

PREVALENCE AND RISK FACTORS FOR POSTANESTHETIC ASPIRATION PNEUMONIA (1999-2009):
A MULTICENTER STUDY

By

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ABSTRACT

INCIDENCE AND RISK FACTORS FOR POST ANESTHETIC ASPIRATION PNEUMONIA (1999-2009): A MULTICENTER STUDY

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To date no multicenter assessment of incidence or risk factors for post anesthetic aspiration in the canine population has been performed. The goal of this study was to estimate incidence and identify risk factors for post anesthetic aspiration pneumonia in the canine patient. Medical record databases from six institutions were searched to identify all cases of pneumonia in dogs that had general anesthesia from 1999 to 2009. After record review, dogs were included in the study if a radiographic diagnosis of aspiration pneumonia was made within 4 days following anesthesia. Each affected dog was compared with two unaffected control dogs. Control dogs were randomly selected from the remaining canine patients coded for one hour of anesthesia in each database. The overall incidence was 1.7 in 1000. Factors associated with increased risk for aspiration pneumonia included: age, weight, ASA status, history of neurological disease or respiratory disease, abdominal exploratory surgery, upper airway surgery, use of continuous rate infusion, megaesophagus, endoscopy, hydromorphone at induction and vomiting or regurgitation anytime during the anesthetic or recovery period. The combined data from the previously described retrospective study and a future prospective study of post anesthetic aspiration risk factors have the potential to create a scale for aspiration pneumonia risk.

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INTRODUCTION

Aspiration pneumonia is becoming a well recognized cause of morbidity and mortality at veterinary teaching hospitals throughout the country. Over the last 10 years retrospective clinical studies have been published from the University of Pennsylvania, the University of California at Davis, the University of Minnesota and Washington State University reporting the incidence and identifying risk factors for the development of aspiration pneumonia in veterinary patients.¹⁻⁷ A 2008 retrospective study from UC Davis identified the top five causes of aspiration pneumonia in dogs as follows: esophageal disease, vomiting, neurologic disorders, laryngeal disease, and post-anesthetic aspiration.⁴ The University of Minnesota found that of all their patients suffering from aspiration pneumonia; the majority of post-anesthetic or post sedation patients exhibited clinical signs within 24 hours after an episode of anesthesia or sedation.⁶ Aspiration pneumonia has been reported in many different animal species including experimental studies in rabbits, clinical studies in dogs, case reports in an oryx and a moose.⁷⁻¹⁰

Post-anesthetic aspiration pneumonia has been extensively studied by the human medical community since 1946 when a physician named Mendelson documented aspiration as the cause for respiratory failure in 66 women during labor.¹¹ The first arguable recorded patient to suffer effects from aspiration pneumonia was a 15 year old girl named Hannah Greener in 1848.¹² Hannah was placed under general anesthesia using chloroform for a

toenail removal. Hannah was “dashed with water” and given brandy to drink after inhalation of chloroform gave her a blanched appearance and weakened pulse according to the doctors notes. Within seconds after swallowing the brandy “with difficulty” Hannah was pronounced dead. A post-mortem exam found Hannah’s lungs “in a very high state of congestion” with patches of deep blue, purplish, or scarlet hue. The lungs were not collapsed and there was a bloody froth on alveolar section. A 1986 study reported post-anesthetic aspiration to occur as infrequently as 1.4 and 6.5 out of every 10,000 anesthetic episodes.¹³ Recent data published, however would, suggest that post-anesthetic aspiration pneumonia occurs more often; one study reports as great as 1 out of every 2000-3000 anesthetics.¹⁴ Higher rates have been reported in children at 1 per every 1200-1600 anesthetic episodes.¹⁴ Many more studies have been performed to determine risk factors for aspiration and effective prophylactic measures to prevent the incidence of post-anesthetic aspiration.

Although this post-anesthetic complication is of concern in all veterinary species the majority of clinical studies have been performed in dogs. Previous studies of post-anesthetic aspiration pneumonia focused on very specific disease processes such as intracranial disease⁷, intervertebral disk disease³, and laparotomy patients.¹⁻² An all encompassing retrospective study examining the overall incidence and risk factors associated with post-anesthetic aspiration pneumonia has not been performed. We hypothesize that there are patient variables and management strategies that influence the prevalence of post anesthetic aspiration pneumonia. Estimating the overall incidence of post-anesthetic aspiration pneumonia will help

to determine the frequency and magnitude of this recognized complication. Determination of post-anesthetic aspiration pneumonia risk factors may help to identify and implement preventative strategies for everyday practice of anesthesia.

The objectives of this study were:

1. To estimate the prevalence of post-anesthetic aspiration pneumonia in the canine patient
2. To distinguish patient and management variables associated with the development of post-anesthetic aspiration pneumonia in dogs

CHAPTER 1

LITERATURE REVIEW

Definition

A 2001 New England Journal of Medicine article suggests that aspiration pneumonia and aspiration pneumonitis should be separated into two clinical entities for accurate diagnosis and to ensure proper treatment is instituted.¹⁵ Aspiration pneumonia should be considered an infectious process, and is defined as a bronchopneumonia that develops secondary to aspiration pneumonitis. Aspiration pneumonitis occurs following aspiration of foreign materials into the bronchial tree, usually oral or gastric contents; it was first scientifically studied and reported in human medical literature by Mendelson in 1946.¹¹ Mendelson described the development of acute respiratory failure in 66 women that aspirated stomach contents during labor. As a result of his work in 1946, Mendelson's syndrome has become a commonly used term to describe aspiration pneumonitis in people.

Pathophysiology

Pathophysiology of aspiration pneumonia is characterized by three phases: airway response, inflammatory response, and secondary bacterial infection.¹⁶ The initial phase of aspiration pneumonia, or airway response, occurs immediately after aspiration. During this phase there is a direct chemical burn of the pulmonary tissue and stimulation of the sensory

nerves located in the airway. Mendelson's syndrome results in necrosis of type 1 pneumocytes. Stimulation of sensory nerves in the affected area results in release of substance P, calcitonin gene-related peptide, and neuropeptide K. These peptides cause an increase in vascular permeability, bronchoconstriction, and an increase in mucus production. Phase 2, the inflammatory phase, occurs 4 to 6 hours following aspiration. This phase is associated with significantly increased capillary permeability, infiltration of neutrophils, and severe pulmonary edema. The inflammatory phase usually lasts for 1 to 2 days or even longer if particulate matter is aspirated. Evidence of inflammation can be seen in areas of the lung that are very distant from the originally affected area. Usually within 24 to 36 hours patients show radiologic evidence of lung consolidation and are febrile. A secondary bacterial infection (phase 3) is most likely to occur if the patient has aspirated particulate matter, but does not necessarily always occur. Secondary bacterial infection should be suspected in any patient which develops a fever in conjunction with evidence of a neutrophilia with a left shift, toxic neutrophils and increased pulmonary densities on radiographs 36 hours or more post aspiration.

Forms of aspirated gastric contents

Aspiration pneumonitis can further be broken down by the type of gastric contents aspirated. Categories are divided up by pH, presence or absence of particles in the fluid, and size of particles. Outcomes for aspiration pneumonitis, leading to pneumonia, worsen depending upon the nature of the aspirated material. A 1946 landmark study by Mendelson using rabbits as experimental models found that more severe clinical signs of aspiration were noted when gastric pH was less than 2.0 and particulate matter was contained within the

fluid.¹¹ Recent experimental animal models have studied the effects of acid aspiration only (ACID), small nonacidified particles (SNAP), and combined acid and gastric food particles (CASP).¹⁷

ACID

Acid only aspiration models are most often induced with intratracheal instillation of hydrochloric acid diluted to a pH of 1.25 with normal saline. A biphasic response as described above with a strong bronchoconstrictive reaction followed by neutrophilic inflammation within four to six hours after the initial insult. This results in microvascular instability with the formation of pulmonary edema which inhibits the diffusion of oxygen molecules through the alveolar membrane into the pulmonary circulation. The influx of plasma protein and other substances results in surfactant dysfunction leading to atelectasis. Improvement in pulmonary function was observed in these experimental subjects when treated with exogenous surfactant instilled intratracheally.¹⁷

SNAP

Small nonacidified particles are obtained from rodent stomach contents; they are washed with normal saline, filtered through gauze, autoclaved, and centrifuged before tracheal instillation. Aspiration of these particles also results in a neutrophilic response within four to six hours; however microvascular instability and therefore pulmonary edema formation is much less severe. In these animals monocyte chemoattractant protein-1 has been noted to be elevated; this mediator has been documented in granuloma formation.¹⁷

CASP

Combined acid and small particles are considered as a two hit injury model for patients suffering from aspiration using rats as the experimental subject. These animals exhibit the most severe pulmonary damage on pulmonary histopathology. Levels of albumin in bronchialveolar lavage fluid are higher in these rats than in ACID or SNAP alone; suggesting that they have even less alveolar membrane to capillary wall integrity. The rats used in this study also demonstrate higher levels of neutrophils for a longer period of time than that of ACID and SNAP subjects. Pulmonary function is so impaired that arterial oxygenation levels have been found to meet the clinical criteria for that of ARDS patients in the 24 hour period after aspiration.¹⁷

