanol in two anesthetic protocols in coatis (*Nasua nasua*). The protocols proved to be effective and safe for anesthesia in this species, providing good sedation, analgesia, muscle relaxation, and recovery. However, it is important to highlight that the coatis were not subjected to any surgical or painful procedures; biological materials were merely collected.

During the timeline of this study, no complications or adverse effects were detected, neither during the surgical or recovery period. This goes in accordance with Trimble *et al*, (2018), which reported that, both methadone and butorphanol administered in dogs, didn´t originated adverse effects. Georoff *et al*. (2004) however, reported the presence of seizures in one coati (*Nasua narica*) anesthetized with medetomidine, butorphanol, and ketamine, as well as myoclonic movements in two other individuals. Ko *et al*. (2000), related that seizure's episodes might be observed when the combination of high doses of ketamine alongside medetomidine are used, thus explaining why these adverse effects didn't occur to the animals in the present study.

These study presents some limitations. The main one is the small sample size, which may not accurately represent the diversity within the species and making it harder to detect significant statistical differences. Furthermore, the small sample size reduces statistical power, preventing reliable statistical conclusions from being drawn. A small sample size leads to another limitation, namely individual variability. Each animal reacts differently to anesthesia, often depending on factors such as age, sex, health, etc. With such a small sample, these individual variations become more evident and influence the results and conclusions. The lack of baseline data for this species constitutes another important limitation. The scarcity of baseline data might hinder the interpretation of results, since there is not enough data of the baseline values, to make a reliable comparison, making it difficult to establish cause and effect relationships. Also, the fact that this species is wild and potentially aggressive, means that parameter measurement has to be performed on pre-sedated animals. This means that the limited information available referring to baseline values, is regarding animals already under the influence of sedative drugs. The use of ketamine as part of the pre-medication, given its analgesic properties, may have obscured the true effects of the administered opioids. Finally, a group control was not used in this study, preventing in this way, the possibility to make definitive comparisons and determine the true effect of the intervention and compare the results of the experiment.

Future research should aim to address these limitations by increasing the sample size and ensuring a more diverse population, with individuals of different ages, sexes, and origins. Another goal should be the collection of comprehensive baseline data, using a diverse sample.

The measurement and analysis of more physiological parameters, such as temperature, should also be undertaken, as well as the evaluation of behavioral factors. The addition of a group control should also be considered.

Chapter V

Conclusion

At the described dosage, both methadone and butorphanol showed intraoperative analgesic efficacy without adverse effects, in the used dosages and for the procedures performed. Sedation with butorphanol was faster than with methadone. No analgesic rescues were required during surgery. Due to the small sample size, the obtained results should be interpreted with caution and therefore, butorphanol and methadone's inclusion in anaesthetic protocols for elective procedures in coatis may require further studies (with adequate sample sizes), as there is currently no adequate scientific evidence.

Bibliography

Ahmad A. A., Wahab N. A., Yeo C. W., Oh J. S., & Chen, H. C. (2019). Comparison of alfaxalone-medetomidine and tiletamine-zolazepam in rescued common palm civets (*Paradoxurus musangus*). *Journal of Veterinary Medical Science*, *81*(1), 48–52. https://doi.org/10.1292/jvms.18-0297

Allerton, F. (2020) Small Animal Formulary – Part A: Canine and Feline, (10th edition), British Small Animal Veterinary Association, Gloucester, UK; BSAVA

Álvarez, E. R., Solé, L. V., & de Carellán Mateo, A. G. (2022). Comparison of subcutaneous sedation with alfaxalone or alfaxalone-midazolam in pet guinea pigs (Cavia porcellus) of three different age groups. Journal of the American Veterinary Medical Association, 1–7. https://doi.org/10.2460/javma.21.02.0104

Amon, T., Kästner, S. B. R., Kietzmann, M., & Tünsmeyer, J. (2021). Plasma levels of a methadone constant rate infusion and their corresponding effects on thermal and mechanical nociceptive thresholds in dogs. *BMC Veterinary Research*, *17*(1). https://doi.org/10.1186/s12917-020-02735-3

Arenillas, M., Canfrán, S., Aguado, D., & Gómez de Segura, I. A. (2021). Sedative and analgesic effects of two subanaesthetic doses of ketamine in combination with methadone and a low dose of dexmedetomidine in healthy dogs. Veterinary Anaesthesia and Analgesia, 48(4), 545–553. https://doi.org/10.1016/j.vaa.2020.11.010

Barros, F. F. P. C., Queiroz, J. P. A. F., Filho, A. C. M., Santos, E. A. A., Paula, V. V., Freitas, C. I. A., & Silva, A. R. (2009). Use of two anesthetic combinations for semen collection by electroejaculation from captive coatis (Nasua nasua). Theriogenology, 71(8), 1261–1266. https://doi.org/10.1016/j.theriogenology.2009.01.003

Beisiegel B.M, (2001) Notes on the coati, Nasua nasua (Carnivora: Procyonidae), in an Atlantic Forest area. Braz. J. Biol. 61(4):689-692. https://doi.org/10.1590/S1519-69842001000400020

Benedetti, I. C., Bublot, I., Ribas, T., Fourel, I., Vogl, C., Dubois, C., Milani, M., Ida, K. K., & Portier, K. (2018). Pharmacokinetics of intramuscular alfaxalone and its

echocardiographic, cardiopulmonary and sedative effects in healthy dogs. *PloS One*, *13*(9), e0204553. https://doi.org/10.1371/journal.pone.0204553

