Primary Secretory Otitis Media in the Cavalier King Charles spaniel

Outcomes and recurrence of clinical signs after myringotomy and tympanostomy procedures

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Summary

In this study, the data of 27 Cavalier King Charles spaniels diagnosed with Primary Secretory Otitis Media (PSOM) and treated at the Department of Clinical Sciences of Companion Animals at the Faculty of Veterinary Medicine of Utrecht University were collected and analyzed. The aim of this study was to assess the time interval in which recurrence of clinical signs occurs after treatment of PSOM with a myringotomy or tympanostomy procedure and to examine if there was any progression of this disease over time or affecting sides. Clinical signs, diagnosis, treatment outcomes and follow-up information of these dogs were collected by using patient records in Vetware and contacting the owners by phone. Results were presented using Kaplan-Meier survival analysis. Results of this study indicate that after a single myringotomy procedure the mean recurrence time is 19.9 months with a median of 13 months and a recurrence rate of 61%. After tympanostomy the time to recurrence was shorter then after myringotomy ($p = 0.022$), which is contrary to the theory which describes that the continual tympanic cavity ventilation by using ventilation tubes may provide a longer symptom-free period. No signs of progression from unilateral to bilateral PSOM were seen.

Introduction

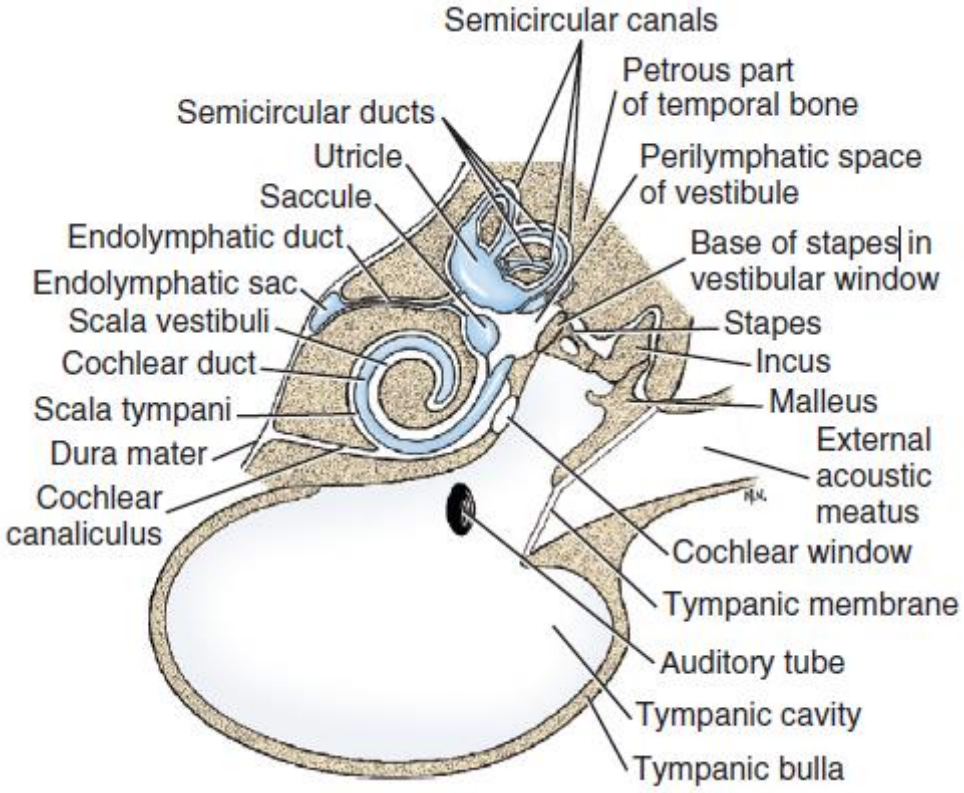
Primary Secretory Otitis Media or PSOM, also known as "glue ear" or "otitis media with effusion" (OME), is a recently more frequently diagnosed disease which is almost exclusively described in Cavalier King Charles spaniels. In this condition, there is a mucous plug in the middle ear, which can occur both unilateral and bilateral (Stern-Bertholtz, Sjostrom et al. 2003). Treatment recommendations include the manual removal of the mucoid effusion from the tympanic cavity through a myringotomy incision and the use of tympanostomy tubes to provide continual tympanic cavity ventilation and pressure equalization. Previous studies showed myringotomy has to be repeated at regular intervals before long term control of clinical signs has been reached and it seems that tympanostomy tubes may be an effective alternative to repeated myringotomy (Corfield, Burrows et al. 2008).

In this retrospective study the treatment outcomes of Cavalier King Charles spaniels (CKCS) with PSOM at the Faculty of Veterinary Medicine of Utrecht University are evaluated and compared with previously published studies. This introduction provides some more information about de anatomy and physiology of the canine ear and the pathogenesis, clinical signs, diagnosis and treatment of PSOM.

Anatomy and physiology of the canine ear

The ear or vestibulocochlear organ not only enables the animal to hear but also provides it with a sense of balance. The canine ear consists of the pinna, the external ear canal, the middle ear and the inner ear. The external ear is composed of the pinna, the vertical ear canal, the horizontal ear canal, the external acoustic meatus and the tympanic membrane (Dyce, Sack et al. 2010). The middle ear is an air-filled tympanic cavity between the tympanic membrane and the inner ear and contains the auditory ossicles. The inner ear, housed in a bony labyrinth in the temporal bone, contains the membranous labyrinth with its sensory organs responsible for hearing and balance (Cole 2010, Macy 1989). As the middle ear plays an important role in PSOM, this part of the organ will be further discussed.

Figure 1. Schematic drawing of the inner ear, middle ear, and external ear canal of a dog (Evans, de Lahunta 2013).



Middle ear

The middle ear is housed in the temporal bone and consists of a small air-filled space known as the tympanic cavity, three auditory ossicles and their associated muscles and ligaments, and the tympanic membrane.

Tympanic membrane

The tympanic membrane is a semitransparent three layered membrane between the external ear canal and the middle ear and can be divided in a small upper pars flaccida and a larger lower pars tensa (Evans, de Lahunta 2013). The pars flaccida is a small, pink, loosely attached region in the upper quadrant of the tympanic membrane and consists of blood vessels. The pars tensa is a thin, tough, gray structure with radiating strands and occupies the rest of the tympanic membrane. A part of the malleus attaches to the medial surface of the pars tensa and the outline, called the stria mallearis, is visible when the tympanic membrane is viewed during otoscopy (Cole 2010).

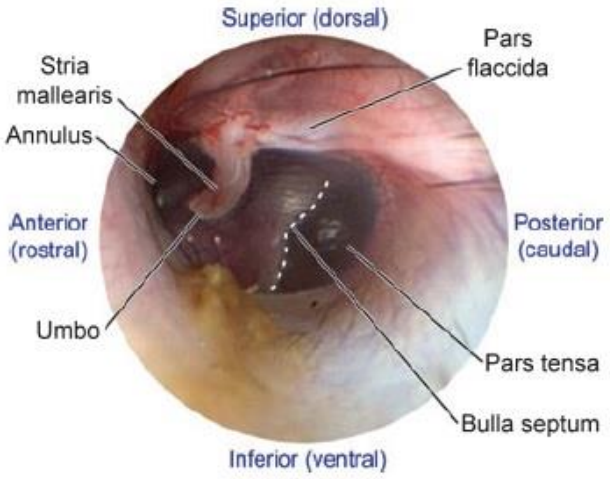


Figure 2. Left tympanic membrane of the dog (Cole 2010).

Tympanic cavity

The tympanic cavity contains an epitympanic recess, a ventral bulla and a tympanic cavity bulla proper. The smallest area, the epitympanic recess, consists of the head of the malleus and incus. The tympanic cavity proper is next to the tympanic membrane. The large ventral bulla is the part within the tympanic bulla (Evans, de Lahunta 2013).

Auditory ossicles

The three auditory ossicles are called the malleus, incus and stapes and carry air vibrations from the tympanic membrane to the inner ear. The malleus is attached to the tympanic membrane, the temporal bone and the incus. The incus is located between the malleus and the stapes. The base of the stapes is connected to the vestibular or oval window, which separates the middle ear from the perilymph fluid of the inner ear (Evans, de Lahunta 2013).

Eustachian tube

The Eustachian tube or auditory tube connects the tympanic cavity with the nasopharynx. This structure consists of a short tube with a narrow lumen that is laterally compressed and usually collapsed. The tube is confined by an inverted cartilaginous through except along its ventral border. The pharyngeal openings of the Eustachian tube are located in the lateral walls of the nasopharynx and are marked by accumulations of lymphoid tissue. The cartilage of the tube extends into the medial wall of the pharyngeal opening and stiffens it.

The function of the Eustachian tube is to allow equalization of the pressures on the two sides of the tympanic membranes. The tubes temporarily open while swallowing or yawning, which allows the slight secretion from the goblet cells and the glands in the lining of the tympanic cavity to escape (Dyce, Sack et al. 2010).

Pathogenesis of PSOM

The pathogenesis of PSOM is unknown. The disease might be caused by an increased production of viscous mucus in the middle ear, by a reduced drainage of the middle ear through the Eustachian tube, or by a combination (Stern-Bertholtz, Sjostrom et al. 2003). The mucous plugs in the middle ear are often found to be sterile on culture (Logas 2013).

Increased production of mucus

The bulla tympanica is covered by a mucociliary mucosa of the same type as in the nasopharynx, which consists of a surface layer of ciliary epithelium and goblet cells (Macy 1989). Mucus glands are located in the connective tissue below the surface epithelium. On the surface of this mucous membrane lies a thin layer of mucus from the glands, to which debris will be attached and is transported through the Eustachian tube with the help of cilia. The consistency of the mucus may vary. In human secretory otitis media, the mucus is very viscous and rubber-like due to changes in the chemical glycoprotein configuration. In this condition, the highly viscous mucus cannot be transported normally and will accumulate in the middle ear (Meyer 1976, Brown, Wetmore et al. 1982). In addition to the limited transport of mucus, the number of secretory cells and glands are also substantially increased in humans with chronic secretory otitis media.