Patient Outcomes

Potential outcomes following an aspiration episode range from no overt clinical signs to acute lung injury (ALI), acute respiratory distress syndrome (ARDS), and possibly death. In a majority of cases patients who aspirate do not exhibit clinical signs.¹⁷ A 1993 study of human peri-operative pulmonary aspiration found that 64% (42/66) of surviving patients that aspirated during surgery showed no respiratory sequelae post-operatively. This study concluded that patients with clinically apparent aspiration that do not develop apparent clinical signs within 2 hours of aspiration are unlikely to experience any respiratory sequelae.¹⁸ No such study has

been performed in veterinary medicine at this time. It has been reported that up to one-third of human post-operative patients who aspirate will develop ALI/ARDS.¹⁷ Humans suffering from ALI/ARDS secondary to aspiration pneumonia are reported to have a 30% mortality rate and these patients account for up to 20% of all deaths attributable to anesthesia.¹⁷

ALI/ARDS

Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) are forms of progressive respiratory failure. These disease processes may be caused by a direct pulmonary insult such as: aspiration, pneumonia, pulmonary embolism, chest trauma, near drowning, or inhalation of noxious gases. ALI and ARDS can also be provoked by systemic diseases such as: bacterial sepsis, pancreatitis, peritonitis, severe burns, hemorrhagic shock, transfusions, or drug overdoses.¹⁹ Clinical characteristics for ALI/ARDS include a rapid, diffuse bilateral lung injury, severe hypoxemia, non-cardiogenic pulmonary edema, low ventilation/perfusion ratios, and abnormal physiologic shunting of oxygen. Clinical definitions for ALI and ARDS are very similar and only differ in the PaO₂/FiO₂ ratio. ARDS is considered to be a more severe physiologic form of ALI. The clinical definition for each of these includes an acute onset within days of exposure to the inciting cause, radiologic evidence of diffuse pulmonary infiltrates consistent with non-cardiogenic pulmonary edema, a PaO₂/FiO₂ of ≤ 300 mmHg for ALI, a PaO₂/FiO₂ of ≤ 200 mmHg for ARDS, and no clinical evidence of left sided heart failure or elevated left atrial pressure (pulmonary arterial catheter wedge pressures ≤ 18 mmHg).¹⁹ Patients with ALI/ARDS usually go through two and may enter three pathologic stages. The initial stage consists of

diffuse pulmonary edema resulting in alveolar damage followed by a proliferative stage during which time the edema resolves. During the proliferative phase type II alveolar cells multiply, squamous cell metaplasia occurs, the interstitium becomes infiltrated with myofibroblast, and collagen is deposited in the parenchyma. In the group of patients that usually die from ALI/ARDS a third fibrotic stage occurs. The fibrotic stage of ALI/ARDS consists of accelerated collagen deposition, destruction of normal lung architecture, diffuse fibrosis, and parenchymal cyst formation.¹⁹

Financial Impact

The financial impact of aspiration pneumonia has also been studied in human and veterinary medical patients. A veterinary study from the University of Minnesota of all canine aspiration pneumonia patients admitted found the average hospital length of stay was 3 days in intensive care with a range of 0-11 days.⁶ Length of hospitalization was also reported in a veterinary study of canine aspiration pneumonia from UC Davis with an average of 5 days (range, 1-23 days) hospitalization for survivors and 5.4 days (range, 1-19 days) for non-survivors.⁵ Average cost for diagnostic workup and treatment of canine aspiration pneumonia patients at the University of Minnesota was \$2,581.48 with a range of \$241.00 to \$10,400.00.⁶ One report from human medicine of post-operative patients was dramatically higher than that of the canine patient with a mean length of 25 days in hospital and an average increase of >6 days (range of 6-21 days) in length of hospital stay. Increases in hospital length of stay resulted

in an average cost of \$58,000 in patients with aspiration pneumonia compared to \$14,000 in patients without aspiration pneumonia. Increase in hospital costs attributable to aspiration pneumonia for non-veterinary patients was estimated to be >\$10,000.00 with a range of \$10,000.00 to \$60,000.00.²⁰

Diagnosis

Diagnosis of aspiration pneumonia can prove challenging if the inciting event is not witnessed. Current literature would suggest that most episodes of aspiration are unobserved.^{15, 17} A diagnosis of aspiration pneumonia in humans after an unwitnessed aspiration event most often occurs after other causes for hypoxia have been ruled out. Current recommendations in the human and veterinary literature for diagnosis of aspiration pneumonia include: history, physical exam, complete blood count, thoracic radiographs (both lateral views and a ventrodorsal view), pulse oximetry and/or arterial blood gas, and transtracheal wash.²¹

Physical exam findings

A recent study from the veterinary teaching hospital at U.C. Davis found that less than half of 88 dogs affected with a radiographic diagnosis of aspiration pneumonia exhibited elevations in temperature, heart rate, or respiratory rate on physical exam.⁴ Dogs were divided into two groups; group one consisted of dogs presenting to the hospital with a known

diagnosis of aspiration pneumonia (65/88) and group two were made up of dogs that acquired aspiration pneumonia following admission while hospitalized (23/88). Sixty-nine percent of all dogs studied reported notable changes in lung sounds. A clinical textbook for physicians reports the most common findings on physical exam to be: altered mental status, periodontal disease/poor oral hygiene, rhonci, and decrease resonance upon percussion of the chest. Rhonci are rattling sounds from the chest similar to snoring caused by secretions in the bronchial airways. Less commonly patients may exhibit: wheezes, crackles, severe dyspnea, or acute respiratory failure.³⁷

Radiographic findings

Radiographic evidence was found to be the most reliable method of detection of all dogs studied with 74% of dogs exhibiting an alveolar infiltrate and 26% of dogs exhibiting an interstitial pattern. The right middle lung lobe was most commonly involved, with single lobe involvement most frequent.⁴ Results from another study of 125 dogs admitted for aspiration pneumonia by the University of Minnesota suggest similar radiographic findings with 69.6% of dogs showing evidence in the right middle lung lobe.⁶ Human literature indicates that radiographs exhibiting consolidation of lower lungs is suggestive of aspiration pneumonia.³⁷

Laboratory findings

Hypoalbuminemia and hypoxemia were also frequently detected in the patients studied.⁴ Hypoalbuminemia was found in 53% of all dogs studied. Hypoxemia was found in 79% of dogs that had arterial blood gas analyses obtained on room air within 48 hours of

aspiration (22/28).⁴ Results of transtracheal wash diagnostics were not reported in the U.C.

Davis study; however the Minnesota study found that 76.6% of dogs sampled did have bacterial

growth.⁶ Of the samples collected *E. coli*, *Mycoplasma* spp., *Pasteurella* spp., and

Staphylococcus spp. were the most common isolates recovered. Slightly more than half of samples (57.1%) from this study grew 3 or more organisms.

Results from laboratory tests from human literature report leukocytosis (WBC >12,000) and occasionally the patient may have evidence of anemia from chronic disease. Sputum, as well as blood, cultures are reported to be low yield. Arterial blood gas is recommended in these patients if respiratory acidosis is suspected.³⁷

Therapy

Human medicine

Pneumonitis v. pneumonia

Literature from human medicine separates aspiration into two different clinical scenarios upon which therapy is predicated, aspiration pneumonitis and aspiration

pneumonia.¹⁷ Aspiration pneumonitis is the term used for aspiration of gastric contents;

whereas aspiration pneumonia is a term reserved for aspiration of colonized oropharyngeal material. (Treatment for both is basically the same with the exception of antimicrobial therapy.)

