ABSTRACT

Title of Thesis:	TOOTH RESORPTION AND RISK FOR ANESTHETIC COMPLICATION DURING ANESTHETIZED DENTAL PROCEDURES IN DOMESTIC FELINES
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Tooth resorption (TR) in felines may present an increased risk for complications during dental procedures, and it is currently unknown whether oral examination is a valid diagnostic method for type 1 TR. Using existing data from 1,530 felines from a large veterinary hospital in Washington, D.C., I examined the association between type 1 TR and complication under anesthesia during a dental procedure, and the validity of oral examination as a diagnostic tool. Controlling for breed, weight, age, sex, hematocrit, total protein, technician, veterinarian, and presence of oral and systemic disease, type 1 TR was associated with a complication under anesthesia during a dental procedure ($p<0.0001$). Sensitivity (93.1%) and specificity (97.6%) support the reliability of oral examination for diagnosing type 1 TR. Veterinarians can proactively anticipate lower blood pressures when anesthetizing felines with type 1 TR. There are similarities between TR in humans and felines, and further research is needed on the pathophysiology and health implications of TR in both species.

TOOTH RESORPTION AND RISK FOR ANESTHETIC COMPLICATION DURING ANESTHETIZED DENTAL PROCEDURES IN DOMESTIC FELINES

by

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List of Abbreviations

AAHA: American Animal Hospital Association (AAHA 2019)

ASA: American Society of Anesthesiologists' physical classification system for anesthetic risk (Brodbelt 2010)

AVDC: American Veterinary Dental College (AVDC 2019)

AVMA: American Veterinary Medical Association (AVDC 2019)

CEJ: cementoenamel junction (Perry and Tutt 2014)

CKD: chronic kidney disease (Greene et al. 2014)

CRI: continuous rate infusion (Robertson et al. 2018)

ECR: External cervical resorption (Patel et al. 2018)

FIV: feline immunodeficiency virus (Clarke and Caiafa 2014)

FCGS: feline chronic gingivostomatitis (Perry and Tutt 2014)

FRL: feline resorptive lesion (Arzi et al. 2010)

MAC: minimum alveolar concentration (Robertson et al. 2018)

MAP: mean arterial pressure (Robertson et al. 2018)

NMdA: N-methyl-d-aspartate (deVries and Putter 2015)

SA: sinoatrial (Vegas et al. 2012)

TR: tooth resorption (Girard et al. 2008)

Chapter 1: Introduction to Tooth Resorption

Introduction

Feline resorptive lesions (FRLs) are common in veterinary medicine, but despite decades of research, the exact mechanism is unknown (DeLaurier et al. 2009). FRLs are categorized as tooth resorption (TR) where there is the loss of dental hard tissue (AVDC 2019). Dental hard tissue is composed of both mineralized and unmineralized components including enamel, cementum and dentin (Patel et al. 2018). Enamel is the mineralized coating over the dentin of the crowns of teeth, and cementum is the unmineralized tissue protecting the dentin of tooth roots (Figure 1) (Clarke and Caiafa 2014). Aside from cats, TR has been observed and studied in many species including chinchilla, dogs, humans and others (Gorrel 2015). Lesions above the cementoenamel junction (CEJ) are described as intraoral or supragingival; whereas, extraoral refers to lesions contained under the gumline (DuPont and DeBowes 2009). Intraoral lesions are associated with significant pain once the dentin is affected (Clarke and Caiafa 2014). Understanding the characteristics that are associated with periodontal disease can lead to more effective prevention and treatment strategies going forward.

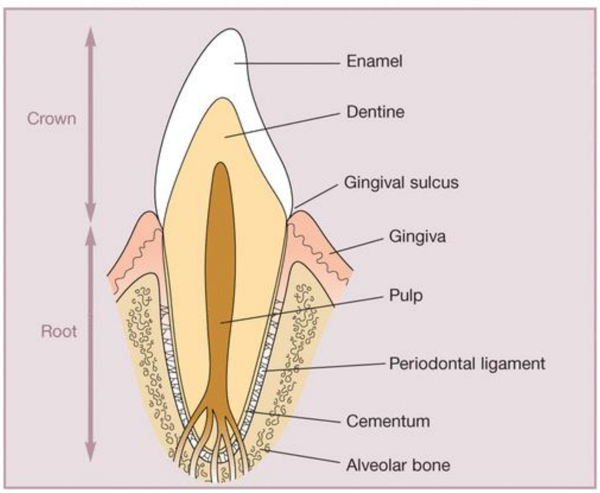

Figure 1. Tooth anatomy including surrounding bone (Clarke and Caiafa 2014)

Two Forms of Periodontal Disease

There are two main forms of periodontal disease including gingivitis, which is reversible gum tissue inflammation, and periodontitis, which is irreversible and progressive tissue and bone deterioration (Perry and Tutt 2014). Clinical signs of oral pain in domestic felines include chattering, hypersalivation, poor coat condition as a result of not grooming, head shaking and halitosis; these symptoms are often present in felines with TR (Figure 2) (Clarke and Caiafa 2014). Owners and clinicians should be aware that cats often hide their oral pain, so in many cases, no symptoms are noticed prior to a thorough dental examination including anesthetized radiographs (Gorrel 2015). Radiographic findings of TR are strongly correlated with a histopathologic diagnosis of TR indicating radiographs are a good measure of TR (Senn et al. 2010).

Figure 2. Photograph of FRLs affecting teeth 407, 408, 409 (Clarke and Caiafa 2014)

Relationship Between Oral and Systemic Disease

Current evidence suggests that the oral pain associated with type 1 TR could have systemic implications (Perry and Tutt 2014). A large case-control study conducted in domestic felines found an association between periodontal disease and chronic kidney disease (CKD) when controlling for weight, thinness, geographic region, sex, breed, recent anesthesia, diabetes, hydration status and several other factors; cats with periodontal disease are at 1.8 times the odds of being diagnosed with CKD compared with the odds in felines without periodontal disease (Greene et al. 2014). The proposed study aims to extend this line of research to consider other health implications of FRLs, specifically, complications during anesthetized dental procedures.

Chapter 2: Research Question and Specific Aims

Investigatory Goals

This study characterizes felines with TR, evaluates the risk of complication under anesthesia for a dental procedure and validates the oral exam by a veterinarian as a useful diagnostic tool for type 1 TR by retrospectively analyzing medical, anesthetic and radiographic records. The target population is domestic felines who receive dental care at large urban veterinary hospitals; the sample population is felines who were anesthetized for a dental procedure at Friendship Hospital for Animals in Washington, D.C., between April 1, 2013, and April 24, 2018, which includes 1,530 felines. Friendship Hospital is a large, urban hospital with over 200 employees. Below are the aims explored; Table 1 depicts the main exposure and outcome variables with potential confounding variables.

- Aim 1: Are certain feline characteristics associated with TR?
    - Covariates: breed, sex, age, weight, concurrent oral and systemic disease
    - Outcome: the presence of at least one FRL as diagnosed by radiograph
    - Goal: to identify characteristics that are associated with TR
- Aim 2: Is TR in cats associated with a complication (i.e. hypotension, bradycardia) that requires an intervention treatment during a dental procedure, and is the association independent of breed, sex, age, weight, concurrent oral and systemic disease, veterinarian, technician, hematocrit (HCT) and total protein (TP)?
    - Covariates: breed, sex, age, weight, concurrent oral and systemic disease, HCT, TP, veterinarian and technician
    - Outcome: if treatment was administered to support heart rate or blood pressure during an anesthetized dental procedure including cleaning, radiographs and extractions, for the feline's first dental procedure in the study period

    - Goal: to advance current understanding of the potential relevance and overall importance of oral health for avoiding complication during dental procedures

- Exploratory Aim: Can an oral exam accurately identify type 1 TR relative to the gold-standard of radiographs?
    - Screening test: oral exam evidence (i.e., the screening test) of type 1 TR
    - Gold-standard assessment: radiographic evidence of type 1 TR
    - Goal: to describe the validity of oral exam as an accurate assessment of oral health and hydration status prior to anesthesia.

Chapter 3: Background on Tooth Resorption and Anesthesia

Gaps in Current Knowledge

Numerous studies have been conducted on FRLs, but substantial gaps in knowledge remain including predisposing factors and systemic implications of FRLs. Increased odontoclastic action at FRLs has been supported by numerous studies and is thought to be associated with inflammatory mediators (Mihaljevic 2012). This study develops knowledge about the feline correlates of the resorptive process, as well as examine whether FRLs warrant consideration before an anesthetic event. This literature review discusses current knowledge on the epidemiology of FRLs, evaluates previous studies, and describes the relationship between resorption and overall health. This chapter delves into the stages of degeneration, the primary types of TR, prevalence estimates, hypotheses on TR, dentistry and anesthetic practice and determinants of blood pressure.