Reduced drainage through the Eustachian tube

As mentioned above, the function of the Eustachian tube is to equalize the pressure between the pharynx and the middle ear and to provide a constant tympanic cavity drainage (Kubba, Pearson et al. 2000, Rose 1978). The first part of the tube from the tympanic bulla is short and osseous and permanently open in a normal dog. Towards the pharynx the tube becomes longer, narrower and more cartilaginous. This portion is closed but can be actively opened through muscular action.

The Eustachian tube remains closed due to the surface tension caused by contact between air and mucus. A combination of phospholipids decreases this surface tension, and reduces the pressure desired to open the tube (Hills 1984). When the tube is closed, the pressure in the middle ear is assumed to become negative in relation to the pressure in the tube, which is always equal to atmospheric pressure (Hagan 1977a). The lack of ventilation causes a negative pressure, which drags out the sterile transudate from the glandular tissues in the middle ear to the surface of the mucous membrane of the Eustachian tube. This negative pressure persists and the accumulation of mucus continues as long as the tympanic membrane is intact and the Eustachian tube is closed. Failure to open the Eustachian tube and thereby release the mucus seems to be the cause of secretory otitis media (Hagan 1977a, Hagan 1977b) and an obstruction of the osseous part of the tube is assumed to be the most general cause (Rose 1978).

Relationship between pharyngeal conformation and PSOM

In humans, otitis media with effusion, which may be similar to PSOM in CKCS, may occur secondary to craniofacial abnormalities such as cleft palate. In a study from Hayes and others (Hayes, Friend et al. 2010) the relationship between nasopharyngeal conformation and OME in CKCS has been evaluated in comparison with boxers and cocker spaniels. The CKCS formed the test brachycephalic group, the boxers formed the brachycephalic control group and the cocker spaniels formed the mesocephalic control group. There was a significant difference in the incidence of OME in the brachycephalic group compared with the mesocephalic group but there was no significant difference between the incidence of OME in the CKCS and boxers. The study of Hayes and others (Hayes, Friend et al. 2010) indicates a relationship between changes in the nasopharyngeal soft tissues and the occurrence of OME, but cannot predict the

nature of this association. The anatomic changes in the nasopharynx may affect the drainage through the Eustachian tube.

Clinical signs of PSOM

The accumulation of mucoid material within the middle ear may cause pain but many dogs do not show visible clinical signs or the signs may be very subtle (Hayes, Friend et al. 2010, Volk, Davies 2011). In a study from McGuinness and others (McGuinness, Friend et al. 2013) the condition is classified as OME, otitis media with effusion, because the cases in this study are not associated with moderate to severe clinical signs.

The clinical signs that are associated with PSOM include pain in the head or neck with spontaneous vocalization and a guarded and horizontal neck carriage, impaired hearing, pruritis without otitis externa, otitis externa, head tilt, nystagmus, ataxia, facial paralysis and fatigue (Corfield, Burrows et al. 2008, Stern-Bertholtz, Sjostrom et al. 2003).

Similar clinical signs in CM and syringomyelia

Some clinical signs associated with PSOM can also occur in Canine Chiari-like malformation (CM) and syringomyelia, like pain in the head and neck areas, scratching, head shaking and spontaneous vocalization. In CM, there is a mismatch between the caudal fossa volume and its contents, the cerebellum and brainstem (Rusbridge, MacSweeny et al. 2000). The neural structures become caudally displaced, which obstructs the foramen magnum and the pressure wave of cerebrospinal fluid out of the head during arterial pulsations. An important consequence of CM is syringomyelia, a condition in which fluid-containing cavities develop within the spinal cord secondary to the obstruction of cerebro-spinal fluid. Cavalier King Charles spaniels are also prone to CM and syringomyelia. Diagnosis requires MRI of the brain and spinal cords, otherwise it is difficult to know to what extent the clinical signs are due to, syringomyelia or PSOM (Rusbridge 2005, Lu, Lamb et al. 2003).

Diagnosis of PSOM

The diagnosis PSOM may be confirmed by otoscopy. When a large, bulging pars flaccida can be identified (figure 3), the diagnosis PSOM can be assumed without the need for further diagnostics (Cole, Samii et al. 2011). However, in many cases the pars flaccida will not bulge. In these cases radiological examination, MRI or CT is indicated for a definite diagnosis (Cole 2012, Cole, Samii et al. 2011).

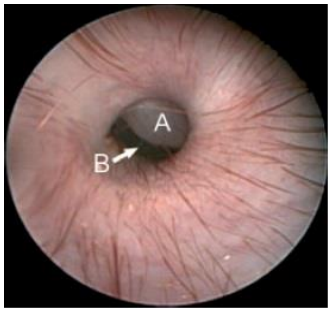


Figure 3. Right tympanic membrane of a Cavalier King Charles spaniel diagnosed with PSOM. Note the bulging pars flaccida. (A) pars flaccida. (B) pars tensa (Cole 2010).

Definitive diagnosis is achieved following a myringotomy to remove a typically viscous opaque, grey to yellow solid plug of mucus from the tympanic bulla (Stern-Bertholtz, Sjostrom et al. 2003) (figure 4). Before examination the external ear canal has to be cleared of wax and other debris. If the tympanum is intact and PSOM is suspected, a myringotomy should be performed. Myringotomy should always be performed in the caudoventral aspect of the tympanum to avoid damage to the oval window and the tympanic ossicles (Logas 2013).

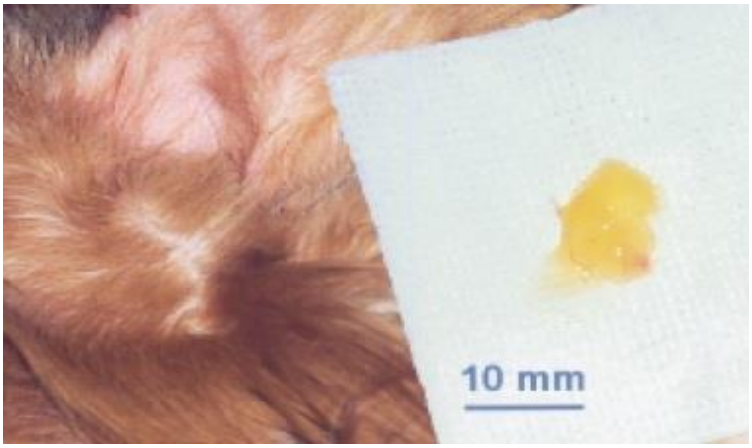


Figure 4. A highly viscous, opaque, solid plug removed from the middle ear during a myringotomy procedure in a Cavalier King Charles spaniel with PSOM (Stern-Bertholtz, Sjostrom et al. 2003).

Computed Tomography

Computed Tomography (CT) evaluation is particularly useful in the diagnosis of otitis media and findings are more apparent in comparison to radiographs. Radiographs show a marked superimposition of structures which make it difficult to evaluate separate structures of the canine skull. In case of normal structures, both bullae should appear symmetric with possible subtle variations. The bulla tympanica has a thin well-defined wall and the lumen of the bullae and external ear canals should be of gas opacity (Bischoff, Kneller 2004). CT provides also an excellent evaluation of bone structures (Lee, Kang et al. 2008). In cases of otitis media, CT findings include thickening and irregularity of the wall of the bulla, lysis of the bulla, soft tissue density representing fluid or tissue within the lumen and signs of otitis externa (figure 5) (Bischoff, Kneller 2004).

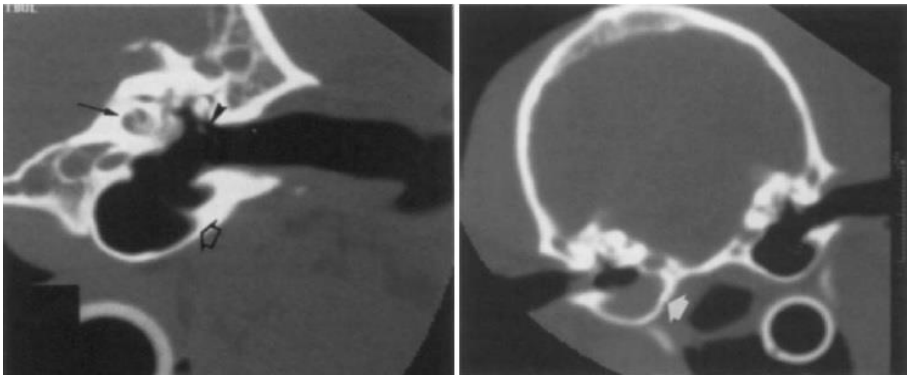


Figure 5. On the left, a high-resolution CT of the ear in a normal dog. Details of the bony structures are clear, including the tympanic bulla (open arrow), the cochlea (fine arrow) and bony ossicles (arrow head). On the right, a high-resolution CT of a 3-year-old Pitbull Terrier with right-sided otitis media. Fluid can be seen filling the ventral part of the tympanic bulla and there is a dorsal meniscus which differentiates the opacity from solid soft tissue (arrow) (Garosi, Dennis et al. 2003).

Magnetic Resonance Imaging

Magnetic Resonance Imaging (MRI) is used less often in the diagnosis of otitis media because of limited availability and high costs. This technique is extremely sensitive to alterations in soft tissue (Lee, Kang et al. 2008). On MRI both gas and cortical bone result in signal void (black), so the wall of the bulla tympanica cannot be differentiated from the air within its lumen. In the cases of otitis media, medium-signal intensity material in the tympanic bulla on T1-weighted images is seen, which is hyperintense on T2-weighted images (figure 6) (Bischoff, Kneller 2004).

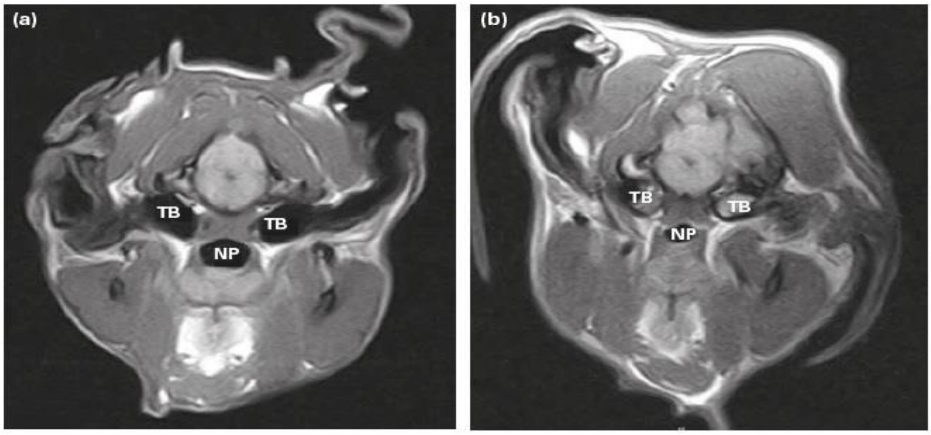


Figure 6. Transverse T1W MRIs from Cavalier King Charles spaniels. (a) Signal voids in the tympanic bullae (TB) from a normal CKCS. (b) Abnormal tympanic bullae from a CKCS with bilateral PSOM (Hayes, Friend et al. 2010).

