**Comparison of two surgical techniques for treatment of canine caudal cervical spondylomyelopathy**

ABSTRACT:

Objective: to compare the prosthetic disc and the vertebral distraction-stabilization in dogs with caudal cervical spondylomyelopathy (CCSM), also known as disc associated wobbler syndrome (DAWS), by evaluating the clinical outcome and the imaging findings at different times after surgery

Study design: prospective cases series

Animals: 25 dogs suffering from CCSM and surgically treated by prosthetic disc (PD) or by vertebral distraction-stabilization (DS)

Methods: dogs presented with clinical signs and MRI findings compatible with CCSM that underwent surgery by implantation of the Adamo’s prosthetic disc (PD) or by vertebral distraction- stabilization (DS) with intervertebral cage, ventral locking plates and dorsal transarticular screws, were enrolled in this study. All dogs were then followed and evaluated clinically for a minimum of 1 year and radiographically for at least 3 months, to asses if there was improvement on neurological status and implant failures, focusing most on subsidence; magnetic resonance exams were also repeated in selected cases

Results: 25 dogs fulfilled the inclusion criteria and Dobermann was the most represented breed (13/25). All dogs with CCSM surgically treaded either by PD implantation (12 cases) or DS (13 cases) underwent pre-operative radiographic and MRI assessment, and immediate post-operative x-rays. Three dogs from PD group dramatically deteriorated within 30 days from surgery: one had severe subsidence at 9 days with relapse of cord compression, and two with moderate subsidence had disc extrusion in the treated spaces. All three required a second surgery and then improved. The most common complication in DS cases was discaospondyltis, involving 3 dogs of 13. Also these patients recovered after antibiotic treatment. Subsidence was identified in 11 out of 12 PD-dogs and it was more relevant when occurred sooner after the surgery. In the DS-group subsidence was identified in 6 of 13 cases and was overall milder and took longer than those treated by PD. No DS dogs developer severe subsidence. radiographs also showed severe reduction or loss of vertebral motion in almost all PD cases and a good bone production/vertebral fusion in all DS cases. MRI was performed in 14 patients and helped in assessing the implant positioning and the cause of deterioration. There was evidence for DS cases to be more prone to clinical improvement and less prone to subsidence than PD casesbut, because small sample size the estimation of effect Treatment was very uncertain (large 95% CI) , more data will be needed, to consolid this evidence.

Conclusion: our preliminary results suggest that the prosthetic disc is more prone to clinical and radiographic failure than distraction-stabilization with cage, locking plates and transarticular screws, especially because of its high tendency to subside more dramatically and early after the surgery. The DS technique as reported herein is a valuable surgical option to treat CCSM dogs with a favorable short and long term clinical and radiographic outcome.

INTRODUCTION:

Canine Caudal Cervical Spondylomyelopathy (CCSM), also known as Disc Associated Wobbler Syndrome (DAWS), affects large breed dogs and particularly Dobermann Pinschers, but also Dalmatian, Weimaraner and many others, that over time become ataxic and paretic on all four limbs.1,4-8 Typical neurological sings has been defined as “two engines gait”, being mostly ataxic on the back legs and hypometric on the front ones. It is usually a progressive disease, due to cervical spinal cord compression and secondary damage, cause by degenerative disc disease and protrusion, hypertrophy of the dorsal longitudinal and sometimes the interarcuate ligaments.1,2,9-12 Most of the CCSM cases and the underlying cord compressions tend also to have a dynamic component, which makes the cord compression itself worse or alleviated for instance in extended or in traction positions. Although Magnetic Resonance Imaging is nowadays commonly accepted as the method of choice to establish the diagnosis, controversy still exits on how to treat this condition, even if it is thought that surgical treatment may provide more benefit than the medical treatment.3-7,9,16-20,46,47,49 A variety of surgical techniques have been proposed for CCSM, with many of the authors claiming success rates between 70% and 90%.21-40 The distraction-stabilization of the affected vertebral segments and more recently the implantation of a prosthetic disc seem to currently represent both valid surgical options. 41-44 Despite their common goal is to relieve the spinal cord compression, a relatively normal vertebral motion should be preserved or restored with the prosthetic disc, whereas the vertebral fusion represents the final aim with the distraction-stabilization.26-36 We prospectively selected dogs with CCSM and then compared the prosthetic disc and the vertebral distraction-fixation, by evaluating the clinical outcome and the imaging findings, both radiographs and magnetic resonance images, at different times after surgery,; a special attention was put on subsidence, since we hypothesized it was superior with the PD technique.