Bortolami, E., Murrell, J. C., & Slingsby, L. S. (2013). Methadone in combination with acepromazine as premedication prior to neutering in the cat. *Veterinary Anaesthesia and Analgesia*, *40*(2), 181–193. https://doi.org/10.1111/j.1467-2995.2012.00736.x

Bubalo, V., Moens, Y. P., Holzmann, A., & Coppens, P. (2008). Anaesthetic sparing effect of local anaesthesia of the ovarian pedicle during ovariohysterectomy in dogs. *Veterinary Anaesthesia and Analgesia*, *35*(6), 537–542. https://doi.org/10.1111/j.1467-2995.2008.00421.x

Burbaitė, E., Čechovičienė, S., Sarapinienė, I., Karvelienė, B., Riškevičienė, V., Daunoras, G., & Juodžentė, D. (2024). Effects of Medetomidine–Butorphanol and Medetomidine–Buprenorphine on Oxidative Stress and Vital Parameters in Dogs Undergoing Ovariohysterectomy. *Animals: An Open Access Journal from MDPI*, *14*(9), 1349. https://doi.org/10.3390/ani14091349

Cardozo, L. B., Cotes, L. C., Kahvegian, M. A. P., Rizzo, M. F. C., Otsuki, D. A., Ferrigno, C. R., & Fantoni, D. T. (2014). Evaluation of the effects of methadone and tramadol on postoperative analgesia and serum interleukin-6 in dogs undergoing orthopaedic surgery. *BMC Veterinary Research*, *10*(1). https://doi.org/10.1186/s12917-014-0194-7

Casoni, D., Spadavecchia, C., & Adami, C. (2015). S-ketamine versus racemic ketamine in dogs: their relative potency as induction agents. Veterinary Anaesthesia and Analgesia, 42(3), 250–259. https://doi.org/10.1111/vaa.12200

Casoria, V., Greet, V., Auckburally, A., Murphy, S., & Flaherty, D. (2023). Comparison of the effects of propofol and alfaxalone on the electrocardiogram of dogs, with particular reference to QT interval. *Frontiers in Veterinary Science*, *10*, 1330111. https://doi.org/10.3389/fvets.2023.1330111

Castañer, J. F., Carmona, S., Q., Bernal, C. M., Morgaz, J. Calvo, R. N., & Machuca, M. M.(2023). Sedation Quality and Cardiorespiratory, Echocardiographic, Radiographic and Electrocardiographic Effects of Intramuscular Alfaxalone and Butorphanol in Spanish Greyhound Dogs. *Animals*, *13*(18), 2937–2937. https://doi.org/10.3390/ani13182937

Cho, H., Yang, S. W., Suh, G. H., Choi, J., (2023). Sedative effect with the combination of butorphanol and midazolam on two-dimensional shear wave elastography of pancreas and kidney in healthy dogs. AVMA, 84(3). https://doi.org/10.2460/ajvr.22.10.0187

Conforti, V. A., de Azevedo, F. C. C., de Oliveira Henriques Paulo, O. L., de Moraes, W., & Deddens, J. A. (2017). Chemical Restraint of Free-ranging South American Coatis (Nasua nasua) with a Combination of Tiletamine and Zolazepam. Journal of Wildlife Diseases, 53(1), 140–143. https://doi.org/10.7589/2016-02-045

Credie, R. G., Teixeira Neto, F. J., Ferreira, T. H., Aguiar, A. J., Restitutti, F. C., & Corrente, J. E. (2010). Effects of methadone on the minimum alveolar concentration of isoflurane in dogs. *Veterinary Anaesthesia and Analgesia*, *37*(3), 240–249. https://doi.org/10.1111/j.1467-2995.2010.00528.x

Cubeddu, F., Masala, G., Sotgiu, G., Mollica, A., Versace, S., & Careddu, G. M. (2023). Cardiorespiratory Effects and Desflurane Requirement in Dogs Undergoing Ovariectomy after Administration Maropitant or Methadone. *Animals: An Open Access Journal from MDPI*, *13*(14), 2388. https://doi.org/10.3390/ani13142388

Decreto-Lei n.º 92/2019 de 10 de julho, Diário da República: I Série, nº 130/2019, Ministério do Ambiente, Lisboa.

Drees, R., Johnson, R. A., Stepien, R. L., Muñoz, A., & François, C. J. (2014). Effects of two different anesthetic protocols on cardiac flow measured by two dimensional phase contrast magnetic resonance imaging, Veterinary Radiology & Ultrasound, 56(2), 168–175. https://doi.org/10.1111/vru.12200

Fehr, M., Neßler, J., Schütter, A., Dziallas, P., Molnár, V., Ludwig, C., Zabke, S., Lehmbecker, A., Tipold, A., & Meyerhoff, N. (2018). Intervertebral disc herniation in two coatis (Nasua nasua) and postoperative laminectomy membrane formation. *Tierärztliche Praxis Ausgabe K: Kleintiere / Heimtiere*, *46*(05), 330–336. https://doi.org/10.15654/tpk-180165

Ferreira, G. A., Nakano-Oliveira, E., Genaro, G., & Lacerda-Chaves, A. K. (2013). Diet of the coati Nasua nasua (Carnivora: Procyonidae) in an area of woodland inserted in an urban environment in Brazil, Revista Chilena de historia natural, V. 86, pg 95-102. http://dx.doi.org/10.4067/S0716-078X2013000100008.

