EVALUATION OF ENDOTRACHEAL TUBE CUFF PRESSURE AND THE USE OF THREE CUFF INFLATION SYRINGE DEVICES IN DOGS

by

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For my parents.

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ABSTRACT

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Title: Evaluation of Endotracheal Tube Cuff Pressure and the Use of Three Cuff Inflation Syringe Devices in Dogs
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Endotracheal intubation is a routine and necessary safety procedure during inhalant anesthesia. The endotracheal tube (ETT) cuff provides a tight seal between the endotracheal wall and the tube to prevent leakage of waste anesthetic gas and aspiration of foreign materials. Both under- and over- inflations of the ETT cuff pose risks to animals under general anesthesia. Under-inflation of the ETT cuff predisposes animals to aspiration of regurgitant or gastric secretions when regurgitation occurs. It also allows the escape of anesthetic gas from the airway which may lead to difficulty in maintaining the appropriate depth of anesthesia and pollution of the operative environment. Over-inflation of the ETT cuff can impede blood circulation of the tracheal mucosa and result in tracheal damage or tracheal necrosis.

Review of published veterinary anesthesia monitoring guidelines reveals that there is no standardized recommendation of routine monitoring ETT cuff pressure in anesthetized patients. The incidence of over- or under-inflation of the ETT cuff in the anesthetized dogs remains unknown. Therefore, the objectives of this two-phase prospective study were 1) to determine the incidence of over- and under-inflation of the ETT cuff in the anesthetized dogs at Purdue Veterinary Medical Teaching Hospital (PVMTH) and 2) to evaluate the performance of three different commercially available syringe devices (a regular injectable syringe, Tru-Cuff™ syringe and AG Cuffill syringe) in inflating the ETT cuff to a recommended safe cuff pressure range (20 to 30 cmH_2O). Besides these two objectives, we also evaluated the ETT cuff pressure changes over time with spontaneous or mechanical ventilation, as well as the effect of body position change on the ETT cuff pressure change. In addition, we investigated a group of dogs that did not require the initial ETT cuff inflation after endotracheal intubation. We hypothesized that there was a high incidence of improper inflation of the ETT cuff in the anesthetized dogs at PVMTH. We also hypothesized that the use of one of the commercially available cuff inflation syringe devices (Tru-Cuff™ syringe and AG Cuffill syringe) would help reduce the incidence of improper inflation of

the ETT cuff compared to using a regular injectable syringe. This study was approved by the Purdue Animal Care and Use Committee (PACUC) (Protocol number: 1804001729).

To evaluate the incidence of over- and under-inflation of the ETT cuff (objective one), a total of 80 dogs undergoing general anesthesia at PVMTH between June and August 2018 were enrolled in the Phase One study. Only dogs intubated with SurgiVet® silicone cuffed endotracheal tubes without wire enforcement were included. The ETT selection and cuff inflation followed the PVMTH's standard operating procedures (SOP). The SOP for ETT cuff inflation includes a leak test and the application of minimum occlusive volume (MOV) technique with a regular injectable syringe. The leak test is carried out by closing the pop-off valve of the breathing circuit of an anesthetic machine and compressing the reservoir bag to a peak airway pressure of 20 cmH_2O. At the same time, the noise of air leakage is checked by listening closely to the dog's airway. If there is an audible air leakage, the MOV technique is carried out by gradually inflating the ETT cuff with a regular injectable syringe to determine the minimal volume of air required to prevent air leakage from the trachea.

The results showed that 50 of the 80 dogs required ETT cuff inflation. Of these 50 dogs, only 14% of the cuffs were normally inflated, 76% were over-inflated and 10% were under-inflated. Collectively, the percentage of improper ETT cuff conditions was 86%. This evidence supported our first hypothesis.

To compare the performance of the three commercially available syringe devices for appropriately inflating the ETT cuff (objective two), 129 dogs undergoing general anesthesia at PVMTH between August and December 2018 were enrolled in the Phase Two study. Among these dogs, 90 dogs required ETT cuff inflation and were subsequently assigned randomly to one of the three treatment groups with 30 dogs in each group. The three syringe treatment groups were a regular injectable syringe, Tru-Cuff™ syringe, and AG Cuffill syringe.

The results showed that the percentage of over-inflation (80%) was significantly higher (both $p < 0.001$, Chi-square and Fisher's exact tests) when a regular injectable syringe was used compared to the other two syringe devices (Tru-Cuff™ syringe [6.7%] and the AG Cuffill syringe [3.3%]). The percentage of normal (proper) inflation was significantly higher (both $p < 0.05$, Chi-square and Fisher's exact tests) in the AG Cuffill syringe group (86.7%) compared to the other two groups (regular injectable syringe [3.3%] and the Tru-Cuff™ syringe [50%]). These findings

supported our hypothesis that using the commercially available cuff inflation syringe devices would help reduce the improper inflation of the ETT cuff.

A subset of 17 dogs that were under the same ventilation type for at least 60 minutes in the operating room in the Phase Two study was included for evaluating ETT cuff pressure changes over time under spontaneous and mechanical ventilation. There was no significant difference ($p = 0.840$, Student's t-test) in ETT cuff pressure changes after 60 minutes (mean ± SD) between dogs receiving mechanical ventilation (-8.4 ± 13.8 cmH_2O; n = 9) and dogs breathing spontaneously (-9.6 ± 8.2 cmH_2O; n = 8). The body position changes were observed in 18 dogs in the Phase Two study (divided into 5 categories based on the direction of the position changed) and the ETT cuff pressure changes ranged from -11 to 3 cmH_2O. A total of 69 dogs out of the 209 studied dogs (33%) did not require the initial ETT cuff inflation after endotracheal intubation. Among these 69 dogs, 30 dogs were continuously monitored following endotracheal intubation and 6 dogs had a subsequent air leakage. All the subsequent air leakages occurred within 10 minutes after endotracheal intubation.

In conclusion, this prospective study showed that there was a high incidence of improper ETT cuff inflation in the canine patients undergoing general anesthesia at PVMTH and regularly monitoring the ETT cuff pressure was recommended to prevent the potential injuries to the trachea. In addition, the use of the commercially available cuff inflation syringe devices, particularly the AG Cuffill syringe, provided a tool to better achieve the accurate and safe cuff pressure range than the regular injectable syringe. We also recommend checking for an air leakage within 10 minutes after endotracheal intubation for those anesthetized dogs which do not require ETT cuff inflation initially after endotracheal intubation.

CHAPTER 1. INTRODUCTION

Endotracheal intubation is routinely performed during anesthesia. It ensures a patent airway for oxygen and inhalant anesthetic gas delivery for the anesthetized patients. The cuff on the endotracheal tube (ETT) provides a seal between the endotracheal wall and the tube. The seal not only facilitates the effectiveness of positive pressure ventilation and prevents environmental contamination with waste anesthetic gases, but also protects the patients from pulmonary aspiration[1]. It is crucial to maintain an appropriate ETT cuff pressure because both excessively high (over-inflation) or low (under-inflation) cuff pressure can lead to serious adverse events. Over-inflation of the ETT cuff can cause tracheal mucosal irritation, tracheal wall ischemia, and necrosis, or even result in tracheal rupture[2–5]. Under-inflation of the ETT cuff has been found to increase the risk of pulmonary aspiration due to the inability of the cuff to prevent aspiration of the regurgitant and/or oral secretion[6].

The ideal ETT cuff pressure should be enough to seal the trachea but not impede tracheal mucosal blood flow. The tracheal capillary perfusion pressure in humans ranges from 22 to 32 mmHg (30 to 43.5 cmH_2O) and in the rabbit ranges from 14 to 28 mmHg (19 to 38 cmH_2O)[7,8]. High ETT cuff pressure has been found to impede tracheal mucosal blood flow in both humans and dogs[5,8]. Currently, there is no recommended guideline or standard reference for the ETT cuff pressure monitoring in veterinary practice. Based on the majority of human literature, cuff pressure between 20 and 30 cmH_2O is considered to be the "standard" ETT cuff pressure range[9–11].

In veterinary medicine, ETT cuff inflation is usually performed with subjective estimation of the cuff pressure. One of the most commonly used ETT cuff inflation techniques is the minimum occlusive volume (MOV) technique[12–14]. It is performed by inflating the ETT cuff with a regular injectable syringe until there is no audible leak noise when applying a peak airway pressure of 15 – 30 cmH_2O in a breathing circuit[1,15,16]. The peak airway pressure used for detecting ETT cuff leak varies in different literature. In a recent study in dogs, Briganti and colleagues found that with MOV technique, only 18% and 8.5% of ETT cuff pressure fell within the ideal range defined in the study (19 – 24 mmHg) when plastic (PVC) tubes and silicon ETT were used, respectively[12]. Direct measurement of the ETT cuff pressure was highly recommended based on the results of human and veterinary studies[17,18].

In humans, several factors have been found to affect the ETT cuff pressure changes during anesthesia, including changes in the patient's body position, the anesthetic agents used and prolonged mechanical ventilation of the intubated patient[19–21]. Movement of the patient's head and neck as well as changing body position from supine to prone have been found to change ETT cuff pressure[19,22]. Nitrous oxide is an anesthetic gas which is occasionally used as an anesthetic adjuvant. Diffusion of nitrous oxide into ETT cuff during anesthesia has been reported and the increased volume of this gas within the cuff significantly increases the cuff pressure[20,23]. ETT cuff pressure was found to decrease over time in mechanically ventilated human patients[24]. To the author's knowledge, there was no study investigating the factors associated with ETT cuff pressure changes in veterinary medicine.

The objectives of this two-phase prospective study were 1) to determine the incidence of over- and under-inflation of ETT cuff in dogs undergoing general anesthesia at Purdue Veterinary Medical Teaching Hospital (PVMTH) and 2) to evaluate the performance of 3 different commercially available syringe devices (regular injectable syringe, Tru-Cuff™ syringe and AG Cuffill syringe) in inflating the ETT cuff to a recommended safe cuff pressure range (20 to 30 cmH_2O). Besides these two objectives, we also evaluated the ETT cuff pressure changes over time with two different ventilation types (spontaneous or mechanical ventilation) and the effect of the body position change on the ETT cuff pressure change. In addition, we investigated a group of dogs that did not require the initial ETT cuff inflation after endotracheal intubation. We hypothesized that there was a high incidence of improper ETT cuff inflation (both over-inflation and under-inflation) in the anesthetized dogs at PVMTH. We also hypothesized that the use of one of the commercially available cuff inflation syringe devices (Tru-Cuff™ or AG Cuffill syringe) would help reduce the incidence of improper ETT cuff inflation in the anesthetized dogs compared to using a regular injectable syringe.

CHAPTER 3. LITERATURE REVIEW

3.1 Background of The Endotracheal Tubes

3.1.1 The Development of Endotracheal Tubes

The evolution of endotracheal tubes (ETTs) has been closely linked with the advance in anesthesia. It can be traced back to the mid-nineteenth century when the surgical procedures were more commonly performed after the introduction of a new anesthetic agent – ether. In 1869, Dr. Friedrich Trendelenburg created a cannula with an inflatable rubber cuff for insertion through tracheostomy, which can prevent the aspiration of blood during surgery of the larynx. In 1893, Dr. Victor Eisenmenger designed a wide-bore semi-rigid orotracheal tube with an inflatable cuff and a pilot balloon for assessing the intracuff pressure. This was the first time the idea of cuffed ETT was described. In the early 1900s, Dr. Franz Kuhn advocated the orotracheal route over the tracheostomy for anesthetic gas delivery. He also emphasized the importance of endotracheal intubation for the removal of pulmonary secretion and in prevention of aspiration. Along with the invention of the laryngoscope, the endotracheal intubation became more accepted. At that time, an anesthetic technique called insufflation was used for gas delivery, with anesthetic gas being blown into the lung and the exhaled gas traveling around the outside of the tube. Due to the risk of aspiration with this technique, in 1926 Dr. Stanley Rowbotham and Dr. Ivan Magill designed a bigger tube that allowed bi-directional air flows with a pharyngeal sponge for the seal. The pharyngeal sponge was more commonly used than the inflatable cuff at that time because it was less cumbersome and easier to be manufactured. Later, when the technical problems were overcome, the inflatable cuff became the mainstream and Dr. Arthur Guedel and Dr. Ralph Waters reintroduced the inflatable cuff to the ETT, which has opened a new period of ETT designs[25–27].