Treatment Methods for PSOM

Myringotomy

One of the treatment methods for PSOM is myringotomy, the manual removal of the mucoid plug from the tympanic cavity through a little incision, often combined with the administration of topical or systemic corticosteroids since it is assumed that hypersensitivity reactions may play a role in the pathogenesis. This treatment method has been described in a retrospective study by Stern-Bertholtz and others (Stern-Bertholtz, Sjostrom et al. 2003), in which 61 cases of PSOM in 43 CKCS were involved. The diagnosis in 57 of 61 episodes of PSOM was made based on visualization of a bulging, opaque, but intact tympanic membrane and the finding of an accumulation of mucus in the middle ear after myringotomy, while in 4 of 61 occurrences the tympanic membrane was already ruptured and the mucus plug was directly visualized. The mucus plug was either removed in one piece with micro ear forceps or by flushing it loose and lifting it out with the tip of a suction catheter. All dogs were treated corticosteroids containing topical betamethasone (82%) and/or systemic prednisolone (82%). Additional systemic treatment consisted of an antibiotic (92%) and/or a mucolytic (57%) while 10% received a topical antibiotic solution.

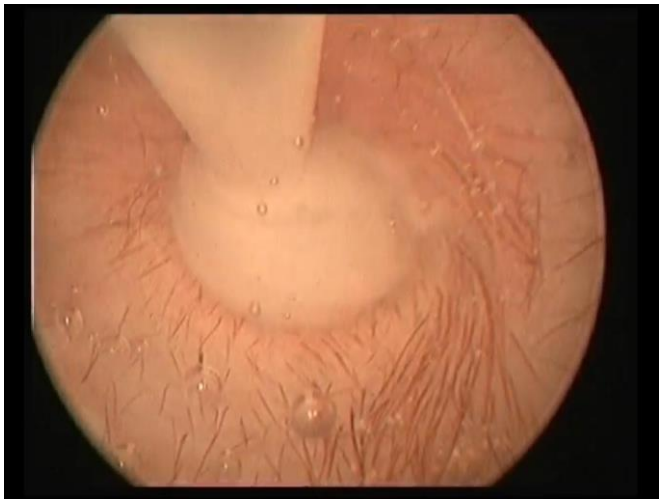


Figure 7. Photograph of a myringotomy procedure in progress

Within 7 to 20 days after the first visit, the dogs were reexamined under anesthesia. All had improved or were asymptomatic but the middle ears already contained mucus again and were reflushed. Of the 51 cases for which the owners pursued treatment, 14 required 2 revisits, 21 required 3 revisits, 10 required 4 revisits, 2 required 5 revisits and 4 required 6 revisits for reflushing of the middle ear before the middle ear was found to be clear of mucus. Twelve of the dogs had 1 or more relapses of PSOM after 6 to 18 months.

All reported cases appeared to benefit from manual removal of the mucoid effusion from the tympanic cavity but unfortunately, repeated procedures appear to be required before long term remission can be achieved (Stern-Bertholtz, Sjostrom et al. 2003).

Tympanostomy

A more recent technique that has been used in the treatment of PSOM is tympanostomy, which is common in human medicine to provide continual tympanic cavity ventilation and drainage in the treatment of OME, Otitis Media with Effusion (Rosenfeld, Culpepper et al. 2004). OME, also known as 'glue ear', is a mucous, viscous effusion within the tympanic cavity (Kubba, Pearson et al. 2000). The viscous properties of the tympanic cavity effusion in human OME are proposed to be similar to those in PSOM (Corfield, Burrows et al. 2008) and with this assumption tympanostomy tubes may provide adequate tympanic cavity drainage, obviating the need for multiple myrinogotomies for the treatment of PSOM in CKCS.

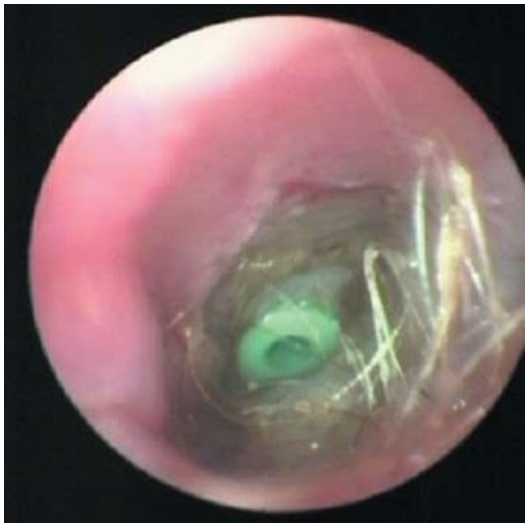


Figure 8. Otoscopic view of the tympanic membrane immediately following ventilation tube placement. (Corfield, Burrows et al. 2008).

Two studies have been published using tympanostomy as an alternative treatment to myringotomy and middle ear flushes in CKCS with OME or PSOM. In both of them the insertion of the tube provided relief of the clinical signs for several months. In the first study (Cox. C. L., Slack et al. 1989) the dog had unilateral OME that was first treated surgically with a lateral wall resection, before the insertion of the tympanostomy tube. The authors of this paper reported symptomatic relief for a period of eight months before extrusion of the tube resulted in recurrence of clinical signs. The only reported complications associated with the implant of the tube were a mild otorrhoea and obstruction of the tube.

In a second study, which described three cases (Corfield, Burrows et al. 2008) of CKCS diagnosed with PSOM, at least one myringotomy was performed before treatment with a tympanostomy tube. Initial improvement was noted in all dogs but clinical signs returned within 2 to 4 weeks. After insertion of the tympanostomy tube, the animals were symptom-free for 8, 6 and 3 months. In the study of Corfield and others no complications associated with insertion of the tubes were described.

Although the insertion of tympanostomy tubes may be an acceptable alternative to repeated myringotomy for the treatment of PSOM, this treatment method may be less suitable for long-term use due to the possibility of extrusion of the tympanostomy tube, the inability to allow the dog's ear to become wet and the possibility for tracking infections (McGuinness, Friend et al. 2013).

Complications associated with myringotomy and tympanostomy

The most common described complications after a myringotomy procedure in human medicine are persistent perforation, atrophic scar and tympanosclerosis at the site of the incision (Bluestone 1983). Complications after placing tympanostomy tubes in human medicine are persistent otorrhea, retained tube for more than 2 years, granulation tissue or foreign body

reaction, atelectasis of monomeric tympanic membrane, perforation after extrusion, tympanosclerosis and cholesteatoma caused by epithelial migration of ear canal lining through ventilation tube (Bluestone 1983, Ho, Chan et al. 2013, Lambert, Roy 2013). No information about complications after myringotomy or tympanostomy in veterinary medicine is found.

Aim of the study

In summary, insertion of a tympanostomy tube may be an alternative to repeated myringotomy and middle ear flushes for the treatment of PSOM, although with this method recurrence of clinical signs on long-term are also described. At the Department of Clinical Sciences of Companion Animals at the Faculty of Veterinary Medicine of Utrecht University (UKG), myringotomy as well as tympanostomy procedures have been performed for the treatment of PSOM. The aim of this research is to present the outcomes of the treatments performed between July 2006 and October 2014, to examine if there is any progression of the disease over time or over affected sides and if there is a difference in recurrence of clinical signs after myringotomy and tympanostomy. In addition, these outcomes will be compared with other results described in literature.

Materials and Methods

Data collection

The medical records of all diagnosed and treated Cavalier King Charles spaniels at the UKG between July 2006 and October 2014 were reviewed. These records are all saved in Vetware, the veterinary practice management software program used at the UKG.

Data including the gender, age at first symptoms and the clinical signs were collected. Following findings were also noted: general clinical examination, otoscopy, results of diagnostic imaging (CT, MRI), number and type of treatments, dates of surgery and results of follow-up visits.

Work up and follow up was similar for all patients included in this study. To monitor the condition of the dogs after their last visit to the UKG the owners were contacted by phone. Information about clinical signs, recurrence and other diseases or causes of death (if applicable) after their last visit to the UKG was obtained.

Animals

The medical records of 35 Cavalier King Charles spaniels diagnosed with PSOM were collected. The median age at referral was 4 (range 1–9). Eight of the 35 dogs were excluded from the study after collecting data due to concurrent disease. Therefore the collected data of the remaining 27 (14 female, 13 male) dogs were used for statistical analysis.

Treatment methods

In 27 Cavalier King Charles spaniels a total of 31 myringotomy and 5 tympanostomy procedures were performed.

Myringotomy

The ears of all dogs were evaluated under general anesthesia and video otoscopy was performed. In 16 cases, cerumen or ointment had to be removed by flushing (13 cases) or by a curette (3 cases). The tympanic membrane was inspected. In the affected ears a bulging, opaque but intact tympanic membrane was found, which indicates a pathological process in the middle ear. None of the tympanic membranes were ruptured. Myringotomy was performed in different ways: by using a myringotomy knife, a Kirscher wire, a curette or a suction catheter. The mucus plug in the affected bulla was removed by flushing with physiological saline solution using a suction catheter.

Tympanostomy

In total 5 tympanostomy procedures were performed in three dogs. All had a single myringotomy performed previously. Tympanostomy tubes were inserted into the myringotomy incision in 4 cases, in 1 case a second incision was made in which the tubes were placed. In all cases Armstrong Grommet ventilation tubes with a 1.1mm internal diameter were used.

Post-treatment

Postoperative medical treatment was not standardized. One dog did not receive any treatment after myringotomy. In 16 cases only antibiotics (Synulox, consisting of amoxicillin and clavulanic acid) were prescribed. Sixteen dogs were treated a combination of antibiotics (Synulox®) and NSAID's (carporal, carprofen or carprodyl). One dog received only NSAID's (carprofen) and 1 dog was treated with a combination of antibiotics (Synulox®) and opioids (tramadol).