Ferreira, T. H., Rezende, M. L., Mama, K. R., Hudachek, S. F., & Aguiar, A. J. A. (2011). Plasma concentrations and behavioral, antinociceptive, and physiologic effects of methadone after intravenous and oral transmucosal administration in cats. American Journal of Veterinary Research, 72(6), 764. https://doi.org/10.2460/ajvr.72.6.764

Fischer, C. P., & Romero, L. M. (2019). Chronic Captivity Stress in Wild Animals Is Highly species-specific. *Conservation Physiology*, *7*(1). https://doi.org/10.1093/conphys/coz093

Fishman, S. M., Wilsey, B., Mahajan, G., & Molina, P. (2002). Methadone Reincarnated: Novel Clinical Applications with Related Concerns. *Pain Medicine*, *3*(4), 339–348. https://doi.org/10.1046/j.1526-4637.2002.02047.x

Fonseca, Â. M., Martins, S. B., Bárisson, J. D., Muehlbauer, E., Borges, N. C., & Moreno, J. C. D. (2017). Anestesia inalatória e anestesia total intravenosa em quatis – estudo comparativo [Inhalational and total intravenous anesthesia in Coatis: a comparative study]. Archives of Veterinary Science, 22(4), 20-30. DOI:10.5380/avs.v22i4.56823

Fowler, M. E. (2008). *Restraint and handling of wild and domestic animals*. Ames, Iowa Wiley-Blackwell.

Franciolli, A. L. R., Costa, G. de M., Mançanares, C. A. F., Martins, D. dos S., Ambrósio, C. E., Miglino, M. A., & Carvalho, A. F. de. (2007). Morfologia dos órgãos genitais masculinos de quati (Nasua nasua, Linnaeus 1766). Biotemas, 20(1), 27–36. Accessed on 16th March, 2023 at: https://periodicos.ufsc.br/index.php/biotemas/article/view/20776

Freitas, E. P., Rahal, S. C., Teixeira, C. R., Teixeira, R. H. F., Mendes, G. M., & Gioso, M. A. (2008). Oral cavity evaluation and dental chart registration of coati (Nasua nasua) in captivity. *Journal of Veterinary Dentistry*, *25*(2), 110–117. https://doi.org/10.1177/089875640802500212

Garofalo, N. A., Teixeira Neto, F. J., Pereira, C. D. N., Pignaton, W., Vicente, F., & Alvaides, R. K. (2012). Cardiorespiratory and neuroendocrine changes induced by methadone in conscious and in isoflurane anaesthetised dogs. *The Veterinary Journal*, *194*(3), 398–404. https://doi.org/10.1016/j.tvjl.2012.03.019

Georoff, T. A., Boo, D., Hammond, E. E., Ferrell, S. T., Radcliffe, R. W. (2004) Preliminary Results of Medetomidine-Ketamine-Butorphanol for Anesthetic Management of

Captive, White-Nosed Coati (Nasua narica). American Association of Zoo Veterinarians Conference 2004. Accessed on May 28, 2024 at: https://www.vin.com/doc/?id=10085256

Geraldene, B. (2012). *Abridged Husbandry Manual for Ring-Tail Coati Nasua nasua (MAMMALIA: PROCYONIDAE, Zoological Institution: Melbourne Zoo*. Accessed in August 30, 2023 from: https://aszk.org.au/wp-content/uploads/2020/06/Ring-Tail-Coati-Nasua-nasua-Geraldene-B.-2012.pdf

Gomes V. H., Peixoto A J., Fernandes, M. E., Campos A. C., Coelho, C. M., & Silva M. F. (2023). Evaluation of lidocaine administration into the ovarian pedicle for the control of intraoperative and early postoperative pain in dogs undergoing ovariohysterectomy. Veterinary Anaesthesia and Analgesia. https://doi.org/10.1016/j.vaa.2023.07.002

Gomes, V. H., Oliveira, R. LS., Marques, J. LR., Coelho, C. MM., & Silva, M. FA. (2018). Comparison of the sedative effects of nalbuphine and butorphanol, alone or in combination with acepromazine in dogs. *Veterinary Anaesthesia and Analgesia*, *45*(1), 68–72. https://doi.org/10.1016/j.vaa.2017.08.003

González-Maya, J. F., Jimenez-Ortega, A. M., Pinto, D., Rodriguez-Bolaños, A. (2011). Recent confirmed records and distribution of the White-nosed Coati Nasua narica in Colombia, Small Carnivore Conservation, Vol. 45:26–30. Accessed in September 17, 2023, from https://www.academia.edu/1097944/Recent_confirmed_records_and_distribution_of_the_White_nosed_Coati_Nasua_narica_in_Colombia

González-Maya, J. F., Vela-Vargas, I. M., Jiménez-Alvarado, J. S., Hurtado-Moreno, A. P., Moreno, C., Aconcha-Abril, I., & Zárrate-Charry, D. A. (2015). First sympatric records of Coatis (Nasuella olivacea and Nasua nasua; Carnivora: Procyonidae) from Colombia; Small Carnivore Conservation 52 & 53: 93–100. Accessed on 27th November, 2023 at: https://www.researchgate.net/publication/289245113_First_sympatric_records_of_Coatis_Nasuella_olivacea_and_Nasua_nasua_Carnivora_Procyonidae_from_Colombia

Grant, R., Montrose, V., & Wills, A. (2017). ExNOTic: Should We Be Keeping Exotic Pets? *Animals*, *7*(12), 47. https://doi.org/10.3390/ani7060047

