



Dutil, G. F. et al. (2022) Otitis media and interna with or without polyps in cats: association between meningeal enhancement on postcontrast MRI, cerebrospinal fluid abnormalities, and clinician treatment choice and outcome. *Journal of Feline Medicine and Surgery*, 24(12), e481-e489.

There may be differences between this version and the published version. You are advised to consult the publisher's version if you wish to cite from it.

<https://eprints.gla.ac.uk/286919/>

Deposited on: 19 December 2022

Enlighten – Research publications by members of the University of Glasgow
<https://eprints.gla.ac.uk>

1 **OTITIS MEDIA AND INTERNA WITH OR WITHOUT POLYPS IN CATS:**
2 **ASSOCIATION BETWEEN MENINGEAL ENHANCEMENT ON POST-**
3 **CONTRAST MRI, CSF ABNORMALITIES AND CLINICIAN TREATMENT**
4 **CHOICE AND OUTCOME**

5
6 Guillaume F Dutil¹ DVM gdutil@live.fr

7 Julien Guevar² DVM, MVM, DECVN, MRCVS julien.guevar@vetsuisse.unibe.ch

8 Daniela Schweizer³ DVM, DECVDI daniela.schweizer@vetsuisse.unibe.ch

9 Petra Roosje⁴ DVM, DECVD, PhD petra.roosje@vetsuisse.unibe.ch

10 Filip Kajin⁵ DVM Filip.Kajin@tiho-hannover.de 0000-0002-8329-9233

11 Holger A Volk⁵ DVM, DECVN, PhD Holger.Volk@tiho-hannover.de

12 Nick J Grapes⁶ BVetMed(hons), PGDipVCP, MRCVS ngrapes@rvc.ac.uk 0000-0002-
13 8849-5508

14 Steven De Decker⁶ DVM, DECVN, PhD SDeDecker@rvc.ac.uk

15 Rodrigo Gutierrez-Quintana⁷ DVM, MVZ, MVM, DECVN, MRCVS

16 Rodrigo.GutierrezQuintana@glasgow.ac.uk 0000-0002-3570-2542

17 Jad Abouzeid⁸ DVM jadle-ab@hotmail.co.uk

18 Paul Freeman⁸ DVM, DECVN, PhD pf266@cam.ac.uk

19 Kiterie Faller⁹ DVM, DECVN, PhD, MRCVS Kiterie.faller@ed.ac.uk 0000-0002-4525-
20 7059

21 Veronika M Stein¹ DVM, DECVN, PhD, DECVN veronika.stein@vetsuisse.unibe.ch

22 Arianna Maiolini¹ DVM, DECVN, PhD, DECVN arianna.maiolini@vetsuisse.unibe.ch

23

24 ¹ *Division of Clinical Neurology, Department of Clinical Veterinary Medicine, Vetsuisse*
25 *Faculty, University of Bern, Bern, Switzerland*

26 ² *Division of Small Animal Surgery, Department of Clinical Veterinary Medicine,*
27 *Vetsuisse Faculty, University of Bern, Bern, Switzerland*

28 ³ *Division of Radiology, Department of Clinical Veterinary Medicine, Vetsuisse Faculty,*
29 *University of Bern, Bern, Switzerland*

30 ⁴ *Division of Dermatology, Department of Clinical Veterinary Medicine, Vetsuisse*
31 *Faculty, University of Bern, Bern, Switzerland*

32 ⁵ *Department of Small Animal Medicine and Surgery, University of Veterinary Medicine*
33 *Hannover, Germany*

34 ⁶ *Department of Clinical Science & Services, Royal Veterinary College, University of*
35 *London, Hatfield, United Kingdom*

36 ⁷ *Small Animal Hospital, School of Veterinary Medicine, University of Glasgow, United*
37 *Kingdom*

38 ⁸ *Division of Clinical Neurology, Cambridge University, Cambridge, United Kingdom*

39 ⁹ *Hospital for Small Animals, Royal (Dick) School of Veterinary Studies, University of*
40 *Edinburgh, Roslin, United Kingdom*

41

42 Corresponding author:

43 Guillaume F Dutil DVM

44 Neuro4Vets

45 13 rue du clos Gilard

46 44120 Vertou France

47 Objectives: To evaluate the association between meningeal enhancement (MgE)
48 and cerebrospinal fluid (CSF) analysis results, their individual association with
49 bacteriology results from affected ear samples, and whether these test results influenced
50 clinicians' therapeutic choice in cats with otitis media and interna (OMI).

51 Methods: Multicentre retrospective study over an eight-year-period. Cats
52 diagnosed with OMI, with or without a nasopharyngeal polyp, leading to peripheral
53 vestibular signs were included. Only cats for which MRI with post-contrast T1 weighted
54 sequences and CSF analyses were available were included in the study. Cats with intra-
55 axial MRI lesions or empyema were excluded.

56 Results: Fifty-eight cats met the inclusion criteria. MgE was reported in 26/58
57 cases of which 9 had an abnormal CSF result (increased total nucleated cell count (TNCC)
58 or total protein); 32/58 cases had no MgE of which 10 showed abnormal CSF results.
59 There was no association between bacteriology results (external ear canal or bulla) and
60 MgE or abnormal CSF results. CSF abnormalities were more commonly detected in acute
61 cases (16/37) compared to chronic cases (3/21), the difference being statistically
62 significant (Fischer test, $P = 0.04$). Prednisolone was prescribed in 10/16 cases with
63 increased TNCC. Among the 42 cases with normal TNCC, 15/42 received prednisolone,
64 and 13/42 received non-steroidal anti-inflammatory drugs. Various antimicrobial drugs
65 were prescribed in 53/58 cats. Antimicrobial therapy duration was similar regardless of

66 positive bacterial culture (5.58 vs 4.22 weeks), increased TNCC (6.13 vs 4.72 weeks) or
67 MgE (5.33 vs 4.90 weeks).