3.1.2 Materials Used for Endotracheal Tubes Manufacture

According to the consensus of American National Standards Institute/International Standards Organization, the materials for ETT should have the following characteristics, including low cost, no tissue toxicity, transparency, easy sterilization and durability with repeated sterilizations (unless it’s specified as disposable), non-flammability, smooth and water-proof surface for both inside and outside the tube to prevent secretion build-up, sufficient tube body to

maintain its shape during intubation and to prevent occlusion by torsion, kinking, or compression, sufficient strength to allow thin wall construction, thermoplasticity to conform to the patient's anatomy when in place, non-reactive to lubricants and anesthetic agents, and latex-free[28]. Currently, there is no single material that fulfills all the aforementioned characteristics.

Red rubber, silicone and polyvinyl chloride (PVC) are the three most commonly used materials for ETTs. Red rubber is one of the very first materials used for the manufacture of ETT. This type of ETTs can be sterilized and reused, but the texture becomes hard and sticky after multiple uses. Lack of transparency and the potential to cause latex allergy are other shortcomings for these tubes. In addition, red rubber ETTs usually don't have a self-sealing valve on the pilot balloon. Therefore, an atraumatic clamp has to be applied on the external tube connecting the cuff and the pilot balloon to prevent cuff deflation following inflation[29]. Silicone ETTs are commonly used in veterinary medicine. This type of tubes is transparent and generally more elastic than the PVC ETTs. They are usually more expensive compared with other types of ETTs but can be sterilized and reused. PVC is the most common type of ETTs used in human medicine. It is usually in a curved shape and for single use only. The desirable characteristics of PVC ETTs include inexpensiveness, no tissue toxicity, transparency, and being able to conform to the patient's airway anatomy at body temperature[1,28,30].

3.1.3 The Designs of Endotracheal Tubes

The common designs of an ETT are illustrated in Figure 2.1. The connector at the machine end is a uniform size in both human and small animal medicine (15 mm outer diameter [OD]), which facilitates its use in all standard anesthetic breathing circuits[1,26]. The patient end is usually beveled, which facilitates endotracheal intubation. The Murphy eye is a hole opposite to the bevel. Its purpose is to serve as an alternative route for gas passage when the patient end of the tube is occluded. The inflatable cuff close to the patient end of the tube is an important structure to provide a seal between the endotracheal wall and the tube, which not only prevents environmental contamination with the anesthetic gas but also protects patients from aspiration. The pilot balloon is a port for cuff inflation and is designed with a self-sealing valve system. The size of ETTs is usually labeled as their internal diameters (ID).

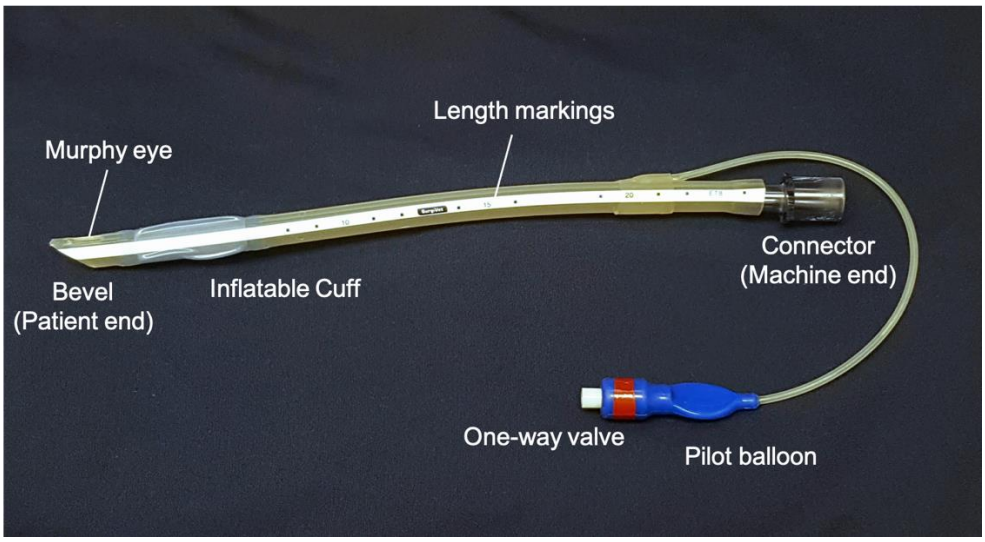

Figure 3.1: Common designs of an endotracheal tube. The endotracheal tube shown here is an 8 mm internal diameter silicon cuffed endotracheal tube (SurgiVet®) without wire enforcement.

3.1.4 Common Cuff systems of Endotracheal Tubes

An ETT cuff system is composed of an inflatable cuff, an external tube connecting the cuff, a pilot balloon, and a one-way valve. The cuffs can be broadly divided into two categories, which are the low-volume, high-pressure (LVHP) cuffs and the high-volume, low-pressure (HVLP) cuffs.

An LVHP cuff generally requires a higher intracuff pressure to achieve a tight seal within the trachea. An intracuff pressure is mainly for overcoming the cuff wall compliances and the pressure exerted on the endotracheal wall is usually smaller than the intracuff pressure[28,30]. Prolonged use of the LVHP cuff can cause ischemic damage to the endotracheal wall and should be prevented[28]. The LVHP cuffs have a small diameter at rest and a low residual volume. When they are inflated, they do not have longitudinal folds and can provide better protection against microaspiration. The characteristic of small diameter at rest also provides a better view during endotracheal intubation.

On the other hand, an HVLP cuff has better compliance to the endotracheal wall, therefore the intracuff pressure correlates closely with the pressure exerted on the endotracheal wall[31]. However, microaspiration is more likely to happen with this type of cuff because the longitudinal folds on the cuff can serve as passages and let the secretion or regurgitant pass through the cuff[32–34]. Applying water-soluble gel around the cuff before endotracheal intubation has been found to effectively reduce microaspiration[35]. The residual volume of the HVLP cuff is higher, hence the

view to the laryngeal opening during endotracheal intubation may be obscured. A comparison of the advantages and disadvantages of the LVHP and HVLP ETT cuffs are summarized in Table 2.1.

Table 3.1: Comparisons of the advantages and disadvantages of the low-volume, high-pressure (LVHP) ETT cuffs and high-volume, low-pressure (HVLP) ETT cuffs.

ETT cuff types	Low-volume, high-pressure (LVHP) ETT cuffs	High-volume, low-pressure (HVLP) ETT cuffs
Advantages	- Better protection against pulmonary aspiration.	- Better compliance with the endotracheal wall. - The intracuff pressure correlates closely with tracheal mucosal pressure.
Disadvantages	- The possibility of causing ischemic damage to the tracheal mucosa following prolonged intubation.	- Microaspiration may develop due to the folds on the ETT cuff.

3.2 Use of Endotracheal Tubes in General Anesthesia

3.2.1 The Purpose of Endotracheal Intubation

The main purpose of endotracheal intubation is to maintain a patent airway for delivering anesthetic gas and oxygen. Most of the anesthetic drugs depress respiratory function and cause hypoxia of the patients[36–39]. In addition, anesthetic drugs reduce the patient's gag reflex which can precipitate pulmonary aspiration. The airway muscle relaxation also makes the anesthetized patients prone to upper airway obstruction[40]. Endotracheal intubation not only can maintain the airway patency but also provides a cuff that can seal the airway to protect the patient from aspirating the regurgitant and airway secretions as well as to permit effective positive pressure ventilation.

3.2.2 Laryngeal Anatomy of The Dogs

The larynx is a musculo-cartilaginous organ located between the pharynx and the trachea. Its functions are to serve as an air passageway, to prevent the aspiration of foreign material and to vocalize (so-called voice box)[41]. The structure of larynx is composed of several cartilages, including epiglottic, thyroid, cricoid, arytenoid, sesamoid, and inter-arytenoid cartilages[41]. The epiglottis is a flap structure mainly formed by the epiglottic cartilage, which functions as a switch between the airway and the esophagus. During endotracheal intubation, the epiglottis would need

to be pushed downward in order to reveal a better view of the opening of the larynx. The glottis is a structure consisting of the vocal folds, arytenoid cartilages, and rima glottides. The rima glottides is the opening between the vocal folds and is the narrowest part of the laryngeal passageway, which determines the size of the ETT a dog can take[41]. The infra-glottic cavity is the portion between the vocal cords and the trachea.

3.2.3 Selection of The Endotracheal Tube Sizes

The selection of the ETT size is crucial because if the size of the ETT is too small for the patient, it increases the risk of over-inflation of the ETT cuff. The small diameter of the ETT also increases the resistance to gas flow, therefore, increasing the patient's work of breathing. On the other hand, if the selected ETT size that is too big for the patient, it causes trauma to the airway if forcibly intubated. The principle of ETT size selection is to choose the largest ETT size possible that will allow passing through the narrowest part of the airway smoothly and seal the trachea snugly without causing trauma[1,13]. The three most common methods for ETT size selection in veterinary medicine include 1) estimation based on the lean body weight of the patient; 2) digital palpation of the tracheal outer diameter (OD) and selecting a comparable size of an ETT; and 3) matching the size of the OD of an ETT with the patient's nasal septal width[13,42]. For the effectiveness of these selection methods in dogs, Lish and colleague demonstrated that the tracheal digital palpation had a higher accuracy (46%) than the nasal septal width matching method (21%)[42]. Recently, Shih and colleague proposed a new method for determining the size of the ETT in dogs by measuring the tracheal internal diameter (ID) on a lateral thoracic radiograph[43]. In the study, eight healthy adult Beagle dogs were evaluated. The result suggested that using 70% of the tracheal ID measured on a lateral thoracic radiograph as a guide for ETT size selection was a feasible method.

3.3 Monitoring of Endotracheal Tube Cuff Pressure

3.3.1 Appropriate Endotracheal Tube Cuff Pressure

3.3.1.1 The Standard in Human Medicine

In humans, tracheal capillary perfusion pressure ranges from 22 to 32 mmHg (30 to 43.5 cmH_2O) and tracheal mucosal blood flow is impaired when the ETT cuff pressure is above 22

mmHg[8]. On the other hand, a persistent ETT cuff pressure below 20 cmH_2O (14.7 mmHg) is associated with an increased risk of aspiration pneumonia in the intubated patient[6]. It was determined that in human patients intubated with a 7.0 mm ID cuffed ETT and ventilated with a peak inspiratory pressure of 20 cmH_2O, the mean intracuff pressure of the ETT required to seal the airway was 19.1 cmH_2O[44]. In the majority of the literature, the ETT intracuff pressure between 20 and 30 cmH_2O is considered to be "standard ETT cuff pressure" in humans[9–11].

3.3.1.2 Veterinary Studies of Endotracheal Tube Cuff Pressure

Very few tracheal capillary perfusion pressures have been studied in animals. It was demonstrated that the rabbits' tracheal capillary perfusion pressure ranged from 14 to 28 mmHg (19 to 38 cmH_2O)[7]. In dogs, Castilho and colleague concluded that maintaining the ETT cuff pressure at 25 cmH_2O avoided significant tracheal mucosal injury[45]. In another study, it was demonstrated that the ETT cuff pressure needed to seal a dog's trachea was approximately 28 mmHg (38 cmH_2O)[5]. When the ETT cuff pressure was set at 20 mmHg (27.2 cmH_2O) in Beagles, the mean air leak pressure was 16.2 cmH_2O[43]. In a study in cats, when the ETT cuff pressure was set at 30 cmH_2O, the mean air leakage pressure was 12 cmH_2O in 95% of the subjects enrolled in that study[18]. In horses, the ETT cuff pressure required to seal the trachea ranged from 80 to 100 cmH_2O[3]. Review of the literature in veterinary medicine and recent American Animal Hospital Association (AAHA) guidelines failed to yield a consistent recommendation for the standard ETT cuff pressure range (Table 2.2)[13,15,29,46]. The "standard" ETT cuff pressure was often extrapolated from human medicine (20 to 30 cmH_2O) and adapted for the use in dogs and cats[14,18].

Table 3.2: The recommended ETT cuff pressure ranges in the veterinary literatures.

Recommended ETT cuff pressure range	Reference
25 – 34 cmH_2O	Hartsfield 2007
No greater than 25 cmH_2O	Dohner & Syring 2012
Maximum 25 mmHg (34 cmH_2O)	Hughes 2016
20 – 25 cmH_2O	Ko 2019

3.3.2 Consequences of Improper Endotracheal Tube Cuff Pressure

3.3.2.1 Human Medicine

In human, sore throat is the most common post-operative complication associated with endotracheal intubation. The incidence of post-operative sore throat ranges from 22% to 100% and is correlated with high ETT cuff pressure[47–50]. The average duration of the sore throat is usually 16 hours but can persist up to a day[47,51]. Other complications caused by improperly high ETT cuff pressure include cough, blood-streaked expectoration, hoarseness and tracheal stenosis[47,52,53]. In contrast to over-inflation, the under-inflation of the ETT cuffs has been found to be a risk factor for microaspiration[6,34,54].