General treatment recommendations

In both cases the patient should be positioned so that the risk for further aspiration is decreased. This can be achieved in the conscious patient by raising the patient's bed to a 45 degree angle with the head up and turning the head laterally to suction the oral and pharyngeal cavities. The patient may or may not require intubation depending on the neurologic status, degree of hypoxemia, hemodynamic stability, and the volume/character of gastric material. Mechanical ventilation may be indicated depending upon the severity of hypoxemia and the hemodynamic stability of the patient. Routine bronchoscopy with lavage may be performed in cases which the aspirated material has large amounts of particulate matter and there is radiographic evidence of severe atelectasis, but is not recommended in most cases. Corticosteroid therapy to reduce inflammation has been used in the past; however recent studies suggest they are of no benefit. In one study, patients showed a higher incidence of Gram negative pneumonia following corticosteroid therapy.¹⁷

Antimicrobial therapy recommendations¹⁷

Empirical antimicrobial therapy is a gray area in human medicine; those against the use of empirical therapy state that it can lead to selection for resistant strains of bacteria in uncomplicated pneumonitis cases. Other physicians call for the empirical use of antimicrobials, reasoning that it is very difficult to distinguish pneumonitis and pneumonia. They equate aspiration pneumonia to ventilator-associated pneumonia in which no adverse effects have been proven when a short course of antibiotic therapy has been initiated and then de-escalated or discontinued based on quantitative microbiology. Empirical therapy is also recommended in

patients that aspirate gastric material who have a short bowel obstruction or other condition associated with colonization of gastric contents. Current literature recommends use of clindamycin in patients not at risk for resistant bacteria. Patients with ventilator-associated pneumonia or those at risk for resistant bacteria should be prescribed piperacillin/tazobactam plus vancomycin or carbapenems with vancomycin. Fluoroquinolones plus clindamycin or metronidazole has also been recommended. It should also be mentioned that once a diagnosis of aspiration pneumonia is made early administration of antibiotics is strongly recommended.³⁷

Veterinary medicine

For veterinary patients current mainstays for treatment of uncomplicated aspiration pneumonia include: oxygen therapy, intravenous fluids, cage rest, nebulization, coughing, and frequently turning the patient from one side to the other. Some sources recommend the inclusion of bronchodilators. Other therapies such as antimicrobial usage are somewhat debated. Empirical therapy with antibiotics to treat secondary bacterial infection is recommended by some references; however other reports argue that empirical therapy may lead to antimicrobial resistant strains of bacteria. These references recommend that antimicrobial therapy be delayed until transtracheal wash can be performed to obtain culture and sensitivity results. Percentage of oxygen therapy is also controversial because of the potential to cause oxygen toxicity in patients that are exposed to high levels of oxygen for sustained periods of time. Evidence suggests that animals without any inflammatory lung injury which are exposed to 100% oxygen for 64 hours or more can exhibit acute respiratory distress.²² It was found that this respiratory distress is secondary to a loss of lung volume,

decreased lung compliance, edema formation, and acute hypoxemia. These changes are linked to type 2 pneumocyte dysfunction causing surfactant abnormalities.²³ Another study reported that exposure to 60% oxygen for up to 3 weeks resulted in only minimal respiratory distress.²⁴ A study from 2000 reported that rabbits which were exposed to 50% oxygen over a 24 hour period following experimental gastric acid aspiration showed increased pulmonary edema, physical signs of respiratory distress, and increased mortality.²⁵ It was proposed by this study that rabbits exposed to high oxygen levels after gastric aspiration may generate more oxygen free radicals resulting in more severe pulmonary damage than those rabbits exposed to lower oxygen levels. Results from this study suggest that aspiration pneumonia patients may require a lower percentage of oxygen delivery than those patients with other types of lung injury.

Prognosis

Reports of survival rates for aspiration pneumonia in dogs range from 95-50% in the veterinary literature. Lowest survival percentages were found a study of dogs that experienced post-operative pulmonary complications following laparotomy (50%),¹ and dogs with pneumonia after intracranial surgery.⁷ Highest survival percentages were reported in dogs following unilateral arytenoid lateralization procedures (95%).²⁶ In a study from UC Davis veterinary teaching hospital, dogs experiencing aspiration pneumonia from a variety of

disorders survival rate was found to be 77%.⁵ The University of Minnesota reported an overall survival rate of 81.6% with the best prognosis in patients with only one lung lobe affected.⁶

Risk Factors

Any patient undergoing anesthesia is at some degree of risk for post-operative aspiration pneumonia as loss of consciousness causes a diminished or even non-existent swallowing reflex.¹⁷ Certain disease processes are associated with increased risk of aspiration and these patients are therefore deemed high risk anesthetic patients. Disease processes associated with post-operative aspiration pneumonia in veterinary literature include: laryngeal paralysis, intracranial disease, megaesophagus, and intervertebral disc disease.^{3, 7,} Pre-disposing risk factors for humans include: diabetes mellitus, pregnancy, and morbid obesity. Patients with diabetes mellitus type I and II are at higher risk for aspiration due to a decrease in the rate of gastric emptying.²⁷ This decrease in gastric emptying is thought to be due to an autonomic neuropathy which can occur in diabetic patients that do not have well regulated blood glucose levels.²⁸ Pregnancy and obesity are thought to increase the risk for aspiration pneumonia due to increased intra-abdominal pressure and delayed gastric emptying resulting in a higher incidence of gastro-esophageal reflux or regurgitation.¹³ Curiously, there are no reported studies in the veterinary literature to suggest that animals are at an increased risk for aspiration pneumonia with diabetes mellitus, pregnancy, or obesity. It is possible that these

factors significantly increase the risk for aspiration in dogs but have not been evaluated yet. Alternatively, difference in anatomy and physiology between humans and veterinary patients may provide another reason for this difference of reports.

Studies documenting aspiration pneumonia in veterinary patients

Laryngeal paralysis

Patients with laryngeal paralysis are considered very high-risk for post-operative aspiration pneumonia by surgeons and anesthesiologists alike. Numerous studies examining the post-operative outcomes of various surgical techniques for the treatment of laryngeal paralysis have produced data that support these concerns. Of the literature reviewed incidence of aspiration pneumonia was 18-23 % of patients studied and survival rates were between 78-95%.^{26, 29} Megaesophagus and/or esophageal disease has been reported in many of these patients pre- and post-operatively. A study from Colorado State University Veterinary Teaching Hospital reported an 11% occurrence of esophageal disease pre-operatively and a 4% incidence of post-operative megaesophagus in 140 canine cases of laryngeal paralysis.²⁹

It was initially believed that post-operative aspiration pneumonia was due to the surgical procedure itself; interestingly however most cases of aspiration pneumonia are reported to occur months post-operatively. A recent study of 32 dogs found 18% of dogs with idiopathic laryngeal paralysis experienced aspiration pneumonia and that those dogs with worse esophageal function were more susceptible to the disease.³⁰ These findings strongly

suggest that idiopathic laryngeal paralysis is syndrome associated with a degenerative polyneuropathy which also causes esophageal dysfunction at or after the initial diagnosis of laryngeal paralysis.³⁰

Central Neurological Disease

Intracranial Disease

Intracranial disease is also a significant risk factor in dogs for post-operative aspiration pneumonia. A 2001 retrospective study from Washington State University Veterinary Teaching Hospital found that 37% of dogs with space-occupying intracranial lesions were diagnosed or highly suspected to have aspiration pneumonia post-craniotomy.⁷ This study found that pneumonia typically occurred within the first week after surgery. Significant risk factors included dogs that experienced vomiting or regurgitation and dogs with megaesophagus. Survival rate for dogs with aspiration pneumonia in this study was about 58%.

Intervertebral Disc Disease

A retrospective study was performed at the University of Pennsylvania Veterinary Teaching Hospital of 707 dogs presenting for diagnosis and treatment of intervertebral disc disease.³ This study compared the incidence of aspiration pneumonia between 1992-1996 and 2002-2006 and looked for specific risk factors associated with anesthesia. Incidence of aspiration pneumonia increased from 0.6% during 1992-1996 to 4.6% during 2002-2006. The authors postulated two potential reasons for this finding. Dogs in the latter period were more

likely to undergo magnetic resonance imaging for diagnosis of intervertebral disc disease at an off-site facility and transported back to the teaching hospital for treatment. It was suggested that these dogs were subject to inadequate monitoring and nursing during the recovery period putting them more at risk to aspirate gastrointestinal contents. Another proposed theory for increased aspiration pneumonia incidence was longer hospital stays in the latter group of dogs putting them at greater risk for nosocomial pneumonia. Risk factors identified by this study include: pre-anesthetic tetraparesis, cervical disc disease, and exposure to magnetic resonance imaging, long anesthetic duration, undergoing more than one anesthetic procedure, and vomiting or regurgitation post-anesthetically. Survival rate for this study was 99% of all dogs included in the study. Survival rate from 1992-1996 was 98.5% and from 2002-2006 was 99%.

Post-operative pulmonary complications

Another 2006 retrospective study from the University of Pennsylvania Veterinary Teaching Hospital looked at incidence and risk factors for post-operative pulmonary complications (PPCs) including aspiration pneumonia. PPC was diagnosed if a dog had physical examination evidence of pulmonary disease and/or dyspnea and developed two or more of the following complications within 24 hours of laparotomy: SpO₂ < 94%; PaO₂ < 85 mmHg; radiographic evidence of pulmonary disease; or cytologic, microbiologic, or histopathologic evidence of acute infectious or inflammatory pulmonary disease.^{1, 2} This study looked at all dogs undergoing exploratory laparotomy over an 11 month period. One hundred sixty-two records were reviewed and 36 (22%) of those dogs experienced post-operative pulmonary complications. Eight of 36 dogs that experienced post-operative pulmonary complications

suffered from pneumonia; of those eight dogs four survived to be discharged from the hospital. Risk factors for post-operative pulmonary complications included: dogs with an ASA status of III or greater, emergency procedures, prolonged anesthetic duration, use of butorphanol or oxymorphone for post-operative pain, dogs that received blood products, dogs that receive reversal of opioids or benzodiazepines, and dogs that recovered in the intensive care unit.

