TOO OLD FOR ANESTHESIA?

The Physiology of Aging, Drugs, Techniques and Tips for Success.

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Abstract

The physiologic changes that occur with ageing include alterations in body composition (less water and muscle and more fat), the central nervous system (decrease in neurons and neurotransmitters), the cardiovascular, pulmonary and renal systems (less reserve) and a less tightly controlled thermoregulatory system. These changes are occurring "below the surface" even in healthy older patients and leave them less able to withstand a challenge such as anesthesia. For example, the requirements for anesthesia, both injectable and inhalant are significantly reduced and the risk of overdosing these patients is real. Suitable anesthetic and analgesic protocols for older cats and dogs include using short acting, titratable and reversible drugs. A delay in recovery from anesthesia is more likely with the number one cause being hypothermia, but a decreased ability to metabolize and excrete drugs can contribute. Delirium and dysphoria are more common in our older patients and this must be differentiated from pain. Algorithms can be used during recovery to problem solve these issues.

Keywords: senior, geriatric, frailty, body composition, functional reserve, hypothermia

Introduction

Anesthesia for dogs and cats at either end of the age spectrum deserves special attention. The unique needs of dogs and cats at different life stages has led to the publication of several

excellent resources. The 2018 American Association of Feline Practitioners Feline anesthesia guidelines also provide expert advice and "go to" algorithms for troubleshooting multiple problems in the perianesthetic period. Anesthetic concerns at different life stages are discussed (see Resources).

Cats tend to age more uniformly than dogs, and a cat is considered senior between 11 and 14 years of age and geriatric from 15 to 25+ years of age. Breeds of dogs (related to their size and weight) age at different rates. Dogs are considered "senior" when they have reached 75% of their expected life span. However, it is more about age alone; it is understanding age-related changes that occur independent of health status plus assessing each patient as an individual – a combination of what you see and know (e.g. via blood work and imaging) and what is going on that you can't directly see (e.g. decrease in vital capacity of major organs).

It is estimated that 30-40% of all patients seen by veterinarians are seniors or geriatrics and many of these may require anesthesia for a variety of reasons including dental procedures which are recommended on a frequent basis in this population. Are the terms senior or geriatric just semantics or significant? In human healthcare a senior is defined as someone who has reached a certain age in an expected lifespan. The term geriatric is applicable to health status, in particular frailty. If a person meets three of the four following criteria, they are considered geriatric.

1. Weakness
2. Fatigue
3. Slowed mobility
4. Weight loss

In veterinary medicine the same terminology can be applied. The weakness that happens with aging is predominantly related to sarcopenia, which is the degenerative loss of skeletal muscle mass and strength associated with aging in all mammals.

Anesthetic mortality related to age

The Confidential Enquiry into Perioperative Small Animal Fatalities (CEPSAF) study provided valuable information on the risks associated with anesthesia in a variety of small animals and also pinpointed some specific risk factors in each species.[1-3] Older cats carry a higher anesthetic risk; cats over 12 years of age are twice as likely to die compared to cats aged 6 months to 5 years and this increased risk was independent from their health or ASA status.[a,(1)] In the CEPSAF study, dogs were grouped by age, but breed or size was not accounted for, therefore although dogs > 12 years had a higher mortality rate than young adults, the risk related to age in this study should be interpreted with caution because a 12 year old small breed dog is very different from a 12 year of large breed dog; they are at very different "places" in their expected lifespan.

Anesthesia for older pets

Although senior and geriatric patients may belong in a specific "life-stage" there is a wide variation in their health status. A sub-classification of the geriatric population has been suggested as follows: [4]

1. Healthy patients with age-related changes
2. Those with subclinical organ dysfunction
3. Those with an overt condition or conditions

Age and disease related changes in organ function and body composition impact on the pharmacokinetics (absorption, distribution, metabolism and elimination) of drugs therefore, dose

and dosing intervals may require adjustment in this patient population. Organ dysfunction may or may not be measurable. In many cases significant decreases in renal and hepatic function can exist yet this will not be reflected by running routine hematology and chemistry tests.