3.3.2.2 Veterinary Medicine

In veterinary medicine, the complications associated with improper ETT cuff pressure have been documented in dogs, cats, and horses. In a case report of tracheal necrosis in a dog, over-inflation of the ETT cuff was suspected to be the cause based on bronchoscopic and histologic examinations[4]. In cats, the association between over-inflation of the ETT cuff and tracheal rupture has been observed in cadavers and reported in a retrospective study[2,55]. The tracheal wall damage due to high ETT cuff pressure has been studied in horses[3]. A necropsy finding of a horse with tracheal necrosis after general anesthesia suggested that the high ETT cuff pressure was most likely to be the cause based on the location and the length of the tracheal lesion[56].

3.3.3 Recommendation for Endotracheal Tube Cuff Pressure Monitoring

3.3.3.1 Human Medicine

Endotracheal tube cuff pressure monitoring is strongly recommended in human anesthesia. Several studies have indicated that ETT cuff inflation with a direct cuff pressure measurement is more accurate in achieving the recommended cuff pressure when compared to the subjective estimation methods[17,53,57]. When a subjective estimation method was used, the average ETT cuff pressures ranged from 35.3 cmH_2O to more than 93 cmH_2O, and only 18.75 – 27% of the patients had an ETT cuff pressure within the recommended range[53,57–61]. The direct ETT cuff pressure measurement not only makes sure the cuff pressure is proper but also lowers the incidence of complications associated with over-inflation (e.g. sore throat, hoarseness)[53]. In addition, it has been shown that the ETT cuff pressure decreases over time without regular pressure adjustments[21].

Continuous monitoring and adjusting cuff pressure would lower the risk of microaspiration and ventilator-associated pneumonia[62,63].

3.3.3.2 Veterinary Medicine

Although there are veterinary literature recommending the direct ETT cuff pressure measurement and monitoring in anesthetized animals, clinical evidence supporting this practice is scarce[1,13,15]. In a study evaluating the efficacy of different ETT cuff inflation methods (all without direct pressure measurement) in dogs, Briganti and colleagues found that only 18% and 8.5% of ETT cuff pressure fell within the ideal range (19 – 24 mmHg measured with an ETT cuff aneroid manometer) when PVC and silicon ETTs were used, respectively[12]. In a cat study, the mean ETT cuff pressures were 41 to 61 cmH_2O when inflating the ETT cuff without a direct cuff pressure measurement. These pressures were significantly higher than the standard cuff pressure (20 to 30 cmH_2O) mentioned[18]. The severity of the tracheal mucosa damage has been showed to correlate with the high ETT cuff pressure in horses and cuff pressure monitoring is strongly recommended[3]. Changes in ETT cuff pressure over time has been noted in dogs and Shih and colleagues suggested to check the ETT cuff pressure in 10 minutes after the onset of anesthesia[64].

3.3.4 Techniques and Devices for Endotracheal Tube Cuff Inflation

Traditionally, ETT cuff inflation is performed with the subjective estimation of cuff pressure. One of the most commonly used techniques is pilot balloon palpation[12,14,18,57,58]. It is performed by digital palpation of the pilot balloon and subjectively estimating whether the ETT cuff pressure is adequate or not. Another common ETT cuff inflation technique is called minimum occlusive volume (MOV) technique[12–16,18]. The MOV technique is combined with a conventional leak test by inflating the ETT cuff with a regular injectable syringe using minimal volume until there is no audible air leakage noise while the peak airway pressure in the patient reached a target number registered in the pressure manometer of a breathing circuit. The suggested peak airway pressure varies in different literature and ranges from 15 to 30 cmH_2O[1,15,16].

Currently, there are several commercial syringe devices specifically designed for ETT cuff inflation with pressure indicators on them. The Tru-Cuff™ syringe is a cuff inflation syringe device with different color marks on the syringe barrel indicating different pressure ranges (https://www.jorvet.com/product/tru-cuff-endotracheal-tube-cuff-pressure-syringe/). The green

zone indicates an adequate ETT cuff pressure (18 to 26 ± 2 cmH_2O) and the red zone indicates that the ETT cuff is over-inflated (40 to 60 cmH_2O) (Figure 2.2). When inflating the ETT cuff using a Tru-Cuff™ syringe, the goal is to keep the black marker on the plunger within the green zone. The efficacy of the Tru-Cuff™ syringe has been validated in a human study and it was recommended as an affordable and reliable syringe device for ETT cuff inflation in a pediatric review articles[65,66]. The AG Cuffill syringe is manufactured with a pressure sensor in the device and is able to detect the ETT cuff pressure during cuff inflation (https://mercurymed.com/product/ag-cuffill-anapnoguard/) (Figure 2.2). Both syringe devices are FDA approved for the use in humans but haven't been evaluated in veterinary medicine.

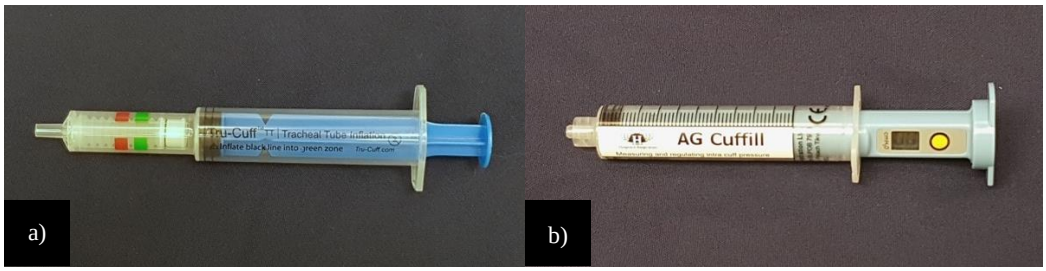

Figure 3.2: Two commercial ETT cuff inflation syringe devices with pressure indicators. a) The Tru-Cuff™ syringe has color marks indicating different pressure ranges (green zone: 18 to 26 cmH_2O; red zone: 40 to 60 cmH_2O). b) The AG Cuffill syringe has a pressure sensor in the device which can detect and display the ETT cuff pressure value on the screen on the plunger. The yellow button allows the rest of the pressure value.

3.3.5 Devices for Endotracheal Tube Cuff Pressure Monitoring

Several devices have been developed to monitor and maintain the ETT cuff pressure[21,67]. The Nosten® device is a pneumatic device which maintains the ETT cuff pressure by connecting the pilot balloon to a cylindrical plastic cuff enclosed in a rigid compartment. A constant pressure is exerted on the cylindrical cuff by an adjustable weight and the ETT cuff pressure can be maintained. This device has been evaluated in animals and human patients and found to be effective in continuous control of the ETT cuff pressure[13,68–70]. Aneroid manometers are portable and convenient devices for ETT cuff pressure monitoring at the bedside. The ETT cuff pressure is measured and monitored by connecting the port on the manometer to the pilot balloon valve. There are several brands of aneroid manometers available on the markets, including Posey Cufflator™ (JT Posey Company, Arcadia, California), Endotest (Rüsch, Duluth, Georgia), Cuff Pressure

Indicator (SIMS-Portex, Keene, New Hampshire) and VBM Cuff Pressure Gauges (VBM, Sulz, Germany)[67,71]. Among all the aneroid manometers mentioned, Posey Cufflator™ has been recommended and used in several animal studies (Figure 2.3)[3,15,72–74].

Figure 3.3: A Posey Cufflator™ is an ETT cuff-specific aneroid manometer which can measure the ETT cuff pressure between 0 to 120 cmH_2O. The ETT cuff pressure can be adjusted by compressing the inflator bulb for increasing pressure and the red air vent button at the back for releasing the excessive air. Note the color areas on the faceplate. The green area represents acceptable cuff pressure range whereas the red area indicates high ETT cuff pressure.

3.3.6 Factors Affecting the Endotracheal Tube Cuff Pressure Changes

3.3.6.1 Changes in Body Position

In human, the ETT cuff pressure change has been found to be associated with altering body position as well as movements of the neck and head. In a study investigating 16 body positions changes in 12 mechanically ventilated patients, the ETT cuff pressure was found to change from the original pressure (25 cmH_2O) with 40.6% of the instances being above the upper limit of the standard cuff pressure range (20 to 30 cmH_2O). Due to the high variability within the patients in that study, the authors couldn't conclude which position would have the most significant impact on the ETT cuff pressure change[75]. In another study, Kako and colleagues found that the ETT cuff pressure increased significantly in 68.1% of the instances, and most of them were observed during head and neck flexion. Decreased ETT cuff pressure was found in 19.1% of the instances and more frequently in head and neck extension[19]. Changing the body position from supine to prone was

associated with both increase and decrease in the ETT cuff pressure in humans[22,76]. Currently, there is no study investigating the influence of body position changes on the ETT cuff pressure changes in veterinary medicine.

3.3.6.2 Anesthetic Agent

Nitrous oxide has been found to increase ETT cuff pressure because the gas can diffuse into the cuff and expand the intracuff volume[20]. The rate of such gas diffusion varies between the ETT cuff materials and the thickness of the cuff wall. The rubber is more permeable than the PVC and the thinner cuff wall allows faster nitrous oxide diffusion[77]. This phenomenon can be prevented by inflating the ETT cuff with a gas mixture that contains the same nitrous oxide concentration as in the anesthetic gas[23].

3.3.6.3 Mechanical Ventilation

Decreased ETT cuff pressure has been noted in human patients receiving mechanical ventilation and the duration of intubation was a risk factor[21,24,78]. In a study with 27 mechanically ventilated human patients, the ETT cuff pressure decreased by 4.9 cmH_2O in 2 hours[24]. In another study with 37 patients, the ETT cuff pressure decreased from 30 cmH_2O to 20 cmH_2O after 7 to 9 hours[79]. To the author's knowledge, there is no study evaluating the ETT cuff pressure changes associated with mechanical ventilation in veterinary medicine.

CHAPTER 4. MATERIALS AND METHODS

4.1 Animals

This study was approved by the Purdue Animal Care and Use Committee (PACUC) (Protocol number: 1804001729). Dogs admitted to Purdue Veterinary Medicine Teaching Hospital (PVMTH) between June and December 2018 and that received general anesthesia for orthopedic and soft tissue surgeries, radiation therapies, diagnostic imaging (e.g. CT and MRI), cardiac interventional procedures and dental procedures were enrolled in this study. To avoid the potential influences of the different endotracheal tube (ETT) designs and materials on the results, only dogs intubated with SurgiVet® silicone cuffed endotracheal tubes without wire enforcement (https://www.smiths-medical.com/products/veterinary/critical-care-consumables/airway-management/cuffed-endotracheal-tube-silicone) were included. Dogs with active upper airway obstruction, those undergoing tracheotomy or thoracotomy, and those with pneumothorax were excluded from this study.

In this study, the body condition scoring (BCS) system used was the 9-point scales[80]. The American Bulldog, Boston Terrier, Boxer, Chihuahua, English Bulldog, Mastiff, Pomeranian, Shih Tzu and Staffordshire Bull Terrier were categorized into Brachycephalic breeds[81–87]. Other breeds were categorized as non-brachycephalic breeds.

4.2 Anesthesia Protocol

For each dog, the anesthetic protocol and whether the dog required mechanical ventilation were determined by the board-certified anesthesiologist on duty based on the health condition of the dog. All the anesthetic machines and ETTs were checked for proper function prior to anesthesia.

Endotracheal tube size selection was based on the lean body weight (BW) of the dog, digital palpation of the tracheal outer diameter (OD) and/or comparing the OD of the ETT with the nasal septal width of the dog[42]. In addition to the selected ETT, additional two sizes (with one size smaller and one size larger than the selected tube) of the ETTs were also prepared as a back-up ETT. The operator would have an option to replace the selected ETT to a larger or a smaller back-up tube based on the degree of difficulty during endotracheal intubation.

4.3 Standard Operating Procedures (SOP) for Endotracheal Tube Cuff Inflation

At PVMTH, the SOP for ETT cuff inflation in small animals includes a leak test and the application of minimum occlusive volume (MOV) technique with a regular injectable syringe. The purpose of the leak test is to check whether there is a proper seal between the ETT cuff and the endotracheal wall. It is applied immediately after endotracheal intubation to determine whether cuff inflation is required for the animal. The leak test is carried out by closing the pop-off valve (i.e. adjusting pressure limiting valve) of the breathing circuit of an anesthetic machine and compressing the reservoir bag to a peak airway pressure of 20 cmH_2O (registered on the circuit pressure manometer). At the same time, the noise of air leakage is checked by a person leaning close toward the animal's head and listening to it. If there is an audible air leakage noise, ETT cuff inflation is indicated.