MATHERIAL AND METHODS

Dogs presented to Diagnostica Piccoli Animali between January 2014 and September 2018, with clinical signs and MRI findings compatible with CCSM or DAWS that underwent surgery, were included. In every patients MRI of the cervical vertebral column was acquired in neutral position and after traction, as previously described.49 Affected spaces were treated either by an Adamo’s prosthetic disc (PD) implantation or by a vertebral distraction-stabilization (DS), obtained by using an intervertebral cage, two ventral locking plates and two dorsal trans-articular screws, all titanium made 42,59. The decision of making a full or a partial ventral slot in the treated spaces, depended on the residual cord compression on post-traction MRI images: if the compression did not fully resolved, a full ventral slot with complete disc removal were performed. Dogs undergoing PD implantation should have had a complete resolution of cord compression after traction. The neurological status and the radiographic appearance were evaluated pre- and post-operatively. Dogs after surgery were neurologically re-evaluated and the neurological status were compared to those pre-treatment, so they were rated as deteriorated, stable, improved or normal, if no neurological deficits were noticed. More importantly, outcome was evaluated within 30 days (short term follow-up), over 30 days and less than 1 year (medium term follow-up) and at 1 year or more (long term follow-up). The radiographs should have taken immediately post-operatively, at 1 month and 3 months after surgery; radiographs were also assessed when taken later, at different intervals after treatment. The radiographs mostly focused on subsidence, described as the percentage of distraction loss between the dorsal borders of the contiguous treated vertebrae and manually measured separately by the two authors with an open-source software for navigating in multidimensional DICOM images (Osirix, www.osirixviewer.com). Subsidence was rated as mild, if the percentage of distraction loss was between 10% and 25%, moderate if from 25 to 50%, severe if more than 50%, and as none, if the loss of distraction was zero or below 10%, as a minimum human margin of error was considered possible and acceptable. The degree of vertebral fusion/bone production for the DS dogs as the degree of residual motion for the prosthetic discs on dynamic x-rays (neutral, flexed and dorsal extended position of the cervical column) were also considered; when present, other changes such as screw rupture or signs suggestive of discospondylitis were reported. MRI images were also repeated at different times after surgery: implant positioning, residual cord compression at the treated sites, new sites of cord compression, vertebral collapse or changes (e.g., bone lysis) and intra-medullary damage were evaluated.

Statistical analysis was performed using a Generalized Linear Mixed Model (GLMM) to compare the subsidence grade after the different treatment options (PD vs DS) with dogs as random effect. Intraclass-coefficient-correlation (ICC) was calculated from variance components of the model, to assess the agreement between the authors on subsidence degree. (Bates D, et al. 2015)

Outcomes after surgery were classified in a multinomial non-ordered categorical variable with three levels: “Improved”, “Stable” and “Worse”, then a multinomial logistic regression (MLR) (Venables WN, Ripley BD (2002) was fitted to predict the outcomes using treatment modality as a predictor factor; All data analysis were performed using R a programming language and environment for statistical computing (R Core Team (2020), with lme4 (Bates et al, 2015) for GLMM , nnet (Venables WN, Ripley BD (2002) for MLR, and accessory packages to handle data and make table and graphs: readxl ( Hadley Wickham and Jennifer Bryan ,2019), , tidyverse(Wickham et al.,2019), sjPlot(Lüdecke D ,2020), ggeffects(Lüdecke D 2018).

