HOW SAFE IS ANESTHESIA FOR DOGS AND CATS?

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Introduction

"What are the risks of anesthesia in dogs and cats today?" – This was a question that until recently we did not have an accurate answer to. The data generated by the Confidential Enquiry into Perioperative Small Animal Fatalities (CEPSAF), a prospective cohort study conducted in the United Kingdom is the most comprehensive information we have available. This study collected data from veterinary practices, including referral centers and universities and recorded patient outcome (alive, dead or euthanized) after pre-medication and within 48 hours of the end of the procedure and calculated species specific (cat, dog, rabbit and "other small animals") risks of anesthetic related death. Anesthesia or sedation related death was defined as "death where surgical or pre-existing medical causes did not solely cause death". This study has generated risk factors for the different species and paves the way for improving anesthetic management in small animals [1-4].

Mortality risks

Animals were assigned a "health status"; "healthy" were animals assigned an ASA status of I or 2 and "sick" were animals assigned an ASA status of 3 to 5. These classifications were based in the American Society of Anesthesiologist's [ASA] classification (Table 1). The CEPSAF study included 98,036 dogs and 79,178 cats. The *overall* risk of death was 0.17% in dogs and 0.24% in cats. In *healthy* dogs and cats the risks were 0.05% and 0.11% respectively. In *sick* dogs and cats the risks were 1.33% and 1.40% respectively (Table 2).

The risk of anesthetic related death in dogs and cats have decreased since the last comparable survey in the mid-1980s but these numbers compare poorly to data for humans where the anesthetic related death rate is reported to be between 0.02 and 0.005%. Differences in the standards of anesthesia including training of those administering anesthesia, having a person dedicated to anesthesia alone, and sophisticated monitoring equipment are likely the reason between the human and animal data, more than species differences alone.

Data from large scale spay and neuter or feral cat clinics is more difficult to obtain in the numbers collected in the CEPSAF study but in a review of 7,502 feral cat anesthetics Williams and others reported an overall anesthetic related mortality rate of 0.23% ^[5].

When do most deaths occur?

Analysis of the CEPSAF results reveals that most deaths occur *post-operatively*; 47% of deaths in dogs occur during this time and in cats the figure is 61% (Table 3). Within the post-operative period, the most critical time appears to be the *first three hours* after the end of anesthesia.

What are the causes of death?

An independent panel reviewed details of each anesthetic death and tried to ascertain a cause. Cardiovascular or respiratory causes accounted for 74% and 72% of deaths in dogs and cats respectively.

As in human anesthetic related deaths, human error plays a role. For example 2 dogs died after the pressure relief valve was left closed.

Risk factors

In both cats and dogs performing a major versus a minor procedure and prolonging the procedure led to an increase in mortality.

The risks for general anesthesia and sedation alone were compared. Although there were fewer sedation only cases in the study it appears that there is less risk of death with sedation alone compared to anesthesia. This suggests that when possible we should try to think of ways to perform simple procedures under sedation combined with local anesthetics.

In previous mortality studies ^[6] the alpha₂-agonist xylazine was associated with an increased risk of death; however in the CEPSEF study medetomidine was not associated with an increased risk.

Dogs

Risk factors in dogs have been identified. Dogs with lower body weights (< 5kg) are at increased risk of anesthetic related deaths (8 times more likely to die than dogs that weigh between 5 and 15kg). This may be a result of hypothermia (see later), inaccuracies in drug dosing, or perhaps because small dogs are more frequently "masked" down because IV access is more difficult.

Mask induction of anesthesia was found to significantly increase mortality (a 5.9 fold increase in risk compared to induction with an injectable agent followed by isoflurane) and must be discouraged; use of premedication followed by induction of anesthesia with injectable drugs is preferred. Inhalant agents are the most cardiovascular and respiratory depressant anesthetic agents we use and "MAC" sparing techniques are encouraged – including premedication with sedatives or tranquillizers and the perioperative use of opioids. There was insufficient data to compare sevoflurane and isoflurane, but it was clear that the use of halothane increased the risks of dying compared to isoflurane.

Senior dogs (> 12 years) are at a significantly higher risk (7 times more likely to die than dogs in the 6 month to 8 year old range). This risk is still real when other confounding factors such as ASA status are accounted for. Special attention must be paid to this population, including careful pre-anesthetic work-up.

Cats

Overall the risk associated with anesthesia in cats is significantly higher than for dogs. Of particular interest is the data showing that the risk in "healthy cats" is greater than in "healthy dogs", but the mortality is similar in both species if they are classified as being "sick" [1].