Differentiating the Types of Tooth Resorption

Periodontitis is a severe infection of the gingiva that can deteriorate underlying jawbone (Perry and Tutt 2014). One study found periodontitis present in 72% of teeth with type 1 TR, while only 15% of teeth with type 2 TR had periodontitis (Lommer and Verstraete 2001). Another study had similar findings in which type 1 TR was significantly associated with localized inflammation while type 2 TR was not (Girard et al. 2008). Type 1 TR initiates on the crown near the gingival sulcus while type 2 TR initiates at the apex of the tooth. Type 3 TR is when both types of FRLs are present on the same tooth, and often in these teeth, the point of initiation is unclear (Mestrinho et al. 2013). Intraoral, type 1, TR is very painful, evident by jaw chattering when the dentin or pulp is touched by eating, drinking or probing (Clarke and Caiafa 2014). The exposed dentin tubules and/or pulp chamber cause pain upon stimulation; the dentin tubules communicate with the innervated pulp chamber, so even if the deterioration has not reached the pulp, the tooth is highly sensitive (Mihaljevic et al. 2012)

Because type 2 TR is associated with a deteriorated the periodontal ligament space, this type of FRL can be addressed by the practicing dental veterinarian by performing a crown amputation of the affected tooth because the root fragments will continue to resorb in the alveolar bone (Mihaljevic et al. 2012). On the other hand, type 1 TR is highly associated with gingivitis and an intact periodontal ligament space, so crown amputation is inappropriate in these cases (Perry and Tutt 2014). Type 1 TR has been found to be highly associated with inflammation and periodontal disease (Gorrel 2015). Figure 3 demonstrates the two main types of TR mentioned (Harvey 2004). It appears that TR on the canines is primarily type 2; however, another commonly occurring process in felines' canine teeth is called buccal bony expansion (Perry and Tutt 2014). This super-eruption of the canine teeth is hypothesized to be caused by the loss of the periodontal ligament space initiated by vertical bone loss and intraoral TR that advances past the CEJ to involve the subgingival root (Perry and Tutt 2014). More research about the forms of resorption is needed because most studies available have clumped the two types together for analysis.

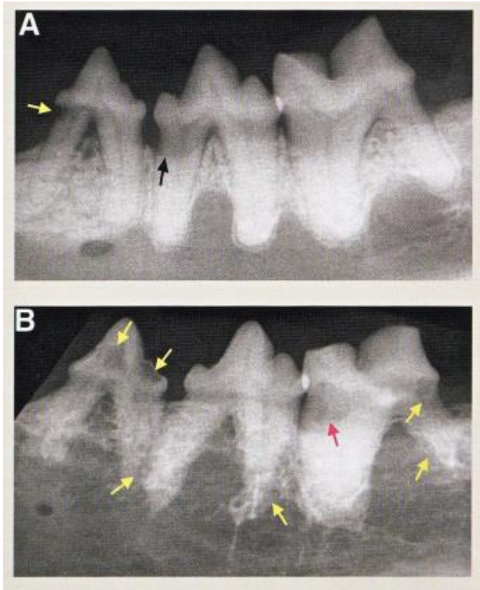

Figure 3. Three types of tooth resorption (TR) demonstrated radiographically. (A) Yellow arrow shows early type 1 TR on lower premolar. Note the traceable periodontal ligament space. (B) Top 3 yellow arrows show type 1 TR; bottom 3 yellow arrows show type 2 TR; red arrow marks tooth with type 3 TR (Harvey et al. 2004).

Differentiating between type 1 and type 2 TR could lead to more precise implications for study results.

Prevalence and Progression of Tooth Resorption

Although FRLs are highly prevalent in domestic felines, researchers and veterinarians are unsure of the exact mechanisms behind TR (DeLaurier et al. 2009). In a study including 109 felines with a standardized population, investigators found the prevalence of TR to be 70% in purebred felines and 38% in mixed-breed felines (Girard et al. 2008). Another study in a population of 96 randomly-selected Swedish felines found that 32% of felines had either gross or radiographic evidence of TR (Pettersson and Mannerfelt 2003). The same study found a positive correlation between age and TR. The authors' suggested that a portion of the variance between prevalence estimates across studies could be due to some studies lacking intraoral radiographs, which underestimates the prevalence, or selection bias, which over-selects for dentistry-specific clinics which tends to overestimate the prevalence (Pettersson and Mannerfelt 2003). Radiographs are essential for diagnosing TR and determining the best treatment approach (Gorrel 2015).

The progression of FRLs is gradual, often resulting in a delay in treatment; for this reason, many of the felines who are seen for dental procedures are being treated because there is a problem, rather than prophylactically (Gorrel 2015). TR has five levels of progression numbered from least severe to most severe degradation (TR1-TR5) (Figure 4) (AVDC 2019). Once dentin the FRL involves the dentin, the tooth is set to continue resorbing (Gorrel 2015). As described by Mihaljevic et al. (2012), TR1 is characterized as mild dental hard tissue loss. TR2 has moderate hard tissue loss with a loss of dentin that does not extend into the pulp chamber. TR3 involves deep dental hard tissue loss with loss of dentin that extends into the pulp chamber; however, the tooth is mostly intact. TR4 has more extensive hard tissue loss compared with TR3, so the tooth is mostly reabsorbed into the alveolar bone now. Finally, TR5 is characterized by a complete gingival covering, and the remnants of hard dental tissue can be seen on a radiograph only (Mihaljevic et al. 2012).

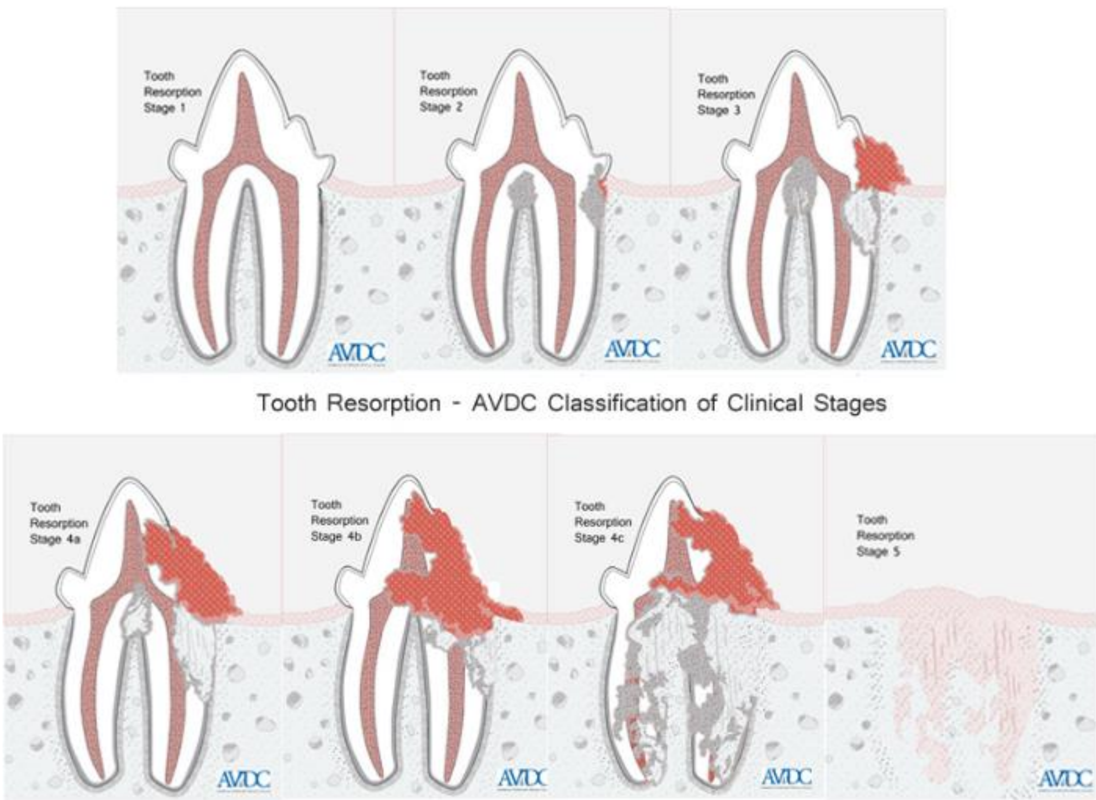

Figure 4. Five Stages of Tooth Resorption (AVDC 2019)

Current Hypotheses on Tooth Resorption

Evidence supports the presence of multiple types of inflammatory cells in association with FRLs including osteoprotegerin (OPG), specific receptor activators (RANK/RANKL), fibroblasts, stem cells and mast cells (Arzi et al. 2010, Gibertoni 2017, Senn et al. 2010). The presence of these cells is hypothesized to be evidence of repair attempts by the body (Senn et al. 2010). One theory on the major difference between cats with FRLs and cats without FRLs is each cat's individual ability to repair TR (Gorrel 2015). The presence of odontoclasts and osteoclasts at FRL sites has been supported by several studies; these cells typically are responsible for the resorption and remodeling of bony tissue during the shedding of deciduous teeth; their presence during other life stages is abnormal (DeLaurier 2009, Wang and McCauley 2011). Odontoblasts and osteoblasts, two dentin producing cells, have also been observed at FRL sites, another indicator of a self-repair attempt (AVDC 2019, Wang and McCauley 2011). Previous studies established mast cell concentrations in the gingival tissue of healthy feline, but one study by Arzi et al. (2010) compared those previous estimates to estimates in felines with feline chronic gingivostomatitis (FCGS), FRLs and periodontitis. This study found that in the gingiva adjacent to teeth affected by FCGS, FRLs or periodontitis have a significantly higher concentration of mast cells compared to that of healthy felines (Arzi et al. 2010).