Guedel, A. E. (1937). Inhalation Anesthesia: A Fundamental Guide. *Anesthesia & Analgesia*, *16*(2), 119. Accessed on 4th June, 2024 at: https://journals.lww.com/anesthesia-analgesia/citation/1937/03000/inhalation_anesthesia_a_fundamental_guide_.19.aspx

Gültiken, N., Gürler, H., Yarım, G. F., Binli, F., Tuncay, M., Büyükbudak, F., Gökçeoğlu, A., & Anadol, E. (2022). Antioxidant and analgesic potential of butorphanol in dogs undergoing ovariohysterectomy. *Theriogenology*, *190*, 1–7. https://doi.org/10.1016/j.theriogenology.2022.07.002

Helgen K, Kays R, Helgen L, Tsuchiya-jerep M, Pinto C, Koepfli K, Eizirik E, Maldonado J (2009) Taxonomic boundaries and geographic distributions revealed by an integrative systematic overview of the mountain coatis, Nasuella (Carnivora: Procyonidae). Small Carnivore Conservation 41: 65-74. Accessed on 9th December, 2023 at: https://repository.si.edu/handle/10088/8168

Hiebert, K., Eshar, D., Sarvi, J., & Beaufrère, H. (2022). Anesthetic effects of alfaxalone-ketamine-midazolam and alfaxalone-ketamine-dexmedetomidine administered intramuscularly in black-tailed prairie dogs (Cynomys ludovicianus). American Journal of Veterinary Research, 83(9). https://doi.org/10.2460/ajvr.21.11.0193

Höglund, O. V., Olsson, K., Hagman, R., Öhlund, M., Olsson, U., & Lagerstedt, A. S. (2011). Comparison of haemodynamic changes during two surgical methods for neutering female dogs. *Research in Veterinary Science*, *91*(1), 159–163. https://doi.org/10.1016/j.rvsc.2010.08.013

Hopkins, A., Giuffrida, M., & Larenza, M. P. (2014). Midazolam, as a co-induction agent, has propofol sparing effects but also decreases systolic blood pressure in healthy dogs. Veterinary Anaesthesia and Analgesia, 41(1), 64–72. https://doi.org/10.1111/vaa.12088

Hyde, M., Bardales, R., Lizarazo, J., Sánchez, F., Payán, E., & Ortiz, R. (2021). First camera-trap evidence of the Western Mountain Coati Nasuella olivacea in San Martin, Peru. Small Carnivore Conservation, 2021, vol. 59, e59001. Accesssed on 15th September, 2023 at: https://smallcarnivoreconservation.com/index.php/sccg/article/view/3454/2890

Imboden, T. J., Pownall, W. R., Rubin, S., Spadavecchia, C., Schöllhorn, B. & Rohrbach, H. (2023). Determination of a safe sedative combination of dexmedetomidine, ketamine and butorphanol for minor procedures in dogs by use of a stepwise optimization method. Acta Veterinaria Scandinavica, 65(1). https://doi.org/10.1186/s13028-023-00697-8

Ingvast-Larsson, C., Holgersson, A., Bondesson, U., Lagerstedt, A.-S., & Olsson, K. (2010). Clinical pharmacology of methadone in dogs. *Veterinary Anaesthesia and Analgesia*, *37*(1), 48–56. https://doi.org/10.1111/j.1467-2995.2009.00476.x

Johnson, J. A., Robertson, S. A., & Pypendop, B. H. (2007). Antinociceptive effects of butorphanol, buprenorphine, or both, administered intramuscularly in cats. *American Journal of Veterinary Research*, *68*(7), 699–703. https://doi.org/10.2460/ajvr.68.7.699

Júnior, L. E. R., Júnior, R. P., Gonçalves, D. D., Kunz, R. O., Cardeal, C., Pachaly, J. R., Cubas, Z. S., & Valle, L. G. E. (2017). Parâmetros comparativos de indicadores bioquímicos plasmáticos de duas populações de quatis (Nasua nasua - LINNAEUS, 1766) com e sem ação antrópica. Arquivo Brasileiro de Medicina Veterinária E Zootecnia, 69(3), 659–666. https://doi.org/10.1590/1678-4162-9110

Juodzente, D.; Macas, A.; Karveliene B.; Petkevicius S.; & Riskeviciene V.; (2018). Comparison of the cardiovascular and respiratory effects and sevoflurane requirement in dogs premedicated with two doses of medetomidine and butorphanol undergoing surgical sterilization. *PubMed*, *21*(1), 101–110. https://doi.org/10.24425/119027

Kanda, T., & Hikasa, Y. (2008). Effects of medetomidine and midazolam alone or in combination on the metabolic and neurohormonal responses in healthy cats. *Canadian Journal of Veterinary Research = Revue Canadienne de Recherche Veterinaire*, *72*(4), 332–339. Accessed on 15th April, 2024 at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2442676/

Kapur, B. M., Hutson, J. R., Chibber, T., Luk, A., & Selby, P. (2011). Methadone: a review of drug-drug and pathophysiological interactions. *Critical Reviews in Clinical Laboratory Sciences*, *48*(4), 171–195. https://doi.org/10.3109/10408363.2011.620601

Kato, K., Itami, T., Nomoto, K., Endo, Y., Tamura, J., Oyama, N., Sano, T., & Yamashita, K. (2021). The anesthetic effects of intramuscular alfaxalone in dogs premedicated with low-dose medetomidine and/or butorphanol. *Journal of Veterinary Medical Science*, *83*(1), 53–61. https://doi.org/10.1292/jvms.20-0330

