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ORIGINAL RESEARCH

# Complications associated with cerebrospinal fluid collection in dogs

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## Abstract

**Background:** This study aimed to identify complications associated with cerebrospinal fluid (CSF) collection in dogs.

**Methods:** This was a prospective, observational multicentre study using data collected from 102 dogs undergoing CSF collection for the investigation of neurological disease. CSF was collected from the cerebellomedullary cistern (CMC), lumbar subarachnoid space (LSAS) or both sites. Pre-, intra- and postprocedural data were collected. Descriptive statistics were performed to outline complications associated with CSF collection.

**Results:** CSF sampling was attempted on 108 occasions, and CSF was acquired on 100 occasions (92.6%). Collection from the CMC was more likely to be successful than that from the LSAS. No dogs exhibited neurologic deterioration following CSF collection. There was no significant difference between pre- and post-CSF collection short-form Glasgow composite measure pain scores in ambulatory dogs ($p = 0.13$).

**Limitations:** The scarcity of complications limited the ability to quantify the incidence of some potential complications reported elsewhere.

**Conclusions:** Our results may be used to inform clinicians and owners that CSF sampling is associated with a low frequency of complications when performed by trained personnel.

## INTRODUCTION

Cerebrospinal fluid (CSF) is normally a clear, colourless fluid that performs several roles within the central nervous system, including distribution of nutrients and metabolites, physical support of the neuroparenchyma and participation in regulation of intracranial pressure.[1,2] Sampling of CSF is frequently employed in both human and veterinary neurology patients and can be helpful in the diagnosis and monitoring of several diseases affecting the meninges, brain, spinal cord and nerve roots.[2,3]

Sampling CSF requires a needle to be advanced into the subarachnoid space (SAS) under aseptic conditions. In humans, the technique performed most frequently is a lumbar puncture, whereas in small animal medicine, the sample can be taken from the cerebellomedullary cistern (CMC) or via a lumbar puncture.[4,5] The placement of this needle is inherently invasive, so CSF sampling is subject to procedural complications. In humans, frequently reported complications following lumbar puncture include a headache and back pain, occurring in up to 40% and 17% of patients, respectively.[6–9] Other complications, including brain herniation, introduction of pathogens, haematoma formation or the development of an intraspinal epidermoid tumour, have the potential for serious consequences but fortunately are rare.[10–13]

While potential complications should always be discussed with dog owners prior to CSF sampling, information about the incidence and nature of complications associated with the procedure has not been well described in veterinary medicine. Until recently, available reports in dogs were limited to a single case of haematomyelia, two cases of ascending–descending myelomalacia and four cases of brainstem injury.[14–16] However, a recent study regarding complications associated with CSF sampling in dogs with intracranial neoplasia identified postprocedural complications in 17% of dogs, which included apneoas, absent pupillary light reflexes, altered level of consciousness and brain parenchymal herniation.[17] The aims of this study

were to therefore evaluate the incidence of complications associated with CSF sampling in dogs, and to characterise the types of complications encountered.

## MATERIALS AND METHODS

### Case selection and inclusion criteria

Dogs undergoing CSF collection at the University of Liverpool and University of Edinburgh between June 2020 and December 2021 were prospectively recruited. Inclusion criteria were that the dog required CSF sampling as part of its diagnostic evaluation, informed client consent had been obtained, and collection of the dog's signalment information and pre-, intra- and postprocedural data were performed. The final diagnosis was recorded (when available) from review of the patient's medical record. Dogs were excluded if pre- or intraprocedural details were incomplete.

### Data collection

The following data were extracted from the patient record at the time of admission: age, breed, sex, neuter status, bodyweight, body condition score (BCS, nine-point scale), neurological examination findings and short-form Glasgow composite measure pain scale (CMPS-SF) score. Hyperaesthesia alone was not considered a neurological deficit. A platelet count was recorded if haematological assessment had been requested by the attending clinician. The premedication agents used prior to induction of general anaesthesia were documented and, in cases in which MRI was performed, whether raised intracranial pressure (ICP) was suspected based on MRI characteristics (effacement of the cerebral sulci, brain herniation, compression of the ventricular system).[18] CSF collection was performed following MRI in all cases, except in cases where disease restricted to the meninges was suspected. Cases that did not undergo CSF sampling due to clinician preference (due to concerns regarding coagulopathy or significant brain herniation) were retrospectively identified from hospital records.