The MOV technique is carried out by gradually inflating the ETT cuff with a regular injectable syringe while performing the leak test to determine the minimal volume of air required to prevent air leakage from the trachea.

4.4 Study Design

This study was divided into two phases. The objective of Phase One was to investigate the incidence of different ETT cuff conditions (e.g. under-inflation, normal inflation, over-inflation) at PVMTH. The objective of Phase Two was to evaluate the performance of three different commercially available syringe devices (regular injectable syringe, Tru-Cuff™ syringe, and AG Cuffill syringe) in inflating the ETT cuff to a recommended safe cuff pressure range (20 to 30 cmH_2O). Besides these two objectives, in Phase Two we also evaluated the ETT cuff pressure changes over time with two different ventilation types (spontaneous and mechanical ventilation) and the effect of body position changes on the ETT cuff pressure changes.

The ETT cuff pressure was measured with a commercial ETT cuff pressure manometer (Posey Cufflator™ Endotracheal Tube Inflator and Manometer) after cuff inflation by attaching the one-way valve on the pilot balloon to the manometer (Figure 3.1). The accuracy of the manometer was verified with a mercury sphygmomanometer daily prior to use. The "standard" or "proper" ETT cuff pressure used in this study was based on published literature in both human and veterinary medicine[9,14,18]. An ETT cuff pressure between 20 and 30 cmH_2O was defined as normal

inflation. An ETT cuff pressure higher than 30 cmH_2O was defined as over-inflation, whereas a cuff pressure below 20 cmH_2O was defined as under-inflation (Figure 3.2). Because the maximum pressure that Posey Cufflator™ could measure is 120 cmH_2O, ETT cuff pressures higher than this threshold were recorded as >120 cmH_2O.

Figure 4.1: The ETT cuff pressure was measured by attaching the one-way valve on the pilot balloon to the port of Posey Cufflator™.

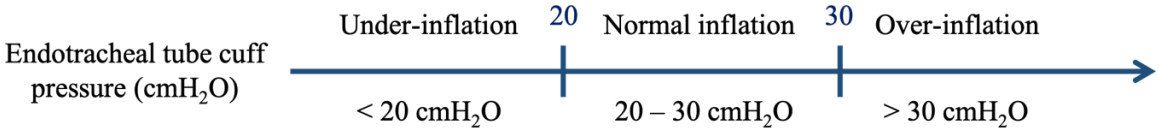

Figure 4.2: Definitions of normal, under- and over- inflation of the ETT cuff pressure of the anesthetized dogs in this study.

4.4.1 Phase One - Assessment of The Incidence of Improper Cuff Pressure

In Phase One, 80 dogs were enrolled from June to August 2018 in PVMTH. After the dog was anesthetized and endotracheally intubated, the leak test and ETT cuff inflation were performed following the SOP. The dogs enrolled in Phase One study were divided into two groups. The first

group was the dogs that required ETT cuff inflation (n=50) and the other group was the dogs that did not (n=30).

For the dogs that required ETT cuff inflation, the ETT cuff pressure was measured with Posey Cufflator™ after cuff inflation. Dogs that did not require ETT cuff inflation (based on the result of leak test in SOP) were closely monitored for 30 minutes and checked if cuff inflation was required during this time. The study design in Phase One is illustrated in Figure 3.3.

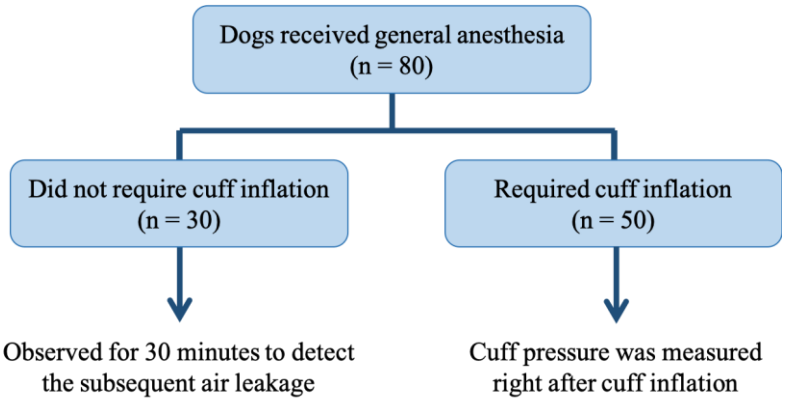

Figure 4.3: Flow chart of the Phase One study design.

4.4.2 Phase Two - Comparisons of Three Syringe Devices in Cuff Inflation

In Phase Two, 129 dogs were enrolled from August to December 2018. Similar to Phase One, after the dog was anesthetized and intubated, a leak test was performed to determine whether the patient required ETT cuff inflation or not. Dogs which did not require ETT cuff inflation (n = 39) were excluded from the randomization but the signalments and the anesthetic protocols of these dogs were recorded. Dogs that required ETT cuff inflation (n = 90) were then randomly assigned to one of the three syringe device treatment groups (30 dogs/group) according to the randomization table. A randomization table for (balanced) treatment assignment was generated from the Research Randomizer website (https://www.randomizer.org).

In the first treatment group, the ETT cuff was inflated with a regular injectable syringe (either 6 ml or 12 ml) and the MOV technique was applied according to the SOP. In the second treatment group, the ETT cuff was inflated with a Tru-Cuff™ syringe according to the manufacturer's recommendation - that is, inflating the ETT cuff until the black marker on the plunger reached the top margin of the green zone (Figure 3.4a). In the third treatment group, the

ETT cuff was inflated with an AG Cuffill syringe until the screen on the plunger displayed 30 cmH_2O, which indicated the cuff pressure detected by the syringe device (Figure 3.4b).

After cuff inflation with the assigned syringe device, all the ETT cuff pressures were measured with Posey Cufflator™. To assess the reliability of Tru-Cuff™ syringe and AG Cuffill syringe in clinical use, a leak test was performed after cuff inflation to check if there was an air leakage from the dog's airway when a positive airway pressure of 20 cmH_2O was applied. If there was an air leakage, the ETT cuff pressure was measured with Posey Cufflator™ once again after the cuff was inflated till there was no audible air leakage noise under the peak airway pressure of 20 cmH_2O. The ETT cuff pressure required to seal the trachea was recorded and further cuff pressure measurement was terminated. The person who assessed the ETT cuff pressure was not blinded to treatment assignment in this study. However, because the ETT cuff pressure was an objective measurement, measurement bias due to non-blinding was not a major concern.

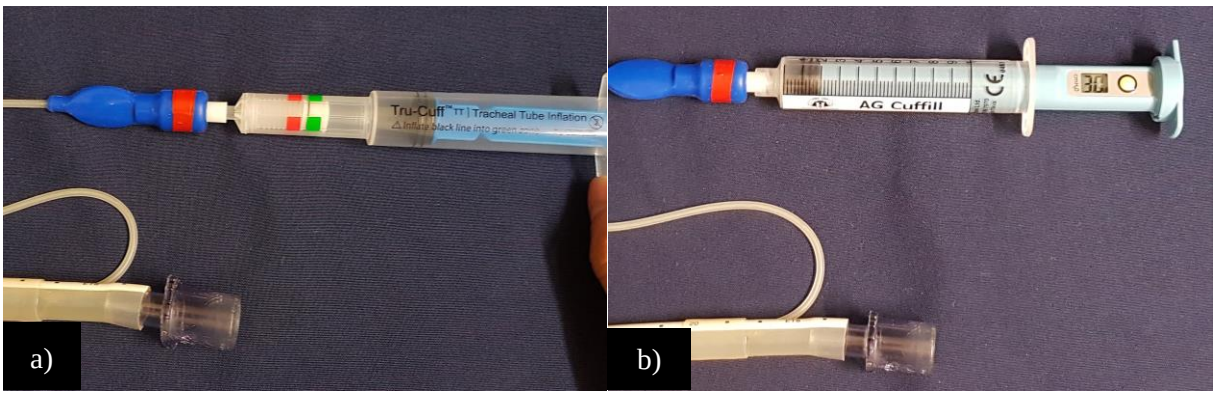

Figure 4.4: Applications of a) Tru-Cuff™ syringe and b) AG Cuffill syringe for ETT (the bottom part of the picture) cuff inflation. Note that the syringes were attached to the one-way valve of the pilot balloon of the ETT cuff.

Within the second and third treatment groups, if there was no air leakage noted from the dog's airway, the ETT cuff pressure was continuously measured with Posey Cufflator™ and recorded every 10 minutes for the next 120 minutes, or until the anesthetic procedure ended, whichever occurred first. The ETT cuff pressure in the first treatment group was measured and recorded in the same way. When a subsequent air leakage developed anytime during the recording period, the ETT cuff pressure was first recorded, and the cuff was inflated again until there was no

audible air leakage noise. After that, the ETT cuff pressure measurement was terminated. The study design of Phase Two is illustrated in Figure 3.5.

For dogs receiving MRI procedures, dental procedures and surgeries at the head and cervical regions, the ETT cuff pressure measurement was terminated after the first measurement right after cuff inflation due to the risk of interference in procedures or contamination of the sterile surgical area.

The ETT cuff pressure changes with the two different ventilation types (mechanical ventilation and spontaneous breathing with intermittent manual assisted ventilation) were evaluated when the dog was in the operating room. Only dogs under the same ventilation type for 60 minutes or more were included in the analysis. The ETT cuff pressure change was calculated as the cuff pressure measured at the 60^{th} minute in the operating room minus the cuff pressure measured at the beginning when the dog was transferred to the operating room. To assess the effect of body position change on the ETT cuff pressure during anesthesia, cuff pressures before and immediately after the body position change were measured and recorded. The changes in body position were categorized as sternal to dorsal, left/right lateral to sternal, sternal to left/right lateral, one side lateral to the other side lateral and dorsal to sternal recumbency.

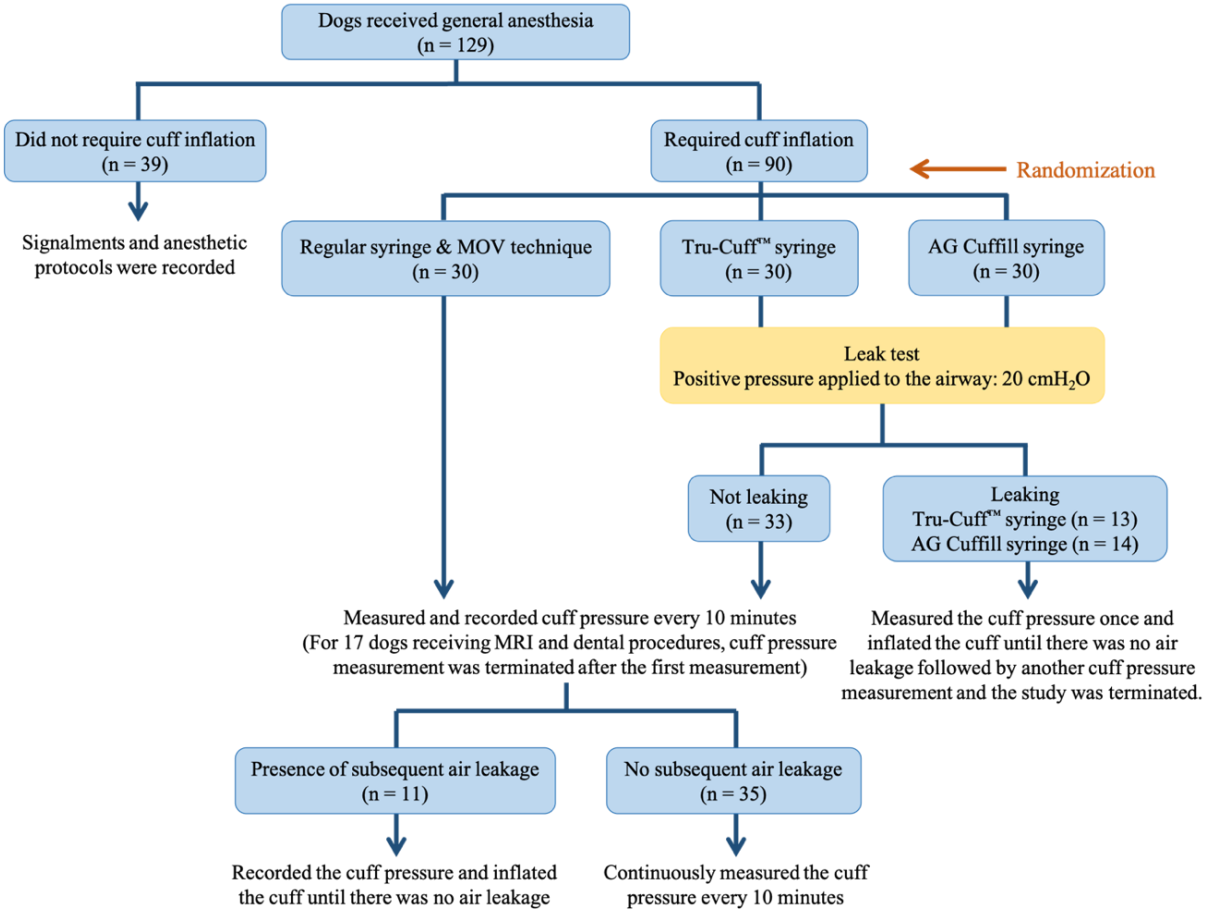

Figure 4.5: Flow chart of the Phase Two study design. Note the 3 treatment groups: regular syringe & MOV technique (first group), Tru-Cuff™ syringe (second group) and AG Cuffill syringe (third group), with 30 dogs randomly assigned to each of the group.