Keating, S., Fries, R., Kling, K., Graham, L., Clark-Price, S., & Schaeffer, D. J. (2020). Effect of Methadone or Hydromorphone on Cardiac Conductivity in Dogs Before and During Sevoflurane Anesthesia. *Frontiers in Veterinary Science*, *7*. https://doi.org/10.3389/fvets.2020.573706

Khaleghi, M., Sarchahi, A. A., Mehrjerdi, H. K., Rasekh, M., & Saadati, D., (2023). Influence of ketamine, propofol or isoflurane on intraocular pressure, heart rate and blood pressure in healthy dogs premedicated with medetomidine and midazolam. Veterinary Medicine and Science, 10(1). https://doi.org/10.1002/vms3.1330

Ko, J. C. H., Fox, S. M., & Mandsager, R. E. (2000). Sedative and cardiorespiratory effects of medetomidine, medetomidine-butorphanol, and medetomidine-ketamine in dogs. *Journal of the American Veterinary Medical Association*, *216*(10), 1578–1583. https://doi.org/10.2460/javma.2000.216.1578

Ko, J. C., Murillo, C., Weil, A. B., Kreuzer, M., & Moore, G. E. (2023). Ketamine-Propofol Coadministration for Induction and Infusion Maintenance in Anesthetized Dogs: Effects on Electroencephalography and Antinociception. Animals: An Open Access Journal from MDPI, 13(21), 3391. https://doi.org/10.3390/ani13213391

Koh, R. B., Isaza, N., Xie, H., Cooke, K., & Robertson, S. A. (2014). Effects of maropitant, acepromazine, and electroacupuncture on vomiting associated with administration of morphine in dogs. *Journal of the American Veterinary Medical Association*, *244*(7), 820–829. https://doi.org/10.2460/javma.244.7.820

Kropf, J., & Hughes, J. M. L. (2018). Effects of midazolam on cardiovascular responses and isoflurane requirement during elective ovariohysterectomy in dogs. Irish Veterinary Journal, 71(1). https://doi.org/10.1186/s13620-018-0136-y

Kukanich, B. & Papich, M. (2018). Opioid analgesic drugs. In: J.E., Riviere & M.G., Papich, 'Veterinary Pharmacology & Therapeutics' (10th edition, pp. 281-307). Wiley-Blackwell, USA.

KuKanich, B., Lascelles, D. X., Aman, A. M., Mealey, K. L., & Papich, M. G. (2005). *The effects of inhibiting cytochrome P450 3A, p-glycoprotein, and gastric acid secretion on the oral bioavailability of methadone in dogs*. *28*(5), 461–466. https://doi.org/10.1111/j.1365-2885.2005.00681.x

Kukanich, B., Wiese, A. J. (2015). Opioids Analgesic Drugs. In: W.J., Tranquilli, L. A., Lamont, K.A., Grimm, S. A., Greene, S. A., Robertson 'Lumb & Jones – Veterinary Anesthesia and Analgesia' (5th edition, pp. 207-221). Blackwell Publishing, USA.

Kunz, R. O., Cardeal, C., Riekher Junior, L. E., Valle, L. G. E., Belettini, S. T., Piau Junior, R., Quessada, A. M., & Pachaly, J. R. (2021). Chemical restraint of coatis by the association of Detomidine, Tiletamine and Zolazepam, in allometrically scaled dosages. Arquivo Brasileiro de Medicina Veterinária E Zootecnia, 73, 108–114. https://doi.org/10.1590/1678-4162-12050

Larenza, M. P., Ringer, S. K., Kutter, A. P. N., Conrot, A., Theurillat, R., Kummer, M., Thormann, W., & Bettschart-Wolfensberger, R. (2009). Evaluation of anesthesia recovery quality after low-dose racemic or S-ketamine infusions during anesthesia with isoflurane in horses. American Journal of Veterinary Research, 70(6), 710–718. https://doi.org/10.2460/ajvr.70.6.710

Leonardi, F., Costa, G. L., Interlandi, C. D., Rosa, J., Ghidelli, A., & Musicò, M. (2019). Immersion anaesthesia in goldfish (Carassius auratus) with three concentrations of alfaxalone. *Veterinary Anaesthesia and Analgesia*, *46*(1), 79–83. https://doi.org/10.1016/j.vaa.2018.08.006

Leppänen, M. K., McKusick, B. C., Granholm, M. M., Westerholm, F. C., Tulamo, R., & Short, C. E. (2006). Clinical efficacy and safety of dexmedetomidine and buprenorphine, butorphanol or diazepam for canine hip radiography. *The Journal of Small Animal Practice*, *47*(11), 663–669. https://doi.org/10.1111/j.1748-5827.2006.00030.x

Liao, P., Sinclair, M., Valverde, A., Mosley, C., Chalmers, H., Mackenzie, S., & Hanna, B. (2017). Induction dose and recovery quality of propofol and alfaxalone with or without midazolam coinduction followed by total intravenous anesthesia in dogs. Veterinary Anaesthesia and Analgesia, 44(5), 1016–1026. https://doi.org/10.1016/j.vaa.2017.02.011

MacPhail, C. M. (2013) Surgery of the Reproductive and Genital Systems In: Fossum, T. W., ‘ Small Animal Surgery’ (4th edition, pp 789-797) Missouri, Elesevier.