Current evidence supports that specific proteins, OPG/RANK/RANKL, are present at resorptive lesion site which is considered evidence of repair attempts by fibroblasts (Senn et al. 2010). Fibroblasts are associated with stem cells; a predominant theory on the mechanism of feline TR is that trauma to the periodontal ligament space from occlusal forces causes type 2 TR in felines (Harvey et al. 2004). The impact of occlusal forces is hypothesized to cause localized trauma to the periodontal ligament space (Gorrel 2015). The friction caused by the repeated irritation begins to cause trauma to the tooth's structure (Harvey et al. 2004). Cytokines are released which attract stem cells which initiates TR in a repair attempt (Harvey et al. 2004). Similarly, Zivkovic et al. (2010) hypothesized that local mechanical trauma is associated with FRL initiation. The study's findings supported the hypothesis, but further research is needed to better understand the relationship between TR and occlusal stress (Zivkovic et al. 2010). The mechanical trauma hypothesis applies to type 2 TR which is akin to ankylosis that occurs in humans and other species (DeLaurier et al. 2009). Ankylosis is thought to be a part of the aging process in which alveolar bone replaces tooth roots; this form of resorption is also referred to as replacement resorption (Clarke and Caiafa 2014). These findings further support the categorization the type of TR present before analyzing the associated data.

On the cellular level, tooth resorption in felines shares similarities to osteoporosis. Osteoporosis is known to be caused by a deficit in bone formation versus concurrent bone resorption process resulting in decreased bone density (Zhao and Ross 2007). Like how odontoclasts have been observed locally to resorb dental hard tissue, osteoclasts have been observed to do the same on the bone tissue of long bones (Zhao and Ross 2007). In addition to the functional similarities, current literature states that both osteoclasts and odontoclasts take advantage of defects in the mineralized border secreting protons and acidic proteases as by-products of resorption (Zhao and Ross 2007). Current evidence suggests that an acidic oral environment is associated with intraoral FRLs, where most of the lesions develop (Muzylak et al. 2007). An acidic environment has been demonstrated to be a regulatory factor of osteoclastogenesis and osteoclastic action in felines (Muzylak et al. 2007). One study in humans described the defect in the hard tissue a "portal of entry" for odontoclasts, as seen in Figure 5 (Patel et al. 2018). During the loss of primary teeth, both osteoclasts and odontoclasts have a role in the normal process resorption and remodeling of

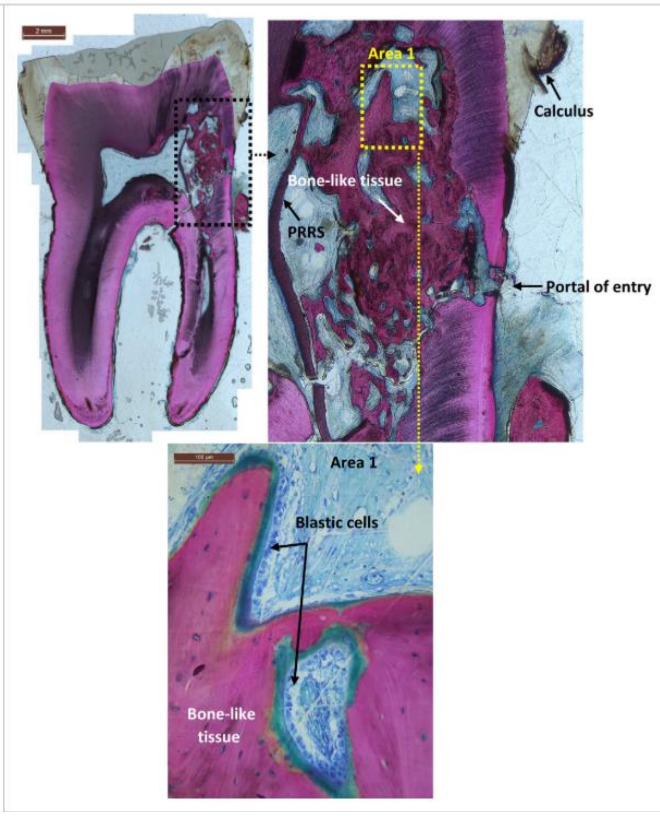

Figure 5. Histological image of human dental tissue illustrates the portal of entry where odontoclasts penetrate the tooth (Patel et al. 2018)

tissue (Wang and McCauley 2011). The problem is the presence of these cells at times other than during the eruption of adult dentition (DeLaurier et al. 2009).

Vitamin D specifically has been hypothesized as a potential nutrient associated with TR, but current research suggests it is not a significant factor for FRLs (Gorrel 2015). Several studies have investigated the relationship of diet and tooth resorption, but the conclusions have been conflicting, so further evaluation is needed to better understand the role of diet in TR if any (Richman 2018).

Dentistry and Anesthetic Practice

To appropriately evaluate and treat animal dentition, there are certain standards that must be upheld to practice veterinary dentistry. The American Veterinary Dental College (AVDC) is recognized by the American Board of Veterinary Specialties of the American Veterinary Medical Association (AVMA) and determines the standards of practice by veterinary dental specialists (AVDC 2019). The American Animal Hospital Association (AAHA) is the accrediting body for veterinary hospitals in the United States and suggests guidelines for medical practice, but individual hospital participation is optional (AAHA 2019). The materials and equipment necessary are extensive and expensive, but each element is important for safety and health. Veterinary dental care is recommended annually for felines over one year of age, and the procedure should include intravenous catheter placement, maintenance fluids and intubation (Holmstrom et al. 2013). Felines who have a history TR should have an oral examination by a veterinarian every six months (AVDC 2019).

Oral procedures carry an increased risk for aspiration and decreased ease of monitoring (deVries and Putter 2015). This is because all procedural steps involve working in and around the oral cavity, where the pulse oximetry rests and the endotracheal tube lies (deVries and Putter 2015). Anesthesia is required for the appropriate evaluation of feline teeth including full-mouth probing and intraoral radiographs; a dental procedure without these two elements is considered inaccurate and incomplete (Holmstrom et al. 2013). Pet-owners are often concerned about the risks associated with anesthetic events, but anesthesia is relatively safe under current guidelines and is necessary for periodontal evaluation and treatment (AHAHA 2019, AVDC 2019).