4.5 Statistical Analysis

Prior to the study, a power analysis was performed to determine the sample size required in Phase Two to detect a clinically important effect using a chi-square test of independence, with the power of 80% and significance level of 0.05. Based on the calculation, a total number of 135 dogs with 45 dogs in each group would be required. During the recruitment period, we noted that a considerable number of dogs in the Tru-Cuff™ syringe (n = 13) and AG Cuffill syringe (n = 14) treatment groups had air leakage after cuff inflation with the assigned syringe device (based on the result of leak test). We, therefore, decided to terminate the study earlier and proceed to data analysis after recruiting 90 dogs (with 30 dogs in each treatment group), which was 67% of the target sample size of 135 dogs.

All the continuous variables were tested for normality by Shapiro-Wilk tests. The primary outcome variable in both Phase One and Phase Two was the ETT cuff inflation conditions (over-inflation, normal inflation, under-inflation), expressed as frequency (percentage). The secondary outcome variable in Phase Two was the ETT cuff pressure change (over 60 minutes under two ventilation types), expressed as mean ± SD. Covariates and other signalments of the dogs were expressed as frequency (percentage) for categorical variables (e.g. sex, breeds, ASA physical status, BCS, procedures performed, drugs, body position), and as median (range) for continuous variables and ordinal variables (e.g. age, BW, ETT size, BCS). Chi-square tests and Fisher's exact tests were used to assess the association between the usage of different cuff inflation syringe devices and ETT cuff inflation conditions. For the significant test results, logistic regression was then used to perform pairwise comparisons between the treatment groups. Bonferroni adjustments were applied. For pairwise comparisons, two binary variables were created: over-inflation: yes/no and normal inflation: yes/no. Chi-square tests and Fisher's exact tests were also used to compare the covariates that were expressed as categorical variables between groups. Student's t-tests were used to compare the ETT cuff pressure changes over 60 minutes under two ventilation types. For the covariates that were expressed as continuous and ordinal variables between two groups, Student's test and Kolmogorov-Smirnov test were the parametric and non-parametric test used, respectively. For the covariates that were expressed as the continuous and ordinal variables between three groups, ANOVA and Kruskal–Wallis tests were the parametric and non-parametric test used, respectively. P value < 0.05 was considered statistically significant.

CHAPTER 5. RESULTS

5.1 Phase One - Assessment of The Incidence of Improper Cuff Inflation

5.1.1 Animals

A total of 80 dogs were enrolled in this phase. Thirty of these 80 dogs did not require endotracheal tube (ETT) cuff inflation. The rest of the 50 dogs were assessed for the incidence of improper ETT cuff inflation. Of these 50 dogs, 20 (40%) were castrated males, 6 (12%) were sexually intact males (26 [52%] males in total), 18 (36%) were spayed females, and 6 (12%) were sexually intact females (24 [48%] females in total). The median age of the dogs during the study period was 6 years (range, 3 months to 17 years) and the median body weight (BW) was 22.95 kg (50.60 lb; range, 1.64 to 50.3 kg [3.62 to 110.89 lb]). The median body condition score (BCS, 9-point scales) was 5 (range, 3 to 8). A total of 29 breeds were enrolled, including mixed breed (n = 10), German Shepherd (5), Labrador Retriever (5), Golden Retriever (3), Yorkshire Terrier (3), Airedale Terrier (1), American Pit Bull Terrier (1), Basset Hound (1), Beagle (1), Belgian Malinois (1), Boston Terrier (1), Boxer (1), Cavalier King Charlies Spaniel (1), Chesapeake Bay Retriever (1), Dachshund (1), English Bulldog (1), Goldendoodle (1), Great Dane (1), Greyhound (1), Italian Greyhound (1), Newfoundland (1), Papillon (1), Rat Terrier (1), Shih Tzu (1), Siberian Husky (1), Soft-coated Wheaten Terrier (1), Toy Poodle (1), West Highland Terrier (1) and Whippet (1).

The American Society of Anesthesiologists (ASA) physical status of these 50 dogs were ASA I (n = 3), ASA II (33), ASA III (12), and ASA IV (2). The following procedures were performed in the enrolled dogs: MRI (n = 8), total hip arthroplasty (6), radiation therapy (5), arthroscopy (4), dental treatment (4), CT (3), stifle arthroscopy and tibial plateau leveling osteotomy (3), implant or wire removal (2), long bone fracture repair (2), wound debridement and closure (2), cryptorchid neuter (1), cystotomy (1), deep ear flush (1), dorsal laminectomy (1), eyelid mass removal (1), femoral head ostectomy (1), hemilaminectomy (1), laparoscopic spay and gastropexy (1), neck radiography (1), ocular ultrasound (1) and unilateral arytenoid lateralization (1).

5.1.2 Anesthetic Protocols

Preanesthetic drugs used for the 50 dogs that required ETT cuff inflation were acepromazine (n = 37), hydromorphone (26), dexmedetomidine (17), butorphanol (14), midazolam (7), methadone (4) and Telazol (1). Anesthetic induction drugs used were propofol (n = 28), propofol with midazolam (13), ketamine with midazolam (3), Telazol (1), alfaxalone (1) and sevoflurane (4).

The ETT sizes used in this phase of the study are summarized in Table 4.1. The median size of the ETT used was 11 mm internal diameter (ID; range, 4 to 14 mm). Due to the size of the enrolled dogs, sizes 11 and 12 mm ID were most commonly used (n = 20; 40%). Most of the dogs were intubated by DVM students (n = 40; 80%), with 1 (2%) and 9 (18%) dogs intubated by the house officer and veterinary technicians, respectively. When inflating the ETT cuff, 26 (52%) dogs were in lateral recumbency, 23 (46%) dogs were in sternal recumbency and only 1 (2%) dog was in dorsal recumbency.

Table 5.1: The ETT sizes (in mm internal diameter) used in Phase One – Assessment of The Incidence of Improper Cuff Inflation.

Internal diameter (ID)	4	5	6	6.5	7	7.5	8	8.5	9	10	11	12	14
No. of tubes	2	0	5	0	6	1	3	1	3	3	10	10	6
Percentage	4	0	10	0	12	2	6	2	6	6	20	20	12

5.1.3 Frequency of Improper Cuff Inflation Conditions

The distribution of the ETT cuff inflation conditions is summarized in Table 4.2. Of the 50 dogs studied, 14% [n = 7; 95% confidence interval (CI), 6.64 – 27.13%) cuffs were normally (properly) inflated (cuff pressure between 20 to 30 cmH_2O), 76% (n = 38; 95% CI, 61.79 – 86.11%) were over-inflated and 10% (n = 5; 95% CI, 4.09 – 22.44%) were under-inflated. Collectively, the total percentage of improper ETT cuff inflation conditions was 86% (43/50). The over-inflated ETT cuff pressures ranged from 36 to 120 cmH_2O, whereas the pressures of the under-inflated ETT cuffs ranged from 0 to 10 cmH_2O.

There was no significant difference in signalment [sex, age, BW, BCS, breeds (brachycephalic vs non-brachycephalic)], ETT size, and who intubated the dogs (student, technician or house officer) among the three ETT cuff inflation conditions (Table 4.3). The

anesthetic protocols of these 50 dogs in three ETT cuff inflation conditions are summarized in Table 4.4.

Table 5.2: The distribution of ETT cuff inflation conditions in the 50 dogs. The ETT cuff pressure of the normal (proper) cuff inflation condition was defined as 20 to 30 cmH_2O.

Cuff Conditions	No. of dogs	Percentage (95% CI)
Normal Inflation	7	14 (6.64 – 27.13)
Over-inflation	38	76 (61.79 – 86.11)
Under-inflation	5	10 (4.09 – 22.44)

Table 5.3: Characteristics of the 50 dogs in three cuff inflation conditions.

Parameters	Normal inflation (n = 7)	Over-inflation (n = 38)	Under-inflation (n = 5)	P-value
Sex [n (%)]				0.561
Male	5 (71.4)	18 (47.4)	3 (60)	
Female	2 (28.6)	20 (52.6)	2 (40)	
Age [years, median (range)]	11 (1 – 17)	5 (0.3 – 15)	9 (1.5 – 12.5)	0.654
BW [kg, median (range)]	35 (4.5 – 46.1)	22.3 (1.64 – 50.3)	34.6 (3.6 – 40.4)	0.699
BCS [median (range)]	7 (5 – 8)	5 (3 – 8)	5 (4 – 7)	0.200
Breeds [n (%)]				0.679
Brachycephalic	1 (14.3)	3 (7.9)	0 (0)	
Non-brachycephalic	6 (85.7)	35 (92.1)	5 (100)	
ETT size [mm ID, median (range)]	12 (6 – 12)	10.5 (4 – 14)	12 (6 – 12)	0.138
Who intubated the dog [n (%)]				0.596
Student	7 (100)	29 (76.3)	4 (80)	
Others (Tech/house officer)	0 (0)	9 (23.7)	1 (20)	

Chi-square and Fisher's exact tests were used to compare the sex, breeds and who intubated the dog between the three cuff inflation conditions.

ANOVA was used to compare age, BW, ETT size, BCS between the three cuff inflation conditions.

Table 5.4: Anesthetic protocols of the 50 dogs in three cuff inflation conditions.

Anesthetic protocol	Normal inflation (n = 7)	Over-inflation (n = 38)	Under-inflation (n = 5)
Premedication (n)			
Acepromazine	3	31	3
Opioids			
Butorphanol	2	9	3
Hydromorphone	2	24	0
Methadone	0	4	0
Dexdomitor	1	15	11
Midazolam	1	4	2
Telazol	0	1	0
Induction methods [n(%)]			
Injectable	5	37	4
Inhalant	2	1	1

5.2 Phase Two - Comparisons of Three Syringe Devices in Cuff Inflation

5.2.1 Animals

One hundred and twenty-nine dogs were enrolled in this phase. Thirty-nine of these dogs did not require ETT cuff inflation and were excluded from randomization. The rest of the 90 dogs were randomly assigned to one of the three syringe device treatment groups with 30 dogs in each group. Of these 90 dogs, 40 (44.4%) were castrated males, 11 (12.2%) were sexually intact males (51 [56.7%] males in total), 31 (34.4%) were spayed females, and 8 (8.9%) were sexually intact females (39 [43.3%] females in total). The median age of the dogs during the study period was 6 years (range, 3 months to 16 years 5 months) and the median BW was 23.95 kg (52.8 lb; range, 2.5 to 62.5 kg [5.51 to 137.79 lb]). The median BCS (9-point scales) was 5 (range, 3 to 8). A total of 42 breeds were enrolled, including mixed breed (n = 22), German Shepherd (6), Greyhound (5), Dachshund (4), Goldendoodle (3), Great Dane (3), Labrador Retriever (3), American Cocker Spaniel (2), American Pit Bull Terrier (2), Beagle (2), Border Collie (2), Chihuahua (2), English Bulldog (2), Golden Retriever (2), Rottweiler (2), Siberian Husky (2), American Bulldog (1), American Eskimo (1), Australia Heeler (1), Australian Shepherd (1), Bichon Frise (1), Bluetick Hound (1), Borzoi (1), Cairn Terrier (1), Cardigan Welsh Corgi (1), Catahoula Leopard (1), Dalmatian (1), English Cocker Spaniel (1), English Shepherd (1), French Bulldog (1), Havanese Terrier (1), Irish Setter (1), Jack Russell Terrier (1), Labradoodle (1), Leonberger (1), Maltese (1),

Miniature Poodle (1), Pomeranian (1), Portuguese Water Dog (1), Staffordshire Bull Terrier (1), Standard Poodle (1) and Weimaraner (1).