In cats, respiratory obstruction as a cause of death was reported more frequently than in dogs indicating that close attention to the airway in this species is important. Respiratory problems were more common in the post-operative period suggesting airway trauma and edema may be involved. The data indicated an increased complication rate related to endotracheal intubation therefore great care should be taken when intubating cats; the propensity for cats to have laryngospasm may play a role. Intubation should be performed under the correct plane of anesthesia (not too light), under direct vision (laryngoscope) and the use of topical local anesthetics are recommended. Patience is required and the tube should only be advanced when the vocal cords are open. In addition the cuff should only be inflated if necessary. The seal can be tested by closing the pop-off valve and squeezing the reservoir bag – air is added in small increments to the cuff until there is no leak at 15 cmH₂O. A small (3ml) syringe should be used to prevent over-inflation. The use of water soluble gel on the cuff will decrease the likelihood of leakage around the cuff $^{[7]}$. Tracheal rupture following endotracheal intubation has been well documented in cats and is often fatal $^{[8, 9]}$.

Cats that weigh less than 2 kg are high risk cases (odds ratio of 15.7 – i.e. over 15 times more likely to die than cats weighing between 2-6 kg). The smaller size of cats may predispose them to hypothermia and its associated complications (see later). The small size of cats may also lead to more problems with intravenous catheter placement, intubation and monitoring. If cats are not accurately weighed, it is likely that relative drug overdoses also occur.

At the other end of the spectrum, obese cats were also at risk, perhaps this is related to a greater risk for respiratory compromise (reduced diaphragmatic excursions due to abdominal and thoracic fat, especially when placed in dorsal recumbency) and reduced cardiovascular reserves (an increase in cardiac output is required as body fat increases).

As with dogs, older cat carry a higher anesthetic risk – cats older than 12 years are twice as likely to die compared to cats aged 6 months to 5 years. This increased risk was independent from the ASA status and may be a result of decreased respiratory and cardiovascular reserve in these patients or decreased anesthetic requirements.

One reason for the higher risk in healthy cats may be the presence of sub-clinical cardiac disease. In "overtly" or "apparently" healthy cats, the incidence of cardiomyopathy may be as high as 15% [10, 11]. Thus cats may be misclassified, but since cats with cardiac disease can be clinically healthy and not all have murmurs it is difficult to detect these patients without echocardiography. A surprising finding was that the use of intravenous fluids increased the risks in both healthy and sick cats. One reason may be inaccurate administration and fluid overload therefore the use of infusion or syringe pumps or a buretrol is advised in cats to ensure accurate volume delivery. With the knowledge that apparently healthy cats may have underlying cardiac disease, it is possible that fluid overload potentially contributes to mortality.

Reducing stress in cats

Although there is no hard data linking stress and anesthetic complications it seems intuitive that stress induced changes in heart rate, blood pressure and catecholamines could adversely affect the anesthetic outcome. There are many simple things that can be done to reduce stress for cats in a veterinary hospital or shelter setting and the following websites have excellent tips:

The catalyst Council: http://catalystcouncil.org
The Feline Advisory Bureau: http://fabcats.org

Association of Shelter veterinarians: http://www.sheltervet.org

Some very simple things that can make anesthesia and recovery go better include the use of pheromones. The use of a synthetic fraction of feline facial pheromones (Feliway®, CEVA Sante Animale) in a spray formulation was assessed for its calming effect on cats in a veterinary clinic before intravenous catheterization ^[12]. The cage was sprayed with Feliway® or placebo prior to placing the cat in it and 30 minutes later cats were videotaped and behavior assessed by a blinded observer. The facial pheromone had additional calming effects in cats given acetylpromazine and, to a lesser degree, helped to calm cats that were not given acetylpromazine and the authors concluded that Feliway® helps to calm cats in unfamiliar surroundings. In another study, significant increases in grooming and interest in food were found in cats exposed to facial pheromones compared with a placebo ^[13]. There were also significant positive correlations between grooming and facial rubbing, interest in food and in a 24-hour period food intake was significantly greater in cats exposed to pheromones and allowed access to a small cat carrier to hide in suggesting that exposure to Feliway® and the provision of a "private" place may be useful in hospitalized cats. The spray can be used in cages, on tables and blankets and a diffuser can be used in the cat area of a clinic.

Monitorina

The use of a pulse oximeter is strongly recommended. In cats, the use of this monitor reduced mortality significantly – likely because it alerted staff to a cardiovascular or oxygenation problem. When selecting a monitor it is important to choose one which has a good audible signal, for example a pulse oximeter or Doppler ultrasonic flow detector, because personnel respond more rapidly to a change in sound than to a visual display – in addition in a busy setting it is not possible to be observing a visual display at all times.