Maiante, A. A., Teixeira Neto, F. J., Beier, S. L., Corrente, J. E., & Pedroso, C. E. B. P. (2009). Comparison of the cardio-respiratory effects of methadone and morphine in conscious dogs. *Journal of Veterinary Pharmacology and Therapeutics*, *32*(4), 317–328. https://doi.org/10.1111/j.1365-2885.2008.01042.x

Marín, P., Belda, E., Laredo, F. G., Torres, C. A., Hernandis, V., & Escudero, E. (2020). Pharmacokinetics and sedative effects of alfaxalone with or without dexmedetomidine in rabbits. *Research in Veterinary Science*, *129*, 6–12. https://doi.org/10.1016/j.rvsc.2019.12.015

Martini, A. C., Monzem, S., Gomes, L. G., Vasconcelos, L. P. S., Farias, D. C., Silva, F. G. da, Paz, R. C. R. da, Souza, R. L., & Guimarães, L. D. (2017). Different Dissociative Anesthesia Protocols For Coatis (Nasua Nasua). *Acta Vet. Bras.*, 200–204. Accessed on 2nd November, 2023, at: https://pesquisa.bvsalud.org/portal/resource/pt/vti-15877

Mayor, P., Montes, D., & López-Plana, C. (2013). Functional morphology of the female genital organs in the wild ring-tailed coati (Nasua nasua) in the northeastern Peruvian Amazon. Canadian Journal of Zoology, 91(7), 496–504. https://doi.org/10.1139/cjz-2012-0331

Medrano-Vizcaíno, P. (2018). The highest altitudinal record of the Mountain coati Nasuella olivacea (Gray, 1865) for Ecuador. Biodiversity Data Journal, vol. 6. https://doi.org/10.3897/BDJ.6.e29160

Menegheti, T. M., Wagatsuma, J. T., Pacheco, A. D., Perez, B., Pacheco, C. M., Abimussi, C. J., dos Santos, P. P., & de Souza Oliva, V. N. (2014). Electrocardiographic evaluation of the degree of sedation and the isolated use of methadone in healthy dogs. *Veterinary Anaesthesia and Analgesia*, *41*(1), 97–104. https://doi.org/10.1111/vaa.12086

Minto, B. W., Nagatsuyu, C. E., Teixeira, C. R., Zanuzzo, F. S., Candido, T. D., Diogo, L. M. I., & Macedo, A. S. (2017). Minimally invasive hysterectomy in Coatis (Nasua nasua). Pesquisa Veterinária Brasileira, 37(6), 627–629. https://doi.org/10.1590/s0100-736x2017000600016

Monteiro, E. R., Figueroa, C. D. N., Choma, J. C., Campagnol, D., & Bettini, C. M. (2008). Effects of methadone, alone or in combination with acepromazine or xylazine, on sedation and physiologic values in dogs. *Veterinary Anaesthesia and Analgesia*, *35*(6), 519–527. https://doi.org/10.1111/j.1467-2995.2008.00412.x

Morici M., Lubian E., Costa G.L., Spadola F. Difference between Cranial and Caudal Intravenous Alfaxalone Administration in Yellow-Bellied Sliders (Trachemys scripta scripta) *Acta Vet. Eurasia.* 2021;47:88–92. doi: 10.5152/actavet.2021.20041.

Moser, K. L., Hasiuk, M. M., Armstrong, T., Gunn, M., & Pang, D. S. (2019). A randomized clinical trial comparing butorphanol and buprenorphine within a multimodal analgesic protocol in cats undergoing orchiectomy. *Journal of Feline Medicine and Surgery*, *22*(8), 760–767. https://doi.org/10.1177/1098612x19886132

Muir, W., Lerche, P., Wiese, A., Nelson, L., Pasloske, K., & Whittem, T. (2008). Cardiorespiratory and anesthetic effects of clinical and supraclinical doses of alfaxalone in dogs. *Veterinary Anaesthesia and Analgesia*, *35*(6), 451–462. https://doi.org/10.1111/j.1467-2995.2008.00406.x

Murdock, M. A., Riccó Pereira, C. H., Aarnes, T. K., Cremer, J., Lerche, P., & Bednarski, R. M. (2020). Sedative and cardiorespiratory effects of intramuscular administration of alfaxalone and butorphanol combined with acepromazine, midazolam, or dexmedetomidine in dogs. AVMA, 81(1), 65-71. https://doi.org/10.2460/ajvr.81.1.65

Mwangi, W. E., Mogoa, E. M., Mwangi, J. N., Mbuthia, P. G., & Mbugua, S. W. (2018). A systematic review of analgesia practices in dogs undergoing ovariohysterectomy. *Veterinary World*, 1725–1735. https://doi.org/10.14202/vetworld.2018.1725-1735

Nascimento, N. A., Souza, P. G. A., Aidar, E. S. A., Silva, M. P. B., Nogueira, A. F. S., Diniz, R. R. F., Scofield, A., & Gering, A. P. (2021). Uso de diferentes protocolos anestésicos na contenção química de Quatis, Nasua Nasua (Linnaeus, 1766) sob parâmetros fisiológicos e recuperação anestésica, Brazilian Journal of Development, 7(7), 74587–74597. https://doi.org/10.34117/bjdv7n7-576

Pascoe, P. and Steffey, E. (2018). Introduction to Drugs Acting on the Central Nervous System and Principles of Anesthesiology. In: J.E., Riviere & M.G., Papich, 'Veterinary Pharmacology & Therapeutics' (10th edition, pp. 167-191). Wiley-Blackwell, USA.