Prevention

Many precautions are taken by the anesthesia team to decrease the perceived risk factors for post-anesthetic aspiration pneumonia. In human hospitals throughout Germany, guidelines recommend that patients are fasted from solids for at least 6 hours and liquids for at least 2 hours prior to surgery.³¹ Veterinary guidelines have not been established by the American College of Veterinary Anesthesia at this time. Care is taken to protect the patient's airway with the placement of a properly fitting endotracheal tube; some studies have suggested frequent monitoring of airway cuff pressure, gel lubrication of the cuff, and the use of an endotracheal tube with a silicone cuff to prevent aspiration of gastric contents.^{32, 33, 34} Patients are usually not extubated until they demonstrated an adequate swallowing reflex. In some hospitals, extubation does not occur until the patient can perform a sustained head lift.³⁵ The upper airway is suctioned if any evidence of regurgitation occurs during anesthesia or any fluid such as blood from a surgical procedure is suspected to be in the pharynx. In human medicine those patients, as listed above, deemed to have a high risk of aspiration may be pre-treated prior to an anesthetic event with antacids, H2 blockers, or proton pump inhibitors in an

effort to increase gastric pH and in turn decrease the severity of pneumonitis in the event of aspiration.³⁶ High risk patients may also experience rapid sequence intubation using a cricoid maneuver. Rapid sequence intubation involves pre-oxygenation of the patient followed by the administration of a hypnotic anesthetic agent and a neuromuscular blocking drug. While performing intubation pressure is applied to the cricoid cartilages pushing them against the cervical vertebrae in an attempt to close off the esophagus from the pharyngeal cavity.³⁶

Summary

Aspiration is emerging as a significant post-anesthetic complication in veterinary patients. It is defined as inhalation of gastric contents into the bronchial tree. Aspiration can fall into one of two clinical scenarios aspiration pneumonitis or aspiration pneumonia. Pathophysiology of aspiration is divided up into three phases: an airway response, an inflammatory response, and an optional secondary bacterial infection.¹⁷ The character of the gastric fluid determines the severity of the pathophysiologic response. Gastric contents with particulate matter and a pH less than 2.0 result in more severe responses.¹¹ Acute lung injury and acute respiratory distress syndrome are two of the more severe outcomes associated with aspiration of gastric contents; however it appears that most patients who aspirate are asymptomatic.¹⁷ Definitive diagnosis for aspiration pneumonia can be made with the help of history, thoracic radiographs, and transtracheal wash with bacterial cultures. Human medical literature suggests that it is very difficult initially to distinguish between pneumonitis and

pneumonia; and that treatment is similar in both scenarios with the exception of use of empirical vs. definitive antimicrobial therapy.¹⁵ Literature for human and veterinary patients suggests that the prognosis for uncomplicated cases of aspiration pneumonitis or pneumonia appears to be very good.

Anesthesia is one of the top five causes for aspiration pneumonia in veterinary patients based on a study from U.C. Davis in dogs with aspiration pneumonia. Other causes of aspiration pneumonia include esophageal disease, neurologic disorders, and laryngeal disease.⁵

Of the other causes found, retrospective studies of post-anesthetic or post-operative canine patients have been performed in patients with intracranial disease, intervertebral disk disease, and laryngeal paralysis. Risk factors for post-anesthetic aspiration from these studies included: tetraparesis, cervical disc disease, magnetic resonance imaging, long anesthetic duration, undergoing more than one anesthetic procedure, megaesophagus, and vomiting or regurgitation in the post-anesthetic period.^{2, 3, 7} Of the three previously mentioned diseases

survival was lowest in patients suffering from intracranial disease. Up to this point there has not been a retrospective study looking at incidence or risk factors for all canine post-anesthetic/post-operative patients.

Preventative measures for post-anesthetic aspiration pneumonia expand beyond the realm of averting the complication as it is very difficult to determine the exact moment aspiration occurs; they also attempt to minimize the severity of the disease process in the event it should occur. Patients considered to be at high risk in human medicine are often pretreated with pharmacologic agents to increase gastric pH and/or increase gastrointestinal transit time. In

veterinary medicine questions still remain as to whether or not more preventative steps should be taken such as: should antacids, H2 blockers, proton pump inhibitors, or metoclopramide be prescribed pre-operatively, should the endotracheal cuff remain inflated until the patient is ready to be extubated, does the administration of opioids immediately after extubation diminish the patient's ability to maintain an adequate swallowing reflex? Moreover it is more obvious in the human patient how lucid they are post-operative as they are able to answer questions and respond to commands when adequately aware enough to be extubated. We do not have the same luxury with our veterinary patients. The question should be asked, when is the patient adequately able to protect their airway during recovery from anesthesia? If these questions and many other potential questions about aspiration pneumonia are to be answered, more research is indicated to determine more tangible risk factors for the looming problem of post-anesthetic aspiration pneumonia. We hypothesize that there are patient variables and management strategies that influence the prevalence of post-anesthetic aspiration pneumonia. The purpose of the study described in this thesis was to estimate the incidence of post anesthetic pneumonia in the general canine population and to distinguish the patient and management variables associated with the development of post-anesthetic aspiration pneumonia in dogs. Records from six veterinary teaching hospitals were reviewed to identify all canine post-anesthetic aspiration pneumonia episodes and multiple variables associated with those cases were identified.

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CHAPTER 2

PREVALENCE AND RISK FACTORS FOR CANINE POST ANESTHETIC ASPIRATION PNEUMONIA (1999-2009): A MULTICENTER STUDY

Summary

Objective – To determine the prevalence of canine post anesthetic aspiration pneumonia and to identify patient variables and management strategies that may put dogs at greater risk for the development of aspiration pneumonia

Animals – 240 dogs affected with aspiration pneumonia and 488 unaffected dogs.

Procedure – In a multicenter, randomized, unmatched case-controlled retrospective study, 2646 records were searched from 6 veterinary teaching hospitals, between January 1999 and December 2009, for radiographic evidence, bacterial culture, and/or necropsy results of aspiration pneumonia following an anesthetic episode. Following identification of affected animals two unmatched control animals were selected from a computer generated randomized list of all dogs that underwent anesthesia during the aforementioned time period. All case and control subjects were further examined to identify risk factors that may be associated with aspiration pneumonia. Factors evaluated were: age, weight, breed, ASA status, history of upper or lower respiratory tract disease, history of central or peripheral neurological disease, megaesophagus, drugs used for anesthetic management (preoperatively, perioperatively, and postoperatively), use of intermittent positive pressure ventilation, epidural administration, type of procedure performed under anesthesia, emergent procedures, regurgitation witnessed during anesthesia, and extubation of the patient during surgery. Mortality of affected dogs was

determined for five of the six institutions in the study. Prevalence was determined by dividing the number of affected patients by the total number of anesthetic episodes over the eleven year period. Preliminary analysis of risk factors was performed using Chi square and student t-test univariate testing. A variance inflation factors of all risk factors indicated multicollinearity between factors. All risk factors were entered into a multivariate logistic regression equation and then deleted according to both univariate and multivariate P values, retaining all factors with a P value of ≤ 0.01 . Previously deleted factors were then individually added back into the multivariate equation and preserved if $P < 0.01$. Univariate and multivariate analysis was performed using SAS software.

Results – Estimated prevalence of post anesthetic aspiration for all sites combined was 1.7/1000 with a range from each site included in the study of 0.03%-0.26% over the 11 year time period. Mortality rates ranged from 14.8%-62.5% at five of the six institution included in the study. Mean age of dogs in the affected group was 7.66 years and mean age of control dogs was 5.57 years old. Mean weight of dogs that aspirated was 28.50 kg and mean weight of control dogs was 23.86 kg. Median ASA status for affected and control dogs was 2 (range of 1-5). Twelve of 57 factors evaluated were strongly associated with the occurrence of aspiration pneumonia. The top six risk factors with the highest odds ratios associated with post anesthetic aspiration pneumonia [including odds ratio (OR)] were: megaesophagus (OR=17.3), upper airway surgery (OR=8.1), history of neurologic disease prior to anesthesia (OR=5.4), endoscopic procedure (OR=5.2), regurgitation or vomiting during anesthetic induction, anesthetic maintenance, or anesthetic recovery (OR=3.6), and history of respiratory disease prior to anesthesia (OR=2.7).

Conclusion and Clinical Relevance – Average prevalence across the institutions was estimated to be about 2 out of every 1000 dogs anesthetized. From these results we can identify that associations with a higher risk for the development of aspiration pneumonia are large breed older dogs with chronic disease processes especially if those diseases are of respiratory or neurological origin. It should be noted that although the odds ratio for factors such as age were low ($OR=1.1$) as age increases the odds for the development of aspiration pneumonia increases by 10% for every one year increase in age. A 10 year old dog has a 61% increased risk for the development of aspiration pneumonia when compared to a 5 year old dog. The same considerations should be made for weight and ASA status. Patients at higher risk for aspiration such as those with one or more of the top six risk factors identified should have their airway protected by endotracheal intubation as quickly as possible at the onset of deep sedation or general anesthesia. Consideration should also be given to suction of the pharynx and esophagus multiple times during and prior to the end of an anesthetic episode to prevent aspiration of gastroesophageal reflux.