Statistics

The collected data were analyzed with Excel (Microsoft Office 365 2013) and SPSS *(*IBM SPSS Statistics 22) software.

Kaplan-Meier survival analysis

The mean recurrence time and the recurrence rate of clinical signs following a myringotomy procedure were estimated by Kaplan–Meier survival analysis which allows calculation of the probability of recurrence of clinical signs based on the number of dogs still under observation at a given time. This statistical method provides the best estimate of the true rate of recurrence if monitoring information is available (Goel, Khanna et al. 2010).

Kaplan-Meier survival analysis was used to calculate the recurrence-free survival time after a single myringotomy procedure in 27 Cavalier King Charles spaniels and after a double procedure. In addition, the time until recurrence after myringotomy and tympanostomy was compared. The time frame used in these Kaplan-Meier survival analyses is 40 months starting from the procedure.

Log rank test

To compare the recurrences between single and double procedures and between myringotomy and tympanostomy procedures, the log rank test was used. The log rank test calculates the chi-square (X^2) for each event time for each group and sums the results. These are added for each group to derive the ultimate chi-square to compare the full curves of each group (Rich, Neely et al. 2010). A p value <0.05 was considered to be statistically significant.

Results

Primary Secretory Otitis Media was diagnosed in 35 Cavalier King Charles spaniels at the UKG between July 2006 and October 2014. Diagnosis was based on findings at MRI or CT examination and the presence of mucous material out of the bulla(e) tympanica(e) during myringotomy.

Features	Values	
Age (years) at clinical signs		
Mean	4.5	
Median	4	
Range	7	
Seks ratio (M/F)	13:14	
Clinical Signs		
Deafness	20	74%
Vestibular problems	4	15%
Head tilt	2	7%
Facial paralysis	2	7%
Scratching	16	59%
Head rubbing	14	52%
Head shaking	15	56%
Pain	5	19%
Radiological examination		
CT	9	33%
Left otitis media	2	7%
Right otitis media	0	
Bilateral otitis media	7	26%
MRI	17	63%
Left otitis media	3	11%
Right otitis media	5	19%
Bilateral otitis media	9	33%
No	1	4%
Number of surgeries		
1	20	74%
2	4	15%
3	3	11%
Types of surgery	36	
Myringotomy	31	86%
Tympanostomy	5	14%

Table 1. Clinical characteristics and details of 27 CKCSs treated for PSOM.

Data were collected from all PSOM patients. In our hospital patient administration software, 37 dogs were identified which had a myringotomy or tympanostomy procedure performed, because PSOM was suspected. Ten of these dogs were excluded from the study. In 2 dogs no mucus was present, thus the clinical signs must have been due to other causes. In 1 dog PSOM was diagnosed as an incidental finding during CT examination for rhinitis, this animal had no clinical signs associated with PSOM. In 7 dogs there was no improvement after the first procedure: in 4 of them, the only symptom was deafness and there was no improvement at all after the procedure: the mucus plug did not cause the impaired hearing, so the deafness has to be caused by another disease. In 3 dogs the clinical signs (scratching, head rubbing, head shaking) persisted after surgery and seemed to associate with syringomyelia or cerebellar herniation, which was also diagnosed with MRI examination in all 3 dogs.

Of the 37 dogs identified in the patient administration software, the collected data of 27 of these animals were used in this study. The male to female ratio was 13:14. Mean age at presentation of first clinical signs was 4,5 with a median of 4.

Clinical signs

Information about first clinical signs was obtained by the owners during their first policlinic appointment and recorded in anamnesis forms. During general clinical examination questions were asked about the presence of signs and their gradation according to the owner.

In 74% (20/27) of the cases the dogs were deaf, 15% (4/27) of the dogs showed ataxia, 7% (2/27) showed a head tilt and 7%% (2/27) showed a facial paralysis of the affected side (figure 9).

In 59% (16/27) of the cases the dogs were scratching, 52% (14/27) of the dogs were rubbing and 56% (15/27) were shaking their heads. In 19% (5/27) of the cases the dogs seemed to experience pain localized to the head or ears according to the owners (figure 10). Gradations of these symptoms were divided in mild, moderate, severe and extreme.

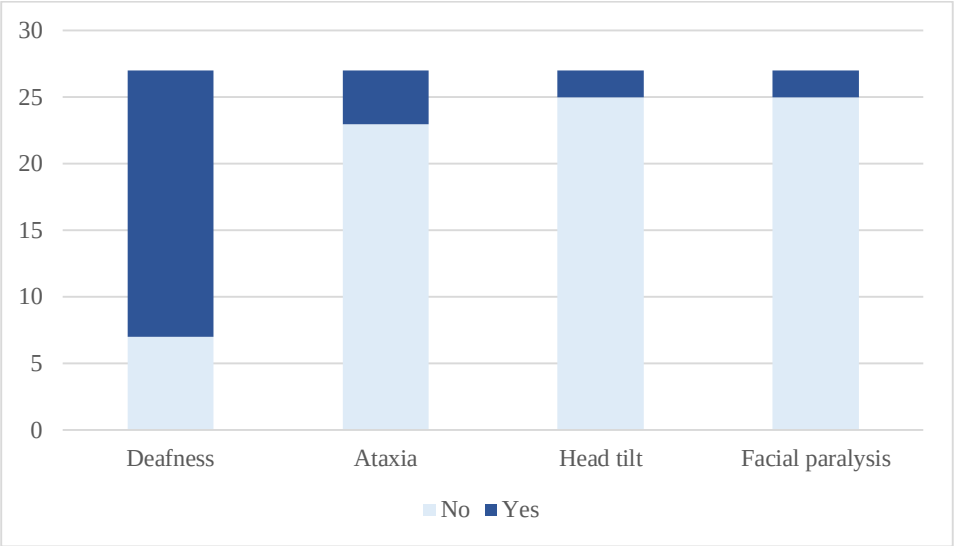


Figure 9. Presence of clinical signs in 27 cases of PSOM according to the owner.

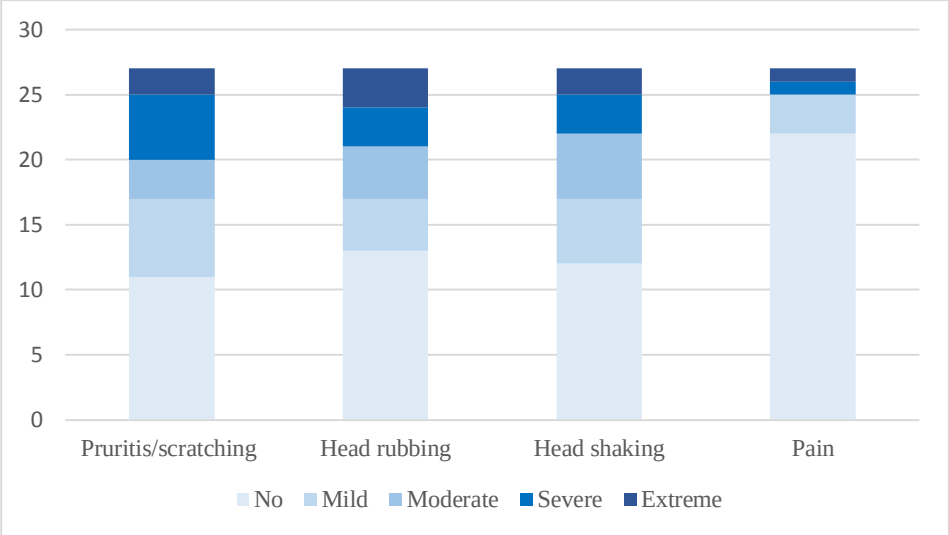


Figure 10. Presence and gradation of clinical signs in 27 cases of PSOM according to the owner.

Diagnostic imaging techniques

In 26 of the 27 dogs radiological examination was used to diagnose PSOM. CT was performed in 9 dogs. Both bullae tympanicae were obliterated by a soft tissue opacity in 7 dogs, in 2 dogs soft tissue opacity was present in only the left bulla tympanica.

MRI was performed in 17 dogs. In 9 dogs, hyperintense material in both bullae tympanicae was detected . In 3 dogs there was only soft tissue opacity present in the left tympanic bulla, in 5 dogs only in the right tympanic bulla.

In general, radiological examination showed bilateral otitis media in 16 dogs, left otitis media in 5 dogs and right otitis media in 5 dogs.

Performed procedures

In 27 Cavalier King Charles spaniels 31 myringotomy and 5 tympanostomy procedures were performed. 20 dogs had a single myringotomy, of which 14 bilateral and 6 a unilateral (3 at the left, 3 at the right side) procedure. 3 dogs had a bilateral myringotomy twice, 1 dog had three bilateral myringotomy procedures. In 1 dog one bilateral myringotomy was followed by a bilateral tympanostomy, 1 dog had one bilateral myringotomy followed by two bilateral tympanostomy procedures, and 1 dog had one bilateral myringotomy followed by a bilateral tympanostomy and a following unilateral (left) tympanostomy (table 2).

	First procedure	Second procedure	Third procedure
Myringotomy			
Bilateral	14	3	1
Unilateral	6		
Tympanostomy			
Bilateral		2	1
Unilateral			1

Table 2. Number and types of procedures performed in 27 CKCSs diagnosed with PSOM.

Affected bullae tympanicae

During the first procedure, mucus was removed out of both bullae tympanicae in 17 cases. In 5 dogs there was only mucus removed out of the left bulla, in 5 dogs out of the right bulla.

The 7 dogs in which a second myringotomy was performed, all had bilateral PSOM at the first procedure. The same outcome was seen in 6 of these dogs. In 1 dog no mucus was removed from both bullae. This animal returned for a third procedure because of persisting symptoms, but still no mucus was present .