Pathan, H., & Williams, J. (2012). Basic opioid pharmacology: an update. *British Journal of Pain*, *6*(1), 11–16. https://doi.org/10.1177/2049463712438493

Peterson, N. W., Buote, N. J., & Bergman, P. (2014). Effect of epidural analgesia with opioids on the prevalence of urinary retention in dogs undergoing surgery for cranial cruciate ligament rupture. *Journal of the American Veterinary Medical Association*, *244*(8), 940–943. https://doi.org/10.2460/javma.244.8.940

Posner, L., P. (2018). Injectable Anesthetic Agents. In: J.E., Riviere & M.G., Papich, 'Veterinary Pharmacology & Therapeutics' (10th edition, pp. 259-364). Wiley-Blackwell, USA.

Queiroz, J., Barros, F., Lima, G., Castelo, T., Freitas, C., & Silva, A. (2010). Assessment of Orchidometry and Scrotal Circumference in Coatis (Nasua nasua). Reproduction in Domestic Animals, 45(6), e382–e386. https://doi.org/10.1111/j.1439-0531.2010.01582.x

Quintavalla, F., Spindler, K. P., Aldigeri, R., & Fidanzio, F. (2022). The Effect of Different Opioids on Acid-Base Balance and Blood Gas Analysis in Hospitalized Dogs. *Frontiers in Veterinary Science*, *9*. https://doi.org/10.3389/fvets.2022.802186

Rankin, D. C. (2015). Sedatives and tranquilizers. In: W.J., Tranquilli, L. A., Lamont, K.A., Grimm, S. A., Greene, S. A., Robertson 'Lumb & Jones – Veterinary Anesthesia and Analgesia' (5th edition, pp. 3-11). Blackwell Publishing, USA.

Regulation (EU), nº 1143/2014 of the European Parliament and the Council, of 22 October 2014, on the prevention and management of the introduction and spread of invasive alien species. Official Journal of the European Union, L 317, 4.11.2014, pp. 35–55.

Ribas, T., Bublot, I., Junot, S., Beaufrère, H., Rannou, B., Gagnière, P., Cadoré, J. L., & Pariaut, R. (2014). Effects of intramuscular sedation with alfaxalone and butorphanol on echocardiographic measurements in healthy cats. *Journal of Feline Medicine and Surgery*, *17*(6), 530–536. https://doi.org/10.1177/1098612x14551187

Rodríguez, A. A.; Buriticá-Gaviria, E., & Echeverry-Bonilla, D. (2016). Intraoperative analgesic effects of intratesticular lidocaine in a dog undergoing elective orchiectomy: case report. ORINOQUIA, 20(2), 78–83. Accessed on 5th June, 2024 at: http://www.scielo.org.co/scielo.php?script=sci_arttext&pid=S0121-37092016000200010

Romero, T., & Aureli, F. (2008). Reciprocity of support in coatis (Nasua nasua). *Journal of Comparative Psychology*, *122*(1), 19–25. https://doi.org/10.1037/0735-7036.122.1.19

Rovirosa-Hernández, M. J., García-Orduña, F., Morales-Mávil, J. E., Hernández-Salazar, L. T., Hermida-Lagunes, J., Lagunes-Merino, O., & Fuentes-Anaya, T. (2012). Hematological and Blood Chemistry values in a semi-free population of white-nosed coatis (Nasua narica) in La Venta Tabasco, Mexico. Acta Zoológica Mexicana, 28(2), 391–400. https://doi.org/10.21829/azm.2012.282841

Saberfard, D., Sarchahi, A. A., & Mehrjerdi, H. K. (2022). Effect of medetomidine, midazolam, ketamine, propofol and isoflurane on spinal reflexes in healthy dogs. Veterinary Medicine and Science, 8(6), 2351–2359. https://doi.org/10.1002/vms3.938

Salcedo-Rivera, G. A., Rodríguez, A. M., Carrascal-Prasca, D., Granados-Peña, R., & González-Maya, J. F. (2022). Confirmation of the current occurrence of Nasua narica (Procyonidae) in the Caribbean region of Colombia. *Neotropical Biology and Conservation*, *17*(1), 21–28. https://doi.org/10.3897/neotropical.17.e70352

Salomón M.,Ramírez J., (2011). Observaciones de forrajeo y defensa de Nasuella olivacea (Carnivora: Procyonidae) en el Volcán Pasochoa, Pichincha – Ecuador, Boletín Técnico 10, Serie Zoológica 7, 47-50. Accessed on 30th November, 2023 at:

https://www.researchgate.net/publication/311912470_Observaciones_de_forrajeo_y_defensa_de_Nasuella_olivacea_Carnivora_Procyonidae_en_el_Volcan_Pasochoa_Pichincha_-_Ecuador

Seddighi, R., Egger, C. M., Rohrbach, B. W., Cox, S. K., & Doherty, T. J. (2011). The effect of midazolam on the end-tidal concentration of isoflurane necessary to prevent movement in dogs. Veterinary Anaesthesia and Analgesia, 38(3), 195–202. https://doi.org/10.1111/j.1467-2995.2011.00615.x

Seo, J.-I., Han, S.-H., Choi, R., Han, J., Lee, L., & Hyun, C. (2015). Cardiopulmonary and anesthetic effects of the combination of butorphanol, midazolam and alfaxalone in Beagle dogs. *Veterinary Anaesthesia and Analgesia*, *42*(3), 304–308. https://doi.org/10.1111/vaa.12223

Shora, J., Myhill, M., & Brereton, J. E. (2018). Should zoo foods be coati chopped. *Journal of Zoo and Aquarium Research*, *6*(1), 22–25. https://doi.org/10.19227/jzar.v6i1.309

Silva, H. V. R., Rodriguez-Villamil, P., Magalhaes, F. F. d., Nunes, T. G. P., Freitas, L. A. d., Ribeiro, L. R., Silva, A. R., Moura, A. A., & Silva, L. D. M. d. (2018). Seminal plasma and sperm proteome of ring-tailed coatis (Nasua nasua, Linnaeus, 1766). Theriogenology, 117(7), 2159–2169. https://doi.org/10.1007/s00436-018-5903-x.