Recorded procedural variables included pre-collection dermatological abnormalities, the collection site (CMC, lumbar subarachnoid space [LSAS] or both sites), length and gauge of spinal needle used, total number of attempts at acquisition (further subdivided into those performed by a resident or a senior clinician), total duration of CSF acquisition procedure, whether the CSF tap was successful or not, and in successful attempts, the total volume (mL) of CSF acquired. The presence or absence of gross blood contamination was noted. A single attempt at CSF collection was defined as insertion of the needle through the skin to the point of needle withdrawal from the skin. The duration of CSF collection was recorded as the time (seconds) from initial skin puncture until final withdrawal of the needle, and thus may have included multiple attempts.

Following CSF sampling and recovery from general anaesthesia, dogs underwent a second neurological examination. A postprocedural CMPS-SF was performed, and the collection site(s) were assessed for the presence of haematoma formation or dermatological abnormalities. Anaesthetic complications associated with the CSF sampling procedure were identified by review of the dogs' anaesthetic records.

### Statistical analysis

Statistical analysis was performed using SPSS 28.0 (SPSS Inc., Chicago, IL, USA). Continuous data were tested for normality using the Shapiro–Wilk test. Most data were not normally distributed, and therefore, descriptive statistics were calculated as medians and interquartile ranges (IQR). The pre- and post-CSF collection CMPS-SF for ambulatory dogs were assessed separately using the Wilcoxon signed ranks test. Statistical significance was set at $p \leq 0.05$.

## RESULTS

A total of 102 dogs met the study's inclusion criteria. Seventy-six cases were recruited from the University of Liverpool and 26 from the University of Edinburgh. There were 63 male cases (36 neutered) and 39 female cases (23 neutered). The median age was 41 months (IQR 62 months). The median bodyweight was 17.15 kg (IQR 18.22 kg) and median BCS was 5 (IQR 2). Among the 102 dogs included, the most frequently represented breeds were crossbreeds ($n$ = 33), pugs ($n$ = 6), Jack Russell terriers ($n$ = 5) and English springer spaniels ($n$ = 5). Seven cases had evidence of dermatological abnormalities prior to CSF collection, all of which were consistent with dermatitis.

A definitive or presumptive diagnosis was available in 81 dogs (79.4%). A diagnosis was not established in 21 dogs (20.6%). The most frequent diagnoses were meningoencephalitis of unknown origin (MUO, $n$ = 14) and idiopathic epilepsy ($n$ = 14), followed by steroid-responsive meningitis arteritis ($n$ = 12), intracranial neoplasia ($n$ = 8) and paroxysmal dyskinesia ($n$ = 6). The remaining patients were undergoing CSF analysis for investigation of a range of clinical signs or potential diagnoses. No dogs were documented to have experienced a deterioration in their neurological status following CSF collection or developed new neurological deficits. No dogs in the study were recorded to have died because of CSF acquisition.

Anaesthetic records were available for review in 100 cases, and abnormalities during or immediately following CSF collection were identified in 14 dogs. Twelve dogs showed signs of lightening of the anaesthetic plane requiring an intravenous bolus of either propofol or alfaxalone, hypotension was observed in one dog with immune-mediated polyarthritis, and postanaesthetic seizure activity was documented in one dog with no definitive diagnosis and no prior history of seizure activity.

Sixty-two dogs were considered neurologically normal and 40 neurologically abnormal on examination prior to CSF collection. Neurological abnormalities included ataxia ($n = 25$), paresis ($n = 19$), abnormal mentation ($n = 14$) and nystagmus ($n = 6$), with the remaining cases having a range of other neurological deficits, such as anisocoria or head tilt. Twenty-eight of the neurologically abnormal dogs were considered ambulatory, and six were non-ambulatory, either due to severe ataxia or paresis. Thirty dogs had evidence of cranial or spinal hyperaesthesia upon examination, of which 10 also had neurological deficits.