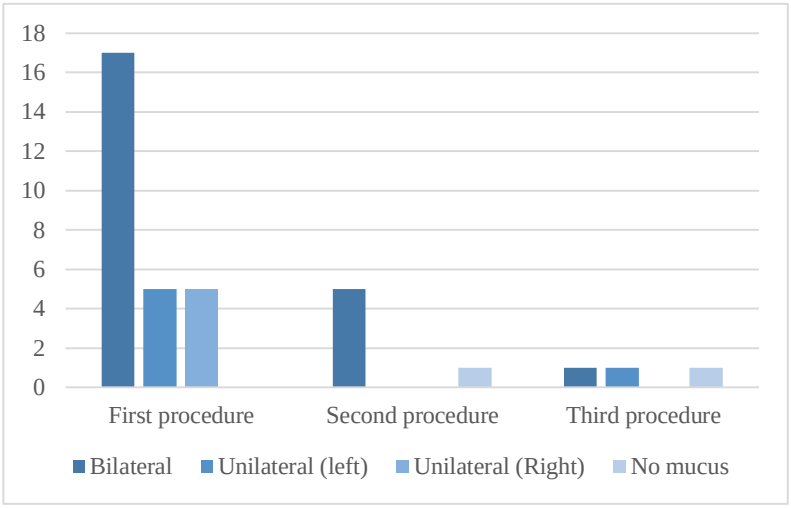


Figure 11. Affected bullae tympanicae during the following procedures in 27 CKCSs diagnosed with PSOM.

In 2 other dogs myringotomy was performed three times. One of them was again bilaterally affected, in the other dog mucus was removed out of the left bulla tympanica only (figure 11).

Recurrence of clinical signs: Kaplan-Meier survival analysis

At the moment the owners were contacted, 15 of the 27 dogs were still alive and 10 of them died over the past few years. They were euthanized due to syringomyelia (5 dogs), heart failure (3 dogs), squamous cell carcinoma (1 dog), or old age (1 dog). Two of the dog owners have not

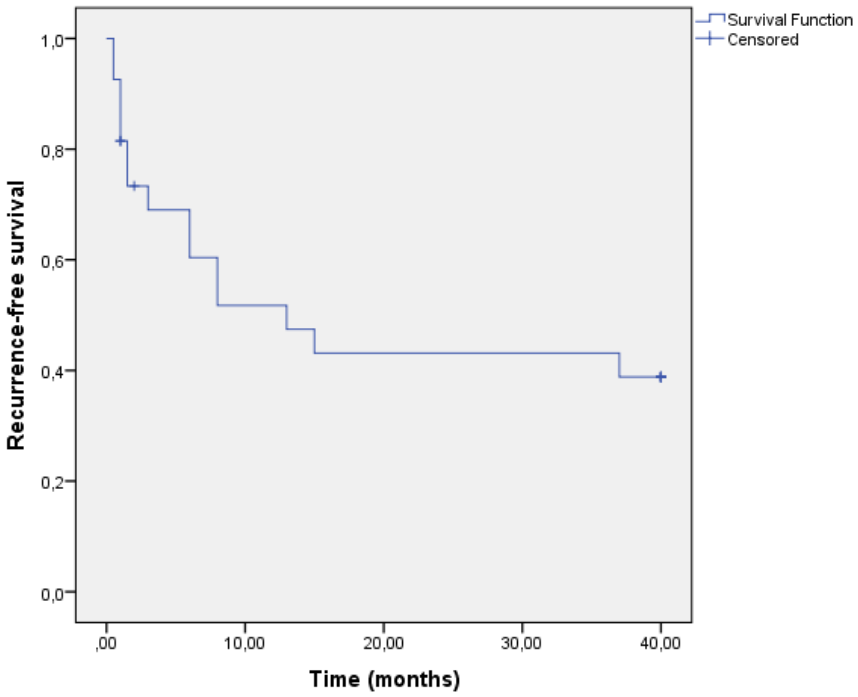
been contacted because of expired phone numbers. These animals are labeled as censored observations in following survival analysis.

Recurrence of clinical signs after first surgery

Standardized telephonic owner questionnaires were used to determine the presence and time of recurrence of clinical signs associated with PSOM. Life table and survival tables are presented in table 3 in the attachments. The recurrence-free curve is shown in figure 12. For all 27 dogs the mean recurrence time was 19.9 months with a median of 13 months and the recurrence rate was 61% over a period of 40 months.

In 16/27 dogs (59%) recurrence of clinical signs occurred, the other 12 dogs were censored. Nine dogs were censored because they did not show any recurring signs of PSOM in a period of 40 months after surgery. Two dogs were censored after 1 month because they were lost-to-follow up, only the information found in Vetware about their follow-up has been used. In both cases the dog was doing great 1 month after surgery. One dog was censored after 2 months, because surgery has been performed only 2 months ago.

Figure 12. Kaplan-Meier estimate of cumulative recurrence-free survival of 27 Cavalier King Charles spaniels after a first myringotomy procedure.



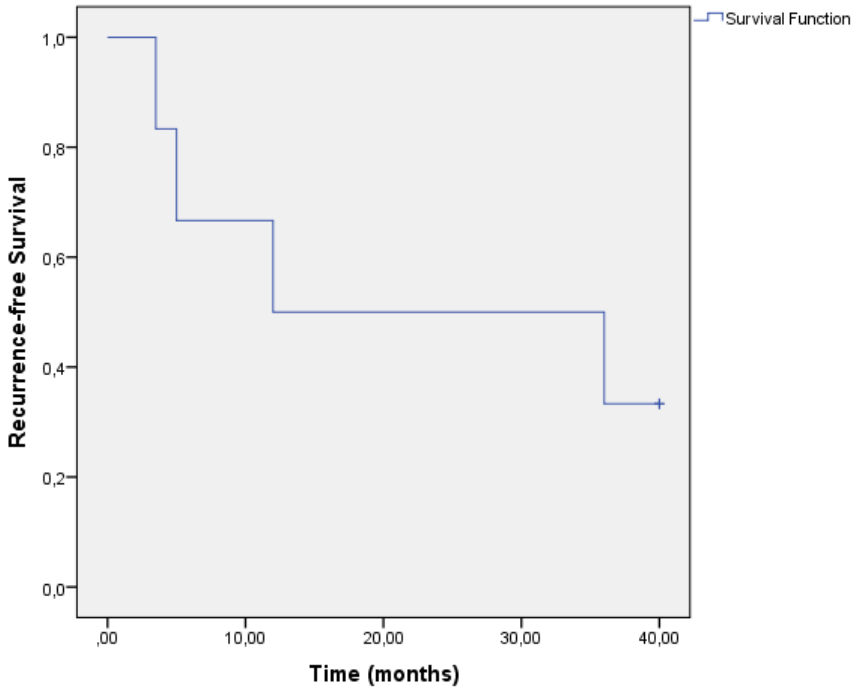
Recurrence of clinical signs after multiple surgeries

In 7 dogs a second procedure has been performed. This was a myringotomy procedure in 4 dogs and a tympanostomy procedure in the other 3 dogs.

In one of these dogs there was no mucus present in both bullae so the clinical signs were not caused by PSOM and this animal was excluded from further research. Life table and survival tables of recurrence after the second procedure are presented in table 4 in the attachments. The recurrence-free curve is shown in figure 13. For these 6 dogs the mean recurrence time was 22.8 months with a median of 12 months and the recurrence rate was 67% over a period of 40 months.

A third procedure was performed in only 2 dogs, in both cases a tympanostomy procedure was performed. The mean recurrence time was 3.3 months with a median of 0,5 months and the recurrence rate was 100%.

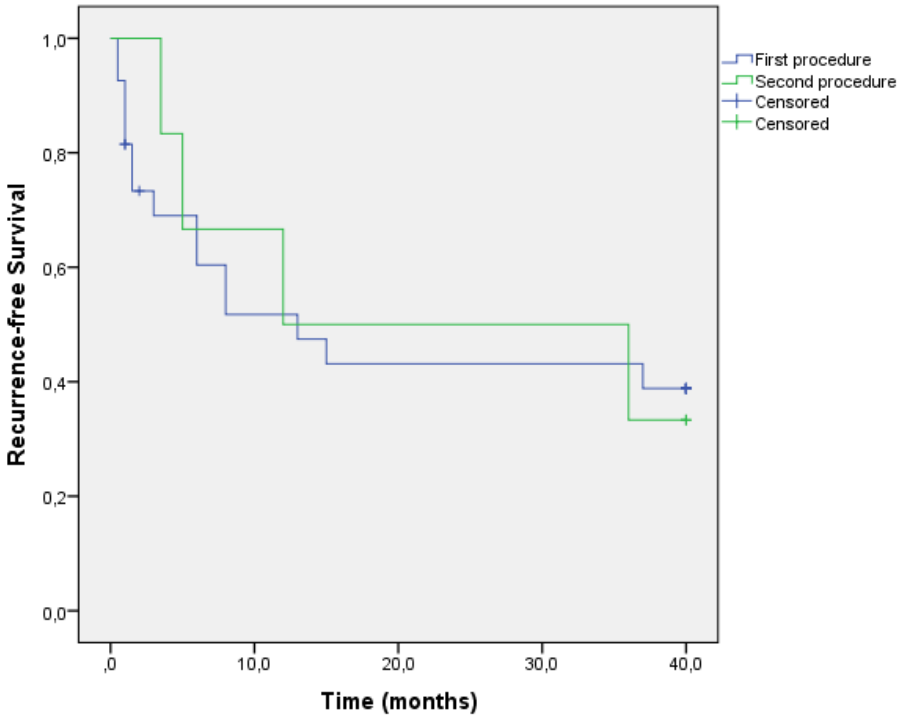
Figure 13. Kaplan-Meier estimate of cumulative recurrence-free survival of 6 Cavalier King Charles spaniels after a second treatment (myringotomy or tympanostomy) procedure.



Comparing recurring clinical signs between first and second procedures

To examine whether the development of mucus production in the middle ear is progressive over time, the recurrence of clinical signs after a first and a second procedure can be compared using the log-rank test. The results of the log rank test are shown in table 5 in the attachments, the compared Kaplan-Meier curves are shown figure 14. There was no statistically significant difference between recurrence of signs after a first and second procedure (p = 0.962).

Figure 14. Kaplan-Meier estimate of recurrence-free survival difference between first and second procedure.