68 Conclusion and relevance: No association was found between CSF and MgE
69 results. Furthermore, no association was found between MgE, CSF or bacteriology
70 findings, respectively. In addition, abnormal CSF results might lead the clinician to treat
71 with corticosteroids but did not have any impact on antimicrobial therapy length. CSF
72 abnormalities are seen significantly less frequently in chronic cases. Outcome tended to
73 be poorer when MgE is detected on MRI.

74

75 Keywords: Otitis media and interna; Peripheral vestibular signs; MRI, Meningeal
76 enhancement; Cerebrospinal fluid

77 **Introduction**

78 Otitis media and interna (OMI) has been reported to be the cause of cause
79 vestibular signs in 43% to 63% of cats with peripheral vestibular signs (PVS) (1,2). OMI
80 in cats is most commonly associated with inflammation caused by upper respiratory
81 infection that has extended through the auditory tube or a nasopharyngeal polyp (1,3,4).
82 It occurs less frequently as a consequence of an otitis externa or neoplasia. Bacterial
83 isolates from OMI include *Staphylococcus* species, *Streptococcus* species, *Pasteurella*
84 *multocida*, *Escherichia coli*, *Enterococcus* species and less frequently *Mycoplasma*
85 species, *Corynebacterium* species and other bacterial species (1,4–8). Apart from
86 bacteria, cats can have other infectious agents being involved, especially fungi
87 (*Malessezia*) (8). Occasionally a nasopharyngeal polyp, a non-neoplastic, inflammatory
88 growth that arises from the middle ear or the auditory tube, can be responsible for OMI
89 (1,2,9,10). Diagnosis of otitis media and bacterial infection in the bulla can be reached
90 via cytological and/or bacterial culture of material retrieved via myringotomy or surgical
91 procedure such as bulla osteotomy (1,8,9). Cats with PVS are clinically recognized with
92 the presence of at least one of the following clinical signs: ipsilateral head tilt, jerk
93 nystagmus, tight circling, positional strabismus and/or vestibular ataxia and the absence
94 of any neurologic signs suggestive of intracranial disease. (11–13). PVS reflect the
95 involvement of the inner ear, while presence of facial nerve deficit and/or Horner
96 syndrome indicates the involvement of the middle ear (11–13).

97 MRI is a sensitive method to diagnose OMI, particularly for inner ear visualization
98 (1,7,14). The fluid composition of endo- and perilymph allows a good visualization of
99 this inner ear part in a fluid sensitive sequence such as T2-weighted (T2W) images or in
100 fluid-attenuated inversion recovery (FLAIR) (14,15). A marked hyperintensity compared
101 to adjacent structures is present on T2W images while a suppression is visible in FLAIR
102 (14,15). Post-contrast T1-weighted images may show abnormality consistent with
103 inflammatory changes in the inner ear. (1) Typical changes raising the suspicion of OMI
104 include isointense material in the bulla on T1W images and hyperintense on T2W images.
105 On post-contrast T1W images, a peripheral enhancement along the inner surface of the
106 tympanic bulla can be observed (7,16). A laminated appearance of the mucosa of the
107 tympanic bulla on T2W images has also been described (17). A reduced signal intensity
108 on T2W or an increase signal intensity on FLAIR images from the intralabyrinthine fluid
109 are MRI finding suggestive of otitis interna (14,16,18). Due to anatomical proximity,
110 intracranial extension of OMI can lead to a meningeal enhancement (MgE) on MRI after
111 intravenous administration of paramagnetic contrast medium (19). Anatomically,
112 perilymph and cerebrospinal fluid (CSF) are connected via the cochlear aqueduct (20).
113 Therefore, CSF analysis is another important diagnostic tool for cats with OMI and is
114 reported to be more sensitive than MRI to identify intracranial inflammatory processes
115 (7,15,21). Thus, an abnormal MRI and/or CSF analysis can provide useful clinical
116 information on the presence of a concurrent meningitis and may influence the therapy.

117 The relationship between MgE and abnormal CSF in cats with OMI has not yet
118 been investigated, neither have their association with bacteriology results and therapeutic
119 management. The aims of this study were to describe the association between MgE and
120 CSF analysis results, their individual association with bacteriology results from affected
121 ear samples, and the influence of the above with therapeutic choice in cats with OMI. We
122 hypothesize that (a) MgE is associated with CSF abnormalities, (b) positive bacteriology
123 is more common if MgE and/or CSF abnormalities are present and (c) positive
124 bacteriology is associated with the choice and length of antimicrobial and/or anti-
125 inflammatory therapy.

126 **Materials and Methods**

127 **Selection criteria**

128 Data were retrospectively collected from six different referral centres across
129 Europe (Vetsuisse-Faculty, University of Bern; University of Veterinary Medicine
130 Hannover, Foundation; Royal Veterinary College London (RVC); School of Veterinary
131 Medicine, University of Glasgow; Queen's Veterinary School Hospital, University of
132 Cambridge, and Royal (Dick) School of Veterinary Studies, University of Edinburgh)
133 over an eight-year-period (January 2012 to December 2020). Only client-owned cats with
134 peripheral vestibular signs that underwent MRI (with post-contrast images) and CSF
135 analysis as part of the diagnostic work up were selected for this study. Inclusion criteria
136 were: (1) clinical signs consistent with peripheral vestibular lesion localisation, (2) a
137 diagnosis of otitis media and interna with or without the presence of a nasopharyngeal
138 polyp based on MRI findings, (3) absence of intra-axial abnormality or imaging findings
139 consistent with empyema on MRI.