Introduction

Aspiration pneumonia has recently become a well recognized phenomenon of morbidity and mortality at veterinary teaching hospitals throughout the country. Over the last 10 years retrospective clinical studies have been performed by the University of Pennsylvania, the University of California at Davis, the University of Minnesota and Washington State University concerning the incidence and identifying some risk factors for aspiration pneumonia or post operative pulmonary complications in veterinary patients.¹⁻⁷ Aspiration pneumonia has been reported in a variety of animal species ranging from prospective experimental studies in rabbits to case reports in an oryx and a moose.⁸⁻¹⁰ A 2008 retrospective study of 88 dogs from UC Davis Veterinary Teaching Hospital identified the top five causes of aspiration pneumonia as follows: esophageal disease, vomiting, neurologic disorders, laryngeal disease, and post-anesthetic aspiration.⁵ The University of Minnesota found that in 125 patients suffering from aspiration pneumonia; the majority of post anesthetic or post sedation patients exhibited clinical signs with 24 hours after an episode of anesthesia or sedation.⁶

Aspiration is defined as inhalation of gastric contents into the bronchial tree. Aspiration can fall into one of two clinical scenarios aspiration pneumonitis or aspiration pneumonia.¹² Following introduction of foreign material into the airway, pathophysiology of aspiration is divided up into three phases: an airway response, an inflammatory response, and an optional

secondary bacterial infection.¹³ The character of the gastric fluid determines the severity of the pathophysiologic response. Gastric contents with particulate matter and a pH less than 2.0 result in more severe responses.¹¹ Acute lung injury and acute respiratory distress syndrome are two of the more severe outcomes associated with aspiration of gastric contents; however it appears that most patients who aspirate are asymptomatic.²² Definitive diagnosis for aspiration pneumonia can be made with the help of history, thoracic radiographs, and transtracheal wash with bacterial cultures. Human medical literature suggests that it is very difficult initially to distinguish between pneumonitis and pneumonia; and that treatment is similar in both scenarios with the exception of use of empirical vs. definitive antimicrobial therapy.^{12, 14} Literature for human and veterinary patients suggests that the prognosis for uncomplicated cases of aspiration pneumonitis or pneumonia appears to be very good.¹⁵

Although aspiration of gastric contents as a post-anesthetic complication is of concern in all veterinary species the majority of clinical studies have been performed in dogs. Retrospective and prospective studies of post-anesthetic canine patients have been performed in dogs with intracranial disease, intervertebral disk disease, and laryngeal paralysis.^{7, 3, 17-19} Surgical procedure has also been considered in dogs undergoing laparotomy that suffered from post operative pulmonary complications including aspiration pneumonia.^{1, 2} Risk factors for post-anesthetic aspiration from these studies identified included: tetraparesis, cervical disc disease, and magnetic resonance imaging, long anesthetic duration, repeated anesthetic procedures, megaesophagus, and vomiting or regurgitation during the post anesthetic period.^{3,}

⁷ Variables associated with increased risk for post operative pulmonary complications included: ASA status ≥ 3 , emergent surgery, longer duration of anesthesia, use of butorphanol or oxymorphone rather than hydromorphone as post operative pain medication, recipients of stored blood products, reversal of opiates or benzodiazepines, recovery in intensive care.²

Survival was lowest in patients suffering from intracranial disease.⁷

Published studies of post-anesthetic aspiration pneumonia have focused on very specific disease processes such as intracranial disease, intervertebral disk disease, and laparotomy patients.^{7, 3, 1-2} There has not been an all encompassing retrospective study examining the overall incidence and risk factors associated with post-anesthetic aspiration pneumonia. We hypothesize that there are patient variables and management strategies that influence the prevalence of post anesthetic aspiration pneumonia. Estimating the overall incidence of post-anesthetic aspiration pneumonia in a large cohort of patients will help to determine the true frequency and magnitude of this recognized complication. Determination of post-anesthetic aspiration pneumonia risk factors may help to identify and implement preventative strategies for everyday practice of anesthesia. The objectives of this study were to estimate the incidence of post-anesthetic aspiration pneumonia in the canine patient and to determine patient and management variables associated with the development of post-anesthetic aspiration pneumonia in dogs. The objectives of this study were addressed by a retrospective review of medical records. Records were reviewed to identify all canine post-anesthetic aspiration pneumonia episodes and multiple variables associated with those cases were identified.

Materials and methods

Criteria for case selection

Six veterinary teaching hospitals participated in the study (Michigan State University, The Ohio State University, the University of Georgia, the University of California at Davis, Colorado State University, and the University of Pennsylvania). Medical record databases from the six veterinary teaching hospitals were searched from January 1999 to December 2009 for any canine patients with a diagnosis of pneumonia and an anesthesia or sedation billing code.

Inclusion criteria for this study consisted of dogs with a witnessed episode of aspiration at any time during the anesthetic period reported in the anesthetic record or with clinical signs of aspiration pneumonia immediately after an anesthetic episode, and a radiographic diagnosis of aspiration pneumonia made within four days after an anesthetic episode. Two dogs were included with a diagnosis of aspiration pneumonia on necropsy within 24 hours after anesthesia. Dogs were excluded from the study if the medical record was missing, incomplete, or a radiographic diagnosis of pneumonia was made immediately prior to an anesthetic episode also qualified for exclusion from the study. Dogs diagnosed radiographically with any respiratory disease (e.g. laryngeal paralysis, lung contusion, collapsing trachea) other than aspiration pneumonia immediately prior to anesthesia were included in the study. Following identification of affected animals two unmatched control animals were selected from a computer generated randomized list of all dogs that underwent anesthesia during the aforementioned time period comparing the same variables as affected dogs.

Medical records review

Information obtained from the medical record of animals included in this study included: signalment, body weight in kilograms, American Society of Anesthesiologists (ASA) physical status classification²³, anesthetic and analgesic drugs used as preanesthetic medication, induction drugs, maintenance drugs, and post operative drugs. Also recorded were: the use of a continuous rate infusion, surgical or diagnostic procedure performed, use of intermittent positive pressure ventilation, epidural placement, and time of day, extubation prior to recovery, and regurgitation /vomiting during anesthesia or recovery. History of neurologic or respiratory disorder prior to anesthesia was also recorded. Patient survival after anesthesia for five of six institutions was also recorded. Patients that were discharged post operatively were included as animals that survived.

Prevalence, mortality, and identification of risk factors

Prevalence was determined by dividing the total number of affected dogs by the total number of anesthetic episodes over the study period. Mortality was determined by dividing the total number of animals that died secondary to aspiration or were euthanized without discharge from the hospital post operatively by the total number of affected cases from each institution. Risk factors were identified from the previously mentioned variables collected from the records of affected dogs. These variables were compared to those findings from all dogs coded for anesthesia or sedation during the study period. Two dogs were selected from a randomized list for each affected dog to act as controls.

Statistical analysis

Preliminary analysis of risk factors was performed using univariate Chi square and student t-test testing, variance inflation factor testing for multicollinearity was performed. Risk factors with a variance of inflation factor greater than 2.5 were deleted from the initial analysis. All risk factors were further analyzed using multivariate logistic regression multivariate testing with a P value of ≤ 0.01 . Previously deleted factors were then individually added back in to the equation and retained if $P \leq 0.01$. Significant risk factors were expressed as odds ratios with their calculated 95% confidence intervals. The frequencies of aspiration pneumonia were compared amongst the six institutions (Chi square with Bonferroni correction factor for multiple comparisons). Mortality was similarly compared (five institutions, Fishers exact test).

Results

A total of 2646 records were available for review from the six veterinary teaching hospitals that participated in the study. Of the 2646 records 240 affected cases satisfied the inclusion criteria and 488 control cases were included in the study. Estimated overall prevalence of post anesthetic aspiration pneumonia was 1.7 out of every 1000 anesthetic episodes. Prevalence of post anesthetic aspiration ranged from 0.3-2.6 out of every 1000 anesthetic episodes. There was a significance difference in prevalence for institution 1 compared with institution 2 through 5 and between institutions 3 and 5 (refer to Table 2.1). Mortality rates of institutions ranged from 14.8%-62.5% of affected dogs (data from institution

6 not included) (Table 2.1). There were no significant differences in mortality rate for the five institutions analyzed, and the mean mortality was 27.6%. (Table 2.1) Mean age for affected dogs was 8 years (range 0.2-17 years) and for control dogs was 6 years (range 0.1-17 years). (Table 2.2) Mean weight for affected dogs was 28 kg (range 1.6-84.1 kg) and for control dogs 24 kg (range 0.73-71.8 kg). (Table 2.2) Median ASA physical status (PS) for affected dogs was PS 2 (range 1-5, mean-2.59) and for control dogs was PS 2 (range 1-5, mean 1.93).