Determinants of Blood Pressure

To support the hypothesis that there is an association between intraoral TR and complication under anesthesia, it is necessary to delve into the determinants of blood pressure. The predominant complication during anesthesia is hypotension which leads to inadequate perfusion of oxygen and nutrients throughout the body (Vegas et al. 2012); generally, the minimum adequate blood pressure is considered to be60 mmHg (Robertson 2018). Blood pressure is determined by the cardiac index (also known as cardiac output) and peripheral

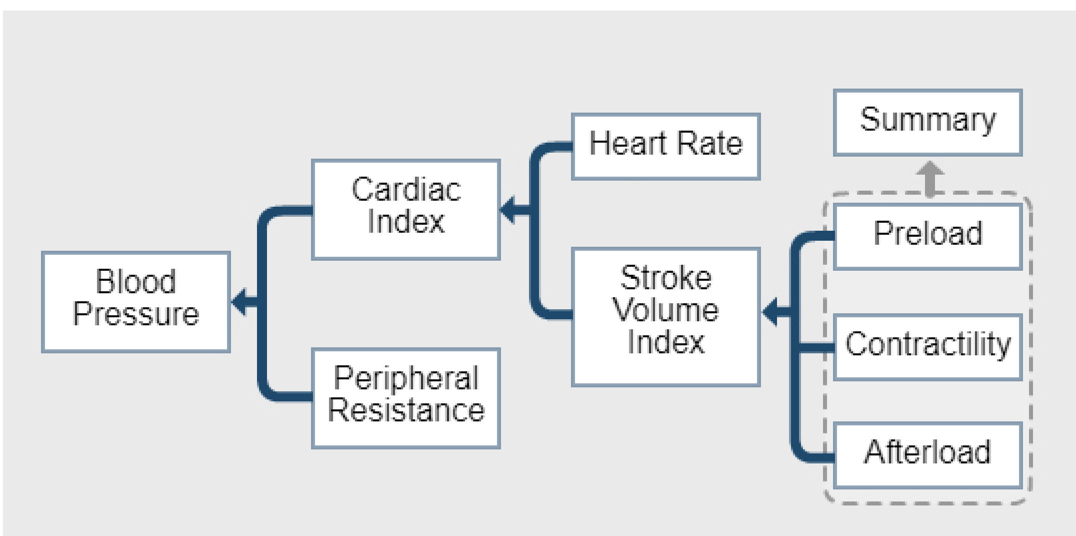

Figure 6. Determinants of blood pressure (Vegas et al. 2012)

resistance by vasculature (also known as total peripheral resistance); Figure 6 is the basic tree of blood pressure determinants (Vegas et al. 2012).

The cardiac index is the volume of blood (L/min) divided by the body's surface area (m^2) and is determined by heart rate and stroke volume (Vegas et al. 2012). If there is a decreased cardiac index, it means there is a deficiency in either the heart rate or the volume of blood in the vasculature relative to body size. Heart rate (beats/min) is determined by the sinoatrial (SA) node firing electrical impulses as signaled by the autonomic nervous system (Vegas et al. 2012). There are four factors that contribute to heart rate by affecting the rate at which electrical impulses are sent by the SA node including intrinsic rate, sympathetic activity, parasympathetic activity and pharmacological response (Vegas et al. 2012). Sympathetic activity induces an increase in heart rate due to the physiological changes associated with the "fight or flight" response, and parasympathetic activity induces a decrease in heart rate due to the physiological changes associated with the "rest and digest" response (Vegas et al. 2012). A pharmacological response can induce an increase or a decrease in heart rate depending on which specific medications are administered (Vegas et al. 2012). On the other hand, stroke volume is the volume of blood in each beat (mL) divided by the body's surface area (m^2), and it is determined by three factors (Vegas et al. 2012). First, preload is the filling pressure in the heart at the end of diastole; the relationship between preload and stroke volume has been demonstrated with Starling's Law (Vegas et al. 2012). Second, contractility is the strength with which the heart muscle contracts during systole and is increased by both sympathetic and pharmacological activity (Vegas et al. 2012). Finally, afterload is the emptying pressure in the heart during systole (Vegas et al. 2012). In summary, these are the determinants of blood pressure, and when troubleshooting hypotension, all these elements must be considered in order to choose the most appropriate treatment option for each individual.

During anesthesia, the determinants of blood pressure are altered by the individual's physical condition and the medications administered. Drugs for each individual are chosen primarily based on comorbidities and procedure being done. For example, drugs with profound cardiac effects are avoided, when feasible, in individuals with heart disease to avoid unnecessary complications and drugs that can cause significant vasodilation are avoided in decompensated individuals to avoid severe hypotension. The broad drug classes are NMDA-receptor antagonists (i.e. ketamine), local anesthetics (i.e. lidocaine, ropivacaine, bupivacaine), NSAIDs (i.e. meloxicam, carprofen), alpha-2 adrenoreceptor agonists (i.e. dexmedetomidine), pure mu agonists (i.e. morphine, oxymorphone, hydromorphone) and partial mu agonists (i.e. buprenorphine, butorphanol) (deVries and Putter 2015). Understanding the drug classes enables the anesthetist to manage anesthesia more effectively by anticipating complications and titrating the maintenance gas appropriately.

Anesthetic Considerations

Each anesthetized individual has a combination of medications on-board, so it is essential that the anesthetist is familiar with how each affects physiology. A special tool for managing an anesthetized dental case is the use of local analgesia. Local nerve blocks are an effective analgesic tool during anesthetized dentals in felines; felines that receive a local block consisting of 0.25 mg/kg each lidocaine and bupivacaine per each maxillary and inferior alveolar site tends to allow for anesthetic maintenance at a lower inhalant concentration and to be associated with reduced heart rate, blood pressure and postoperative pain compared with cats who received a placebo (Aguiar et al. 2014). Figure 7 outlines the expected cardiac effects

Drug	Heart rate	Inotropy	Cardiac output	Vascular resistance	Arterial blood pressure
Acepromazine	↔	↔	↔	↓	↓
Midazolam	↔	↔	↔	↔	↔
Diazepam	↔	↔	↔	↔	↔
Butorphanol	↔	↔	↔	↔	↔
Buprenorphine	↔	↔	↔	↔	↔
Methadone	↓	↔	↔	↔	↔
Fentanyl	↓	↔	↔	↔	↔
Xylazine Medetomidine Dexmedetomidine	↓↓	↔	↓	↑	↑↓
Ketamine	↑	↑	↑	↑	↑
Propofol	↔	↓	↓	↓	↓
Thiopental	↑	↓	↓	↓	↓
Alphaxalone	↑	↓	↓	↓	↓
Etomidate	↔	↔	↔	↔	↔
Isoflurane	↑	↔	↔	↓	↓
Sevoflurane	↔	↔	↔	↓	↓

↓: Decrease ↑: Increase ↓↓: pronounced decrease ↔: no influence ↑-↓: initially increase, then decrease

Figure 7. Cardiovascular effects of commonly used veterinary anesthetics (Steinbacher and Dorfelt 2012)

of commonly used medications; this figure has been included to exemplify the relationship previously mentioned between pharmacological agents and heart rate (Steinbacher and Dorfelt 2012). Medications from the table that the dental service from this thesis utilized acepromazine, midazolam, dexmedetomidine, butorphanol, buprenorphine, oxymorphone, hydromorphone, morphine, ketamine, propofol and isoflurane during the study period. Based on the figure, midazolam, butorphanol and buprenorphine have no cardiovascular effects, so these medications are not going to affect the individual's blood pressure. Drugs including acepromazine, isoflurane and propofol typically decrease blood pressure through vasodilation (decreased vascular resistance) (Steinbacher and Dorfelt 2012). Alpha-2 agonists such as dexmedetomidine cause a significant increase in vascular tone which causes an increase in blood pressure, so as a reflex, the heart rate is profoundly decreased (deVries and Putter 2015). Finally, ketamine is beneficial for maintaining blood pressure due to increased heart rate and vascular tone and is often used as an induction agent with propofol to provide smooth induction and anesthesia (Steinbacher and Dorfelt 2012). Overall, the drug protocol for the anesthetized procedure is chosen thoughtfully, and during monitoring which medications were given as a part of the pre-medication and induction protocol are relevant to consider before treating a complication for animal safety and comfort.

Troubleshooting Anesthetic Complications

In the presence of an inhalant anesthetic and the absence of surgical or procedural stimuli, hypotension is a common occurrence, so doing a full assessment before treating any condition under anesthesia is vital for maximizing safety and comfort while minimizing unnecessary administration of medications and fluids (Robertson et al. 2018). It should be noted that dental procedures are considered elective, so the individuals being anesthetized have either no concurrent disease or well-controlled, stable disease processes. If a complication arises, the first step is to evaluate if the inhalant can be decreased based on the patient's anesthetic depth (Robertson et al. 2018). It is unlikely that during a dental that a reversal agent would need to be administered, but in certain cases of complication under anesthesia, a reversal agent can be given to render the drug inactive. The next step is to provide a fluid bolus, crystalloid or colloid, but caution must be exercised in patients with heart disease or who are anuric. Alternatively, the second step could be to administer an anticholinergic, such as glycopyrrolate or atropine, to increase the heart's contractility if hypotension is observed concurrently with bradycardia. Third, the addition of a minimum alveolar concentration (MAC) reductant can enable the inhalant concentration to be turned down to decrease the side effects experienced by the patient (Robertson et al. 2018). Finally, after euvolemia is reached, but hypotension persists, a positive inotrope, such as dopamine, can be added as a continuous rate infusion (CRI) to increase heart rate, and subsequently, the increase in heart rate will increase and maintain the blood pressure (Robertson et al. 2018).