140 Retrospective information collected from the medical records included
141 signalment, history, therapy prior and after referral, side of PVS, MRI and CSF findings,
142 bacteriology results from affected ear, and outcome.

143 **MRI**

144 The MRI images of the skull were obtained under general anesthesia, using
145 anesthetic protocols at the discretion of the anesthesiologist in charge. High-field MRI
146 were used at all institutions (except for one cat) and varied between centres: a Philips
147 Panorama HFO 1.0 T (Philips Medical Systems Nederland B.V., Best, Netherlands) for
148 Bern, a Philips Achieva 3.0 T (Philips Medical Systems, Best, The Netherlands) for
149 Hannover, 1.5T (Intera; Philips Medical Systems, Amsterdam, Netherlands) for RVC,
150 1.5T (Magnetom Essenza Siemens) for Glasgow, 0.27T (Esaote VetMR Grande, Genova,
151 Italy) or 1.5 T (Phillips Achieva, Phillips Healthcare, Best, Netherlands) for Cambridge
152 and 1.5 T (Intera; Philips Medical Systems, Amsterdam, Netherlands) for Edinburgh.
153 Although MRI protocols varied between centres, in all cats, at least T1-weighted T1W,
154 T2W and T1W post-contrast images were available (IV of 0.2 mmol/kg gadoteric acid
155 [Dotarem; Guebert Laboratories] for Bern and Hannover, IV of 0.1 mmol/kg gadoterate
156 meglumine [Dotarem; Guerbet, Milton Keynes, UK] for RVC, [Gadovist, Bayer] for
157 Glasgow & Cambridge and 0.1 mmol/kg gadopentate dimeglumine [Magnevist, Bayer]
158 for Edinburgh). All MR images had been evaluated by a board-certified veterinary
159 radiologist or a board-certified veterinary neurologist. Information about OMI with or
160 without nasopharyngeal polyp and MgE were collected directly from MRI reports.

161

162 **CSF analysis**

163 Abnormal CSF was defined as a total nucleated cell count (TNCC) ≥ 5 leukocytes
164 per μL and/or increased total protein > 0.3 g/L for cisterna magna samples and > 0.45 g/L
165 for lumbar samples. Albuminocytologic dissociation was defined as an increase in total
166 protein without an increased TNCC. Neutrophilic (respectively monocytic) pleocytosis is
167 identified if there is $> 70\%$ of neutrophils (respectively monocytes) in a CSF with
168 abnormal TNCC. (22)

169

170 **Medical treatment**

171 Antimicrobials were categorized as first or second line of treatment. First line
172 included amoxiclav, cephalosporin, metronidazole, clindamycin and doxycycline.
173 Second line contained marbofloxacin, enrofloxacin, cefovecine, pradofloxacin and
174 cefixime. (23)

175 Anti-inflammatory drugs were categorized as steroidal (eg, prednisolone,
176 dexamethasone) or non-steroidal (eg, meloxicam, robenacoxib).

177

178 **Statistical analysis**

179 The presence or absence of MgE on MRI, the CSF results and bacteriology culture
180 results were compared using a χ^2 test. The choice of therapy based on MgE, CSF and
181 bacteriology results were compared using a χ^2 test or a Fischer's exact test if a group
182 contained less than 5 cats. Duration of therapy was compared using a Student's t-test. Test
183 values were performed two-sided and a value of $P \leq 0.05$ was considered statistically
184 significant. All analyses were performed using R version 3.6.3.

185 **Results**

186 A total of fifty-eight cats met the inclusion criteria. Domestic shorthair cats were
187 the most common breed (32/58 cats). Other breeds were Maine Coon (9), Siamese (4),
188 British Short Hair (2), Burmese (2), Russian Blue (2), Bengal (1), Egyptian Mau (1),
189 Norwegian (1), Ocicat (1), Persian (1), Ragdoll (1), and Snowshoe (1). There were 27
190 females (four intact, 23 spayed) and 31 males (four intact, 27 neutered; sex ratio
191 male/female = 1.15). The mean age of the cats was 6.9 years (median = 7.3 years, range:
192 3.7 months to 14.7 years). Half of the cases had left vestibular signs at time of
193 presentation. Clinical signs were acute (≤ 14 days) in 37 cats and chronic (> 14 days) in
194 21 cats. Medical treatment before presentation was given in 32 cats. Nine cases received
195 antimicrobial therapy alone, eight had an antimicrobial therapy with non-steroidal anti-
196 inflammatory drugs, nine had an antimicrobial therapy with corticosteroids, and two had
197 an antimicrobial therapy, non-steroidal anti-inflammatory drugs, and corticosteroids. Five
198 cats received only corticosteroids and one only a non-steroidal anti-inflammatory drug.
199 All clinical information from cases are available in supplementary material.

200 Forty-five cats (78%) were diagnosed with OMI alone (without a nasopharyngeal
201 polyp) (Figure 1 (a), 2 (a) and (c)): three based on histology of material obtained from
202 bulla osteotomy, three based on findings during bulla osteotomy, 26 based on otoscopy
203 and cytology results obtained through myringotomy and 13 were suspected on MRI only.
204 The remaining cats (13/58, 22%) were diagnosed with OMI secondary to a polyp (Figure

205 3 (a) and 4 (a): six based on histology of material obtained from bulla osteotomy, two
206 based on findings during bulla osteotomy, two based on otoscopy and/or cytology results
207 obtained through myringotomy and two were suspected on MRI only.