Hypothermia (The Big Chill)

Small veterinary patients commonly lose heat when anesthetized ^[14] but the impact of this on the patient is greatly underestimated. Maintaining body temperature within a narrow range is important for cardiac function, metabolism, normal enzyme activity, nerve conduction, and hemostasis.

Thermal balance

Homeothermy is a balance between heat loss and heat gain and involves complex sensing mechanisms that will drive the mechanisms controlling heat loss or gain in the correct direction, therefore thermoregulation is a closed loop system. Heat gains can be obligatory or facultative. Obligatory gains occur independently of thermoregulation and include heat from basal metabolism, eating and exercise. Facultative gains act to restore thermal balance and the most important source is from shivering. Three-

quarters of heat loss occurs from the body surface and the remainder is lost from the respiratory tract. Losses occur through convection, conduction, evaporation and radiation.

Anesthesia and thermoregulation

When an animal is anesthetized many factors interrupt normal thermoregulation. Anesthesia abolishes behavioral responses (the animal can no longer seek out a warm environment), reduces metabolic rate, alters hypothalamic function, reduces muscle tone and effector responses (shivering). In addition operating room environments and surgical procedures impose large thermal stresses on the animal.

Under general anesthesia there is a much wider range of core temperature where the animal does not respond to maintain normothermia. Vasoconstriction can occur in an anesthetized patient and although it may slow down the rate of heat loss it will have a negative effect on tissue perfusion. This reflex will be counteracted or greatly obtunded if acetylpromazine and other vasodilating agents such as isoflurane or sevoflurane are used.

The greatest amount of heat is lost immediately after induction and during the first 20 minutes of anesthesia due to redistribution of heat from the core to periphery. Heat continues to be lost after the initial steep drop but at a lower rate. There is also an increase in the difference between core (esophageal) and peripheral (rectal) temperature over time. The smaller the animal the greater its body surface area to weight ration and the more prone it is to hypothermia. When no attempt was made to preserve body heat, dogs and cats weighing < 10 kg dropped below their normal temperature by 3.4°C compared to 1.5°C after an average of one hour of anesthesia. The severity of hypothermia will also be influenced by the environmental temperature, duration of anesthesia, and exposure of body cavities.

Negative impact of hypothermia

A drop in core temperature to 34°C (93.2°F) should give rise to concern. As the core temperature falls, the myocardium becomes more irritable and the sino-atrial node beats more slowly. This is in part associated with increases in circulating catecholamines. There is a drop in cardiac output and blood pressure and at subnormal temperatures; atropine and glycopyrrolate are unlikely to correct the bradycardia. Changes in cardiac rhythm may be noted and at temperatures approaching 32.2°C (90°F), asystole or fibrillation may occur.

Fluid shifts from the vasculature resulting in hemoconcentration, blood viscosity increases and red blood cells sludge. Increased bleeding can occur secondary to prolonged coagulation times and alterations in platelet function.

Tissue perfusion is impaired by hypothermia and the shift in the oxyhemoglobin curve to the left decreases oxygen unloading. This however, may be counteracted by the developing metabolic acidosis. Lactate levels can be expected to rise secondary to poor perfusion and decreased hepatic metabolism. Blood glucose levels may rise and complicate interpretation of laboratory results.

Metabolism is slowed and liver function is impaired, delaying metabolism of anesthetic drugs which delays recovery. The requirements for inhalant agents drop and if anesthetic depth is not closely monitored, animals will receive a relative overdose. In addition, as a patient cools, the amount of anesthetic required to produce apnea decreases and the animal's responses to hypercapnia and hypoxia are blunted.

In several human studies, accidental intra-operative hypothermia has been linked to increased post-operative wound infection. This is likely a result of poor perfusion to the periphery, vasoconstriction and low oxygen tension at the surgical site. In addition, hypothermia impairs immune function, including the killing ability of neutrophils. One veterinary study linked would infection to duration of surgery [15] and no doubt maintaining normothermia is in the best interests of the patient.

In the post-operative period, cold animals take longer to recover, shiver violently and look miserable. Shivering increases their metabolic rate and heat production, but also increases their oxygen demand by up to 300%. This, combined with a decreased ventilatory drive can lead to hypoxemia if they are

breathing room air and can have serious consequences in sick animals or those with cardiac abnormalities. Pain from the surgical incision is also likely to be worse when an animal shivers.

Techniques for maintaining body temperature

Thermal losses should be minimized in all patients. Although rewarming is possible in the post-operative period, this can be associated with so-called "rewarming shock". Rapid rewarming can cause vasodilation, which is not well tolerated by some surgical patients.