Chapter 4: Research Design and Methods

Study Design and Variables

This MPH thesis addresses two primary aims and one exploratory aim. The first objective examines the association between FRLs and characteristics including breed, sex, age, weight and concurrent disease, both systemic and oral. Next, the association between type 1 TR and intervention during anesthesia was analyzed while controlling for feline characteristics including breed, sex, age, weight, HCT, TP and concurrent disease and procedure characteristics including veterinarian and technician. Finally, the validity of the oral examination was evaluated by comparing the diagnostic capability of the oral exam with the radiograph for type 1 TR. If anywhere in the medical record other than the radiographic comments contained a note indicative of TR, then the feline was considered to have TR on oral examination.

This research was conducted using a retrospective analysis of hospital cohort data. The data were extracted from Friendship Hospital for Animals' database; all feline dentistry patients between April 1, 2013, and April 24, 2018 were included. The entire five-year hospital cohort of 1,530 felines has been included in the study, but individuals missing information on any variable of interest were excluded from the study population. After exclusion criteria were applied, the sample remaining was 1,337 felines; 12% of records were lost due to missing information. The most common missing variable was radiographic information. In 2013, 2014 and much of 2015, radiographs were performed on every abnormal tooth on the oral examination, but it was not routine practice to take full-mouth radiographs until mid-2015 when the radiography equipment was updated.

Data were extracted from medical, anesthetic and radiographic records. Age, breed, weight, HCT, TP, systemic and oral disease status variable information were included as potential confounders based on previous research and observational findings. Specifically, FCGS was included as a potential confounder due to the known association with oral pain and inflammation (Perry and Tutt 2014). Jaw fractures and cancerous oral masses were included as oral disease processes possibly associated with oral pain. One hypothesis on the relationship between systemic and periodontal diseases is that the presence of oral bacterial biofilm, such as in those with periodontal disease, advances periodontal pocketing enabling bacteria to become systemic via the pocket epithelium (Perry and Tutt 2014). Systemic diseases included in this study were categorized as none, cardiac, renal, other and multiple; categorization was based on veterinarian diagnosed conditions. Other diseases included diabetes mellitus, hyperthyroidism and liver diseases. The medical records were completed by either the dental coordinator, the attending veterinarian or a combination of the two. There was moderate variability in the amount of history contained in each medical record. If the information was missing on the first place in the record checked, then further investigation was done to find that information elsewhere in the record. For example, each anesthesia sheet had both technicians working in the dental suite that day recorded, so I relied on who placed the intravenous catheter and handwriting. A total of three veterinarians and 12 technicians were included in the study; three lead technicians were evaluated individually, and 9 technicians were grouped together as "everyone else." I evaluated the medical record and radiographs to categorize the type of TR present. During the collection and analysis, each variable was handled as follows (Table 1). All associations in this study were evaluated at the 95% significance level. SAS Studio 9.4 was utilized for all analyses.

Table 1: Sample Charactersitics

Variable	Type of Data	Categories	Primary Source of Data	Role in Study	Aim(s) Addressed
Age (years)	Continuous	--	Medical record^	Covariate	Aim 1, 2
Weight (kg)	Continuous	--	Medical record	Covariate	Aim 1, 2
Breed	Continuous	--	Medical record	Covariate	Aim 1, 2
Hematocrit (%)	Continuous	--	Medical record	Covariate	Aim 2
		Yes-at least one tooth affected		Outcome	Aim 1, Exploratory Aim
Type 1 TR	Binary	No-no teeth affected	Radiographic record	Exposure	Aim 2
		Yes-oral mass, FCGS, jaw fracture			
Oral Disease	Categorical	No-concurrent disease process	Medical record	Covariate	Aim 1, 2
		None			
		Renal			
		Cardiac			
Systemic Disease	Categorical	Other	Medical record	Covariate	Aim 1, 2
		One			
		Two			
Veterinarian	Categorical	Three	Medical record	Covariate	Aim 2
		One			
		Two			
		Three			
Technician	Categorical	Everyone else	Anesthetic record	Covariate	Aim 2
Total Protein (g/dL)	Continuous	--	Medical record	Covariate	Aim 2
		Male			
Sex	Categorical	Female	Medical record	Covariate	Aim 1, 2
		Yes-at least one tooth affected			
TR on Oral Exam	Binary	No-no teeth affected	Medical record	Exoposure	Aim 3

Anesthetic Protocol

During the study period, the dental anesthetic protocols varied. The boarded veterinary anesthesiologist was added to hospital staff in late 2014 and added changes to the overall protocol. Each individual cat's anesthetic plan was completed the morning of the procedure by the dental doctor practicing that day. Each feline during this period received one dose of an antibiotic, clindamycin, intravenously at a 5.5 mg/kg dosage. As discussed in Chapter 3, pre-medications, induction and intraoperative medications are each important to consider when both designing and executing the anesthetic plan. Prior to 2015, an intravenous catheter was placed, and pre-medications, typically acepromazine, and an opioid, typically hydromorphone, were given swiftly intravenously and quickly followed by a propofol (2-4 mg/kg) and midazolam (0.2 mg/kg) induction. The doses used for the pre-medications were not clear from the medical files available. From 2015 onward, the dental anesthetic protocol was subcutaneous or intramuscularly injected pre-medications of acepromazine (0.02-0.05 mg/kg), dexmedetomidine (5-10 ug/kg) or midazolam (0.2 mg/kg) plus an opioid (partial or pure mu agonist). The technician waited until the feline showed signs of sedation and placed an intravenous catheter. An induction of propofol or ketamine plus propofol was used for each feline. The result of the change, observationally, was fewer cases of dysphoria, but there was no significant difference in the number of patients treated for complications before and after addition of anesthesiologist ($p>0.05$).

The entire study period shared relatively the same protocol for maintenance anesthesia. Inhalant anesthesia was started at 3% isoflurane in oxygen and decreased to 1-2% for maintenance after the palpebral response was lost. The technician was the primary anesthetist for all cases, but the veterinarian was in the room for the duration of the procedure. An anesthetic record was kept for each feline, and the recording of vitals took place every ten minutes. If a complication, such as hypotension or bradycardia, occurred, then the technician and veterinarian typically chose a treatment option together. If a crystalloid bolus was indicated, typically sodium-lactate solution was administered at 5-10 mL/kg, and if a colloid bolus was indicated, typically hydroxyethyl starch was administered at 3 mL/kg for felines. If bradycardia was being addressed, glycopyrrolate was almost always the drug of choice in this study and was administered at 0.01 mg/kg. If these options were ineffective at maintaining blood pressure, then a dopamine CRI was started at 5 ug/kg/min and titrated up to 10 ug/kg/min gradually, as needed. Often the duration of dental procedures, especially in felines, was too short to require a CRI to maintain the blood pressure.

After the feline was anesthetized and initially stable, the technician began the dental procedure by rinsing the mouth with 0.12% chlorhexidine solution to decrease both oral and aerosolized bacteria (Holmstrom et al. 2013). Each tooth was then scaled and polished. The veterinarian then completed a full-mouth examination by running a periodontal probe around the gingival sulcus of each tooth feeling for any defects, pockets, FRLs and abnormalities while the technician charted the findings on the anesthetic record. The technician then performed intraoral radiographs with digital imaging software. Prior to 2015, radiographs were only taken on teeth with notes from the oral examination; after 2015, full-mouth radiographs were taken on each feline because the standards of practice had changed (AAHA 2019, AVDC 2019). The radiographs were assessed by the veterinarian to decide the best treatment plan for that feline.

If extractions were indicated, then a local nerve block was administered intraorally; this block was a combination of 1 mg (0.05 mL) of lidocaine and 0.5 mg (0.1 mL) of bupivacaine. Caudal mandibular nerve blocks were performed on cats who had extractions anywhere on the lower jaw from the canines caudally, and rostral maxillary (infraorbital) nerve blocks were done for extractions on the maxilla. In cases were only the canines or incisors on the mandible need extracting, then mental nerve blocks were performed. An NSAID was administered subcutaneously shortly after extubation for pain control following extractions for healthy patients; otherwise, a single dose of buprenorphine was administered subcutaneously.

Chapter 5: Statistical Analysis and Results

Analysis

First, I examined the associations between each individual feline characteristic and FRLs in a series of univariate analyses. The exposures of interest included age, breed, sex, weight, oral disease status and systemic disease were analyzed against the binary outcome of any type of TR (types 1-3) as identified by radiograph. All continuous variables in the analysis were found not to be normally distributed, so non-parametric analyses were utilized; primarily skewness and kurtosis were assessed to come to this conclusion. The analysis of the continuous variables included the mean and standard deviation, and the p-values were calculated using the Wilcoxon rank-sum test; the analysis of the categorical characteristics included the frequencies, and the p-values were calculated using the chi-square test.