208

209 Meningeal contrast enhancement was present in 26/58 cases (45%) (Figure 2 (b)
210 and 4 (b)) while 32/58 cases (55%) did not show MgE (Figure 1 (b) and 3 (b)). CSF
211 analysis was abnormal in 19/58 (33%) cats. Eleven of them with only increased TNCC,
212 five with both increased TNCC and total protein and three with albuminocytologic
213 dissociation. Increased TNCC ranged between five and 1205 leukocytes / μ L (median =
214 12) and increased total protein in CSF ranged between 0.34 and 0.77 g/L (median = 0.56).
215 Neutrophilic pleocytosis was seen in nine cases, monocytic pleocytosis was seen in one
216 case and mixed cell pleocytosis in six cases.

217 Nine of 58 cats (16%) presented both MgE and abnormal CSF (five with only
218 increased TNCC, two with both increased TNCC and total protein and two with
219 albuminocytologic dissociation). MgE was detected in 17/58 cats (29%) with normal
220 CSF. Abnormal CSF was seen in a total of 10/32 cats (31%) without MgE: 6 with only
221 increased TNCC, three with both increased TNCC and total protein and one with
222 albuminocytologic dissociation. No significant association (χ^2 test, $P = 0.79$) was found
223 between CSF results and MgE findings (Table I).

224 CSF abnormalities were more commonly detected in acute cases (16/37)
225 compared to chronic cases (3/21), the difference being statistically significant (Fischer
226 test, $P = 0.04$), while MgE was similar in acute (15/37) and chronic (11/21) cases.
227 Furthermore, none of the chronic cases presented an abnormal CSF without MgE (Table
228 II). No association was found between the use of anti-inflammatory drugs before MRI
229 and CSF analysis (Table III) or the presence or absence of a polyp (Table IV) and MgE
230 or CSF abnormalities.

231

232 Bacterial culture was performed in 45/58 cases. Samples were collected from bulla
233 osteotomy in 13 cases, myringotomy in 28 cases, and external ear canal in four cases.
234 Negative bacterial culture was observed in 33/45 cases, of which thirteen (39%) received
235 antimicrobial therapy before sampling. The percentage of negative bacterial culture was
236 73% in both acute (21/30) and chronic (11/15) cases.

237 Twelve cases showed a positive bacterial culture: six for *Staphylococcus* species,
238 three for *Pasteurella* species, one for *Streptococcus canis*, one for *Actinomyces pyogenes*
239 and one with both *Streptococcus equi subspecies zooepidemicus* and *Staphylococcus felis*.
240 Among these cases, seven out of twelve (58%) received antimicrobial therapy before
241 sampling.

242 The results of the bacterial culture depending on presence/absence of MgE and
243 normal/abnormal CSF findings are summarized in Table V. No statistical association was

244 found between a positive bacterial culture and MgE (χ^2 , $P = 0.82$) or CSF results (χ^2 test,
245 $P = 0.15$). One observation was that if no MgE was seen on MRI images and no
246 abnormality was detected on CSF analysis, the likelihood to get a **negative ear sample**
247 bacterial culture from myringotomy or bulla osteotomy was only about 12% (2/17 cases).
248 One cat had a positive culture from CSF (*Clostridium beijerinckii* and *Enterococcus*
249 *faecalis*) despite no positive bacterial culture ear sample from myringotomy and
250 clindamycin therapy for three days.

251

252 Twenty-five cats received corticosteroids and 13 received non-steroidal anti-
253 inflammatory drugs after diagnosis. Choice of anti-inflammatory drugs according to
254 MgE, CSF or bacteriology findings is summarized in Table VI. No significant difference
255 (χ^2 test, $P = 0.53$ for MgE; Fischer test, $P = 0.08$ for CSF; Fischer test, $P = 0.62$ for
256 bacteriology) was identified although corticosteroids seem to be chosen more often in
257 case of abnormal CSF (11 cases versus 1 case). A total of 54 cats (93%) received
258 antimicrobial therapy after diagnosis. Twenty-six out of 54 (48%) had antimicrobial
259 therapy started prior to referral while it was started by the referral centre after diagnosis
260 in twenty-eight cases (52%). Thirty-nine received first line antimicrobials, seven received
261 second line and eight received both. Duration of antimicrobial treatment depending on
262 MgE, CSF or bacteriology findings are summarized in Table VII. Antimicrobial therapy
263 duration tended to be longer in case of positive culture (5.58 vs 4.22 weeks) or when CSF

264 findings were abnormal (5.83 vs 4.76 weeks), although this difference was not
265 statistically significant (Student's t-test).