Cardiac disease can also have a silent presence; a patient may have no detectable heart murmur or history of exercise intolerance, yet echocardiography may show evidence of decreased cardiac function; not enough to cause overt disease, but enough to cause concern with some of the agents used for anesthesia and sedation.

When we give a drug, we are looking for a specific pharmacodynamic effect and in geriatric patients what we say may be different compared to a younger animal due to changes in body composition (e.g. decreased lean body mass), drug receptors and neurotransmitters. Age and disease related changes in pharmacokinetics and pharmacodynamics can result in adverse effects unless the clinician individualizes each anesthetic and analgesic plan.

Senior and geriatric animals may respond poorly to changes in their environment and many have clinical signs suggestive of cognitive dysfunction.[5-6] Faced with a hospitalization, or extensive in-patient treatments, some of these pets seem to "give up" within moments of being in a strange environment. This might be something as mild as refusing to interact with caretakers but could also result in more serious issues such as refusal to eat, or drink water. Encourage caregivers to bring familiar toys or blankets to be left with their pet, which are often a comfort to any animal, but especially to older animals. Keeping the hospital stay as short as possible will be beneficial; when possible schedule these patients first thing in the morning so that they can be discharged on the same day.

The most important age-related changes in cardiac function are decreased ventricular compliance and cardiac reserve. This renders older animals less tolerant of acute changes in intravascular

volume – both fluid loss and fluid overload. Older patients also have a decreased respiratory reserve. Vital capacity is reduced, the chest wall and lungs become less compliant and the anatomic dead space and work of breathing increase making them more susceptible to hypoxemia and hypercapnia. With a decrease in respiratory reserve, older animals may rapidly desaturate in the immediate post-induction period before they are intubated. For this reason, pre-oxygenation is recommended.[7] Pre-oxygenation takes 3 minutes and is time well spent. It builds in a large safety factor if there is difficulty achieving an airway, for example in a brachycephalic breed.

As animals age, renal blood flow decreases as does glomerular filtration rate and the number of functional glomeruli. Older animals may have underlying renal pathology which is well compensated for until they are stressed or challenged in the perioperative period (e.g. fasting, fluid deprivation, blood loss and hypotension) therefore a decline in post-anesthetic renal function is a concern. These patients may already be receiving non-steroidal anti-inflammatory drugs (NSAIDs) for chronic pain or may be administered NSAIDs as part of a perioperative analgesic protocol for surgery. These drugs block prostaglandin production which is important for maintaining renal blood flow during periods of hypotension. If an NSAID is used in the peri-anesthetic period, preventing, recognizing and treating hypotension is essential to maintain normal fluid balance and renal perfusion.

Brain mass decreases with age because of neuronal loss, cerebral blood flow declines and the quantity of neurotransmitters is reduced. Specific age-related changes indicative of neurodegeneration similar to those seen in aged people have been identified in the brain, brainstem and spinal cord of cats.[8] Although the exact reasons are unclear, but probably linked to decreased brain mass, older humans have decreased anesthetic requirements which is well

documented for the inhalant agents.[9] This phenomenon has also been confirmed for the commonly used agents isoflurane and sevoflurane in dogs.[10-11] Because of the documented decrease in anesthetic requirements in older patients the depth of anesthesia must be closely monitored (e.g. by assessing jaw tone, general muscle tone and eye position) to prevent anesthetic overdose. Hypothermia also decreased anesthetic requirements.