Five dogs had MRI features associated with increased intracranial pressure. Two dogs that were diagnosed with MUO and one dog with a glial cell tumour had evidence of caudal transtentorial herniation alone. One dog with MUO had herniation of the cerebellar vermis into the foramen magnum and attenuation of the SAS overlying the cerebrum and cerebellum. The remaining dog had evidence of both caudal transtentorial herniation and herniation of the cerebellar vermis via the foramen magnum and was subsequently diagnosed with MUO. Five of these dogs had CSF sampled from the CMC, and the remaining dog had CSF sampled from the LSAS after CMC collection failed. Seven dogs were retrospectively identified as not undergoing CSF sampling due to clinician concerns regarding raised intracranial pressure in six dogs and the suspicion of coagulopathy in one dog.

Fifty cases had a platelet count performed prior to CSF collection. The median platelet count of dogs included in the study was $263 \times 10^3/\mu$L (IQR $100 \times 10^3/\mu$L). In only one case was the platelet count considered below the reference interval (less than $150 \times 10^3/\mu$L), with a platelet count of $132 \times 10^3/\mu$L.

The most frequently employed spinal needle for CSF collection was a 1.5 inch, 22 G ($n = 80$), followed by a 2.5 inch, 22 G ($n = 20$). The 3 inch, 20 G needle was infrequently used ($n = 2$).

A total of 336 CSF collection attempts were documented. Six dogs had collections performed from both the CMC and LSAS. In five cases, this was performed as standard for the work-up of steroid-responsive meningitis arteritis, and in a single case, this was performed due to a failure to acquire CSF from the CMC. In total, CSF was successfully acquired on 100 occasions (92.6%), with collection unsuccessful on eight occasions (7.4%). Collection from the CMC was performed 72 times, and CSF was successfully acquired in 69 cases (95.8%) with a median number of attempts of 1 (IQR 2). Collection from the LSAS was performed 36 times, and CSF was successfully acquired in 31 cases (86.1%) with a median number of attempts of 2 (IQR 3).

CSF collection was unsuccessful in eight dogs (7.8%). The median bodyweight of these dogs was 21.45 kg (IQR 13.70 kg), compared to a median study population bodyweight of 17.15 kg (IQR 18.23 kg). The median BCS was 4 out of 9, compared to a median study population BCS of 5 out of 9. The dogs from which CSF sampling was unsuccessful included two crossbreed dogs and one each of French bulldog, English springer spaniel, cocker spaniel, Newfoundland and greyhound. Sampling was unsuccessful at the CMC in three cases (4.2%) and at the lumbar site in five cases (13.9%).

Twenty-five dogs had CSF sampling attempted by two or more clinicians. This was from the CMC in 12 cases and the LSAS in 15 cases, with two dogs having CSF sampling attempted from both the CMC and LSAS. CSF collection was unsuccessful in six of these dogs requiring attempts by multiple clinicians (two CMC and four LSAS).

The median volume of CSF obtained was 1.0 mL (IQR 0.75 mL). Gross blood contamination was evident in 28 CSF samples (28.0%), with 13 (13.0%) obtained from the CMC and 15 (15.0%) from the LSAS. The median volume of CSF collected (in mL/kg) from the CMC was 0.085 mL/kg (IQR 0.094 mL/kg) and from the LSAS was 0.061 mL/kg (IQR 0.071 mL/kg). Seven dogs had more than 0.20 mL/kg of CSF taken for sampling. The median weight of these dogs was 4.65 kg (IQR 2.31 kg), with the median volume sampled being 0.26 mL (IQR 0.30 mL).

The duration of CSF acquisition was recorded in 100 cases. The median duration of CSF collection from the CMC was 149 seconds (IQR 255 seconds), from the LSAS was 386 seconds (IQR 403 seconds) and when both sites were attempted was 297 seconds (IQR 361 seconds). Excluding dogs in which CSF acquisition was unsuccessful, the median duration was 147 seconds (IQR 191 seconds) from the CMC and 345 seconds (IQR 417 seconds) from the LSAS.

Ten dogs developed a subcutaneous haematoma following CSF collection (five CMC and five LSAS). The median bodyweight of dogs that developed a subcutaneous haematoma was 16.5 kg (IQR 17.3 kg). The median number of attempts performed in dogs that developed a subcutaneous haematoma was 3 (IQR 5), and CSF was successfully acquired in all dogs. In no dogs was the subcutaneous haematoma deemed clinically significant or required any specific treatment.