266 Association between CSF results, MgE and outcome are described in table VIII.
267 Good outcome is defined by an improvement of clinical signs (and euthanasia unrelated
268 to the disease after several months). Poor outcome is defined by an absence of
269 improvement or euthanasia. Although cases with MgE tend to have poorer outcome
270 (5/18) than without MgE (3/26), the difference was not statistically relevant (Fischer test,
271 $P = 0.24$). No association was found between outcome and CSF abnormalities (Fischer
272 test, $P = 1$). Bulla osteotomy was performed in 14 cases (8 polyps and 6 OMI), between
273 one and 78 days after diagnosis (median = 5). Delayed bulla osteotomies were due to
274 absence of improvement or relapse of clinical signs after initial medical management.
275 Improvement of neurological signs after surgical management was seen in 11 cases (time
276 of follow-up varies between one and 104 weeks including five cases with more than eight
277 weeks of follow-up), relapse in one (three months after surgery) and three cases were lost
278 to follow-up. None of the surgical cases were euthanized for reasons related to the OMI.
279 Medical management resulted in improvement in 23/44 cases (time of follow-up varies
280 between one and 78 months including 12 cases with more than eight weeks of follow-
281 up). Two cases improved and were euthanized due to unrelated reasons four months and
282 17 months after diagnosis of OMI respectively due to carcinoma and polyarthritis. Three
283 cases did not improve after one month but owners declined surgery. Four cases were

284 euthanized following diagnosis or several weeks after with no improvement on medical
285 therapy. One case showed intermittent vestibular signs and was euthanized 20 months
286 after diagnosis due to seizure-like episodes. Eleven cases were lost to follow-up.

287 **Discussion**

288 The findings of this study show that in a cohort of 58 cats with PVS diagnosed
289 with OMI, MgE is seen in approximately 50% of cases but only 27% of these cases had
290 an abnormal CSF analysis. There was no association between MgE and abnormal CSF
291 results. Chronic cases had significantly fewer abnormal CSF findings. When a treatment
292 was given, its duration was similar regardless of a positive bacterial culture, abnormal
293 CSF analysis or meningeal enhancement. Cases with MgE tend to have poorer outcome.

294

295 The use of MRI to investigate the cause of PVS is common practice in clinical
296 neurology, particularly if concurrent meningitis is suspected. Administration of
297 gadolinium-based contrast medium in MRI has been demonstrated as a more sensitive
298 method to diagnose experimental bacterial meningitis in dogs compared to MRI without
299 contrast or post-contrast CT (23). However, only severe meningeal inflammation at
300 necropsy was correlated with MRI findings while mild inflammation was not detected in
301 MRI leading to the conclusion that the absence of meningeal enhancement does not rule
302 out bacterial meningitis (24). False positive results of diffuse MgE on MRI images
303 without CSF abnormalities have also been previously described (25). MRI also allows a
304 better evaluation of fluid containing inner ear structures than CT and otitis interna can be
305 assessed on T2W images (16,26). More recently, d'Anjou *et al.* (2012) and Keenihan *et*
306 *al.* (2013) compared MR sequences for detecting MgE in dogs. Post-contrast T1W and

307 T1W fat suppression were found to be the sequences of choice to detect meningeal
308 inflammation (27,28). In previous studies in cats with OMI, only one case with focal
309 meningitis resembled our population of cats with MgE, without intra-axial lesion or
310 empyema. This case had an abnormal CSF analysis (1). In dogs, few studies describe
311 naturally occurring OMI leading to meningeal enhancement in T1W images after
312 gadolinium administration but no large study focusing on this aspect has been done;
313 therefore its clinical consideration remains unknown (16,29,30).

314 Despite the first hypothesis that MgE is associated with abnormal CSF findings,
315 a discrepancy between MgE and CSF results was found in 47% of cases. Indeed, MgE
316 was seen more frequently in cases with unremarkable CSF analysis (65%) and abnormal
317 CSF can be found without MgE in up to 31% of cases. To the best of the authors'
318 knowledge, no previous report of cats with OMI evaluated the association between the
319 MRI findings and CSF analysis. In previous reports of cats diagnosed with OMI and intra-
320 axial lesions or empyema on MRI, an abnormal CSF was detected in 22/25 cases in which
321 CSF analysis was performed (1,7,31). MgE was specifically described in one of these
322 studies, where none of the five cats with chronic vestibular clinical signs had a MgE while
323 all of the six acute or subacute cases showed MgE (7). The prevalence of MgE is in
324 contrast with our results, in which 11 of 21 chronic cases and 15 of 35 acute cases showed
325 MgE. When available, abnormal CSF analysis was detected in all acute or subacute cases
326 (5/5) and only in 1 of 4 chronic cases (7). These results reflect our findings with

327 significantly fewer CSF abnormalities in chronic cases. Previous treatment with anti-
328 inflammatory drugs or presence of a polyp did not affect presence/absence of MgE or
329 CSF results.

330

331 The second hypothesis was that there would be an association between MgE
332 and/or CSF abnormalities and a positive bacteriology culture. In case of absent MgE and
333 normal CSF, the likelihood of a positive bacterial culture from myringotomy or bulla
334 osteotomy is low (~ 12%). Even if this result is not statistically significant, it could make
335 the clinician aware of the possible need to alter antimicrobial therapy after receiving
336 culture results. Bacteriology results between acute or chronic cases did not differ
337 significantly.

338 We finally hypothesized that positive bacterial culture would influence the choice
339 and length of antimicrobial and/or anti-inflammatory therapy. Due to the retrospective
340 and multicentre aspect of our study, medical management was very variable, making the
341 investigation of the last hypothesis difficult. Generally, a long term (4 to 8 weeks), broad-
342 spectrum antimicrobial therapy or, ideally, a therapy based on *in vitro* antimicrobial
343 sensitivity profile, is recommended to treat OMI in cats and dogs (8). In the current study,
344 duration of therapy was slightly longer in cases of positive bacterial culture than in cases
345 of negative bacterial growth culture (respectively 5.58 weeks vs 4.22 weeks), although

346 the difference was not significant. The similar length of therapy may be due to initial
347 prescription with no improvement of clinical signs or a lack of short-term follow-up by
348 the referring centre. Also, if anti-inflammatory drugs were to be implemented after
349 abnormal CSF results, clinicians tended to use corticosteroids more frequently. These
350 results could reflect a clinicians' preference for corticosteroids in case of CNS
351 inflammation. However, clinicians need to remember about the lack of CSF abnormalities
352 in chronic cases, despite meningeal inflammation.