Second, I used logistic regression to examine the relationship between type 1 TR on radiograph and if an intervention was required to treat a complication during the anesthetized dental procedure. I conducted a sequential model-building approach that included five models. I added HCT and TP in successive models because of the non-independence of HCT and TP.

Third, I examined the validity of oral examination to document TR to complement the information learned about the relationship of FRLs and complications under anesthesia. The sensitivity (sn) (sn=TP/(TP+FN)) and specificity (sp) (sp=TN/(FP+TN)) were both calculated.

Results

Aim 1

The median age for all felines in the sample was 9.0 years [5.9-12.0], and the mean ages for felines with TR and without TR were 10.0 years [7.2-12.5] and 7.3 years [4.8-11.1], respectively (p=0.0001); see Table 2. For weight, the median of the total sample was 5.0 kilograms (kg) while the median weights for felines with TR and without TR, respectively, were 5.0 kg [4.0-6.0] and 5.1 kg [4.1-6.0] (p=0.55). The study population included 47.5% (n=645) female and 52.5% (n=713) male felines, and females were more likely to have TR than males (p=0.001). Breed was unrelated to the presence of TR (p=0.26), and the large majority (84.3%) of the study subjects were mixed-breed felines. Oral disease was found in 7.9% of the study population, but only 2.9% of the study population with oral disease had concurrent TR (p=0.001). The large majority of felines in the study were free from systemic disease (78.7%, n=1,068), and the most common systemic disease was cardiac disease with 9.7% (n=131) felines affected.

Table 2: Bivariate associations between feline characteristics and tooth resorption (n=1,337)					
Chacteristic	Strata	≥1 Type 1-3 TR present	No TR Present	Total Sample	p-value
Age (yr)		10.0 [7.2-12.5]	7.3 [4.8-11.1]	9.0 [5.9-12.0]	0.0001*
Weight (kg)		5.0 [4.0-6.0]	5.1 [4.1-6.0]	5.0 [4.1-6.0]	0.55
Sex	Female	27.2% (n=363)	20.7% (n=281)	47.5% (n=645)	0.001*
	Male	25.0% (n=334)	27.4% (n=372)	52.5% (n=713)	
Breed	Fancy	7.6% (n=102)	8.1% (n=108)	15.7% (n=210)	0.26
	Mixed	44.5% (n=595)	39.8% (n=532)	84.3% (n=1,144)	
Oral Disease	Yes	2.9% (n=39)	5.0% (n=67)	7.9% (n=106)	0.001*
	No	49.2% (n=658)	42.9% (n=573)	92.1% (n=1,231)	
Systemic Disease	None	39.6% (n=530)	39.3% (n=533)	78.7% (n=1,068)	0.05*
	Cardiac	5.6% (n=75)	4.1% (n=56)	9.7% (n=131)	
	Renal	1.9% (n=25)	1.9% (n=26)	3.8% (n=51)	
	Other	2.5% (n=33)	1.1% (n=15)	3.7% (n=50)	
	Multiple	2.5% (n=34)	1.7% (n=23)	4.3% (n=58)	
*p≤0.05					

Aim 2

Using a logistic regression model to examine the relationship between type 1 TR on radiograph and intervention to treat a complication during a dental procedure, adjusting for signalment characteristics including age, weight and breed. Age was the only variable that was associated with treatment for anesthetic complication (p=0.01, see Table 3 Model 1). The odds of a feline requiring intervention for an anesthetic complication increase by 1.04 (95% CI (1.01,1.07)) times for every year increase in age. In Model 2, when type 1 TR, HCT and breed were added to the model, then age was no longer significant (p=0.39), but felines with type 1 TR had 1.94 times the odds of complication (95% CI (1.51, 2.48)) compared with those without TR. In Model 3, which included the previous models' covariates plus systemic and oral disease status, only type 1 TR was associated with treatment, where felines with type 1 TR were at

1.99 times the odds of needing treatment for a complication (95% CI (1.55, 2.56)) relative to a feline without TR. The results were similar when the model additionally included a categorical variable to adjust for the veterinarian who completed the dental procedure (see Model 4). Notably, one veterinarian had lower odds of treating for a complication compared to the reference veterinarian (OR=0.69 (95% CI (0.51, 0.94)). This veterinarian performed 18.3% of all feline dentals during the study period. All other covariates in Model 4 had p>0.05.

The final model, Model 5, includes all covariates of the previous models and adds technician, sex and TP. In this model, type 1 TR (p<0.0001), veterinarian (p=0.03) and technician (p=0.0005) were significant to the outcome treatment for anesthetic complication. Regarding technicians, technician one and two did 21.2% (n=282) and 21.5% (n=287) of the dentals, respectively, technician three did 16.3% (n=218) of the dentals and everyone else combined as technician four did 41% (n=548) of the dentals. When technicians were analyzed against the reference technician, only technician one treated significantly more or less with an increased odds of 1.50 (95% CI (1.00, 2.25) times for treating for a complication. The difference is statistically significant, but further data analyses would need to be performed to better understand the circumstances of this finding. I suspect there is variation between anesthetists' individual practices when it comes to treating complications. The same veterinarian who had decreased odds of the outcome in the previous model had 0.71 (95% CI (0.52, 0.97)) times the odds of treating for a complication during the dental procedure (p=0.03). All other covariates were not statistically significant (p>0.05).

Table 3: Multivariate analysis of tooth resorption (TR) and the odds of an intervention during an anesthetized dental procedure (n=1,337)

		Model 1		Model 2		Model 3		Model 4		Model 5	
Chacteristic	Strata	Odds Ratio (95% CI)	p- value	Odds Ratio (95% CI)	p- value	Odds Ratio (95% CI)	p- value	Odds Ratio (95% CI)	p- value	Odds Ratio (95% CI)	p- value
Age (yr)		1.04 (1.01, 1.07)	0.01 *	1.02 (0.98, 1.05)	0.39	1.01 (0.98, 1.05)	0.47	1.01 (0.98, 1.05)	0.53	1.01 (0.98, 1.05)	0.49
Weight (kg)		0.96 (0.89, 1.03)	0.24	0.96 (0.88, 1.03)	0.24	0.96 (0.89, 1.04)	0.32	0.96 (0.88, 1.05)	0.35	0.96 (0.88, 1.05)	0.36
Breed	Fancy	0.90 (0.65, 1.25)		0.92 (0.67, 1.28)		0.92 (0.67, 1.28)		0.93 (0.67, 1.29)		0.97 (0.69, 1.34)	
	Mixed	Reference	0.54	Reference	0.62	Reference	0.64	Reference	0.66	Reference	0.83
Hematocrit (%)				0.99 (0.96, 1.01)	0.27	0.99 (0.96, 1.01)	0.33	0.99 (0.96, 1.01)	0.33	0.99 (0.97, 1.01)	0.41
Type 1 TR	Yes			1.94 (1.51, 2.48)		1.99 (1.55, 2.56)		2.05 (1.59, 2.64)		2.10 (1.63, 2.72)	
	No			Reference	<0.0001*	Reference	<0.0001*	Reference	<0.0001*	Reference	<0.0001*
Oral Disease	Yes					1.51 (0.94, 2.44)		1.52 (0.94, 2.45)		1.45 (0.89, 2.36)	
	No					Reference	0.09	Reference	0.09	Reference	0.13
Systemic Disease	None					1.03 (0.54, 1.98)	0.92	1.03 (0.54, 1.98)	0.92	1.01 (0.53, 1.97)	0.95
	Cardiac					0.82 (0.40, 1.68)	0.59	0.86 (0.42, 1.76)	0.68	0.82 (0.40, 1.69)	0.58
	Renal					2.08 (0.79, 5.50)	0.14	2.14 (0.81, 5.66)	0.13	2.17 (0.81, 5.79)	0.12
	Other					1.66 (0.64, 4.31)	0.30	1.58 (0.61, 4.12)	0.35	1.57 (0.59, 4.16)	0.36
	Multiple					Reference	--	Reference	--	Reference	--
Veterinarian	One							Reference	--	Reference	--
	Two							0.69 (0.51, 0.94)	0.02*	0.71 (0.52, 0.97)	0.03*
	Three							1.25 (0.77, 2.04)	0.37	1.41 (0.85, 2.32)	0.18
Technician	One									1.50 (1.00, 2.25)	0.05*
	Two									0.71 (0.48, 1.05)	0.09
	Three									Reference	--
	Four									1.22 (0.85, 1.75)	0.28
Total Protein (g/dL)										1.08 (0.87, 1.35)	0.48
Sex	Female									Reference	
	Male									1.01 (0.78, 1.32)	0.92

**p≤0.05

Exploratory Aim

The exploratory aim collected additional information regarding FRLs. The specificity and sensitivity of the oral exam were 97.6% and 93.1%, respectively.