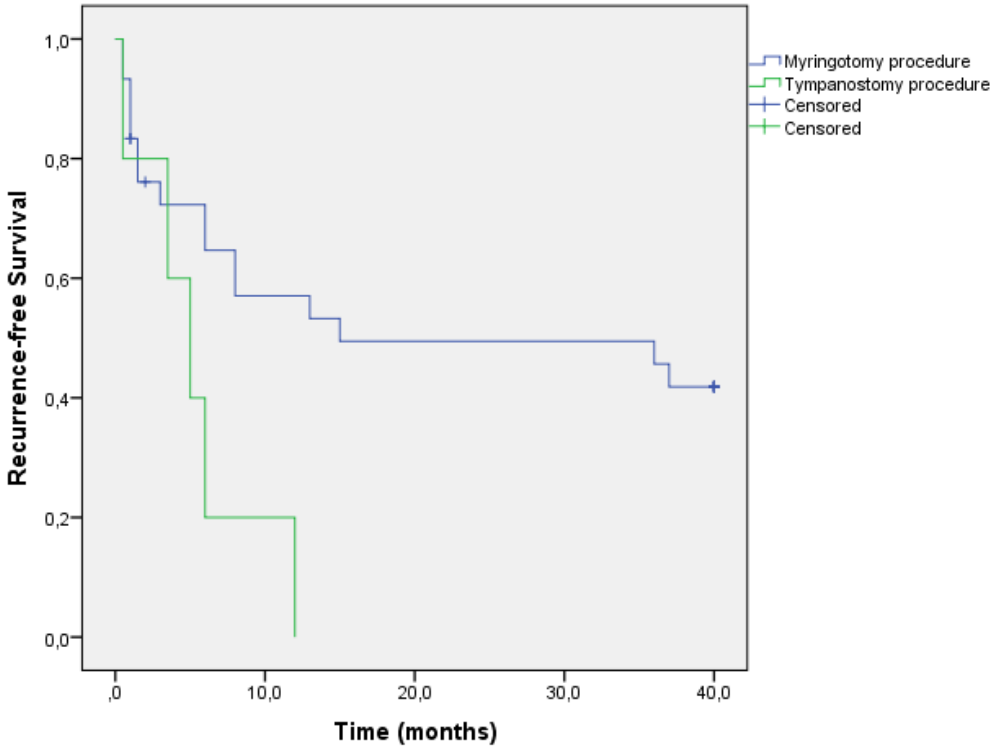


Comparing recurring clinical signs between myringotomy and tympanostomy procedures

The log-rank test was also used to compare the recurrence time after myringotomy to tympanostomy procedures. For this analysis all recurrence information was used, so the recurrence times after first, second and third procedures. Life tables, survival tables and the log-rank results are presented in table 6 in the attachments. The compared Kaplan-Meier curves are shown in figure 15.

Overall, the mean recurrence time after myringotomy was 22 months with a median of 15 months and a recurrence rate of 58% over a period of 40 months, and the mean recurrence time after tympanostomy was 5.4 months with a median of 5 months and a recurrence rate of 100% over a period of 12 months. By using the log rank test a statistically significant difference between the recurrence of signs after myringotomy or tympanostomy procedures is found (p = 0.022), which means according to the information of the owners, recurrence of signs occurs faster after tympanostomy in comparison to myringotomy.

Figure 15. Kaplan-Meier estimate of recurrence-free survival difference between myringotomy and tympanostomy procedures.



Conclusion

Recurrence after a single and second procedure

After a single myringotomy procedure the mean recurrence time in 27 dogs in which clinical signs occur is 19.9 months with a median of 13 months and a recurrence rate of 61%. After a second procedure in 6 dogs the mean recurrence time is 22.8 months with a median of 12 months and a recurrence rate of 67%. There is no statistically significant difference in time frame in which PSOM relapses between a first and a second procedure (p = 0.962).

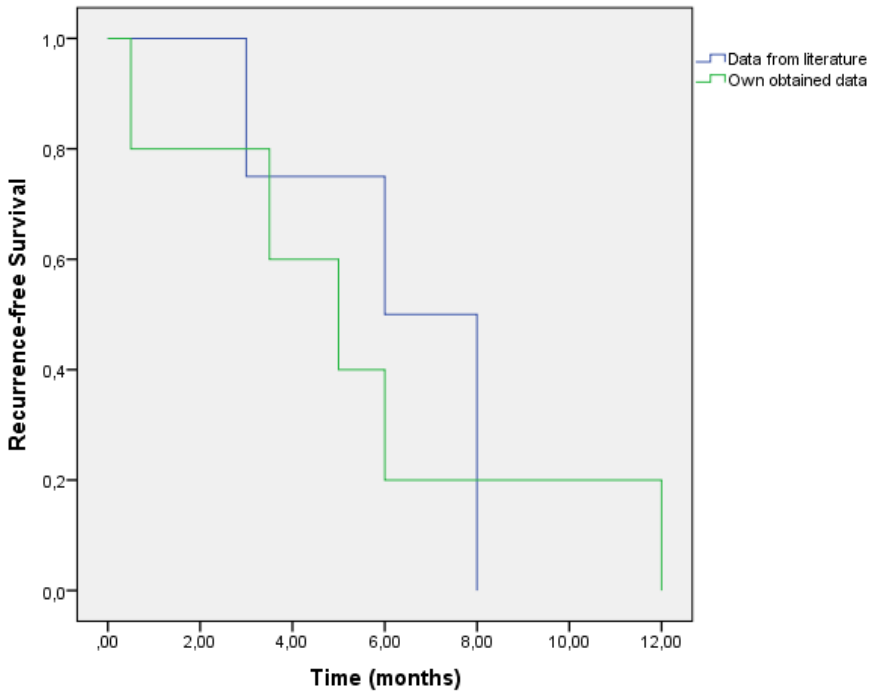
Comparisons with other studies are difficult to make. Stern-Bertholtz and others (Stern-Bertholtz, Sjostrom et al. 2003) set up a clinical review about recurrence after myringotomy. In this study, 43 CKCSs all had improved or were asymptomatic in 7-20 days after the first myringotomy, but all middle ears were examined again and contained mucus. The procedure had to be repeated between one and five times before the middle ear was found to be free of mucus. These results are not comparable with the results in this study, because no revisits have taken place and there is only information about recurrence of the clinical signs.

Recurrence after tympanostomy in comparison with myringotomy procedures

In this study, a significant difference was determined between recurrence after myringotomy and tympanostomy procedures (p = 0.022): recurrence of clinical signs occurs faster after tympanostomy in comparison with myringotomy.

These outcomes are contrary to the theory which describes that the continual tympanic cavity ventilation by using ventilation tubes may provide a longer symptom-free period and be a good alternative to repeated myringotomy procedures. In 4 cases described in literature (Cox. C. L., Slack et al. 1989, Corfield, Burrows et al. 2008), symptomatic relief was reported for a period of 3, 6, 8 and 8 months. If we compare these with our own results (0.5, 3.5, 5, 6 and 12 months) by plotting these in a Kaplan-Meier curve and using the log-rank test, a p-value of 0.746 is found, which indicates there is no statistically significant difference. Means and medians and log-rank results are shown in table 7 in the attachments, compared Kaplan Meier curves are shown in figure 16.

Figure 16. Kaplan-Meier estimate of recurrence-free survival difference between tympanostomy procedures described in this study and tympanostomy procedures described in previous studies.



Affecting sides

In this study no progression over affecting sides is seen. In a study from McGuinness and others (McGuinness, Friend et al. 2013) it is suggested that otitis media in CKCSs is an acquired and progressive condition: in this study 34 CKCSs were MRI scanned on two different dates. 9 (26.5%) of the cases had progressed at the second MRI examination, 3 from unilateral to bilateral effusion, 6 to acquire an effusion. 8 dogs remained with the same effusion as the first time and no cases with otitis media at the first MRI had resolved at the time of the second. It is not possible to do a direct comparison of this study to the described study due to lack of precise data about the condition of the dogs after the treatment.

Complications

Regarding complications after a myringotomy procedure, one of the dogs showed persistent otorrhea after the first myringotomy procedure for a period of two months. This was diagnosed as a secondary otitis externa chronica and treated with antibiotics and corticosteroids. No complications were seen in the other 26 dogs.

Discussion

Limitations of this study

Data collection

Outcomes of this study have to be interpreted carefully because of the many limitations. Limitations of the study are firstly the way in which data are obtained. The occurrence of relapsing clinical signs after surgery is defined by the dog owner which results in very subjective information. The long time between this study and the treatment procedures did make it hard for some of the owners to recall the precise condition and any possible moment of recurrence of clinical signs of their dog.

The knowledge of the dog owners does not really confirm that PSOM has or has not returned. If the clinical signs returned over a few weeks, a new mucus plug may have formed in the middle ear, but there can also be another cause of the signs. On the other hand, if the owner didn't notice any signs after surgery, the PSOM may have been resolved but this isn't sure: a mucus plug in the middle ear(s) can be present (so PSOM has returned) but not cause any signs. Moreover, deafness is a very difficult clinical sign to estimate for the owner. To be sure about the recurrence of PSOM the diagnose has to be determined by radiological examination or a repeated myringotomy procedure.

There were no control visits at the faculty after the performed procedures , which was achieved in the study of Stern-Bertholtz and others (Stern-Bertholtz, Sjostrom et al. 2003) and several owners did not return to the clinic when the dog started to show clinical signs again. Various reasons were given: the dog did only suffer from deafness, of which the dog became used to and no repeating of the procedure was necessary according to the owner; the owners did not want to take their dog for a surgery for a second or third time because of the high costs or other diseases arised and took priority.

Results would be more reliable when an explicit protocol of follow-up and re-exanimation of the bullae by otoscopy, radiological examination or repeated myringotomy were performed. Therefore, it is difficult to compare these outcomes with other results found in literature, because in those cases re-examination has been performed and conclusions were able to make about the diagnosis. However, an attempt was made in the former chapter.

Statistics

As a second limitation of this study, the study was underpowered due to the small sample sizes. The group of dogs which had a first myringotomy procedure was 27, the group of dogs which had a second surgery was only 6, and the amount of tympanostomy procedures was only 5: these are such small numbers which do not have the power to rule out a real difference.

Another limitation is the amount and distribution of censored subjects. In the Kaplan-Meier curve of recurrence after the first myringotomy procedure, 12 of the 27 dogs were censored. Nine dogs were censored because they did not show any signs in a period of 40 months after surgery. These dogs did not change the survival probability: it graphically tells us that the survival was at least this long. Three dogs were censored because they were lost-to-follow-up (2 dogs) after a month or because the procedure has been performed only two months ago (1 dog). These dogs materially reduced the cumulative survival between intervals. The more patients that are censored in a study, the less reliable is the survival curve. After the first patient is censored the survival curve becomes an estimate, since we do not know if censored patients would have experienced a recurrence at some point later in their life.