Risk factors for development of post anesthetic aspiration pneumonia

Twelve of 57 factors were found to be significant risk factors for the development of post anesthetic aspiration pneumonia. The 12 risk factors were sorted into categories which included: Patient Demographics, Anesthetic Management, Procedure Type, and Other. In the Patient Demographic category the following variables were found to be significant: age ($P = 0.002$), weight ($P = 0.0003$), ASA physical status ($P = 0.0005$). (Table 2.2) The Anesthetic Management category had two significant variables: patients receiving hydromorphone at induction ($P = 0.003$) and the use of a continuous rate infusion of any anesthetic or analgesic agent at anytime during anesthesia ($P = 0.006$). (Table 2.2) The Procedures Type category found significant risk factors for the development of post anesthetic aspiration pneumonia to be patients undergoing: exploratory laparotomy ($P = 0.003$), endoscopy ($P = 0.009$), or upper airway surgery ($P < 0.0001$). (Table 2.2) Significant risk factors in the Other category included: patients with megaesophagus ($P = 0.01$), patients that regurgitated/vomited during any point of anesthesia ($P = 0.007$), patients with a history of neurologic disease prior to anesthesia ($P < 0.0001$), and patients with a history of respiratory disease prior to anesthesia ($P 0.001$). (Table 2.2)

Odds ratios were calculated for all significant risk factors, the top six risk factors for post anesthetic aspiration were megaesophagus, upper airway surgery, regurgitation or vomiting anytime during the anesthetic period, histories of respiratory or neurological disease prior to anesthesia, and endoscopy. Patients with megaesophagus were 17.3 (95% CI 2-150) times more likely to suffer from aspiration pneumonia than unaffected animals. Other patient factors of concern included those patients with a history of respiratory disease prior to anesthesia with a risk of aspiration 2.7 (95% CI 1.5-4.9) times greater than those unaffected by respiratory disease. Patients with a history of neurologic disease were 5.4 (95% CI 3.3-9) times more likely to experience aspiration pneumonia. Procedures with an increased risk for aspiration included patients undergoing upper airway surgery who were 8.1 (95% CI 3-21.5) times more likely to aspirate and endoscopic patients with a 5.2 (95% CI 2-17.7) times greater risk of aspiration.

Discussion

Risk for post anesthetic aspiration was highest in patients with a history of megaesophagus. In our study dogs with megaesophagus were 17 times more likely to suffer from post anesthetic aspiration pneumonia than those patients without megaesophagus. Ninety-five percent confidence intervals for this finding were very wide (2-151). The explanation for such sizeable confidence intervals lies in the small subpopulation of patients that had megaesophagus and underwent an anesthetic procedure. Megaesophagus was also found to be a significant risk factor for post anesthetic aspiration pneumonia in dogs that underwent intracranial surgery.⁷ This study (from Washington State) found that dogs with megaesophagus were nine times more likely to aspirate post operatively than those without

the disorder; similar to our study confidence intervals for this group of patients were wide. Findings from both of these studies would suggest that dogs with megaesophagus are at a higher risk for the development of post anesthetic aspiration pneumonia. Care should be taken to protect the airway of these animals and indeed any animal with esophageal dysmotility, at all times during the anesthetic and post-anesthetic periods.

Differences in anesthetic management between institutions as a cause for increased risk for aspiration in some aspects can be difficult to prove due to the retrospective nature of this study. As there is no documented proof as to the most likely time for aspiration to occur in veterinary patients during anesthesia one could postulate that patients are most at vulnerable at times of a reduced level of consciousness with an unprotected airway. During anesthesia there are two time periods at which both of the criteria stated above occur: at the time of induction and during recovery from anesthesia. Although the anesthetic record can be a very good account of the events that take place during the maintenance of anesthesia; it often lacks detail as to the timing and actions taken during intubation and extubation of the anesthetized patient. From time spent reviewing numerous records ideal induction information would include: position of the patient (lateral v. dorsal v. sternal) at the time of intubation, type of tube and cuff (low pressure high volume v. high pressure low volume), time from the first injection of induction agent to intubation with inflation of the cuff, cuff inflation pressure, and the nature of any difficulty of intubation. Plus any reported regurgitation under anesthesia and the volume removed upon any suctioning performed. Details for extubation would include subjective and objective assessment of awareness before extubation, position of the patient during extubation, timing of cuff deflation during recovery, and a subjective or preferably

objective method to determine the capacity of the swallowing reflex during recovery. The goal upon completion of this study is to undertake a prospective study which would include the previously described data that were not obtained due the retrospective nature of this data collection.

When comparing anesthetic management practices, anesthetic drug protocols should be taken into account. We observed that different institutions use very diverse anesthetic protocols with minimal impact on the risk of aspiration; our study found that use of hydromorphone at induction and the use of continuous rate infusions were the exceptions to this observation. Odds ratios for both of these anesthetic management practices were less than three; with three of the six institutions we studied using hydromorphone at induction and all using continuous rate infusions. One other study of canine post operative aspiration found the use of hydromorphone intra-operatively to be a significant risk factor in dogs suffering from intervertebral disc disease.³ The results from this study found that patients undergoing a second episode of anesthesia for surgical correction of intervertebral disc disease, after a first anesthetic episode for diagnosis, were more likely to experience aspiration pneumonia after receiving hydromorphone during the intra-operative period. These findings agree with our detection of an increase in the risk of aspiration when hydromorphone was used at induction although these findings contrast those of Brainard et al. 2006. Interestingly our study and the previously mentioned study found that patients did not have a statistically significant risk for aspiration pneumonia when hydromorphone was used as an anesthetic premedication. With the exception of hydromorphone at induction, the results from this study would suggest that in

the majority of canine anesthetic cases drug choice is not likely to increase or decrease the risk for aspiration of gastric contents.

Regurgitation or vomiting was found to be a significant risk factor for the development of aspiration pneumonia in our study which was expected. Three out of four studies investigating post operative aspiration pneumonia or pulmonary complications also found regurgitation or vomiting were significant risk factors for the development of these problems. Retrospective studies examining aspiration pneumonia in the general canine hospital population from UC Davis and the University of Minnesota also found regurgitation or vomiting to be among the top five reasons patients aspirated.^{5, 6} In comparing our odds ratios to that of a study in pneumonia in post-craniotomy dogs we found similar results with an odds ratio of 3.6 (95% CI 1.4-9) from our study and an odds ratio of 2.7 (95% CI 1-8.6) from the craniotomy study.⁷ These results suggest that we should again focus our efforts on protecting the airway during the two periods of anesthesia at which the patient is most vulnerable, that being during induction and recovery. Increased vigilance of the airway well into the recovery period is recommended because it is typically during this phase that patients become more independent of anesthetic nursing care, despite being still consciously impaired.

Dogs with a history of respiratory disease immediately prior to anesthesia carried 2.7 (95% CI 1.5-4.9) times greater risk of developing post anesthetic aspiration pneumonia than those dogs without. In our study any dog with an upper airway abnormality or disease, such as brachycephalic syndrome or laryngeal paralysis, and dogs with lower airway disease, such as bronchitis, previous pneumonia, or traumatic lung contusions, were included within this group.

Dogs with a history of upper airway disease and intervertebral disc disease have also been reported to have increased risk for aspiration pneumonia post operatively in a 2009 study from the University of Pennsylvania.³ Reports in current medical literature about post anesthetic aspiration pneumonia state that the majority of patients that aspirate gastric material do not show clinical signs of aspiration pneumonitis.²² Compromised pulmonary defense mechanisms in animals with previous respiratory disease could make them more vulnerable to the sequelae of aspiration pneumonitis resulting in pneumonia. It is not of great surprise that this subpopulation of patients would be at higher risk for the development of aspiration pneumonia as they have experienced previous respiratory insults which may have compromised pulmonary defense mechanisms. A major innate pulmonary defense mechanism is the mucociliary clearance (MCC) apparatus has been documented in humans to be impaired in chronic respiratory diseases such as asthma. It has been reported that histopathologic samples from asthmatic patients exhibited a reduced number of ciliated cells, goblet cell metaplasia, and large amounts of hyperviscous mucus, thereby decrease the function of the MCC.²⁴ Patients with chronic obstructive pulmonary disease have been found to have increased turbulence and high local velocities in flow-limiting segments (FLS). Sites of FLS include the trachea and lobar bronchi. Areas of FLS are associated with expiratory particle deposition of inhaled materials into small airways.²⁵ Deposition into small airways limits clearance of inhaled materials from the respiratory tract increasing the likelihood of infection. Veterinary patients with severe tracheal/bronchial collapse may also experience deposition of inhaled materials secondary to FLS increasing the probability for aspiration pneumonia.