Seven dogs developed dermatitis following the procedure (two CMC and five LSAS). One dog required treatment for the resulting dermatitis (topical betamethasone and fusidic acid gel) due to significant pruritus being reported by the owner. In the remaining dogs, this resolved without intervention.

All dogs received an opioid as part of their premedication, with 66 dogs (64.7%) receiving butorphanol, 34 methadone (33.3%), one pethidine (1.0%) and one buprenorphine (1.0%). One hundred and one dogs received a second premedication drug, with a single dog receiving methadone as a solitary premedication drug. The second premedication drug used in those 101 cases included acepromazine in three dogs (3.0%), medetomidine in 77 dogs (76.2%), dexmedetomidine in 20 dogs (19.8%) and midazolam in one dog (1.0%). Pre- and post-CSF collection CMPS-SF were obtained for 29 ambulatory dogs. The post-CSF collection CMPS-SF assessment was performed for a median of 2 hours following CSF collection (IQR 1.1). The median pre-CSF collection CMPS-SF was 1 (IQR 3),

and the median post-CSF collection CMPS-SF was 1.5 (IQR 3). There was no significant difference between pre- and post-CSF collection CMPS-SF in ambulatory dogs ($p = 0.13$) when pain scoring was conducted within this time frame. Only three non-ambulatory dogs underwent pre- and postprocedural CMPS-SF; therefore, statistical analysis could not be performed for this group of dogs.

## DISCUSSION

The purpose of this study was to identify and characterise complications associated with CSF sampling in dogs. We found that CSF sampling is associated with a low frequency of complications when performed by board-certified neurology specialists or neurology residents in training. Those encountered in our sample population were considered minor, such as dermatitis, which was suspected to be associated with aseptic preparation, or the development of a subcutaneous haematoma. Significant complications such as paraparesis, haematomyelia, myelomalacia or iatrogenic brainstem injury were not encountered. The historical scarcity of these complications supports that when CSF sampling is performed by suitably trained professionals, these complications are considered fortunately rare.

The most frequently reported complication associated with lumbar puncture in humans is a post-dural puncture headache (PDPH). PDPH is currently defined as a headache occurring within 5 days of a lumbar puncture caused by CSF leakage through the dural puncture. The headache should spontaneously remit within 2 weeks or after application of an autologous epidural blood patch.[19] The incidence of PDPH is variable among studies but has been reported in up to 24.8% of patients.[9] The mechanism resulting in PDPHs in humans is uncertain, with the favoured theory currently being that downwards stretch of pain-sensitive structures (meninges, intracranial blood vessel walls and nerves) occurs upon adoption of an orthostatic posture secondary to CSF hypovolaemia.[20] The headache frequently improves or resolves upon supination.[21] Given their quadrupedal stance, it could be postulated that PDPH would be less frequently encountered in dogs than humans. Unfortunately, clinical assessment of headache disorders in veterinary species is considered difficult and subjective. Previous attempts to make objective assessment of this syndrome in animals have utilised specialised equipment (such as von Frey monofilaments and aesthesiometers).[22] These techniques were not employed in this study because most patients were discharged from the hospital shortly following recovery from anaesthesia. Interpreting such tests in client-owned dogs would also potentially be very different than in other experimental settings. Grimace scales have been validated as a tool for assessment of pain in laboratory mice used in migraine research; however, no such scales currently exist for dogs.[23] This represents an area of research in which further work is required before PDPHs can be identified in dogs, should they exist. Other reported complications associated with lumbar punctures in humans, such as infection or spinal haematoma formation, are considered very rare (incidence less than 0.01%) and no dogs were suspected to have experienced such complications in the present study.[11,24] Radicular pain was additionally not identified in any of our dogs that underwent postprocedural pain scoring.

Back pain is a common complication in humans following lumbar puncture, occurring in up to 17% of people in a large, multicentre study.[8] CSF sampling was not associated with a statistically significant increase in CMPS-SF in our study. These findings suggest that CSF sampling is not associated with a significant increase in short-term patient discomfort or that any such discomfort is amenable to standard anaesthetic and analgesic protocols. However, no follow-up pain assessment was performed in our patients, and it is possible that discomfort occurred during the period following hospital discharge.