Table 4: Validation of oral examination for diagnosing feline tooth resorption: sensitivity and specificity

Measure	**Test Statistic**
Sensitivity	93.1%
Specificity	97.6%

Chapter 6: Discussion

Discussion

This thesis captured data from 1,337 felines who underwent anesthetized dental procedures at the same hospital within a five-year period. The data were analyzed to examine which characteristics were associated with TR, if the presence of TR was correlated with receiving treatment for an anesthetic complication, and if an oral examination is an accurate diagnostic for TR. FRLs were more common in females than males, and felines with TR tended to be older than those without TR. Felines with TR were more likely to have at least one concurrent systemic disease than felines without TR, but felines with a concurrent oral disease are less likely to have TR. TR, veterinarian and technician were correlated with treatment for an anesthetic complication. The oral examination was supported as a valid diagnostic tool for TR using intraoral radiographs as the "gold-standard" diagnostic for this condition.

Aim 1

Many findings for Aim 1 were consistent with current literature. First, age and sex were associated with TR ($p \leq 0.001$), as were oral and systemic diseases (p-values = 0.001 and 0.05, respectively). For example, according to one previous study, TR is most commonly seen in cats over six years of age (Clarke and Caiafa 2014). Weight was not significant to TR (p=0.55).

Contrary to current literature on breed and TR, no association was found between breed and TR (p=0.26). This contrasts with a study that found 70% purebred and 38% mixed breed had TR (Girard et al. 2008). Some authors have commented that it may be important to stratify breed by age to draw a more meaningful comparison (Gorrel 2015).

The current study found a relationship (p=0.001) between oral disease and TR. Type 1 TR is associated with inflammation, and oral disease, such as FCGS, that are also associated with inflammation. Current literature supports FRLs and FCGS as separate disease processes; although, both are associated with inflammation (Farcas 2014). Previous studies support the link between viral exposure and FCGS; while collecting data, I observed feline immunodeficiency virus (FIV) positive status to be more common in cats with FCGS versus cats without FCGS, in agreement with current literature (Clarke and Caiafa 2014). Similar to other current research, systemic disease (binary) was significant to TR (p=0.05). The analysis used none, cardiac, renal, other (thyroid, pancreas, liver), multiple (>1 disease present) as categories, but future studies could use a different method of categorizing disease to focus on diabetes, hyperthyroidism, cardiac, renal and FIV. Hyperthyroidism was rare in this population. A future study could include biological samples with blood serum values to evaluate how well-controlled or advanced a systemic disease is. It should be noted that certain medications given to cats with CKD have been demonstrated to be associated with increased gingival hyperplasia; specifically, amlodipine, a calcium-channel blocker has been demonstrated to cause this overgrowth of gingival tissue (Perry and Tutt 2014). Further research is needed on the relationship between FCGS and concurrent or historical disease processes.

Although this aim did not hypothesize a significant difference in the ratio of felines with TR versus felines without TR, I analyzed the frequencies of TR diagnosis for each veterinarian. This step also allowed me to evaluate the number of dentals done by each doctor to provide a rough idea of the doctor's experience. I found that the majority of the dentals (74.0%), as expected, were performed by the most senior dentistry veterinarian who practiced 3-4 days a week during the study period, and there was no significant difference between veterinarians as far as odds of diagnosing TR ($p=0.08$).

To provide additional information, I performed a multivariate analysis for Aim 1 using logistic regression. The model including age, weight, breed, oral disease and systemic disease was a good fit for the data (deviance $p<0.0001$). Males were at decreased risk for TR compared to females (OR=0.64, 95% CI (0.50,0.85)), and those with oral disease were at decreased risk of TR compared to those with none (OR=0.55 95% CI (0.36, 0.85)). Characteristics associated with an increased risk of TR included age (OR=1.16, 95% CI (1.12, 1.20)) and increasing weight (OR=1.09, 95% CI (1.00, 1.18). These findings could be used to develop future hypotheses on FRLs.

Aim 2

Each model in the series of logistic regression models for Aim 2 was a good fit of the data (deviance $p<0.0001$). The primary exposure and outcome variables, type 1 TR and treatment for complication under anesthesia, respectively, were significantly associated in all models tested (Models 3-5) ($p<0.0001$), supporting the hypothesis of Aim 2. In addition, when type 2 TR was included in the full model instead of type 1 the relationship was also significant (p<0.0001). This relationship may be explained by the severity of the cases seen by this veterinary hospital because by the time the cases were treated, the FRLs had typically advanced into type 3 TR, so no point of initiation could be determined. Type 3 TR is related to both types 1 and 2 TR by definition (Gorrel 2015). In addition to substituting type 2 TR for type 1 TR, I tested the full model handling TR as a binomial and found the relationship between TR and treatment was significant (p<0.0001).

Exploratory Aim

Assessing an individual's risk for complications before anesthesia help the anesthetist be practice proactively, and the exploratory aim supported the validity of an oral examination as a necessary part of a complete feline evaluation. The high specificity (97.6%) and high sensitivity (93.1%) indicate the oral exam by a dental-trained veterinarian is an effective diagnostic tool for type 1 TR. The results also indicated that observation of TR on the oral exam was highly predictive of there being TR evident on radiograph (PPV=98.5%). The NPV of 89.2% indicates that, although typically no TR on oral exam correlates with no TR on radiograph, the oral examination is more likely to have a false negative than a false positive result. For comparison, when applied as a diagnostic tool for FRLs computed-tomography (CT) has a high specificity between 92.8% and 96.3% but a low sensitivity between 42.2% and 57.7% using intraoral radiographs as the "gold standard" (Lang 2016). Based on current data, the oral examination is highly effective for diagnosing TR in felines, under nearly-ideal circumstances as far as feline cooperation and veterinarian experience. Although this was a limitation of the study design, the validity of the oral examination supports its use for diagnosing FRLs with accuracy.

Measure Reliability

Overall the measure reliably of this study was high based on the use of medical records as the data source. The criteria for low blood pressure did not change during the study period; in clinical practice, experience-level and comfortability handling anesthetic complications varies by the individual doctor, technician and interaction of the two, which was evident in this thesis explored by Aim 2. Additionally, hospital-wide veterinarian comfortability with diagnosing TR could have advanced over the study period. Because I was a practicing dental technician during the study period, I included myself in the pool of nine technicians that was compared to three other senior dental technicians. If I completely excluded myself, it would have added bias to the study because I performed a large percentage (16.6%) of the feline dentals during the study period.

No pre-anesthetic fluids were routinely given in practice, operating under the philosophy complications could be treated for as needed, to avoid the risk of fluid overloading the cat (deVries and Putter 2015). The definition of TR remained standard during the time of the study; although, radiography equipment and technology did improve over time. In addition, many previous studies excluded incisors while this study included them. I expect this has no effect on the measure reliability because rarely were incisors, and if they did have TR, there were other teeth in the mouth also with TR. Typically if radiographs were missing, it was from years 2013, 2014 and 2015 before full-mouth radiographs were taken on each patient. Most records, for all years, were missing information on type 2 TR. Even with this limitation of underreporting, type 2 TR was found significant to treatment for anesthetic complication when controlling for all covariates.

Strengths and Limitations

There are several strengths of this study which can be attributed to the design and plan for analysis. One major benefit of the retrospective aspect of the design is that the data were derived from medical records, rather than retrospective reports by owners which would be susceptible to recall bias. Another benefit of the design is the ability to examine multiple exposures against one outcome for each aim. Additionally, the large sample size (n=1,530) using the entire cohort of feline dental patients from a five-year period at a specific hospital adds validity to the study by increasing generalizability; this sample size is especially large for a veterinary health study. The downside is the ability to relate findings to the average feline in the United States (as described in detail, below); however, the findings could be applied to similar veterinary hospital settings. Even after excluding any subject missing data on a covariate, the final sample included 1,337 cats. By stratifying the sample by physical and health characteristics the confounding variables observed in previous studies could be controlled for while assessing the relationship between the variables of interest.

The potential effect of hidden confounding by characteristics that the type of owners who seek feline dental care share. The control group of felines without TR serves as a counterfactual model to the cases of felines with TR decreasing confounding bias and increasing validity. By using a single hospital cohort, it is expected that the sample was comprised of a relatively homogenous population in terms of owner socioeconomic status (SES), geography and education. The effect of these variables could potentially lead to a study population of felines that receive better care compared to the general domestic feline population in the United States. There is evidence of an oral healthcare disparity in human populations based on income-level; higher SES was associated with improved oral health and decreased prevalence of CKD compared with lower SES (Ruospo et al. 2013). Furthermore, using the entire cohort enables the interpretation to be applied in similar large, urban veterinary hospitals. Additionally, this population is more likely to contain purebred cats than the general feline population in the United States based on the same owner traits. This population trait could have resulted in an increased rate of TR compared to the general population if there were a confounding effect of breed on TR. No significant relationship was found between breed and TR, contradictory to several previous studies that contained a smaller prevalence of purebred felines.