There is a growing consensus by the biomedical scientific community not to use the significant / non-significant dichotomy for the interpretation of the results on the basis of a predetermined cut-off of the p-value (Amrhein, et al 2019, Wasserstein R.L. et al 2019). In accordance with what is also indicated by the American Statistical Association (ASA) regarding the recent statement on the use and meaning of the p-value (Ronald L. Wasserstein & Nicole A. Lazar (2016) ), we focused attention on the extent of the estimate of the treatment effect and on its uncertainty, reporting the p-value exclusively as a measure of the evidence against the null hypothesis (the treatment are equal) without defining a cut-off value of p that defines the significant or insignificant results.

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RESULTS

25 dogs fulfilled the inclusion criteria and Dobermann was the most represented breed (13/25); 4 were Weimaraner, 2 Bernese Mountain dogs and then 1 per each of the following: Rottweiler, Deutsch Kurzhaar, Hannoverscher Schweisshund, German Shepherd dog, Beauceron, and Mongrel. As per the inclusion criteria, all dogs with CCSM were surgically treaded either by PD implantation (12 cases: 2 cases C5-C6 and C6-C7, 10 cases C6-C7) or DS (13 cases: 2 cases C5-C6 and C6-C7, 11 cases C6-C7) and underwent pre-operative radiographic and MRI assessment. Mean surgery duration in PD-group was 1 hour 18 minutes for dogs with one single space and 2 hours for those with C5-C6 and C6-C7; in the DS-group the mean duration was 3 hours for 1 single space and 4 hours for two sites. Despite rare, most common intra-operative complication was bleeding, especially when a full slot was performed. All dogs had immediate post-operative x-rays. All dogs were discharged within 24-36 hours after the surgery; mild deterioration was occasionally witnessed only in dogs that underwent full ventral slot and improved spontaneously within a week.

Clinical follow-up (table1)

Within the first month after surgery (short term follow-up) only three dogs deteriorated, all from the PD-group: one became mildly ambulatory tetraparetic at 9 days because of severe subsidence and relapse of cord compression, as shown by repeat radiographs and MRI, and two dogs developed severe neck pain and mild to moderate tetraparesis respectively at 15 and 25 days, due to disc extrusion associated with moderate subsidence in the treated spaces in both cases, as shown by repeat MRI. These three cases required a second surgery: the first dog was treated by DS technique and the other two cases by removal of the extruded disc through a lateral hemilaminectomy.55

Amongst the remaining 22 dogs, 16 improved (5 PD and 11 DS) and 6 were stable (3 PD and 3 DS); no dogs were normal.

24 dogs were clinically re-evaluated between 1 month and 1 year after surgery (medium term follow-up), since one dog from DS group suddenly died at 30 days after surgery, for unknown reasons. 8 cases were stable (6 PD and 2 DS), 3 dogs deteriorated from DS group because developed discospondilitys at 45 days, 6 months and 10 months after surgery. Discospondilitys affected the intervertebral space cranial to the treated site in the first two dogs and the space caudal to the treated one in the third case. All dogs received amoxicillin and clavulanic acid (20 mg/kg BID) in association with enrofloxacin (5 mg/kg SID) and improved with therapy duration varying from 90 to 120 days. Other 2 dogs deteriorated from the PD group, respectively at 2 and 4 months after surgery; both developed neck pain and one also became mildly tetraparetic. Both cases had severe subsidence on radiographic recheck and were treated conservatively with tapering dose of prednisolone and gabapentin (10 mg/kg BID); neck pain improved in both dogs with a mean time of 60 days, but never the gait. In the DS group it was also enrolled the dog previously treated with PD that required a second surgery at 9 days because of severe subsidence with relapse of cord compression; although this dog was clinically monitored and assessed from the clinical and radiographic post of view for more than 1 year, it was not used for statistical purposes. All three dogs from PD that deteriorated at short term revaluation improved after the second surgery.