Aging can result in altered drug concentrations at their site of action and altered drug actions *per se.* Some of these changes are related to altered body composition, blood flow and organ perfusion and some are a result of altered metabolism and excretion and changes in the number and density of receptors in target organs. Advanced age can result in unpredictable drug effects therefore careful drug choices and administration techniques, combined with close monitoring is essential for a good outcome. It is prudent to choose drugs that are:

1. Reversible
2. Can be given "to effect" and
3. Have a short duration of action

As with all patients a complete history and physical examination are essential. Clinical findings will dictate what pre-anesthetic blood work should be run and what additional tests may be required (e.g. thoracic radiographs, echocardiography, N-terminal pro-brain natriuretic peptide [NT-proBNP]). In humans there are no agreed upon or mandated laboratory tests based solely upon age.[12] Abnormal laboratory tests were less predictive of outcome in elderly surgical patents than ASA[a] classification or surgical risk.[13] A compete blood count and chemistry plus a urine analysis is generally warranted in this patient population both for evaluation of major body systems and as a baseline for comparison later.

Sedation and premedication

One of the most commonly made mistakes when anaesthetizing older patients is to depend primarily on inhalant agents and avoid premedicant agents in the misunderstanding that inhalant agents are somehow "safer" because they go "in and out" and are minimally metabolized. Sedation is recommended to decrease anxiety and fear which lead to increased catecholamine release, cardiac arrhythmias, peripheral vasoconstriction, increased cardiac work and decreased tissue perfusion. Acepromazine is not always contraindicated in geriatric patients although dose requirements (on an mg/kg basis) may be markedly decreased and careful thought must be given to patient selection. Acepromazine is an anti-emetic and anti-arrhythmic but one of its most important properties is its anesthetic sparing effect.[14] Two studies have examined the effects of acepromazine on systemic blood pressure and glomerular filtration rate (GFR) measured by scintigraphy in clinically normal dogs.[15-16] Acepromazine appears to protect renal function despite a decrease in blood pressure. Acepromazine combined with butorphanol provided excellent sedation for dogs undergoing nuclear scintigraphy procedures, and GFR was no different after sedation compared to measurements obtained from the same dogs without sedation, despite a decrease in systolic, diastolic and mean blood pressure.[15] In the same study, diazepam and ketamine resulted in significant increases in heart rate and blood pressure and resulted in a lower GFR compared to the acepromazine + butorphanol combination. Tachycardia should be avoided in our older patients as it increases cardiac work and myocardial oxygen demand. As previously stated, preserving renal blood flow and GFR is especially important in older patients who may have decreased renal reserve or are receiving NSAIDs for acute or chronic pain. The concerns related to acepromazine are its long duration of action, that it is not reversible, and vasodilation enhances heat loss in a population that is already vulnerable to hypothermia.

Benzodiazepines such as midazolam and diazepam produce more reliable sedation in older patients than in younger ones. For premedication, midazolam has an advantage over diazepam because it can be given intramuscularly. These drugs are also reversible with flumazenil should an adverse event or delay in recovery occur. Opioids produce sedation and provide analgesia and should be a part of all anesthetic protocols. Butorphanol provides good sedation in both dogs and cats. In dogs, opioids are significantly anesthetic sparing, but this effect is less in cats.

Induction agents

Ketamine causes an increase in heart rate and blood pressure which may be detrimental to some older patients. However, ketamine plays a role in preventing central plasticity (sensitization) and in the face of hypovolemia supports cardiovascular function and does not impair tissue oxygenation.[17-18] The pros and cons of ketamine in each individual must be considered before it is used. A good move is to use it as an infusion during surgery preceded by a loading dose which is far lower than an induction dose and has fewer cardiovascular side effects. For example, up to 5 mg/kg is required for induction, but a sufficient loading dose prior to infusion is 0.25 to 0.5 mg/kg. Propofol can be titrated slowly "to effect" without causing excitement and when used after premedication the dose required for induction is significantly reduced. When used in combination (co-induction technique) with intravenous diazepam or midazolam, induction is smooth, and the dose can be reduced. It is important to avoid large doses of propofol and to administer it slowly to prevent profound hypotension. Propofol is metabolized in the liver but this is not significantly affected by poor liver function perhaps because it is also cleared by the lungs. There are no active metabolites therefore no "hang over" effect. However, the pharmacokinetics of propofol in older dogs is different; they require less to reach a plane of anesthesia sufficient for intubation, and clearance of the drug is slower than reported in young

dogs.[19] Alfaxalone is a suitable induction agent in dogs and cats, but as with propofol large doses given rapidly will cause cardiorespiratory depression. Etomidate has minimal cardiopulmonary depressant effects and can be a valuable induction agent in older dogs and cats, those with cardiac disease or in the face of fluid losses.[20]