On the other hand, there are several limitations to acknowledge due to the study design. One limitation of the study is the retrospective data which indicates the exposure and outcome data were collected concurrently. There are certain biases associated with retrospective analyses including selection bias, so to maintain consistency I was the sole investigator and took detailed notes on my specific methods during data collection. This measure was also beneficial to prevent investigator bias. These effects appear to be minimal based on the study results' comparability to previous studies. If a record is missing a piece of information there was no possibility to capture the missing data, so the subject had to be excluded from the analysis. When using a hospital cohort, there is likely a selection bias for felines who need more intensive dental treatment. Often owners fail to seek medical care for their pets until the symptoms are severe enough to cause observable side effects (Gorrel 2015). Another limitation to this study is the potential for a variance in the testing conditions over the five-year span of data. During this time period, there was a change in staff, radiography equipment and anesthetic protocols. To address this limitation, I included veterinarian and technician as covariates. Although this study excluded specific drug protocols used on each patient, no difference between cases and controls as far as drug selection and anesthetic protocols was expected based on the lack of previous research on this topic.

Chapter 7: Public Health Significance

Overlap with Human Health

Although the focus of this thesis is to improve the understanding of feline TR, there is significant overlap in the resorptive process that occurs in both human and feline species. TR in humans is similar to TR in felines based on the presence of odontoclasts (DeLaurier et al. 2009, Patel et al. 2018). Resorptive lesions typically present similarly in both species with a pink band of inflammation at the gingival sulcus (Patel et al. 2018). The primary exposure related to TR in people is orthodontics related trauma or other oral trauma, and the most commonly affected teeth are the central maxillary incisors followed by the maxillary canines (Mavridou et al. 2017). Different occlusal patterns of stress and wear between humans and felines have resulted in different teeth being most commonly affected. In people, 72% of resorptive lesions are maxillary (Mavridou 2017), and in cats, 82% of teeth affected are mandibular molars (DeLaurier et al. 2009). Significant evidence supports the association between painful periodontal disease and a decreased quality of life in humans (Cunha-Cruz 2008, Needleman et al. 2004).

Recommendations

Based on the analyses of this study, I have several recommendations for feline dental veterinarians and technicians. First, this study supports the need to consider TR as a factor related to complications under anesthesia such as bradycardia and/or hypotension. Even though the study design limits the ability to deduce a causal relationship between TR and anesthetic complication, there is enough evidence including relevant covariates that there is an association between these two variables. Preemptively planning for lower blood pressure under anesthesia in felines with TR could avoid complications while maintaining an appropriate plane of anesthesia; this could include choice of opiate (pure mu agonist vs. partial mu agonist), choice of sedative combination (dexmedetomidine vs. acepromazine, ketofol vs. propofol), and utilization of local blocks (procedure start vs. immediately prior to extractions). The administration of local blocks earlier in the procedure could render the feline less reactive to oral stimuli and enable to anesthetist to decrease the inhalant concentration more than without a local block and avoid unnecessary complication (AAHA 2019).

In addition to being cognizant of analgesic options on a patient-by-patient basis, the current study's findings suggest the anesthetist should give particular attention and care to patients with TR based on their increased odds of experiencing complication under anesthesia for their dental procedures. Anesthetic practice standards (AVDC 2019) state vitals be charted every five to ten minutes; the protocol at the study's hospital followed this standard, but dentistry was the only service which recorded measurements every ten minutes. Understandably, doing readings half as often may allow the anesthetist, who is also performing much of the procedure, to work more efficiently. However, potentially taking readings every five minutes instead of every ten could prevent unnecessary anesthetic depth through more frequent patient assessments because patient safety is the priority. Frequent evaluations enable to anesthetist to adjust inhalant gas, add local blocks or add additional MAC reductants to account for change that occurred during the time since the previous measurement of vitals.

Although the ability to perform a thorough oral examination is highly variable depending on veterinarian experience and feline temperament. In practice, clinicians can focus their efforts during the examination to look at each cat's 307 and 407 due to the high prevalence reported on these specific teeth (DeLaurier 2009, Girard et al. 2008, Lang 2016, Mestrinho et al. 2013). These two teeth are the first premolars on the mandible; one study found the prevalence of TR on each of these teeth (307/407) was 10.6% (Mestrinho et al. 2013). During this quick evaluation the veterinarian should attempt to see the characteristic pink banding at the gumline, or in more advanced cases, the gingiva covering the tooth (Mestrinho et al. 2013, Patel et al. 2018). Additionally, missing teeth are correlated with the presence of TR, so if any missing teeth with no history of dental extractions, then an anesthetized dental should be recommended (Gorrel 2015).

Glossary

Ankylosis: alveolar bone replaces tooth roots as a part of the aging process, also called replacement resorption (Clarke and Caiafa 2014)

Anuric: not producing urine (Robertson et al. 2018)

Apex: the tip of the root of the tooth (Perry and Tutt 2014)

Bradycardia: low heart rate (Steinbacher and Dorfelt 2012)

Buccal bony expansion: the super-eruption of the canine teeth is caused by the loss of the periodontal ligament space caused by vertical bone loss and external TR that moves below the gumline (Perry and Tutt 2014)

Cementum: layer covering dentin of the tooth root (AVDC 2019)

Cementoenamel junction (CEJ): the natural margin between root and crown of a tooth, where gingiva meets tooth crown (Perry and Tutt 2014)

Dentin: mineralized tissue around the pulp chamber (AVDC 2019)

External cervical resorption (ECR): odontoclastic resorption, the presence of odontoclasts results in deterioration of dental hard tissue (Patel et al. 2018)

Extraoral: used to describe something located under the gumline (DuPont and DeBowes 2009)

Feline resorptive lesion (FRL): tooth resorption in cats (Arzi et al. 2010)

Feline chronic gingivostomatitis (FCGS): a painful periodontal disease that causes severe inflammation which crosses the mucogingival junction and affects areas of the oral cavity, not limited to the gingiva (Perry and Tutt 2014)

Gingiva: gum tissue, covering of alveolar bone (Perry and Tutt 2014)

Hypotension: low blood pressure (Robertson et al. 2018)

Intraoral: used to describe something located above the gumline within the oral cavity, also referred to as supragingival (DuPont and DeBowes 2009)

Minimum alveolar concentration (MAC): minimum concentration of anesthetic inhalant required in alveoli to maintain desired anesthetic plane, can be reduced using a multimodal approach to anesthesia and analgesia by incorporating multiple sedative and pain control medications to achieve a surgical anesthetic plane (Robertson et al. 2018)

Odontoblasts: mesenchymal cells for dentin formation (dentinogenesis) (AVDC 2019)

Odontoclasts: resorb and remodel tooth mineral, have a role in the loss of primary teeth (Wang and McCauley 2011); associated with the resorption of retained teeth during maturation (Girard et al. 2008)

Osteoclasts: resorb and remodel bone mineral, have a role in the loss of primary teeth (Wang and McCauley 2011)

Periodontal disease: general term for disease involving teeth and surrounding bone (Perry and Tutt 2014)

Periodontitis: infection of gingiva that can spread to the underlying bone (Perry and Tutt 2014)

Tooth resorption (TR): progressive tooth material loss (Girard et al. 2008)

Master of Public Health Competencies

Epidemiology Core Competencies

a. Identify vital statistics and other key sources of data for epidemiological purposes
b. Describe a public health problem in terms of magnitude, person, time and place.
c. Comprehend basic ethical and legal principles pertaining to the collection, maintenance, use and dissemination of epidemiologic data.
d. Explain the importance of epidemiology for informing scientific, ethical, economic and political discussion of health issues.
e. Apply the basic terminology and definitions of epidemiology.
f. Calculate basic epidemiology measures.
g. Communicate epidemiologic information to lay and professional audiences.
h. Differentiate among the criteria for causality.
i. Draw appropriate inferences from epidemiologic data.
j. Describe epidemiologic study designs and assess their strengths and limitations.
k. Evaluate the strengths and limitations of epidemiologic reports.

Epidemiology Cognate Competencies

a. Calculate advanced epidemiology measures.
b. Design, analyze, and evaluate an epidemiologic study.
c. Demonstrate skills in public health data collection and management.

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