At 12 months after surgery (long term follow-up) 24 dogs were available for neurological assessment: compared to the pre-operative status, 12 improved (4 PD and 8 DS), 8 were stable (4 PD and 4 DS) and 4 deteriorated (3 PD and 1 DS). All three dogs from DS group that developed discospondilitys improved after antibiotic treatment, as said above; the extra 2 PD-dogs that deteriorated at medium term follow-up, improved pain-wise, but one remained tetraparetic. At 2 year telephone follow-up 15 owners reported an unchanged status from last time (5 PD and 10 DS); one owner of a dog from DS group noticed a mild deterioration, describing a more ataxic gait, especially on the pelvic limbs. Only 6 dogs were available for follow-up at 3 years (2 PD and 4 DS), including the dog that already deteriorated at 2 years: this dog underwent an MRI scan at this stage and a progression of the intramedullary damage was deemed responsible for the worsening ataxia and paresis of all four limbs. The remains 5 dogs were deemed unchanged from previous assessment. From the statistic point of view, at the short term follow up, dogs treated with PD, had an odds 6.60 times greater than dogs treated with DS to be stable, an odds 8.80 times greater than dogs treated with DS to be worse and an odds 0.11 lower than DS dogs to be improved (Table 2). At long term follow-up (12 months) PD dogs had an odds 8.00 times greater thanks DS dogs to be stable and an odds 2.67 times greater than DS dogs to be worse and an odds ratio 0.17 lower than DS dogs to be improved (Table 2). 95% CI was very large for all the categories examined, because of the small sample size of this study

Imaging follow-up (Table 3)

Radiographs were repeated in 23 dogs, from 30 to 90 days; 4 of these 23 dogs also had extra-radiographs at 6 months and 2 over 1 year. One PD dog had lost radiographic follow-up, because it was deemed unnecessary by the owners, considering the improvement of the neurological status of their dog. The other dog that lost the radiographic follow-up was those from the DS-group that died at 30 days from surgery, for unknown reasons. Overall, subsidence was identified in 10 out of 11 PD-dogs, it tended to become more evident over time, and varied from mild in 3 patients (20-30%), to moderate in 3 dogs and severe in 4 cases. As previously stated, the 2 dogs with disc extrusions had moderate subsidence and the PD-dog that deteriorated at 9 days and was treated with DS had severe subsidence. The remaining three cases with severe subsidence had a relevant new bone production at 90 days radiographic recheck and almost a complete vertebral fusion in 1 patient, whereas in two dogs mild residual vertebral movement was still present on flexion and extension x-rays. Of these three dogs, one was neurologically unchanged compared to the preoperative assessment, and two only had deterioration of clinical signs, characterized by neck pain in both cases and mild tetraparesis in one dog; they both were treated conservatively, with partial improvement as stated above. 1 PD dogs had no subsidence on 30 and 90 days radiographs and neurologically improved. In the PD group the degree of vertebral motion, evaluated in flexed and extended neck position, was preserved in only 1 dog (without subsidence), while it was from decreased to absent in the remaining ones, in proportion to the severity of subsidence: a high tendency to vertebral-fusion with new bone production and spondylosis were most likely if subsidence was severe or moderate.

In the DS group subsidence was overall identified in 6 of 13 cases and was rated as mild in 2 cases and moderate in 4 (31-50%); no dogs suffered from severe subsidence. Subsidence was associated with screw rupture in 3 cases (2 screws in 2 cases and 1 screw in 1 case) and with discospondylitis in the dog that deteriorated 45 days after the surgery; no other major radiographic implant failure or other evident causes in the remaining case. 7 dogs had no subsidence at 3 months: 5 of those dogs showed also no subsidence when x-rays were repeated later, respectively at 6, 10, 12, 16 and 36 months. Good bone production-vertebral fusion was witnessed in all dogs, but it became radiographically more obvious after 90 days.