While the population of dogs undergoing CSF sampling in this study with MRI features suggestive of increased ICP was small, none of those dogs clinically deteriorated following the procedure. Concerns regarding CSF sampling in patients with increased ICP relate to the possibility of subsequent neuroparenchymal herniation secondary to movement of neural structures down a cranio-spinal subarachnoid pressure gradient, the steepness of which may be increased during CSF sampling.[25] Given the small population in our study, we cannot recommend that this practice is performed routinely. Our study does suggest, however, that the suspicion of raised ICP on MRI should not always contraindicate CSF sampling if the potential risks are adequately communicated to the dog's owner and the potential benefits of obtaining a sample are high.

Our study identified that sampling from the LSAS was more liable to failure compared to the CMC. Collection of CSF from the LSAS appears most important in patients with spinal cord disease compared to intracranial disease, given its greater sensitivity for diseases of the spinal cord in comparison to samples from the CMC.[26,27] The LSAS collection site also required a greater number of attempts to successfully obtain a sample in comparison to the CMC and was more likely to be blood contaminated, with 48.3% of LSAS samples being blood contaminated. This finding is similar to that observed in another study in which 32.5% of samples obtained from the LSAS were blood contaminated, which also identified the LSAS collection site to be a risk factor for blood contamination.[28] While the significance of blood contamination on downstream analysis is controversial, it is considered at least undesirable, and therefore, subsequent collection from the CMC should be considered in heavily contaminated LSAS samples. In this study, CSF acquisition was unsuccessful in 7.8% of dogs. Unfortunately, due to the limited number of cases, predictive factors

for an unsuccessful sample could not be established. This study has at least provided a figure that may be used to manage dog owners' expectations prior to CSF acquisition and has highlighted an area in which further research is required.

The duration of CSF sampling in our paper appeared relatively short and therefore had little impact on the duration in that patients remained anaesthetised.

A commonly applied recommendation is not to sample more than 0.2 mL/kg of CSF from dogs.[29] Seven dogs in the present study had more than 0.2 mL/kg of CSF sampled, none of which experienced neurological deterioration. While the median volume of CSF taken from these dogs was still just 0.26 mL, this provides evidence that, if necessary, the 0.2 mL/kg recommendation may be exceeded for diagnostic purposes if felt indicated.

This study is subject to several limitations. While 102 dogs were initially recruited into the study, only 29 ambulatory dogs underwent pre- and postprocedural CMPS-SF. This was due to limited uptake at the host institution, and therefore pain scoring was not consistently performed. While our clinical experience and expectation were that there would be no significant difference in pre- and postprocedural CMPS-SF, a larger number of dogs would have allowed this finding to be more reliable. A small number of non-ambulatory dogs underwent pre- and postprocedural CMPS-SF; however, these cases were subsequently excluded from pain score analysis due to an insufficient number with which to perform statistical analysis. The scarcity of non-ambulatory dogs undergoing CSF analysis may reflect that most dogs with non-ambulatory status had non-medical conditions such as intervertebral disc extrusions and, as a result, did not undergo CSF analysis.

In this study, the CSF sampling procedure was performed by neurology residents in training and board-certified neurology specialists. The low incidence of complications may be, in part, due to the operator's familiarity with the procedure. As a result, this may limit the generalisability of the study's findings to companion animal first-opinion practice, where the incidence of complications may be higher due to operator unfamiliarity. The study's sample size was also considered relatively small, meaning that complications considered rare were liable to be missed. While no cases of postprocedural paraparesis or ataxia were documented in our population, these complications do occur anecdotally, and it remains important to be aware of their occurrence. Given the low incidence of complications associated with CSF sampling, statistical analysis to identify risk factors for such events could not be performed; thus, risk factors for complications were not explored.

In conclusion, this study has demonstrated that CSF sampling in dogs is associated with a low patient morbidity and that it may safely be performed in most patients, with no dogs undergoing neurological deterioration following CSF sampling. Extensive research is required before the presence and incidence of PDPHs can be evaluated in dogs.

## AUTHOR CONTRIBUTIONS

Rita Gonçalves conceived the project. Data were collected by all authors. Rory Fentem and Megan Madden collated the data. Rory Fentem performed the data analysis and descriptive statistics. The manuscript was written by Rory Fentem, and all authors reviewed the draft and writing of the final manuscript.

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## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## ETHICS STATEMENT

Ethical approval for use of clinical data was granted by the ethics committee of the University of Liverpool (VREC713).

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