The ASA physical status of these 90 dogs were ASA I (n=12), ASA II (58), ASA III (17), ASA IV (2) and ASA V (1). The following procedures were performed in these dogs: dental treatment (n = 12), MRI (9), radiation therapy (9), stifle arthroscopy and tibial plateau leveling osteotomy (7), CT (6), tibial plateau leveling osteotomy (5), arthroscopy (3), exploratory laparotomy (3), arthrodesis (2), balloon valvuloplasty (2), cystotomy (2), incisional biopsy (2), long bone fracture repair (2), pin or implant removal (2), total hip arthroplasty (2), caudectomy (1), cystotomy and stent placement (1), cystotomy and urethrotomy (1), ear mass excision (1), evisceration and prosthesis placement (1), hemilaminectomy (1), hip luxation reduction (1), intrapelvic mass removal (1), mandibular fracture repair (1), median sternotomy and thymoma removal (1), medial patella luxation surgery (1), nephrotomy (1), neuter and laparoscopic gastropexy (1), patent ductus arteriosus occlusion (1), perineal hernia repair (1), perianal mass removal (1), soft tissue sarcoma removal (1), spay (1), stifle arthrotomy & tibial plateau leveling osteotomy (1), thyroidectomy (1), urethrostomy revision (1) and wound debridement (1).

5.2.2 Anesthetic Protocols

Preanesthetic drugs used for these 90 treatment group dogs were acepromazine (n = 59), hydromorphone (48), dexmedetomidine (38), butorphanol (24), methadone (12), fentanyl (4), Telazol (2), alfaxalone (1), diazepam (1) and midazolam (1). All the dogs were induced with injectable anesthetic drugs. Anesthetic induction drugs used for these dogs were propofol with midazolam (n = 68), propofol (14), alfaxalone with midazolam (3), etomidate with midazolam (3), alfaxalone (1) and Telazol (1).

The ETT sizes used in this phase of the study are summarized in Table 4.5. The median size of the ETT used in this phase was 11 mm ID (range, 5 to 16 mm). The 11 mm and 12 mm ID were most commonly used (n = 44; 48.9%). Most of the dogs were intubated by DVM students (n = 76; 87.8%), with 3 (3.3%) and 11 (12.2%) dogs intubated by the house officers and veterinary technicians, respectively. When inflating the ETT cuff, 53 (58.9%) dogs were in sternal recumbency, 32 (35.5%) were in lateral recumbency and 5 (5.6%) dogs were in dorsal recumbency.

Table 5.5: The ETT sizes (in mm internal diameter) used in the 90 treatment group dogs in Phase Two – Comparisons of Three Syringe Devices in Cuff Inflation.

Internal diameter (ID)	5	6	7	7.5	8	8.5	9	10	11	12	14	16
No. of tubes	2	5	7	2	10	2	8	4	20	24	5	1
Percentage	2.2	5.6	7.8	2.2	11.1	2.2	8.9	4.4	22.2	26.7	5.6	1.1

5.2.3 Comparisons of Cuff Inflation Conditions in Three Syringe Treatment Groups

There was no significant difference in signalment [sex, age, BW, BCS, breeds (brachycephalic vs non-brachycephalic)], ETT size, who intubated the dog (student, technician or house officer) and the induction drugs used among the three syringe device treatment groups (Table 4.6 & 4.7). The distribution of ETT cuff inflation conditions by the three syringe device treatment groups is summarized in Table 4.8. The percentage of over-inflation was significantly higher in the regular syringe treatment group (80%) compared to the other two treatment groups (Tru-Cuff™ syringe treatment group [6.7%] and regular syringe treatment group [3.3%]; both $p < 0.001$). The percentage of normal inflation was significantly higher in the AG Cuffill syringe treatment group (86.7%) compared to the other two treatment groups (Tru-Cuff™ syringe treatment group [50%; $p = 0.012$] and regular syringe treatment group [3.3%; $p < 0.001$]). The Tru-Cuff™ syringe treatment group also had a significantly higher percentage of dogs having normally inflated cuffs (50%) than in the regular syringe group (3.3%; $p = 0.006$).

The number of dogs with the presence of air leakage after ETT cuff inflation with each syringe device is summarized in Table 4.9. There was a significantly higher percentage of the presence of air leakage in the Tru-Cuff™ (13/30; 43.3%) and the AG Cuffill (14/30; 46.6%) syringe treatment groups than the regular syringe treatment group (0/30; 0%; both $p < 0.001$), when subjected to the SOP leak check. No significant difference in the presence of air leakage was detected between the Tru-Cuff™ syringe and the AG Cuffill syringe treatment groups ($p = 1.000$).

Of the 13 dogs in Tru-Cuff™ syringe treatment group which had an air leakage, 7 dogs had under-inflated ETT cuffs and 6 had normally inflated ETT cuffs. All 14 dogs in the AG Cuffill group had normally inflated ETT cuffs. The mean ± SD cuff pressure after the ETT cuff was inflated until the air leakage noise was absent in all 27 dogs was 65.5 ± 21.3 cmH_2O.

Table 5.6: Characteristics of the 90 dogs in three syringe device treatment groups.

Parameters	Regular syringe & MOV technique (n = 30)	Tru-Cuff™ syringe (n =30)	AG Cuffill syringe (n = 30)	P-value
Sex [n (%)]				1.000
Male	17 (56.7)	17 (56.7)	17 (56.7)	
Female	13 (43.3)	13 (43.3)	13 (43.3)	
Age [years, median (range)]	7.5 (0.2 – 16.5)	5.7 (0.7 – 13)	5.5 (0.7 – 13)	0.500
BW [kg, median (range)]	27 (4.2 – 53.7)	25.6 (4.4 – 62.5)	22.9 (2.5 – 58.7)	0.364
BCS [median (range)]	5 (3 – 8)	5 (4 – 8)	5 (4 – 8)	0.614
Breeds [n (%)]				0.522
Brachycephalic	1 (3.3)	3 (10)	4 (13.3)	
Non-brachycephalic	29 (96.7)	27 (90)	26 (86.7)	
ETT size [mm ID, median (range)]	11 (7 – 14)	11 (5 – 16)	9 (5 – 14)	0.138
Who intubated the dog [n (%)]				0.910
Student	27 (90)	25 (83.3)	24 (80)	
Others (Tech/House officer)	3 (10)	5 (16.7)	6 (20)	

Chi-square and Fisher's exact tests were used to compare sex, breeds and who intubated the dog between the three syringe device treatment groups.
Kruskal–Wallis test was used to compare age and BW between the three syringe device treatment groups.
ANOVA was used to compare the ETT size and BCS between the three syringe device treatment groups.

Table 5.7: Anesthetic protocols of the 90 dogs in three syringe device treatment groups.

Anesthetic protocols [n (%)]	**Regular syringe & MOV technique (n = 30)**	**Tru-Cuff™ syringe (n =30)**	**AG Cuffill syringe (n = 30)**	**P-value**
Premedication				
Acepromazine	18	21	20	
Opioids				
Butorphanol	11	8	5	
Hydromorphone	10	18	20	
Methadone	7	2	3	
Fentanyl	2	1	1	
Dexdomitor	11	11	16	
Midazolam	0	1	0	
Diazepam	1	0	0	
Telazol	1	0	1	
Alfaxalone	0	1	0	
Induction drugs				0.086
Propofol & midazolam	19 (63.3)	26 (86.7)	23 (76.7)	
Propofol alone	8 (26.7)	2 (6.7)	4 (13.3)	
Etomidate & midazolam	2 (6.7)	0 (0)	1 (3.3)	
Alfaxalone/Telazol	1 (3.3)	2 (6.7)	1 (3.3)	
Telazol	0 (0)	0 (0)	1 (3.3)	

Chi-square and Fisher's exact tests were used to compare the induction drugs between the three syringe device treatment groups.

Table 5.8: Distribution of the cuff inflation conditions after the regular syringe, Tru-Cuff™ and AG Cuffill syringe treatments.

Treatment group (30 dogs in each group) ETT cuff condition	**No. of dogs**	**Percentage (95% CI)**
Regular syringe		
Normal inflation	1	3.3 (0.4 – 22.2)
Over-inflation	24[a,b]	80 (60.8 – 91.2)
Under-inflation	5	16.7 (6.7 – 35.7)
Tru-Cuff™ syringe		
Normal inflation	15[c]	50 (31.9 – 68.1)
Over-inflation	2	6.7 (1.5 – 24.7)
Under-inflation	13	43.3 (26.2 – 62.2)
AG Cuffill syringe		
Normal inflation	26[d,e]	86.7 (68.0 – 95.2)
Over-inflation	1	3.3 (0.4 – 22.2)
Under-inflation	3	10 (2.0 – 28.3)

CI: Confidence interval.

Chi-square and Fisher's exact tests were used to compare the ETT cuff conditions between the three syringe device treatment groups. Logistic regression was then used to perform pairwise comparisons between the treatment groups and Bonferroni adjustments were applied.

[a] Significant difference ($p < 0.001$) between the regular syringe and Tru-Cuff™ syringe treatment groups.

[b] Significant difference ($p < 0.001$) between the regular syringe and AG Cuffill syringe treatment groups.

[c] Significant difference ($p = 0.006$) between Tru-Cuff™ syringe and regular syringe treatment groups.

[d] Significant difference ($p < 0.001$) between AG Cuffill syringe and regular syringe treatment groups.

[e] Significant difference ($p = 0.012$) between AG Cuffill syringe and Tru-Cuff™ syringe treatment groups.

Table 5.9: The number of dogs with the presence of air leakage after endotracheal tube cuff inflation in the regular syringe, Tru-Cuff™, and AG Cuffill syringe treatment groups.

Treatment group (30 dogs in each group)	**Number of the dogs with an air leakage after cuff inflation (n)**	**Percentage (95% CI)**
Regular syringe	0	0
Tru-Cuff™ syringe	13[a]	43.3 (26.2 – 62.2)
AG Cuffill syringe	14[b]	46.6 (29.0 – 65.2)

CI: Confidence interval

Chi-square and Fisher's exact tests were used to compare the number of dogs with an air leakage between the three syringe device treatment groups.

[a] Significant difference ($p < 0.001$) between Tru-Cuff™ syringe and regular syringe treatment groups.

[b] Significant difference ($p < 0.001$) between AG Cuffill syringe and regular syringe treatment groups.

5.2.4 Comparisons of Cuff Pressure Changes Under Two Ventilation Types

Seventeen of the 90 treatment group dogs in Phase Two were selected for evaluating their ETT cuff pressure changes over 60 minutes under two types of ventilation. Mechanical ventilation was applied to 9 dogs and the other 8 dogs were allowed to breathe spontaneously with intermittent manual assisted ventilation. No significant difference was noted in signalment (sex, age, BW, BCS) and the ETT size between the two ventilation groups (Table 4.10). The anesthetic protocols of these 17 dogs in two ventilation groups are summarized in Table 4.11. There was no significant difference in the ETT cuff pressure changes over 60 minutes between dogs breathing spontaneously (-9.6 ± 8.2 cmH_2O) and those with mechanical ventilation (-8.4 ± 13.8 cmH_2O; p = 0.836) (Figure 4.1).

Table 5.10: Characteristics of the dogs in two ventilation groups.

Parameters	Mechanical ventilation (n = 9)	Spontaneous breathing (n = 8)	P-value
Sex [n (%)]			1.000
Male	6 (66.7)	5 (62.5)	
Female	3 (33.3)	3 (37.5)	
Age [years, median (range)]	4.6 ± 2.9	3.9 ± 2.7	0.605
BW [kg, median (range)]	30.5 ± 14.1	27.3 ± 17.6	0.684
BCS [median (range)]	6 (4 – 7)	5 (4 – 6)	0.642
ETT size [mm ID, median (range)]	12 (8 – 14)	12 (7 – 16)	0.782

Chi-square and Fisher's exact tests were used to compare sex between the two groups.
Student's t-test was used to compare age, BW, BCS and ETT size between the two groups.

Table 5.11: Anesthetic protocols of the dogs in two ventilations groups.