One of the top five risk factors for post anesthetic aspiration found in our study included dogs that had a surgical procedure to the upper airway. Our group of patients classified as having upper airway surgery included dogs with: laryngeal paralysis, tracheal collapse, and brachycephalic syndrome. Patients that undergo upper airway surgery, especially dogs suffering from laryngeal paralysis, have historically been a group of concern to be at increased risk for aspiration pneumonia. Multiple retrospective studies have been performed in the early and late 2000s looking at outcomes and post operative complications following unilateral arytenoid lateralization.¹⁷⁻¹⁸ Results from the majority of these studies found that aspiration pneumonia occurred days to weeks after the initial surgical procedure rather than the immediate post operative period. Most recently a prospective case controlled study by Stanley et al unearthed evidence that patients with idiopathic laryngeal paralysis can and in most cases do also suffer from esophageal dysfunction.¹⁹ Literature addressing to brachycephalic syndrome and gastrointestinal disorders from 2005 reported a significant association between the severity of digestive and respiratory tract diseases in certain brachycephalic type dogs, namely French bulldogs, large brachycephalic dogs, and males.²⁰ The nature of clinical signs of digestive tract disease reported in the study included: pytalism, regurgitation, and vomiting. A follow-up study from 2006 examining the long term results of surgical correction for brachycephalic syndrome and simultaneous medical management of gastrointestinal tract disorders in 51 brachycephalic dogs found no evidence of aspiration pneumonia immediately post operatively in any study subjects.²¹ In consideration of the previously described studies

we would attribute our findings to the types of dogs requiring these types of surgeries and the concurrent digestive issues associated with these respiratory disorders.

Although extubation prior to complete recovery from an anesthetic episode might be expected to be a highly significant risk factor for the development of aspiration pneumonia it has not been reported in any published veterinary studies. In the case of our study, early extubation (prior to complete recovery from anesthesia), whether intentionally to check the integrity of an upper airway procedure or accidentally, was a significant risk factor for aspiration pneumonia upon univariate analysis with Chi square testing. When early extubation was entered into multivariate analysis it was deemed not to be a significant risk factor. Upon further analysis it was discovered that multicollinearity existed between upper airway procedures and pre-emptive extubation and therefore the significance early extubation was annulled by the significance of upper airway procedures.

Emergency laparotomy procedures have been reported previously in the veterinary literature to be significant risk factors for the development of post operative pulmonary complications which included aspiration pneumonia.² The reason stated for this finding was the possibility of a full stomach or a fast of unknown duration leading to gastroesophageal reflux and aspiration. Our study did not find any significance for procedures performed after hours in comparison to those performed between the hours of 8AM and 5PM; however we also found laparotomy to be a procedure that is strongly associated with the development of aspiration pneumonia. It is possible that we overlooked a number of emergency procedures by attempting to identify emergency cases based on the time of day at which anesthetic procedures occurred. The subjects referenced from the post operative pulmonary complications study were identified

using the emergency ASA status classification and time of day. We chose to identify our emergency cases based on the time of day the procedure occurred because many of the records examined lacked an ASA status or were not classified as emergency status even though the procedures occurred after regular business hours. We believe using the time of day only to identify emergency anesthetic procedures may have limited our ability to distinguish this emergent cases as a significant factor associated with aspiration pneumonia. It is also possible that emergent cases may not be associated with post-operative aspiration pneumonia. Results from this study enhance our ability to detect factors for canine patients associated closely with the development of post operative aspiration pneumonia.

Twelve of 57 variables analyzed were highly significant risk factors for aspiration. Variables with the greatest odds ratios associated with aspiration were: patients with megaesophagus, patients with a history of respiratory disease prior to anesthesia, patients with a history of neurologic disease prior to anesthesia, those that underwent an upper airway procedure, and those that underwent an endoscopic procedure. Patient signalment and ASA physical status did not pose the most substantial odds for risk of post anesthetic aspiration pneumonia. This is not to say that age, weight and ASA status are to be ignored when trying to identify patients at a higher risk for aspiration, it should be noted that although the odds ratio for continuous factors such as age were low ($OR=1.1$) as age increases the odds for the development aspiration pneumonia by 10% for every one year increase in age. Simply stated a 10 year old dog has a 61% increased risk for the development of aspiration pneumonia when compared to a 5 year old dog. Based on these results, older large breed dogs placed under anesthesia with respiratory co-morbidities should be carefully monitored during the anesthetic

and post anesthetic period for signs of aspiration pneumonia. In addition to increased measures of vigilance for these patients owners should be informed as to the increased risk for and consequences of this post operative complication.

Our study also evaluated the number of the significant factors associated with aspiration pneumonia for each individual dog.(Figure 2.4) Eighty-one percent (195/240) of affected dogs had three or more significant factors and 0.8% (2/240) of affected dogs had no significant factors at the time of anesthesia. In comparison to affected dogs, 78% (383/488) of control dogs had four or less factors associated with aspiration pneumonia and 2% (10/488) had no significant factors at the time of anesthesia. None of the patients included in the study had all twelve risk factors. Three percent (8/240) of dogs that aspirated had at maximum nine of twelve significant factors associated with risk for aspiration pneumonia. In the control dog group 0.8% (4/488) had a maximum of nine significant factors. Not all factors have equal influence on the risk of aspiration, as demonstrated by varying odds ratios. To determine an individual dog's risk for aspiration pneumonia, the odds ratios are multiplied together and the product is then multiplied by prevalence.

Limitations for this study included its retrospective nature; incomplete anesthetic records with the loss data such as ASA status, weight, extubation time, identification of anesthetic maintenance drugs, patient signalment, patient position, and post-operative medications used. Many cases were excluded due to incomplete medical records missing radiology reports and anesthetic reports. Radiographs were not performed on every patient post anesthetic and therefore prevalence may be underreported due to a population of subclinical cases. Mortality data was not collected from all institutions and the limited number

of aspiration cases may have resulted in a type II error for comparisons of mortality between institutions. Drug dosages were not evaluated in this study and may also be a factor associated for the development of aspiration pneumonia. Time under anesthesia was also not evaluated by this study.

This study found the estimated prevalence of post anesthetic aspiration pneumonia to be 1.7 out of every 1000 anesthetic episodes in the general canine population. The results of our study agreed with our hypothesis that there are both patient and management variables which influence the prevalence of canine post anesthetic aspiration pneumonia. In addition to patient and management variables procedure also appears to influence the prevalence of canine post anesthetic aspiration pneumonia. Based on these results, patient co-morbidities such as megaesophagus and previous history of respiratory disease along with procedure most highly influence post anesthetic aspiration pneumonia prevalence. Identification of these risk factors should be a small step into the direction of determining when patients are most likely to aspirate and how we should attempt to prevent this post anesthetic complication from occurring or hopefully diminish the severity of this complication should it occur. Future studies should attempt to pinpoint when post anesthetic aspiration pneumonia is most likely to occur.

Table 2.1 Prevalence and Mortality Results

Prevalence and Mortality

Institution	Anesthetized	Aspirated	Lived	Died	Prevalence	Mortality
1	22816	8	3	5	0.04%*	62.50%
2	20106	42	25	17	0.21%	40.47%
3	23413	27	23	4	0.12%*	14.81%
4	16666	23	19	4	0.14%	17.39%
5	32738	85	64	21	0.26%*	24.71%
6	24972	54			0.22%	
All	140711	240	134	51	0.17%	21.34%

Prevalence and mortality are broken down for each individual institution. Institutions numbered in first column starting from the left. Second column equals total number of dogs anesthetized during the study time period. Third column equals number of dogs that aspirated post anesthesia. Fourth column equals the number of dogs that lived after aspirating. Fifth column equals the number of dogs that were euthanized or died after aspirating. Sixth column equals the prevalence for each institution. Seventh column equals the mortality rate for each institution after an aspiration event.

Table 2.2 Significant factors

Factor	Mean (Aspirated/ Control)	Odds ratio	95% Confidence Intervals	P value
Age (years)	7.7/5.6	1.1	1.0-1.2	0.0022
Weight (kg)	28.0/24.1	1.02	1.0-1.0	0.0003
ASA status	2.6/1.9	1.6	1.2-2.0	0.0005

Factor	N (Aspirated/ Control)	Odds ratio	95% Confidence Intervals	P value
Exploratory Laparotomy	56/76	2.4	1.3-4.3	0.0033
Endoscopy	12/13	5.2	1.5-17.7	0.0088
Megaesophagus	15/1	17.3	2.0-150.5	0.0099
Regurgitation during anesthesia	29/17	3.6	1.4-9.0	0.0072
History of neurologic disease before anesthesia	89/81	5.4	3.3-8.9	< 0.0001
Hydromorphone at induction	47/38	2.6	1.4-4.7	0.0025

Table 2.2 cont.