Suggestions for preventing hypothermia:

- Surgical preparation avoid the use of cold prep solutions especially alcohol and use them sparingly. Warm sterile saline is a good choice in small patients.
- Surgery time should be kept to a minimum.
- Ambient temperature Normal operating room temperatures are often cool. Warmer temperatures would benefit the patients but may increase the surgeon's discomfort. The induction and recovery areas should be kept very warm.
- Warm inspired gases this requires specialized anesthetic equipment that is rarely available in veterinary medicine. However, if a circle system is used; low flow anesthesia will minimize heat loss from the respiratory tract.
- Warm mattresses Circulating warm water blankets are effective in small patients ^[16]. These blankets are more effective when placed on the limbs than on or under the trunk ^[17]. Electric blankets must be avoided as severe skin burns can occur in hypothermic animals.
- Forced warm air devices are effective in veterinary patients [18]. Examples include the Bair Hugger® (http://www.arizant.com/us/bairhuggertherapy/warmingunits).
- Blankets fleece blankets and thermal insulating blankets can minimize radiation and convective losses.
- Simple things including jackets and socks can be placed on small patients to decrease heat loss.
 Pieces of polystyrene, "packing peanuts" placed in a plastic bag and "bubble packing" are good surfaces to lay small patients on and newspaper is a good insulating layer to place over metal tables.
- Infra-red lamps great care should be used when using these devises as skin burns can occur
- Warm intravenous fluids when large volumes of fluid are given to patients they should be warmed to minimize thermal stress. Dextrose fluids should NOT be warmed.

Take home lessons

- Animals with a higher ASA status are more at risk therefore careful attention to choice of anesthetic techniques, monitoring and post-anesthetic care are especially important in the patient population.
- An increase in duration of the procedure contributes to mortality therefore every effort should be
 made to ensure procedures are done as quickly as possible and no "wasted" anesthesia time
 occurs because of poor scheduling or planning.
- Having a person dedicated to the anesthetic needs of the animal and specialized training of this
 person reduces anesthetic mortality.
- Because most deaths occur in the first three hours after the end of a procedure, the recovery
 area should be well staffed and animals should be continued to be monitored. More attention
 should be given to patient monitoring and support during this time, including providing warmth,
 fluids, maintaining a patent airway and providing pain relief.
- Small patients are more at risk therefore they should be accurately weighed and anesthetic drugs carefully calculated and if necessary diluted to increase accuracy of dosing.
- The negative impact of hypothermia is often underestimated. All efforts to decrease heat loss are worthwhile and many are inexpensive and simple to implement.
- When possible techniques that involve sedation with local anesthesia should be explored since the risks of sedation are lower than general anesthesia.

Although anesthetic related mortality in cats and dogs has decreased over the past 2 decades, there is still room for improvement and some key factors to focus on have been identified by the CEPSAF study.

Cardiopulmonary resuscitation

In the event that a cardiac arrest does occur, one should be prepared. This includes regular training sessions for staff and regular checking of CPR equipment and drugs. A centrally located, but mobile "crash cart" which contains equipment solely for CPR is a good investment. It can be stocked with intubation supplies, drugs, fluids etc and have a CPR chart attached to it, so that it is easy to draw up drugs without doing calculations. Excellent CPR charts (algorithms and drugs doses) can be purchased from the Veterinary Emergency and Critical Care Society - http://www.veccs.org

Cardiopulmonary resuscitation procedures in small animals were reviewed by Plunkett and McMichael in 2008 [19]. The recommendations for animals follow closely those of the American Heart Association (http://www.heart.org) and these were most recently updated in 2010. One of the new recommendations in these guidelines is to follow a CAB (compressions, airway, breathing) approach rather than an ABC approach (airway, breathing, compressions). This is because effective chest compressions are key to blood flow. What this means for us is that if the animal is not already intubated, or intubation supplies are not immediately available one should not wait to secure an airway before starting chest compressions. The most important drugs to have available are still epinephrine, atropine and lidocaine.

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Table 1. ASA classification of patients

ASA STATUS	DESCRIPTION
1	A normal healthy patient
2	A patient with mild systemic disease
3	A patient with severe systemic
	disease
4	A patient with a severe systemic
	disease that is a constant threat to life
5	A moribund patient who is not
	expected to live without the proposed
	surgical procedure

Table 2. Mortality rates in dogs and cats, derived from the CEPSAF study

	%	%
OVERALL	0.17	0.24
HEALTHY ASA 1-2	0.05	0.11
SICK ASA 3-5	1.33	1.40

Table 3. Time of anesthetic death (% of total)

TIME OF DEATH		
AFTER PREMEDICATION	1	1
INDUCTION	6	8
MAINTENANCE	46	30
POST-OPERATIVELY	47	61