Anesthetic protocol [n (%)]	Mechanical ventilation (n = 9)	Spontaneous breathing (n = 8)
Premedication		
Acepromazine	8	5
Opioids		
Butorphanol	0	1
Hydromorphone	8	4
Methadone	1	1
Fentanyl	0	2
Dexdomitor	6	2
Diazepam	0	1
Induction drugs		
Propofol & midazolam	8	5
Propofol alone	1	2
Etomidate & midazolam	0	1
Inhaled anesthetic gas		
Isoflurane	9	8

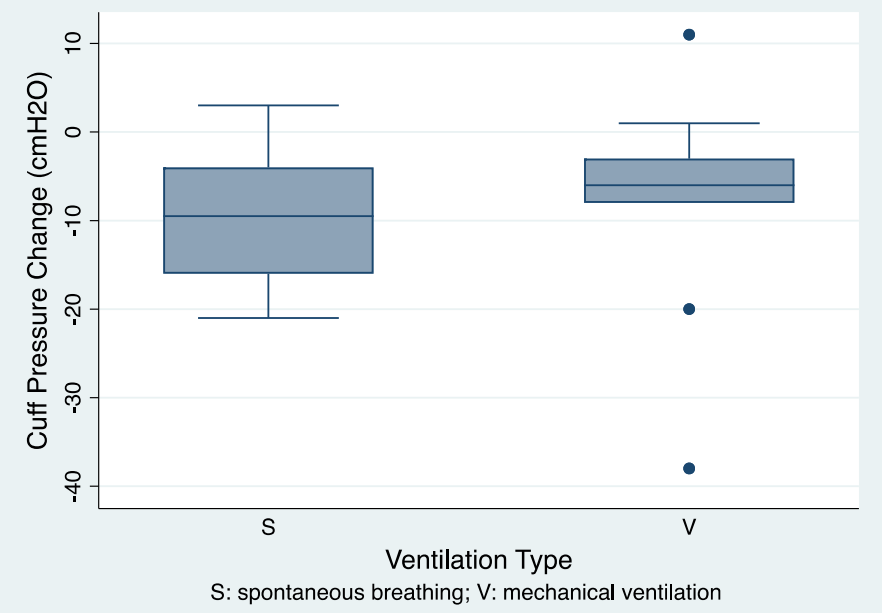

Figure 5.1: The ETT cuff pressure changes over 60 minutes in the spontaneous breathing (mean ± SD, -9.6 ± 8.2 cmH_2O; n = 8) and mechanical ventilation (mean ± SD, -8.4 ± 13.8 cmH_2O; n = 9) groups. There was no significant difference in ETT cuff pressure changes over 60 minutes between the two groups (p = 0.836).

5.2.5 The Effect of Body Position Change on The Cuff Pressure Changes

The changes of body position were observed in 18 of the 90 treatment group dogs in Phase Two. The median ETT cuff pressure change after position change was 0 cmH_2O (range, -11 to 3 cmH_2O). The changes in body position and the subsequent ETT cuff pressure change are summarized in Table 4.12 and Figure 4.2. Only one dog developed a subsequent air leakage (detected by the presence of audible air leaking noise during ventilation) after position changed from sternal to dorsal recumbency.

Table 5.12: The cuff pressure changes associated with the body position changes in 18 dogs.

Directions of the Body Position Change	No. of dogs (n = 18)	Cuff Pressure Changes (cmH_2O)
Sternal to dorsal	8	2, 2, 2, 0, 0, 0, -4, -11
Left/Right lateral to sternal	4	3, -2, -4, -8
Sternal to left/right lateral	3	2, 0, -4
One side lateral to the other side	2	1, 0
Dorsal to Sternal	1	0

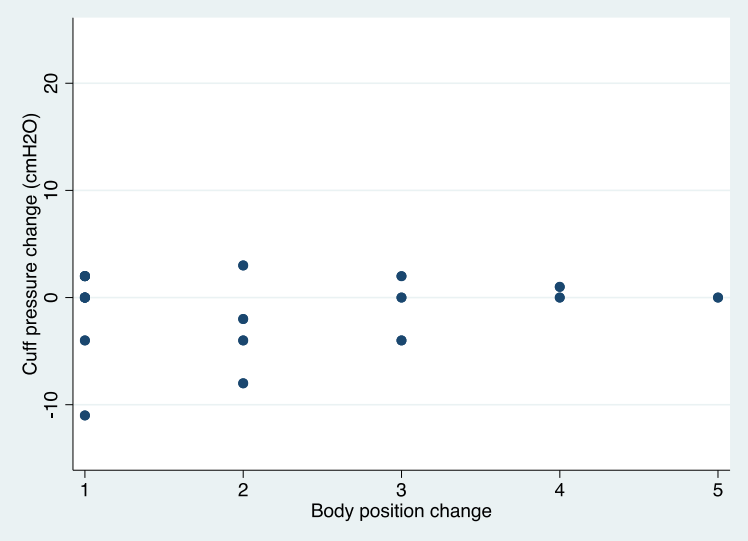

Figure 5.2: The directions of body position changes and the individual ETT cuff pressure changes. Group 1: sternal to dorsal (n = 8; individual cuff pressure changes: 2, 2, 2, 0, 0, 0, -4, -11 cmH_2O); Group 2: left/right lateral to sternal (n = 4; individual cuff pressure changes: 3, -2, -4, -8 cmH_2O); Group 3: sternal to left/right lateral (n = 3; individual cuff pressure changes: 2, 0, -4 cmH_2O); Group 4: one side lateral to the other side lateral (n = 2; individual cuff pressure changes: 1, 0 cmH_2O); Group 5: dorsal to sternal (n = 1; individual cuff pressure change: 0 cmH_2O).

4.2.6 The Development of a Subsequent Air Leakage

Of the 46 out of 90 treatment group dogs in which the ETT cuff pressure was continuously monitored, a subsequent air leakage was noted in 11 dogs (including the one which developed immediately after body position change). Except for the dog which had an air leakage after the body position change, the median time from the ETT cuff inflation to the air leakage being detected in the rest of the 10 dogs was 17.5 minutes (range, 5 to 40 minutes). The median ETT cuff pressure when the air leakage was detected (by the presence of audible air leaking noise during ventilation) was 49.5 cmH_2O (range, 20 to 120 cmH_2O). There was no significant difference in signalment [sex, age, BW, BCS, breeds (brachycephalic vs non-brachycephalic)], initial ETT cuff pressure and cuff inflation conditions between dogs which developed a subsequent air leakage and which did not (Tables 4.13). The median ETT size in dogs with a subsequent air leakage (9 mm ID) was significantly smaller than that in dogs with no subsequent air leakage (11 mm ID; $p = 0.031$).

Table 5.13: Characteristics of the dogs which developed a subsequent air leakage (n = 10) and which did not (n = 35). The dog which the air leakage was developed immediately after body position change is not included in this table.

Parameters	Presence of a subsequent air leakage (n = 10)	No subsequent air leakage (n = 35)	P-value
Sex [n (%)]			0.292
Male	8 (80)	21 (60)	
Female	2 (20)	14 (40)	
Age [years, median (range)]	8 (1 – 13)	5 (0.3 – 16.5)	0.077
BW [kg, median (range)]	16.5 (4.2 – 46.7)	27.1 (4.4 – 62.5)	0.257
BCS [median (range)]	6 (5 – 7)	5 (3 – 8)	0.134
Breeds [n (%)]			1.000
Brachycephalic	1 (10)	4 (11.4)	
Non-brachycephalic	9 (90)	31 (88.6)	
ETT size [mm ID, median (range)]	9 (6 – 11)	11 (5 – 16)	0.031
Initial cuff pressure [cmH_2O, median (range)]	50 (20 – 120)	46 (12 – 120)	0.486
Cuff condition [n (%)]			0.168
Normal inflation	4 (40)	10 (28.6)	
Over-inflation	6 (60)	15 (42.9)	
Under-inflation	0 (0)	10 (28.6)	

Chi-square and Fisher's exact tests were used to compare sex, breeds and the cuff condition between the two groups.
Student's t-test was used to compare BW and ETT size and BCS between the two groups.
Kolmogorov-Smirnov test was used to compare age and the initial cuff pressure between the two groups.

5.3 Investigation of Dogs That Did Not Require Cuff Inflation

5.3.1 Animals

Of the 209 dogs enrolled in this study (Phase One and Phase Two), 69 (33%; 95% CI, 26.68 – 39.84%) dogs did not require ETT cuff inflation based on the result of the SOP leak test. Of these 69 dogs, 21 (30.5%) were castrated males, 15 (21.7%) were sexually intact males (36 [52.2%] males in total), 26 (37.7%) were spayed females, and 7 (10.1%) were sexually intact females (33 [47.8%] females in total). The median age of the dogs during the study period was 6 years (range, 3 months to 17 years 2 months) and the median BW was 25.4 kg (56.0 lb; range, 2.02 to 65.5 kg [5.45 to 144.4 lb]). The median BCS (9-point scales) was 5 (range, 3 to 9). A total of 33 breeds were enrolled, including mixed breed (n = 13), Labrador Retriever (7), Golden Retriever (6), Boxer (3), Rottweiler (3), Shih Tzu (3), American Bulldog (2), English Bulldog (2), French Bulldog (2), Great Dane (2), Mastiff (2), Saint Bernard (2), Yorkshire Terrier (2), American Cocker Spaniel (1), American Pit Bull Terrier (1), American Staffordshire Terrier (1), Border Collie (1), Boston Terrier (1), Chihuahua (1), Dachshund (1), German Shepherd (1), German Wirehaired Pointer (1), Great Pyrenees (1), Greyhound (1), Havanese Terrier (1), Miniature Schnauzer (1), Papillon (1), Pomeranian (1), Puggle (1), Rhodesian Ridgeback (1), Shiba Inu (1), Siberian Husky (1) and Vizsla (1).

The ASA physical status of these 69 dogs were ASA I (n = 6), ASA II (40) and ASA III (23). The following procedures were performed in these dogs: long bone fracture repair (9), MRI (5), stifle arthroscopy and tibial plateau leveling osteotomy (5), total hip arthroplasty (5), dental treatment (4), exploratory laparotomy (4), radiation therapy (4), arthroscopy (3), medial patella luxation surgery (3), balloon valvuloplasty (2), enucleation (2), laparoscopic spay and gastropexy (2), limb amputation (2), portal systemic shunt correction (2), chain mastectomy (1), CT (1), cystotomy & liver biopsy (1), electrodiagnosis (1), episioplasty (1), neuter and laparoscopic gastropexy (1), patent ductus arteriosus occlusion (1), photodynamic therapy (1), pin removal (1), rostral mandibulectomy (1), sialoadenectomy (1), spay (1), tibial plateau leveling osteotomy (1), total colectomy (1), total ear canal ablation (1), transfrontal craniotomy (1) and splenectomy (1).

5.3.2 Anesthetic Protocols

Preanesthetic drugs used for these 69 dogs were acepromazine (n = 48), hydromorphone (41), dexmedetomidine (25), butorphanol (16), methadone (8), midazolam (4) and fentanyl (2).

Anesthetic induction drugs used for these dogs were propofol with midazolam (n = 32), propofol (26), ketamine with midazolam (4), etomidate with midazolam (3), alfaxalone with midazolam (2), alfaxalone (1) and sevoflurane (1).

The ETT sizes used in these 69 dogs are summarized in Table 4.14. The median size of the ETT was 11 mm ID (range, 5 to 16 mm). Sizes 11, 12 and 14 mm ID were most commonly used (n = 38; 55%). Most of the dogs were intubated by DVM students (n = 63; 91.3%), with only 2 (2.9%) and 4 (5.8%) dogs intubated by the house officers and veterinary technicians, respectively. When inflating the ETT cuff, 36 (52.2%) dogs were in sternal recumbency, 26 (37.7%) were lateral recumbency and 7 (10.1%) dogs were in dorsal recumbency.

Table 5.14: The ETT sizes used in the 69 dogs that did not require ETT cuff inflation.

Internal diameter (ID)	**5**	**6**	**6.5**	**7**	**7.5**	**8**	**9**	**10**	**11**	**12**	**14**	**16**
No. of tubes	3	6	1	3	1	3	4	9	15	13	10	1
Percentage	4.3	8.7	1.4	4.3	1.4	4.3	5.8	13.0	21.7	18.8	14.5	1.4

5.3.3 Presence of a Subsequent Air Leakage

Of these 69 dogs that did not require ETT cuff inflation, 30 dogs were observed in Phase One for 30 minutes in order to investigate if there was a subsequent air leakage. Subsequent air leakages were noted in 6 dogs. The median time from the first leak test immediately after endotracheal intubation to the presence of an air leakage was 7.5 minutes (range, 4 to 10 minutes).

5.3.4 Factors Affecting the Need for Cuff Inflation

The characteristics and anesthetic protocols of the dogs that required ETT cuff inflation and dogs that did not are summarized in Table 4.15 and Table 416, respectively. The proportion of brachycephalic breeds was significantly higher in dogs that did not require ETT cuff inflation (24.6%) than in dogs that required ETT cuff inflation (8.6%; $p = 0.002$). No significant difference was noted in other characteristics, ETT size, who intubated the dog and the induction agents used.

Table 5.15: A comparison of the characteristics of the dogs that required ETT cuff inflation (n = 140) and those without the need of ETT cuff inflation (n = 69).