Simon, B. T., & Steagall, P. V. (2016). The present and future of opioid analgesics in small animal practice. *Journal of Veterinary Pharmacology and Therapeutics*, *40*(4), 315–326. https://doi.org/10.1111/jvp.12377

Simon, B. T., Scallan, E. M., Siracusa, C., Henderson, A., Sleeper, M. M., & Larenza Menzies, M. P. (2014). Effects of acepromazine or methadone on midazolam-induced behavioral reactions in dogs. The Canadian Veterinary Journal, 55(9), 875–885. Accessed on 15th May, 2024 at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137930/

Slingsby, L. S., Sear, J. W., Taylor, P. M., & Murrell, J. C. (2016). Effect of intramuscular methadone on pharmacokinetic data and thermal and mechanical nociceptive thresholds in the cat. *Journal of Feline Medicine and Surgery*, *18*(11), 875–881. https://doi.org/10.1177/1098612X15605164

Solano, A. M., Pypendop, B. H., Boscan, P. L., & Ilkiw, J. E. (2006). Effect of intravenous administration of ketamine on the minimum alveolar concentration of isoflurane in

anesthetized dogs. American Journal of Veterinary Research, 67(1), 21–25. https://doi.org/10.2460/ajvr.67.1.21

Tamura, J., Ishizuka, T., Fukui, S., Oyama, N., Kawase, K., Miyoshi, K., Sano, T., Pasloske, K., & Yamashita, K. (2015). The pharmacological effects of the anesthetic alfaxalone after intramuscular administration to dogs. *The Journal of Veterinary Medical Science*, *77*(3), 289–296. https://doi.org/10.1292/jvms.14-0368

Thomas, A. A., Leach, M. C., & Flecknell, P. A. (2012). An alternative method of endotracheal intubation of common marmosets (Callithrix jacchus). *Laboratory Animals*, *46*(1), 71–76. https://doi.org/10.1258/la.2011.011092

Thomas, L. D., Piccoli, R. J., Bernardi, P. E. Q., Sinotti, J. F., Silva, V. A., Souza, C. F. de, & Fukushima, F. B. (2021). Bloqueio do plexo-braquial e peridural lombossacra em um quati (Nasua nasua). Acta Sci. Vet. (Online), Pub. 651–Pub. 651. Accessed on 15th December, 2023 at: https://pesquisa.bvsalud.org/portal/resource/pt/vti-32658

Tranquilli, W. J., Grimm, K. A. (2015). Introduction: Use, Definitions, History, Concepts, Classification, and Considerations for Anesthesia and Analgesia. In: W.J., Tranquilli, L. A., Lamont, K.A., Grimm, S. A., Greene, S. A., Robertson 'Lumb & Jones – Veterinary Anesthesia and Analgesia' (5th edition, pp. 196-206). Blackwell Publishing, USA.

Trescot, A. M., Datta, S., Lee, M., & Hansen, H. (2008). Opioid Pharmacology. Pain Physician, 11(S133-S153). Accessed on 30th October , 2023 at: https://www.painphysicianjournal.com ISSN 1533-315

Trimble, T., Bhalla, R. J., & Leece, E. A. (2018). Comparison of sedation in dogs: methadone or butorphanol in combination with dexmedetomidine intravenously. *Veterinary Anaesthesia and Analgesia*, *45*(5), 597–603. https://doi.org/10.1016/j.vaa.2018.03.008

Vinyals, A. (2015). Ovariohisterectomía en un coatí. Argos: Informativo Veterinario, 172 (Cirugía y laparoscopia), 60–60. Accessed on 17th January, 2024 at : https://dialnet.unirioja.es/servlet/articulo?codigo=7271021

Warne, L. N., Beths, T., Whittem, T., Carter, J. E., & Bauquier, S. H. (2015). A review of the pharmacology and clinical application of alfaxalone in cats. *The Veterinary Journal*, *203*(2), 141–148. https://doi.org/10.1016/j.tvjl.2014.12.011

Warne, L. N.; Thierry B.; Holm, M.; Bauquier, S. H. (2013). *Comparison of perioperative analgesic efficacy between methadone and butorphanol in cats. Journal of the American Veterinary Medical Association, 243(6), 844–850*

Wells, S. M., Glerum, L. E., & Papich, M. G. (2008). Pharmacokinetics of butorphanol in cats after intramuscular and buccal transmucosal administration. *American Journal of Veterinary Research*, *69*(12), 1548–1554. https://doi.org/10.2460/ajvr.69.12.1548

Zapata, A., Laredo, F. G., Escobar, M., Agut, A., Soler, M., & Belda, E. (2018). Effects of midazolam before or after alfaxalone for co-induction of anaesthesia in healthy dogs. Veterinary Anaesthesia and Analgesia, 45(5), 609–617. https://doi.org/10.1016/j.vaa.2018.04.002