Head Rubbing

In the 27 dogs in this study, 14 of the 27 dogs were rubbing their head. Head rubbing (against the floor or other surfaces) has, with the exception of dermatitis and allergies (Bruet, Bourdeau et al. 2012), only been associated with syringomyelia and CM and an unknown syndrome of behavioral signs of discomfort in the CKCS in former literature (Rusbridge 2005, Rusbridge, Carruthers et al. 2007). Only 7 of these 14 dogs were also diagnosed with CM/SM at the moment of the occurring clinical signs. After the myringotomy procedure, all clinical signs, including the head rubbing, were resolved in all 14 dogs for a period varying from four weeks to years. It seems that in these cases, the head rubbing was caused by the overfilled bulla(e) tympanica(e) and therefore this clinical sign can also be associated with PSOM.

Diagnostic imaging techniques

The bullae tympanicae which contained mucus during myringotomy were all already appointed during radiographic examination. This implies that no case of PSOM was missed during CT and MRI. Although definitive diagnosis is achieved following a myringotomy in which a mucus plug is removed, CT and MRI examination seem to be efficient methods to diagnose PSOM.

In 26 dogs diagnostic imaging techniques were used in determining the diagnose of PSOM. CT was performed in 9 animals, while MRI was performed in 17 animals. Usually MRI is used less often than CT in the diagnosis of otitis media because of limited availability and high cost (Bischoff, Kneller 2004). In this study MRI is used more often. This is because the first reason for radiological examination was screening of syringomyelia which only can be diagnosed with MRI examination and thereby the PSOM was accidentally found, or because a distinction between PSOM and syringomyelia had to be made to explain the clinical signs.

Affected bullae tympanicae

Because no unilateral PSOM has expanded to a bilateral PSOM, there is no sign of progression of the disease from unilateral to bilateral. In addition, all 10 unilaterally affected dogs did not show any recurring clinical signs, while 7 of the 17 bilaterally affected dogs did. If we assume that the information from the owners about no recurrence of clinical signs is equal to no recurrence of PSOM, this means that 100% (10/10) of the unilaterally affected ears were cured after one myringotomy procedure, while this was only 59% (10/17) in the dogs with bilaterally affected PSOM. This indicates a difference between unilateral and bilateral PSOM, in which unilateral PSOM is less likely to return after treatment then bilateral PSOM.

However, there is no further information about the 20 dogs which had no second myringotomy procedure or other diagnostic exam. It is not possible to do a direct comparison of this study to the described study of McGuinness and others (McGuinness, Friend et al. 2013), in which it is suggested that otitis media in CKCs is a progressive condition, due to lack of precise data about the condition of the dogs after the treatment. In this study there was no second moment of diagnostics.

Overall conclusions

Primary Secretory Otitis Media is a recently more frequently diagnosed disease which is almost exclusively described in Cavalier King Charles spaniels and describes a condition in which there is a mucous plug in the middle ear. This disease causes clinical signs like deafness, pain localized in the head or neck, head tilt, nystagmus and facial paralysis. Treatment recommendations include the removal of the mucoid effusion from the tympanic cavity through a myringotomy incision and the use of tympanostomy tubes to provide continual tympanic cavity ventilation and pressure equalization. Former studies showed myringotomy has to be repeated at regular intervals before long term control of clinical signs has been reached and it seems that tympanostomy tubes may be an effective alternative to repeated myringotomy.

The aim of this study was to assess the time interval in which recurrence of clinical signs occurs after treatment with a myringotomy or tympanostomy procedure performed at the Faculty of Veterinary Medicine of Utrecht University, and to examine if there is any progression of PSOM over time or affecting sides. Results of this study indicate that after a single myringotomy procedure the mean recurrence time is 19.9 months with a recurrence rate of 61%. There is no statistically significant difference between recurrence after a single and a double procedure ($p = 0.962$). After tympanostomy the time to recurrence was shorter then after myringotomy ($p = 0.022$), which is contrary to the theory which describes that the continual tympanic cavity ventilation by using ventilation tubes may provide a longer symptom-free period. No signs of progression from unilateral to bilateral PSOM was seen.

Comparing the results of this study with other results is hard because of the lack of comparable information in previous studies. This study does not contain similar data-sets as used in other studies. More valuable results would have been obtained when a clear and definite follow-up with repeating of diagnostics of the dogs was performed. Outcomes of this study are all obtained by different subjective opinions of the dog owners and give only information about the recurrence of clinical signs associated with PSOM, not about the true presence of this disease.

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Attachments

Table 3a.. Life table in survival analysis of 27 Cavalier King Charles spaniels after a first myringotomy procedure. The recurrence rate was obtained by subtracting the cumulative proportion surviving at 40 months of 100%.

Interval Start Time	Number Entering Interval	Number Withdrawing during Interval	Number Exposed to Risk	Number of Terminal Events	Proportion Terminating	Proportion Surviving	Cumulative Proportion Surviving at End of Interval	Std. Error of Cumulative Proportion Surviving at End of Interval	Probability Density	Std. Error of Probability Density	Hazard Rate	Std. Error of Hazard Rate
0	27	0	27,000	2	,07	,93	,93	,05	,074	,050	,08	,05
1	25	2	24,000	5	,21	,79	,73	,09	,193	,077	,23	,10
2	18	1	17,500	0	,00	1,00	,73	,09	,000	,000	,00	,00
3	17	0	17,000	1	,06	,94	,69	,09	,043	,042	,06	,06
4	16	0	16,000	0	,00	1,00	,69	,09	,000	,000	,00	,00
5	16	0	16,000	0	,00	1,00	,69	,09	,000	,000	,00	,00
6	16	0	16,000	2	,13	,88	,60	,10	,086	,058	,13	,09
7	14	0	14,000	0	,00	1,00	,60	,10	,000	,000	,00	,00
8	14	0	14,000	2	,14	,86	,52	,10	,086	,058	,15	,11
9	12	0	12,000	0	,00	1,00	,52	,10	,000	,000	,00	,00
10	12	0	12,000	0	,00	1,00	,52	,10	,000	,000	,00	,00
11	12	0	12,000	0	,00	1,00	,52	,10	,000	,000	,00	,00
12	12	0	12,000	0	,00	1,00	,52	,10	,000	,000	,00	,00
13	12	0	12,000	1	,08	,92	,47	,10	,043	,042	,09	,09
14	11	0	11,000	0	,00	1,00	,47	,10	,000	,000	,00	,00
15	11	0	11,000	1	,09	,91	,43	,10	,043	,042	,10	,10
16	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
17	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
18	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
19	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
20	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
21	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
22	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
23	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
24	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
25	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
26	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
27	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
28	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
29	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
30	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
31	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
32	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
33	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
34	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
35	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
36	10	0	10,000	0	,00	1,00	,43	,10	,000	,000	,00	,00
37	10	0	10,000	1	,10	,90	,39	,10	,043	,042	,11	,11
38	9	0	9,000	0	,00	1,00	,39	,10	,000	,000	,00	,00
39	9	0	9,000	0	,00	1,00	,39	,10	,000	,000	,00	,00
40	9	9	4,500	0	,00	1,00	,39	,10	,000	,000	,00	,00

a. The median survival time is 13,404

Table 3b. Survival table in Kaplan-Meier survival analysis of 27 Cavalier King Charles spaniels after a first myringotomy procedure.

	Time	Status	Cumulative Proportion Surviving at the Time		N of Cumulative Events	N of Remaining Cases
			Estimate	Std. Error		
1	,500	1	.	.	1	26
2	,500	1	,926	,050	2	25
3	1,000	1	.	.	3	24
4	1,000	1	.	.	4	23
5	1,000	1	,815	,075	5	22
6	1,000	0	.	.	5	21
7	1,000	0	.	.	5	20
8	1,500	1	.	.	6	19
9	1,500	1	,733	,087	7	18
10	2,000	0	.	.	7	17
11	3,000	1	,690	,092	8	16
12	6,000	1	.	.	9	15
13	6,000	1	,604	,098	10	14
14	8,000	1	.	.	11	13
15	8,000	1	,518	,102	12	12
16	13,000	1	,475	,102	13	11
17	15,000	1	,431	,101	14	10
18	37,000	1	,388	,100	15	9
19	40,000	0	.	.	15	8
20	40,000	0	.	.	15	7
21	40,000	0	.	.	15	6
22	40,000	0	.	.	15	5
23	40,000	0	.	.	15	4
24	40,000	0	.	.	15	3
25	40,000	0	.	.	15	2
26	40,000	0	.	.	15	1
27	40,000	0	.	.	15	0

Table 3c. Means and medians for survival time in Kaplan-Meier survival analysis of 27 Cavalier King Charles spaniels after a first myringotomy procedure.

Mean[a]				Median			
		95% Confidence Interval				95% Confidence Interval	
Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
19,941	3,564	12,955	26,927	13,000	5,312	2,589	23,411

a. Estimation is limited to the largest survival time if it is censored.

Table 4a. Life table in survival analysis of 6 Cavalier King Charles spaniels after a second treatment (myringotomy or tympanostomy) procedure. The recurrence rate was obtained by subtracting the cumulative proportion surviving at 40 months of 100%.