Parameters	Required cuff inflation (n = 140)	No cuff inflation required (n = 69)	P-value
Sex [n (%)]			0.768
Male	77 (55)	36 (52.2)	
Female	63 (45)	33 (47.8)	
Age [years, median (range)]	6 (0.2 – 17)	6 (0.3 – 17)	0.073
BW [kg, median (range)]	23.85 (1.64 – 62.5)	25.4 (2.02 – 65.5)	0.708
BCS [median (range)]	5 (3 – 8)	5 (3 – 9)	0.356
Breeds [n (%)]			0.002
Brachycephalic	12 (8.6)	17 (24.6)	
Non-brachycephalic	128 (91.4)	52 (75.4)	
ETT size [mm ID, median (range)]	11 (4 – 16)	11 (5 – 16)	0.713
Who intubated the dog [n (%)]			0.194
Student	116 (82.9)	63 (91.3)	
Others (Tech/house officer)	24 (17.1)	6 (8.7)	

Chi-square and Fisher's exact tests were used to compare sex, BCS, breeds and who intubated the dog between the two groups.

Student's t-test was used to compare the BCS between the two groups.

Kolmogorov-Smirnov test was used to compare age, BW and ETT size between the two groups.

Table 5.16: A comparison of the anesthetic protocols of the dogs that required ETT cuff inflation (n = 140) and those without the need of ETT cuff inflation (n = 69).

Anesthetic protocol [n (%)]	Required cuff inflation (n = 140)	No cuff inflation required (n = 69)	P-value
Premedication			
Acepromazine	96	48	
Opioids			
Butorphanol	38	16	
Hydromorphone	74	41	
Methadone	16	8	
Fentanyl	4	2	
Dexdomitor	55	25	
Midazolam	8	4	
Diazepam	1	0	
Telazol	3	0	
Alfaxalone	1	0	
Induction drugs			0.514
Propofol & midazolam	81 (57.9)	32 (46.4)	
Propofol alone	42 (30)	26 (37.7)	
Sevoflurane	4 (2.9)	1 (1.5)	
Others (Etomidate, Alfaxalone)	13 (9.3)	10 (14.5)	

Chi-square and Fisher's exact tests were used to compare the induction drugs between the two groups

CHAPTER 6. DISCUSSION

In this study, we found a high incidence of over-inflation of the ETT cuff in the anesthetized dogs at PVMTH and using the commercial cuff inflation syringe devices significantly reduced the incidence of improper ETT cuff inflation.

The ETT cuff inflation with the MOV technique has been investigated in dogs and cats. In a prospective clinical study in dogs, Braganti and colleagues found that the percentage of ETT cuff pressure beyond the normal pressure range (19 to 24 mmHg) after inflating the cuff with MOV technique was 65.5%[12]. The frequency of over-inflation of the ETT cuff in the current study was 76%, which was higher than the Briganti's study. This difference may be due to the different definitions of the normal ETT cuff pressure (19 – 24 mmHg [25.8 – 32.6 cmH_2O] vs 20 – 30 cmH_2O) and different operators who performed the procedures. Regardless of this difference, over-inflation still represents the majority of the ETT cuff condition. In another clinical study in cats, the mean ETT cuff pressure after cuff inflation with MOV technique was 61 cmH_2O, which was above the recommended safe cuff pressure range (20 to 30 cmH_2O)[18]. All these studies point out that the MOV technique is an unreliable method for reaching a standard (safe) cuff pressure for ETT cuff inflation and a direct ETT cuff pressure measurement during cuff inflation is highly recommended.

The Tru-Cuff™ and AG Cuffill syringes are commercially available devices for ETT cuff inflation. Comparing to the aneroid manometer (the standard cuff pressure measurement device), these cuff inflation syringe devices are cheaper and easy to carry. To the author's knowledge, there is no study evaluating their performance in veterinary medicine. This study served as pioneer research in assessing the performance of these commercially available cuff inflation syringe devices in dogs. Our results demonstrated that both Tru-Cuff™ syringe and AG Cuffill syringe devices can effectively reduce the frequency of over-inflation of the ETT cuff in dogs. However, when the Tru-Cuff™ syringe device was used for ETT cuff inflation, 43.3% of the ETT cuff were under-inflated. This frequency was higher than that using a regular injectable syringe (16.7%). In a study evaluating the use of Tru-Cuff™ syringe devices in humans, the authors found that 26% of the green zone pressure measurements were less than the manufacturer reported pressure range. Most of the discrepancy of these measurements were ≤ 3 cmH_2O of the reported lower limit value[65]. In our study, we used the Tru-Cuff™ syringe pressure indicator to reach the upper limit of the

normal cuff pressure (the top margin of the green zone) as our inflation method, yet there was still a substantial number of the ETT cuffs below the manufacturer reported pressure range. Based on all the information, we concluded that although the use of Tru-Cuff™ syringe device was able to reduce the frequency of over-inflation, caution should be taken to prevent the under-inflation of ETT cuffs which can lead to respiratory complications.

While both Tru-Cuff™ and AG Cuffill syringe devices were able to lower the incidence of over-inflation of the ETT cuff, some dogs still had an air leakage when the SOP leak test was applied (Tru-Cuff™ syringe [43.3%]; AG Cuffill syringe [46.6%]). This could be explained by 1) 7 dogs in the Tru-Cuff™ syringe treatment group had an under-inflated ETT cuff that could not create a proper seal within the trachea 2) the ETT size selected based on the SOP was not big enough for some dogs and a higher cuff pressure was required to seal the trachea, and 3) the peak airway pressure used in the leak test (20 cmH_2O) is unnecessarily high for the dogs. The leak test in the SOP was integrated with the MOV technique to check whether there was a proper seal within the trachea during positive pressure ventilation. The MOV technique was first described in human medicine[88]. In humans, nearly all the anesthetized patients are paralyzed for endotracheal intubation and mechanically ventilated during inhalant anesthesia. For this reason, it is necessary to apply the leak check with positive airway pressure in order to simulate the positive pressure ventilation. On the other hand, the majority of the anesthetized small animals are not paralyzed and allowed to breathe spontaneously with negative airway pressure during anesthesia. However, the manual positive ventilation is often applied to these small animal patients to recruit the atelectatic alveoli and to treat hypoventilation. Therefore, using a positive pressure leak test to check for the proper seal within the trachea is reasonable to prevent the environmental contamination with the anesthetic gas when recruiting the alveoli. But the peak airway pressure used in the leak test should be judicious. In Shin's study, when the ETT cuff pressure was within the safe pressure range [20 mmHg (27.2 cmH_2O)], the mean air leak pressure was 16.2 cmH_2O[43]. In veterinary literature, the suggested peak inspiratory pressure for small animals ranges from 8 to 15 cmH_2O and the high peak inspiratory pressure can cause barotrauma[1,89]. Based on these findings, the peak airway pressure of 20 cmH_2O used in the leak test is unnecessarily high, which can lead to over-inflation of the ETT cuff.

Our study found that there was no significant difference in the ETT cuff pressure changes between the dogs breathing spontaneously and the dogs receiving mechanical ventilation.

However, in both ventilation groups, the ETT cuff pressures decreased during the 60 minutes observation period. This downward trend of the ETT cuff pressure is consistent with the previous studies in dogs and horses. In an experimental study, Shin and colleagues found that ETT cuff pressure decreased from 25 mmHg (34 cmH_2O) to 10.9 mmHg (14.8 cmH_2O) in 60 minutes when dogs were breathing spontaneously[64]. In another study in horses, the ETT cuff pressure tended to decrease during the first 30 minutes of anesthesia[3]. Decreases in ETT cuff pressure over time was also documented in mechanically ventilated human patients[21,24,79]. The possible explanations for the decrease in ETT cuff pressure without pressure correction include tracheal muscle relaxation and the fatigue of the cuff materials[43]. Further study focusing on the causes of decreased ETT cuff pressure over time is warranted to facilitate ETT cuff pressure management.

In this study, the ETT cuff pressure change after body position change ranged from -11 to 3 cmH_2O. In a human study, Minonishi and colleagues found that the mean ETT cuff pressure had a 4.7 cmH_2O decrease when the body position was changed from supine to prone (with face rotating to right in the prone position), and the ETT displacement was noted at the same time in most of the patients[76]. In another study, Kim and colleagues found that the ETT cuff pressure increased from 26 cmH_2O to 31.5 cmH_2O after changing the body position from supine to prone[22]. The potential causes for such changes included the compression of the trachea and ETT cuff by the spine, muscles and major vessels, and the increased intra-thoracic pressure in prone position due to the compression of the anterior chest wall and the abdomen[22]. In this study, we can't draw a conclusion about the effect of body position changes on the ETT cuff pressure changes due to the small number of observations. Further study with a larger number of observations may help to elucidate the correlation between the body position changes and the ETT cuff pressure changes in dogs.

After the initial ETT cuff inflation, there were a number of dogs developing a subsequent air leakage during anesthesia regardless of the ETT cuff condition. This could be due to relaxation of the tracheal muscles induced by the inhalant anesthetic agents. The effects of inhalant anesthetic agents on the airway smooth muscles have been studied in various tracheal models. In an *in vitro* study using canine tracheal tissues, it was shown that inhalant anesthetic agents (halothane, enflurane, isoflurane, sevoflurane) inhibit tracheal smooth muscle contraction by reducing the intracellular calcium ion concentration and by directly suppressing the muscle contractility[90]. The inhalant anesthetic agents also cause tracheal smooth muscle relaxation by inhibiting the post-

ganglionic cholinergic neuroeffector transmission in the trachea[91]. In our study, of the dogs that had a subsequent air leakage, their median ETT size was significantly smaller than the dogs that did not have a subsequent air leakage. When the body weights of these dogs were taken into consideration, the ETT size corresponded to their respective body sizes, therefore we don't think that the selection of the smaller ETT size played a role in causing a subsequent air leakage in these dogs.

In this study, 33% (69/209; 95% CI, 26.68 – 39.84%) of the total enrolled dogs did not require an initial ETT cuff inflation after endotracheal intubation. This was unexpected, because to the author's knowledge, this condition has not been reported in any of the previous literature involving dogs or cats. Of these dogs that did not require ETT cuff inflation, some of them developed a subsequent air leakage (all within 10 minutes). This air leakage can be explained by the action of the inhalant anesthetic agents inducing tracheal muscle relaxation[90,91]. We also found the dogs that did not require ETT cuff inflation had a 3 times higher proportion of brachycephalic breeds than the dogs that required ETT cuff inflation. Brachycephalic breeds are prone to have anatomical abnormalities of the upper respiratory tract, including stenotic nares, elongated soft palate, everted laryngeal saccules and hypoplastic trachea[81,92,93]. Dogs with hypoplastic trachea have abnormally narrowed tracheal diameters along the entire trachea due to the small tracheal cartilage (c-shaped) with overlapped ends[94,95]. Therefore, when using the routine ETT size selection methods in brachycephalic breeds, the ETTs are likely to fit more tightly within the trachea and form a better seal without cuff inflation.

The limitations of this study include 1) only one type of the ETT (SurgiVet® silicone cuffed ETT without wire enforcement) was evaluated so the conclusions of this study may not be applied to other types of ETTs (e.g. PVC ETTs), and 2) most of the enrolled dogs were medium to large sizes so the results may not be extrapolated to the population which the majority of the dogs are small sizes. Future studies in different body sizes and different types of ETTs will provide a more comprehensive view of the ETT cuff pressure monitoring in veterinary medicine. In addition, since the complications associated with improper ETT cuff inflation have also been documented in horses and cats, the studies in these species are also strongly suggested. Furthermore, this study can also be extended to the animals in ICU under mechanical ventilation, since the ventilator-associated pneumonia (VAP) has been found to be associated with improper ETT cuff pressure in human patients.

CHAPTER 7. CONCLUSIONS

The study confirmed our hypothesis and showed that currently there was a high incidence (86%) of improper ETT cuff inflation in dogs in our hospital with 76% of them being over-inflated and 10% being under-inflated. The use of Tru-Cuff™ and AG Cuffill syringes both effectively reduced the frequency of improper inflation of the ETT cuff. Among the three syringe devices, the AG Cuffill syringe provided the best accuracy in reaching the safe ETT cuff pressure range (20 to 30 cmH_2O). The types of ventilation did not play a role in ETT cuff pressure changes in this study. However, the ETT cuff pressure did decrease over time and continuous monitoring of the ETT cuff pressure with corrective action is necessary to maintain the proper ETT cuff pressure. A total of 69 dogs out of the 209 enrolled dogs (33%) did not require ETT cuff inflation immediately after endotracheal intubation. For these dogs, we recommend that another leak test should be performed 10 minutes later to prevent subsequent air leakage.

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