Co-induction techniques

Using an injectable induction agent in combination with a benzodiazepine reduces the dose of induction agent required. For example, in premedicated dogs, giving 1.0 mg/kg of propofol followed by midazolam (0.25 mg/kg), then titrating propofol until dogs could be intubated resulted in a total dose of 1.1 ± 0.2 mg/kg propofol compared to 3.2 ± 0.6 mg/kg when using propofol alone.[21] When midazolam was given before propofol, dose reduction was reported but was less than when propofol was given first, and some dogs became excited.(21)

Speed of injection

The rate of injection makes a difference in the induction dose of propofol in healthy dogs. A rate of 1.3 mg/kg/minute resulted in a total dose of 3.5 ± 1.2 mg/kg being required for intubation compared to 4.8 ± 0.6 mg/kg if given at 0.4 mg/kg/minute.[22] A slow rate of administration is especially important in older patients because cardiac output and circulation times are usually lower and slower respectively; this means you must give sufficient time for the drug to travel from the injection site to the brain before giving more.

Maintenance of anesthesia

For all but the shortest procedures inhalant agents are most commonly used for maintenance of anesthesia. All inhalant agents are potent cardiorespiratory depressant agents making the use of anesthetic sparing drugs and techniques important. Intra-operative infusions including opioids and low doses of ketamine reduce inhalant agent requirements and provide additional analgesia.

Lidocaine infusions can be used in dogs but are not recommended in cats because of documented decreases in cardiac output and perfusion.[23,24] The use of locoregional techniques (e.g. epidural placement of local anesthetics and / or opioids and specific nerve blocks) are extremely beneficial in older patients as they decrease anesthetic requirements, improve post-operative comfort and result in more alert patients because they need fewer systemic drugs that can cause sedation.

Most anesthetic deaths occur in the first three hours of recovery, probably because this is a time when physiological support is withdrawn; for example, animals go from breathing 100% oxygen to room air at a time when their requirements for oxygen may increase if they are cold and shivering. This is especially detrimental in older patients with reduced cardiac and respiratory reserves. For these reasons, supplemental oxygen should be given until animals are normothermic. Because older dogs and cats have a smaller muscle mass than younger animals, they generate less heat via shivering therefore rewarming and return to normal body temperatures takes longer. The close monitoring that occurred during anesthesia is often withdrawn in recovery, but it should be continued during this high-risk time.

Other tips for older pets

Older dogs may have problems with slippery floors. Using yoga mats outside their cage or kennel is very helpful as is placing a harness, so you can assist them to travel around the clinic and get up after a procedure. Whenever possible schedule them for early in the day so they can be an outpatient; getting back to a normal routine is important especially for pets with cognitive dysfunction. Older pets do not thermoregulate well, so extra efforts are needed to keep them warm; hypothermia is the number one cause of delayed recovery. Willingness to eat soon after anesthesia is also important and adding maropitant and / or ondansetron to the protocol will

decrease the time to voluntary feeding and increase caloric intake in the first 24 hours after surgery. Although our older patients may be “more delicate” and challenging to anaesthetize, with careful assessment and choice of anesthetic protocols a good outcome should be the rule and not the exception.

Resources

AAFP = American Association of Feline Practitioners

AAHA = American Animal Hospital Association

- The AAFP-AAHA Feline Life Stages Guidelines: www.aahanet.org
- The AAFP Senior Care Guidelines: http://catvets.com
- The AAHA Senior Care Guidelines for Dogs and Cats: www.aahanet.org
- 2018 AAFP Feline Anesthesia Guidelines https://catvets.com/guidelines/practice-guidelines/anesthesia-guidelines

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[a] American Society of Anesthesiologists physical status classification: www.asahq.org

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