Interval Start Time	Number Entering Interval	Number Withdrawing during Interval	Number Exposed to Risk	Number of Terminal Events	Proportion Terminating	Proportion Surviving	Cumulative Proportion Surviving at End of Interval	Std. Error of Cumulative Proportion Surviving at End of Interval	Probability Density	Std. Error of Probability Density	Hazard Rate	Std. Error of Hazard Rate
0	6	0	6,000	0	,00	1,00	1,00	,00	,000	,000	,00	,00
1	6	0	6,000	0	,00	1,00	1,00	,00	,000	,000	,00	,00
2	6	0	6,000	0	,00	1,00	1,00	,00	,000	,000	,00	,00
3	6	0	6,000	1	,17	,83	,83	,15	,167	,152	,18	,18
4	5	0	5,000	0	,00	1,00	,83	,15	,000	,000	,00	,00
5	5	0	5,000	1	,20	,80	,67	,19	,167	,152	,22	,22
6	4	0	4,000	0	,00	1,00	,67	,19	,000	,000	,00	,00
7	4	0	4,000	0	,00	1,00	,67	,19	,000	,000	,00	,00
8	4	0	4,000	0	,00	1,00	,67	,19	,000	,000	,00	,00
9	4	0	4,000	0	,00	1,00	,67	,19	,000	,000	,00	,00
10	4	0	4,000	0	,00	1,00	,67	,19	,000	,000	,00	,00
11	4	0	4,000	0	,00	1,00	,67	,19	,000	,000	,00	,00
12	4	0	4,000	1	,25	,75	,50	,20	,167	,152	,29	,28
13	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
14	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
15	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
16	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
17	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
18	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
19	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
20	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
21	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
22	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
23	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
24	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
25	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
26	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
27	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
28	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
29	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
30	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
31	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
32	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
33	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
34	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
35	3	0	3,000	0	,00	1,00	,50	,20	,000	,000	,00	,00
36	3	0	3,000	1	,33	,67	,33	,19	,167	,152	,40	,39
37	2	0	2,000	0	,00	1,00	,33	,19	,000	,000	,00	,00
38	2	0	2,000	0	,00	1,00	,33	,19	,000	,000	,00	,00
39	2	0	2,000	0	,00	1,00	,33	,19	,000	,000	,00	,00
40	2	2	1,000	0	,00	1,00	,33	,19	,000	,000	,00	,00

a. The median survival time is 36,000

Table 4b. Survival table in Kaplan-Meier survival analysis of 6 Cavalier King Charles spaniels after a second treatment (myringotomy or tympanostomy) procedure.

	Time	Status	Cumulative Proportion Surviving at the Time		N of Cumulative Events	N of Remaining Cases
			Estimate	Std. Error		
1	3,500	1	,833	,152	1	5
2	5,000	1	,667	,192	2	4
3	12,000	1	,500	,204	3	3
4	36,000	1	,333	,192	4	2
5	40,000	0	.	.	4	1
6	40,000	0	.	.	4	0

Table 4c. Means and medians for survival time in Kaplan-Meier survival analysis of 6 Cavalier King Charles spaniels after a second treatment (myringotomy or tympanostomy) procedure.

Mean[a]				Median			
		95% Confidence Interval				95% Confidence Interval	
Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
22,750	6,608	9,799	35,701	12,000	18,984	,000	49,208

a. Estimation is limited to the largest survival time if it is censored.

Table 5. Results of the recurrence-free survival analyses for the impact of the moment of procedure (first versus second procedure).

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	,002	1	,962

Test of equality of survival distributions for the different moments of procedure.

Table 6a. Life table in survival analysis of 30 myringotomy procedures in 27 Cavalier King Charles spaniels diagnosed with PSOM. The recurrence rate was obtained by subtracting the cumulative proportion surviving at 40 months of 100%.

Interval Start Time	Number Entering Interval	Number Withdrawing during Interval	Number Exposed to Risk	Number of Terminal Events	Proportion Terminating	Proportion Surviving	Cumulative Proportion Surviving at End of Interval	Std. Error of Cumulative Proportion Surviving at End of Interval	Probability Density	Std. Error of Probability Density	Hazard Rate	Std. Error of Hazard Rate
0	30	0	30,000	2	,07	,93	,93	,05	,067	,046	,07	,05
1	28	2	27,000	5	,19	,81	,76	,08	,173	,070	,20	,09
2	21	1	20,500	0	,00	1,00	,76	,08	,000	,000	,00	,00
3	20	0	20,000	1	,05	,95	,72	,08	,038	,037	,05	,05
4	19	0	19,000	0	,00	1,00	,72	,08	,000	,000	,00	,00
5	19	0	19,000	0	,00	1,00	,72	,08	,000	,000	,00	,00
6	19	0	19,000	2	,11	,89	,65	,09	,076	,052	,11	,08
7	17	0	17,000	0	,00	1,00	,65	,09	,000	,000	,00	,00
8	17	0	17,000	2	,12	,88	,57	,09	,076	,052	,13	,09
9	15	0	15,000	0	,00	1,00	,57	,09	,000	,000	,00	,00
10	15	0	15,000	0	,00	1,00	,57	,09	,000	,000	,00	,00
11	15	0	15,000	0	,00	1,00	,57	,09	,000	,000	,00	,00
12	15	0	15,000	0	,00	1,00	,57	,09	,000	,000	,00	,00
13	15	0	15,000	1	,07	,93	,53	,10	,038	,037	,07	,07
14	14	0	14,000	0	,00	1,00	,53	,10	,000	,000	,00	,00
15	14	0	14,000	1	,07	,93	,49	,10	,038	,037	,07	,07
16	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
17	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
18	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
19	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
20	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
21	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
22	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
23	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
24	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
25	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
26	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
27	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
28	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
29	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
30	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
31	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
32	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
33	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
34	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
35	13	0	13,000	0	,00	1,00	,49	,10	,000	,000	,00	,00
36	13	0	13,000	1	,08	,92	,46	,10	,038	,037	,08	,08
37	12	0	12,000	1	,08	,92	,42	,10	,038	,037	,09	,09
38	11	0	11,000	0	,00	1,00	,42	,10	,000	,000	,00	,00
39	11	0	11,000	0	,00	1,00	,42	,10	,000	,000	,00	,00
40	11	11	5,500	0	,00	1,00	,42	,10	,000	,000	,00	,00

a. The median survival time is 15,851

Table 6b. Life table in survival analysis of 5 tympanostomy procedures in 3 Cavalier King Charles spaniels diagnosed with PSOM. The recurrence rate was obtained by subtracting the cumulative proportion surviving at 40 months of 100%.

Interval Start Time	Number Entering Interval	Number Withdrawing during Interval	Number Exposed to Risk	Number of Terminal Events	Proportion Terminating	Proportion Surviving	Cumulative Proportion Surviving at End of Interval	Std. Error of Cumulative Proportion Surviving at End of Interval	Probability Density	Std. Error of Probability Density	Hazard Rate	Std. Error of Hazard Rate
0	5	0	5,000	1	,20	,80	,80	,18	,200	,179	,22	,22
1	4	0	4,000	0	,00	1,00	,80	,18	,000	,000	,00	,00
2	4	0	4,000	0	,00	1,00	,80	,18	,000	,000	,00	,00
3	4	0	4,000	1	,25	,75	,60	,22	,200	,179	,29	,28
4	3	0	3,000	0	,00	1,00	,60	,22	,000	,000	,00	,00
5	3	0	3,000	1	,33	,67	,40	,22	,200	,179	,40	,39
6	2	0	2,000	1	,50	,50	,20	,18	,200	,179	,67	,63
7	1	0	1,000	0	,00	1,00	,20	,18	,000	,000	,00	,00
8	1	0	1,000	0	,00	1,00	,20	,18	,000	,000	,00	,00
9	1	0	1,000	0	,00	1,00	,20	,18	,000	,000	,00	,00
10	1	0	1,000	0	,00	1,00	,20	,18	,000	,000	,00	,00
11	1	0	1,000	0	,00	1,00	,20	,18	,000	,000	,00	,00
12	1	0	1,000	1	1,00	,00	,00	,00	,200	,179	2,00	,00

a. The median survival time is 5,500

Table 6c. Survival table in Kaplan-Meier survival analysis of 30 myringotomy (M) procedures compared to 5 tympanostomy (T) procedures.

Procedure	Time	Status	Cumulative Proportion Surviving at the Time		N of Cumulative Events	N of Remaining Cases
			Estimate	Std. Error		
M 1	,500	1	.	.	1	29
2	,500	1	,933	,046	2	28
3	1,000	1	.	.	3	27
4	1,000	1	.	.	4	26
5	1,000	1	,833	,068	5	25
6	1,000	0	.	.	5	24
7	1,000	0	.	.	5	23
8	1,500	1	.	.	6	22
9	1,500	1	,761	,079	7	21
10	2,000	0	.	.	7	20
11	3,000	1	,723	,084	8	19
12	6,000	1	.	.	9	18
13	6,000	1	,647	,091	10	17
14	8,000	1	.	.	11	16
15	8,000	1	,571	,095	12	15
16	13,000	1	,533	,096	13	14
17	15,000	1	,495	,096	14	13
18	36,000	1	,457	,096	15	12
19	37,000	1	,418	,095	16	11
20	40,000	0	.	.	16	10
21	40,000	0	.	.	16	9
22	40,000	0	.	.	16	8
23	40,000	0	.	.	16	7
24	40,000	0	.	.	16	6
25	40,000	0	.	.	16	5
26	40,000	0	.	.	16	4
27	40,000	0	.	.	16	3
28	40,000	0	.	.	16	2
29	40,000	0	.	.	16	1
30	40,000	0	.	.	16	0
T 1	,500	1	,800	,179	1	4
2	3,500	1	,600	,219	2	3
3	5,000	1	,400	,219	3	2
4	6,000	1	,200	,179	4	1
5	12,000	1	,000	,000	5	0

Table 6d. Means and medians for survival time in Kaplan-Meier survival analysis of 30 myringotomy procedures compared to 5 tympanostomy procedures.

Procedure	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
M	22,003	3,359	15,419	28,587	15,000	18,307	,000	50,883
T	5,400	1,893	1,689	9,111	5,000	1,643	1,779	8,221
Overall	19,353	3,049	13,376	25,329	12,000	4,831	2,531	21,469

a. Estimation is limited to the largest survival time if it is censored.

Table 6e. Results of the recurrence-free survival analyses for the impact of the type of procedure (myringotomy versus tympanostomy).

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	5,211	1	,022

Test of equality of survival distributions for the different sorts of procedures.

Table 7a. Means and medians for survival time in Kaplan-Meier survival analysis of 5 tympanostomy procedures in this study compared to 4 tympanostomy procedures previously described.

	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
Data	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
Literature	6,250	1,181	3,934	8,566	6,000	1,667	2,733	9,267
Own data	5,400	1,893	1,689	9,111	5,000	1,643	1,779	8,221
Overall	5,778	1,118	3,586	7,970	6,000	,707	4,614	7,386

a. Estimation is limited to the largest survival time if it is censored.

Table 7b. Results of the recurrence-free survival analyses for the impact of the sort of procedure (obtained data in this study versus described data in previous studies).

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	,105	1	,746

Test of equality of survival distributions for the different levels of VAR00003.