Continuous Rate Infusions of anesthetic or analgesic agent	70/80	2.1	1.2-3.5	0.0059
Upper Airway Surgery	40/11	3.0-21.5	8.1	< 0.0001
History of respiratory disease before anesthesia	78/60	1.5-4.9	2.7	0.01

Table displays all significant factors by multivariate logistic regression analysis. Column 1 names factor. Column 2 given the mean or number of affected and control animals with factor. Column 3 gives odd ratio for each factor. Column 4 gives confidence intervals for those factors. Column 5 gives P value for each factor

Table 2.3 All factors

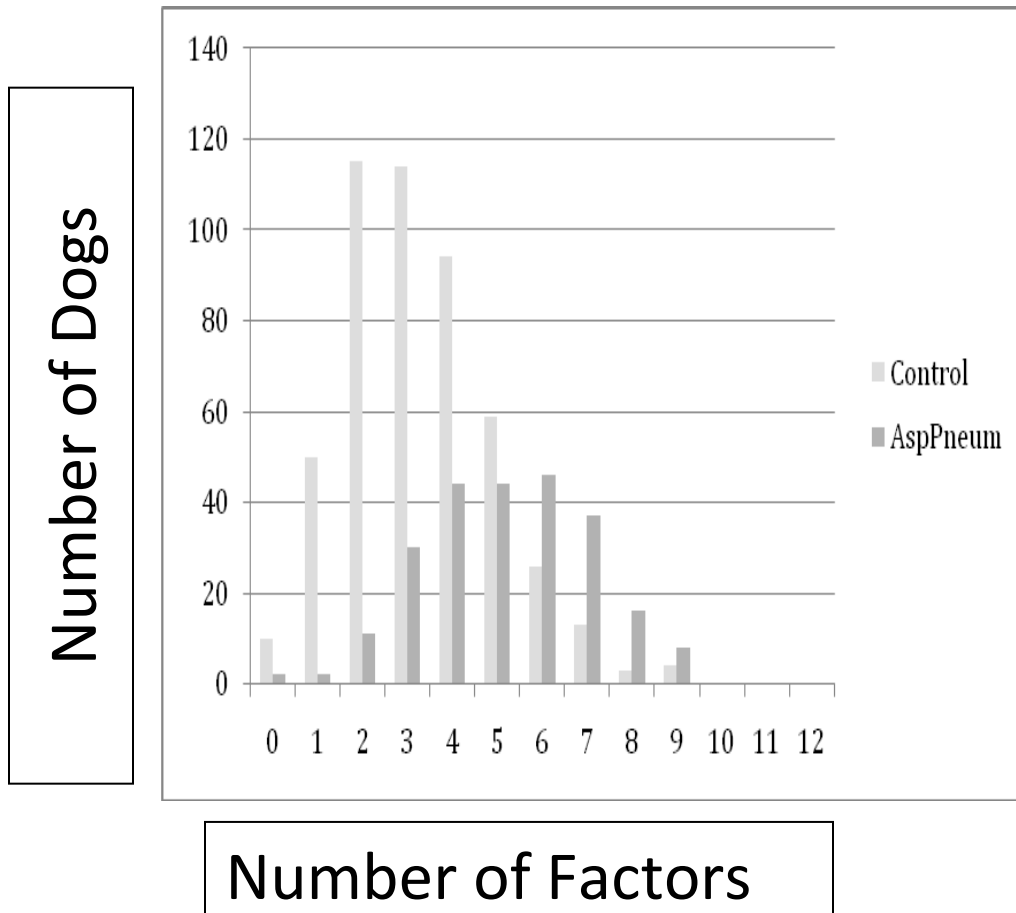
		VIF	aspirated	control	P
Premedications	acepromazine	1.94	41	165	<0.0001
	atropine	2.04	42	91	0.72
	buprenorphine	1.16	6	5	0.12
	butorphanol	1.91	21	48	0.65
	diazepam	1.29	9	32	0.13
	glycopyrrolate	1.77	51	135	0.07
	hydromorphone	3.28	52	187	<0.0001
	medetomidine	1.26	7	15	0.91
	methadone	1.59	14	20	0.29
	midazolam	1.53	41	75	0.53
	morphine	2.40	21	70	0.03
	oxymorphone	2.16	33	77	0.49
	xylazine	1.12	2	8	0.38
Induction agents	diazepam	2.38	90	143	0.02
	etomidate	1.50	19	26	0.17
	fentanyl	1.43	25	15	<0.0001
	hydromorphone	1.96	47	38	<0.0001
	ketamine	2.32	28	58	0.95
	lidocaine	1.50	32	46	0.1
	midazolam	1.79	41	64	0.15
	oxymorphone	1.24	3	4	0.51
	propofol	2.87	117	235	0.84
	thiopental	3.11	60	180	0.002
Maintenance agents	fentanyl cri	2.69	55	50	<0.0001
	isoflurane	2.48	206	410	0.77
	nitrous oxide	1.12	0	5	0.11
	propofol cri	1.38	11	7	0.01
	sevoflurane	2.20	17	28	0.51
Management	after hours	2.33	94	203	0.53
	cri	2.48	76	74	<0.0001
	epidural	1.42	21	71	0.03

Table 2.3 cont. All factors

	ippv	1.66	137	224	0.001
	post op pain meds	1.31	132	224	0.02
Complications	early extubation	1.58	33	11	<0.0001
	regurgitation	1.23	30	16	<0.0001
Co-morbidities	megaesophagus	1.20	15	1	<0.0001
	h/o neuro disorder	1.93	92	78	<0.0001
	h/o resp disorder	1.79	80	58	<0.0001
Procedure	bronchoscopy	1.26	5	5	0.25
	laparotomy	2.55	56	76	0.01
	endoscopy	1.27	12	13	0.1
	neuro sx	1.94	46	23	<0.0001
	ophtho sx	1.41	3	26	0.01
	ortho sx	2.89	10	103	<0.0001
	other	2.82	111	248	0.25
	thoracotomy	1.34	9	5	0.01
	upper airway sx	2.37	40	11	<0.0001
Signalment	brachycephalic	1.26	34	63	0.64
	retriever	1.25	52	84	0.15
	VIF	m(asp)	f(asp)	P	
Sex	1.16	145	95	0.03	
neutered	1.36	111	73	0.21	
	VIF	mean(asp)	s.e.m.	P	
age (years)	1.56	7.66	0.25	<0.0001	
weight (kg)	1.32	28.5	1.13	0.12	
	VIF	median(asp)		P	
ASA	1.73	2			

Table of all factors studied included,, variance inflation factor to determine if multicollinearity present between factors (VIF), a breakdown of total number of patients that aspirated and the controls that had the factor, and the P value for each factor.

Figure 2.1 Number of significant risk factors per dog



Number of significant factors present for each individual affected and control dog at the time of anesthesia. Continuous variables (e.g. age, weight, ASA status) were averaged, all dogs at or above average were considered to have the factor associated with risk for aspiration and those below did not have the factor associated with risk for aspiration.

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SUMMARY, CONCLUSIONS, AND FUTURE INVESTIGATIONS

This research demonstrated that there are differences in patient variables and management strategies which influence the prevalence of post anesthetic aspiration pneumonia. Estimated prevalence of post anesthetic aspiration was 1.7/1000 with a range of 0.3/1000-2.6/1000 of all canine anesthetic cases performed over the 11 year time period. Mortality rates ranged from 14.8%-62.5% at five of the six institution included in the study. Twelve of 57 factors were strongly associated with the occurrence of aspiration pneumonia. The top six risk factors associated with post anesthetic aspiration pneumonia were: megaesophagus (OR=17.3), upper airway surgery (OR=8.1), history of neurologic disease prior to anesthesia (OR=5.4), endoscopic procedure (OR=5.2), regurgitation or vomiting during the anesthetic period (OR=3.6), and history of respiratory disease prior to anesthesia (OR=2.7).

Based on the results from this study it would appear that the factors posing greatest risk for aspiration are not heavily dependent on pharmacologic interventions prescribed by the anesthesiologist. Exceptions to this theory would include significant risk factors such as hydromorphone at induction and the use of continuous rate infusions of anesthetics and analgesics during the anesthetic period. These findings warrant further investigation as to whether or not dosage may play a role in the cause for these risks.

Co-existing disease, whether that be previously or concurrently, complications during anesthesia or recovery, and surgical or diagnostic procedures pose a greater risk of aspiration for the canine anesthetic patient based on these results. These findings lead us into many

directions of future investigation of this post anesthetic complication. Further study of the use of histamine 2 receptor antagonists and proton pump inhibitors in high risk veterinary patients to decrease the severity of aspiration pneumonia should it occur. Study of these gastric protectants should include determining effective dosage needed in our veterinary patients to increase gastric pH above 4 for a satisfactory time period. We should re-evaluate the dosage and effects of metoclopramide needed prior to and during the anesthetic period to prevent gastroesophageal reflux and decrease gastrointestinal transit time. We should attempt to determine the point during the anesthetic or recovery period that aspiration of gastric contents is most likely to occur.

Finally, we should add some new variables to study in a prospective clinical study that weren't able to be adequately evaluated retrospectively. Timing of extubation should be evaluated to determine when the animal's swallowing reflex is most competent to protect the airway from aspiration of gastric content. We should study more thoroughly the anesthesia recovery period at least 24 hours post extubation to determine if postoperative analgesic side effects such as nausea and vomiting may also be playing a role in the risk of aspiration. Endotracheal tube cuff type or cuff lubrication could also be evaluated in the veterinary patient as it has been in the human patient to determine if it could play a preventative role in aspiration during the anesthetic period.

The combined data from the previously described retrospective study and a future prospective study of post anesthetic aspiration risk factors have the potential to create a scale for aspiration pneumonia risk. Although aspiration pneumonia has a low but variable prevalence in the general canine population anesthetized throughout the country, the financial

and physical ramifications of canine post anesthetic aspiration pneumonia sequalae are much too consequential to ignore.