353 Culture results from samples taken from the external ear canal have to be
354 interpreted with caution. Common microorganisms can be detected in the tympanic bulla
355 of healthy cats in up to 25% of cases (32). Bacteria have been previously cultured from
356 48% of healthy canine external ears (33). Moreover, up to 67% of myringotomies
357 performed via video-otoscopy might be contaminated even if microorganisms were
358 detected only in 15.4% of the samples (34). The presence or absence of bacteria on culture
359 should not be considered as critical in formulating a treatment plan as the type of bacteria
360 that are cultured (that is, whether they are likely of external ear canal origin and/or
361 possible iatrogenic contaminants versus a likely cause of middle ear infection). The lack
362 of a cultured infectious agent in our case series with the presumed presence of OMI raises
363 the question of a purely inflammatory mechanism leading to otitis interna.

364 Age of cats, uni- or bilateral vestibular signs distribution, proportion of OMI with
365 or without polyps and type of bacteria cultured were similar to previously published

366 literature (1,2,13,35). In this cohort cases with identified MgE tend to have poorer
367 prognosis than those without MgE however this difference was not statistically
368 significant, while an abnormal CSF result was not associated with any difference in
369 outcome. This finding might help clinicians to anticipate and maybe adapt the therapy for
370 such cases. Surgical treatment with bulla osteotomy was performed in fourteen cats
371 (24%), including four in which it was performed several weeks after diagnosis. This was
372 different to other published studies in which none of the cases with vestibular signs
373 underwent surgery and up to 30% of otitis media cases without neurological signs
374 received bulla osteotomy (1,4). In another study focusing on OMI in cats with intracranial
375 complications, ventral bulla osteotomy was performed more often (12/18 cases, 67%)
376 (31). Surgically managed cases lead to an improvement of neurological status for all cases
377 (13/13) while medical management showed an improvement in 23/31 cases (74%). These
378 results are slightly better than those for cats with OMI and intracranial complication (31).

379

380 There are several limitations to this study. First of all, the retrospective nature is
381 associated with incomplete data and did not allow long term follow-up of cases. A
382 multicentre study with different MRI machines, clinicians and protocols will result in
383 differences in the evaluation of MR images and the clinical management of cases.
384 Concerning case recruitment, cases without MRI and/or CSF analysis were excluded,
385 which may have biased the study population towards potentially more severely affected

386 cases. Clinicians may decide against CSF analyses in those cases where clear MgE is seen
387 on MRI, biasing the population towards a higher number of cases without MgE. A similar
388 bias could also impact the choice of therapy in the cases of the present study. Moreover,
389 the use of medication prior to presentation might have impacted the results of the current
390 study. We decided to exclude all cases presented with intra-axial lesions or empyema on
391 MRI images despite presumed peripheral vestibular lesion localisation as brainstem signs
392 may not be clinically obvious in the neurological examination and might have impacted
393 CSF results (36,37). In dogs, it has been shown that bacterial culture obtained via
394 myringotomy can be contaminated by bacteria from the external ear canal and this could
395 be one limitation for our bacteriology results (34). Time of acquisition in dogs and higher
396 dose of gadolinium in humans may induce false negative meningeal enhancement
397 (28,38). False positive MgE may also occur (25).

398

399 **Conclusion**

400 In this study, no association was found between MgE and CSF results. Nearly half
401 of the cases (47%) showed a discrepancy between MRI and CSF findings. Additionally,
402 the lack of MgE in MRI does not rule out the presence of a meningitis pathologically.
403 Hence, CSF analysis may be useful to detect the presence of possible concurrent
404 meningitis in cats with OMI. CSF findings and MgE results were not associated with
405 likelihood of a positive or negative middle ear bacterial culture. Abnormal CSF results
406 seemed to influence the clinicians' choice of anti-inflammatory drugs with a preference
407 for glucocorticoids versus non-steroidal anti-inflammatory drugs. Abnormal CSF results
408 were seen less frequently in chronic cases than acute cases in this study. Additionally, the
409 identification of an abnormal CSF analysis did not seem to notably influence the length
410 of antimicrobial therapy, which remains the mainstay for this presumed infectious
411 disease. Outcome tend to be poorer when MgE is detected on MRI.