A reduction of subsidence of 29.03 unit (95% CI: -47.78 – -10.28) in dogs treated by DS, compared to those treated by PD were observed from GLMM model results, with a strong evidence (p=0.02) against null hypothesis that the surgical technique are equal in term of subsidence grade The two authors in rating the degree of subsided, showing a very high agreement ( ICC=0.97).

Overall MRI was repeated in 14 patients (7 PD and 7 DS) for a total of 18 studies: 7 were acquired immediately after the surgery (2 PD-dogs and 5 DS-dogs) and showed good implant positioning with none to minimal residual cord compression in all cases. 6 cases were scanned because of worsening of their neurological status: 3 PD-dogs respectively at 9, 15 days and 25 days (disc extrusion and moderate subsidence in two cases a severe subsistence with relapse or cord compression in one case) and 3 DS cases respectively at 45 days, 5 months and 10 months all with discospondyltis. 3 dogs had extra MRI at 90 days post-operatively for a routine re-check in one and to assess if there were changes in the remaining two dogs, since radiographs showed screw rupture and mild to moderate subsidence: in both cases no relevant MRI changes nor residual or new cord compressions were identified. In 2 cases MRI was repeated at 12 and 36 months and it showed progression of the intramedullary damage in both cases; amongst those two dogs, the damage was deemed responsible for mild worsening of the gait only in the dog receiving the MRI at 36 months, as previously described.

DISCUSSION

Preliminary results from this study suggest that canine caudal cervical spondylomyelopathy could be surgically treated with success using both techniques; however, prosthetic disc seems to be more prone to clinical and radiographic failure than distraction-stabilization with cage, plates and trans-articular screws.

Canine caudal cervical spondylomyelopathy (CCSM) or disc associated wobbler syndrome (DAWS) in Dobermann and in other large breed-dogs more frequently affect the C6-C7 intervertebral disc space, in association with involvement of C5-C6 in about 35% of the cases, with subsequent single or multiple compression and damage of the spinal cord.1-5,10 The changes causing the spinal cord compression are mainly represented by disc protrusion and hypertrophy of the dorsal longitudinal ligament;1-5,10-11 they might be static or dynamic, based on the variability of the degree of cord compression with flexion, extension, and traction/distraction applied to the cervical spine. 1-3,10,12-15,20,48 According to the dynamic response on myelographic, computed tomography or MRI studies, it is possible to distinguish between static and dynamic lesions or, more correctly, between traction non-responsive and traction-responsive cord compressions.1,10,12,14,15,17,19-20,49,54