412 **References**

- 413 1. Negrin A, Cherubini GB, Lamb C, et al. **Clinical signs, magnetic resonance**
414 **imaging findings and outcome in 77 cats with vestibular disease: A**
415 **retrospective study.** *Journal of Feline Medicine and Surgery.* 2010 Apr
416 1;12(4):291–9.
- 417 2. Grapes NJ, Taylor-Brown FE, Volk H, et al. **Clinical reasoning in feline**
418 **vestibular syndrome: which presenting features are the most important?**
419 *Journal of Feline Medicine and Surgery.* 2021 Aug 1;23(8):669–78.
- 420 3. Harvey RG, Haar G ter. **Ear, Nose and Throat Diseases of the Dog and Cat.**
421 Boca Raton: CRC Press; 2016. 520 p.
- 422 4. Swales N, Foster A, Barnard N. **Retrospective study of the presentation,**
423 **diagnosis and management of 16 cats with otitis media not due to**
424 **nasopharyngeal polyp.** *Journal of Feline Medicine and Surgery.* 2018
425 Dec;20(12):1082–6.
- 426 5. Ackermann AL, Lenz JA, May ER, et al. **Mycoplasma infection of the middle**
427 **ear in three cats.** *Veterinary Dermatology.* 2017;28(4):417-e102.
- 428 6. Henneveld K, Rosychuk RAW, Olea-Popelka FJ, et al. **Corynebacterium spp. in**
429 **Dogs and Cats with Otitis Externa and/or Media: A Retrospective Study.**
430 *Journal of the American Animal Hospital Association.* 2012 Sep 1;48(5):320–6.
- 431 7. Sturges BK, Dickinson PJ, Kortz GD, et al. **Clinical Signs, Magnetic Resonance**
432 **Imaging Features, and Outcome After Surgical and Medical Treatment of**
433 **Otogenic Intracranial Infection in 11 Cats and 4 Dogs.** *Journal of Veterinary*
434 *Internal Medicine.* 2006;20(3):648–56.
- 435 8. Gotthelf LN. **Diagnosis and treatment of otitis media in dogs and cats.**
436 *Veterinary Clinics of North America: Small Animal Practice.* 2004
437 Mar;34(2):469–87.
- 438 9. Vernau KM, LeCouteur RA. **Feline Vestibular Disorders. Part II: Diagnostic**
439 **Approach and Differential Diagnosis.** *Journal of Feline Medicine and Surgery.*
440 1999 Jun 1;1(2):81–8.

- 441 10. Kudnig ST. **Nasopharyngeal polyps in cats.** *Clinical Techniques in Small*
442 **Animal Practice.** 2002 Nov 1;17(4):174–7.
- 443 11. Cook LB. **Neurologic evaluation of the ear.** *Veterinary Clinics of North*
444 *America: Small Animal Practice.* 2004 Mar 1;34(2):425–35.
- 445 12. Garosi LS, Lowrie ML, Swinbourne NF. **Neurological Manifestations of Ear**
446 **Disease in Dogs and Cats.** *Veterinary Clinics of North America: Small Animal*
447 *Practice.* 2012 Nov 1;42(6):1143–60.
- 448 13. Rossmeis JH. **Vestibular Disease in Dogs and Cats.** *Veterinary Clinics of North*
449 *America: Small Animal Practice.* 2010 Jan 1;40(1):81–100.
- 450 14. Castillo G, Parmentier T, Monteith G, et al. **Inner ear fluid-attenuated inversion**
451 **recovery MRI signal intensity in dogs with vestibular disease.** *Veterinary*
452 *Radiology & Ultrasound.* 2020;61(5):531–9.
- 453 15. Foth S, Meller S, De Decker S, et al. **Unilateral decrease in inner ear signal in**
454 **fluid-attenuated inversion recovery sequences in previously suspected canine**
455 **idiopathic vestibular syndrome.** *The Veterinary Journal.* 2021 Nov
456 1;277:105748.
- 457 16. Garosi LS, Dennis R, Penderis J, et al. **Results of magnetic resonance imaging in**
458 **dogs with vestibular disorders: 85 cases (1996–1999).** *Journal of the American*
459 *Veterinary Medical Association.* 2001 Feb 1;218(3):385–91.
- 460 17. Dvir E, Kirberger RM, Terblanche AG. **Magnetic Resonance Imaging of Otitis**
461 **Media in a Dog.** *Veterinary Radiology & Ultrasound.* 2000;41(1):46–9.
- 462 18. Bischoff MG, Kneller SK. **Diagnostic imaging of the canine and feline ear.**
463 *Veterinary Clinics of North America: Small Animal Practice.* 2004 Mar
464 1;34(2):437–58.
- 465 19. Mellema LM, Samii VF, Vernau KM, et al. **Meningeal Enhancement on**
466 **Magnetic Resonance Imaging in 15 Dogs and 3 Cats.** *Veterinary Radiology &*
467 *Ultrasound.* 2002;43(1):10–5.
- 468 20. Salt AN, Hirose K. **Communication Pathways to and from the Inner Ear and**
469 **their Contributions to Drug Delivery.** *Hear Res.* 2018 May;362:25–37.

- 470 21. Bohn AA, Wills TB, West CL, et al. **Cerebrospinal fluid analysis and magnetic**
471 **resonance imaging in the diagnosis of neurologic disease in dogs: a**
472 **retrospective study.** *Veterinary Clinical Pathology.* 2006;35(3):315–20.
- 473 22. Cook J, Levine G. Chapter 14 - **Cerebrospinal Fluid and Central Nervous**
474 **System Cytology.** In: *Diagnostic Cytology and Hematology of the Dog and Cat.*
475 4th ed. Elsevier; 2014. p. 222–43.
- 476 23. Beco L, Guaguère E, Méndez CL, et al. **Suggested guidelines for using systemic**
477 **antimicrobials in bacterial skin infections: part 2— antimicrobial choice,**
478 **treatment regimens and compliance.** *Veterinary Record.* 2013;172(6):156–60.
- 479 24. Mathews V, Kuharik M, Edwards M, et al. Dyke award. **Gd-DTPA-enhanced**
480 **MR imaging of experimental bacterial meningitis: evaluation and comparison**
481 **with CT.** *American Journal of Roentgenology.* 1989 Jan 1;152(1):131–6.
- 482 25. Ives EJ, Rousset N, Heliczner N, et al. **Exclusion of a Brain Lesion: Is**
483 **Intravenous Contrast Administration Required after Normal Precontrast**
484 **Magnetic Resonance Imaging?** *J Vet Intern Med.* 2014;28(2):522–8.
- 485 26. Benigni L, Lamb C. **Diagnostic imaging of ear disease in the dog and cat.** In
486 *Practice.* 2006 Mar 1;28(3):122–30.
- 487 27. Keenihan EK, Summers BA, David FH, et al. **Canine Meningeal Disease:**
488 **Associations Between Magnetic Resonance Imaging Signs and Histologic**
489 **Findings.** *Veterinary Radiology & Ultrasound.* 2013;54(5):504–15.
- 490 28. d’Anjou MA, Carmel ÉN, Blond L, et al. **Effect of Acquisition Time and**
491 **Chemical Fat Suppression on Meningeal Enhancement on Mr Imaging in**
492 **Dogs.** *Veterinary Radiology & Ultrasound.* 2012;53(1):11–20.
- 493 29. Garosi LS, Dennis R, Schwarz T. **Review of Diagnostic Imaging of Ear Diseases**
494 **in the Dog and Cat.** *Veterinary Radiology & Ultrasound.* 2003;44(2):137–46.
- 495 30. Orlandi R, Gutierrez-Quintana R, Carletti B, et al. **Clinical signs, MRI findings**
496 **and outcome in dogs with peripheral vestibular disease: a retrospective study.**
497 *BMC Vet Res.* 2020 May 25;16:159.
- 498 31. Moore SA, Bentley RT, Carrera-Justiz S, et al. **Clinical features and short-term**
499 **outcome of presumptive intracranial complications associated with otitis**

- 500 **media/interna: a multi-center retrospective study of 19 cats (2009–2017).**
501 Journal of Feline Medicine and Surgery. 2019 Feb 1;21(2):148–55.
- 502 32. Klose TC, MacPhail CM, Schultheiss PC, et al. **Prevalence of select infectious**
503 **agents in inflammatory aural and nasopharyngeal polyps from client-owned**
504 **cats.** Journal of Feline Medicine and Surgery. 2010 Oct 1;12(10):769–74.
- 505 33. Matsuda H, Tojo M, Fukui K, et al. **The aerobic bacterial flora of the middle**
506 **and external ears in normal dogs.** Journal of Small Animal Practice.
507 1984;25(5):269–74.
- 508 34. Reinbacher E, Kneissl S, Hirt R, et al. **Myringotomy in dogs: Contamination**
509 **rate from the external ear canal - a pilot study.** Vet Anim Sci. 2020
510 Dec;10:100125.
- 511 35. Rosser EJ. **Causes of otitis externa.** Veterinary Clinics: Small Animal Practice.
512 2004 Mar 1;34(2):459–68.
- 513 36. Bongartz U, Nessler J, Maiolini A, et al. **Vestibular disease in dogs: association**
514 **between neurological examination, MRI lesion localisation and outcome.**
515 Journal of Small Animal Practice. 2020 Jan;61(1):57–63.
- 516 37. Boudreau CE, Dominguez CE, Levine JM, et al. **Reliability of interpretation of**
517 **neurologic examination findings for the localization of vestibular dysfunction**
518 **in dogs.** Journal of the American Veterinary Medical Association. 2018 Mar
519 19;252(7):830–8.
- 520 38. Runge VM, Wells JW, Williams NM, et al. **Detectability of Early Brain**
521 **Meningitis with Magnetic Resonance Imaging.** Investigative Radiology. 1995
522 Aug;30(8):484–95.

524 **Figures**

525 Figure 1 - MRI (Philips Panorama HFO 1.0 T) transverse images in T1W sequence (a)
526 and T1W post-contrast sequence (b) of a cat presented with an otitis media-interna
527 without polyp (*) and without meningeal enhancement.

528

529 Figure 2 - MRI (Philips Panorama HFO 1.0 T) transverse images in T1W sequence (a),
530 T1W post-contrast sequence (b) and T2W sequence (c) of a cat presented with a bilateral
531 otitis media-interna without polyp (*), with meningeal and vestibulocochlear nerve
532 enhancement (white arrowhead) and otitis interna (yellow arrowhead).

533

534 Figure 3 - MRI (Philips Panorama HFO 1.0 T) transverse images in T1W sequence (a)
535 and T1W post-contrast sequence (b) of a cat presented with an otitis media-interna
536 associated with a polyp (X) and without meningeal enhancement.

537

538 Figure 4 - MRI (Philips Panorama HFO 1.0 T) transverse images in T1W sequence (a)
539 and T1W post-contrast sequence (b) of a cat presented with an otitis media-interna
540 associated with a polyp (X) and with meningeal and vestibulocochlear nerve
541 enhancement (white arrowhead).

542 **Supplementary material**

543 The following file is available online: table of cases

544

545

546 **Conflict of Interest**

547 The authors declared no potential conflicts of interest with respect to the research,

548 authorship, and/or publication of this article.

549

550

551 **Funding**

552 The authors received no financial support for the research, authorship, and/or publication

553 of this article.

554

555

556 **Ethical Approval**

557 The work described in this manuscript involved the use of non-experimental (owned or

558 unowned) animals. Established internationally recognised high standards ('best practice')

559 of veterinary clinical care for the individual patient were always followed and/or this work
560 involved the use of cadavers. Ethical approval from a committee was therefore not
561 specifically required for publication in JFMS. Although not required, where ethical
562 approval was still obtained, it is stated in the manuscript.

563

564

565 **Informed consent**

566 Informed consent (verbal or written) was obtained from the owner or legal custodian of
567 all animal(s) described in this work (experimental or non-experimental animals, including
568 cadavers) for all procedure(s) undertaken (prospective or retrospective studies).

569 No animals or people are identifiable within this publication, and therefore additional
570 informed consent for publication was not required.