Despite the treatment for dynamic CCSM lesions is still controversial, medical management generally results only in transient clinical improvement, and progression to severe tetraparesis is common.1,6-7,45 A recent study found that a beneficial outcome was associated with nonsurgical treatment in 54% of dogs and with surgical therapy in 81% of dogs; however, the difference between these two outcomes was not statistically significant, probably because the low patients number.1,6-7,10 Overall, there is the tendency of considering the surgical treatment superior than the conservative one, especially with regards to medium-long term improvement, as also reported for the human counterpart.6 A variety of surgical techniques have been proposed for treatment of CCSM in dogs, with success rate varies between 70 and 90 %.21-40 ,44 The goal of surgical intervention is improving the neurological deficits or at least to stop or slow down their progression, by relieving the spinal cord compression and stabilizing the cervical vertebrae, anytime a dynamic component is suspected.1,10 Various types of spinal decompression and vertebral stabilization techniques were reported for the treatment of cervical disc pathology in humans and the use of intervertebral body cages with or without adjuvant locking plates to achieve interbody arthrodesis rapidly gained acceptance and more recently it became popular also in dogs.50-53,30-36 Based on our previous experience on more than 30 cases, the use of the intervertebral cage alone was often insufficient to maintain the required inter-vertebral body distraction, despite the good clinical outcome. We therefore developed a system where the interbody spacer was also supported by the use of two ventral parallel locking plates and two dorsal transarticular screws through the affected facets, similar to what previously described.58 As opposed to the vertebral distraction-stabilization, another theory more recently suggested in dogs with DAWS, also inspired by the human counterpart, is that a normal vertebral motion should be preserved or restored and for this purpose a prosthetic disc has been designed, with the goal also to provide vertebral distraction and neural decompression.41-44,51-52 We then decided to compare these two very different surgical techniques, by evaluating the clinical and the radiographic outcome at different time after surgery and, as previously stated, the prosthetic disc resulted more prone to failures, especially in the early stages after surgery. In fact, even if the surgery led to neurological improvement in the vast majority of cases regardless of the surgical technique, many of the PD-treated patients tended to deteriorate more often and sooner than the DS-dogs, that have fewer complications, less severe and later. The most critical period in PD-treated cases seemed to be especially the first month after the operation, mostly due to moderate-severe subsidence associated with worsening of cord compression, also in conjunction with disc extrusion in two cases. In some of these cases a second surgery was necessary to relieve the spinal compression and to counteract the effects of subsidence. We hypothesized that the discs extruded in two cases as a consequence of collapse of the intervertebral disc space that forced the residual disc material into the vertebral canal. The selection of a surgical technique should take into consideration the success rate as well as the potential risks of complication such as implant failure, potentially related also to subsidence in CCSM patients.10,25-37,44 Subsidence is in fact commonly witnessed with many of the surgical techniques used to treat CCSM and, from its human counterpart, it has been defined as sinking of a body with a higher elasticity modulus (e.g. graft, cage, spacer) in a body characterized by a lower elasticity modulus (e.g. vertebral body), resulting in 3D changes of the spinal geometry and eventually in a partial o total failure of the vertebral distraction-stabilization.44,50,52,53 Although even in human neurosurgery there is no general agreement regarding its role for the complications after cervical fixation-fusion surgeries, it seems to predispose to implant failure and then it should be avoided. Many studies have been conducted with the primary goal to identify surgical techniques capable of minimizing or eliminating the subsidence. As also for the data showed herein, subsidence is not only a radiographic failure but it is often associated with clinical deterioration, especially when moderate or severe or when it happens early in the post-operative period. Subsidence was witnessed in almost all PD-cases, with only tone dog not showing any signs of subsidence and maintaining a good vertebral motion, supporting that the subsidence could be deleterious for a good outcome. We confirmed our hypothesis that subsidence is more commonly seen with PD technique compared to DS and we hypothesized that a potential cause for the high incidence in the PD-group is most likely represented by the small size of the artificial disc, when compared to the size of the intervertebral space; we in fact supposed that the loading surface of the prosthetic disc is too small compared to those of the vertebral end plates, which eventually tend to incorporate the disc itself. Moreover, we believe that its stiff nature is not capable to adsorb the vertebral movements of the caudal cervical region without sinking into the vertebral end plates themselves. As a direct consequence of such severe subsidence, the caudal cervical vertebrae lost the distraction and tended to fuse, either partially or totally, also lacking the restored motion.

Most common causes for deterioration in DS-dogs were discospondylitis, which developed in three cases, about 20% of all DS cases; one case worsened due to the progression of intramedullary damage as identified at three years post-operative MRI recheck. With the exception of one case, where discospondylitis developed at 45 days after surgery, in the other two dogs it developed relatively late, respectively at 5 and 10 months. Surprisingly, the infected spaces were close to the treated ones, but never those that have been operated on. Though in the first cases a direct relationship with the surgical procedure is likely, in the remaining two dogs we did not identified a relevant correlation. However, we felt that the surgery would cause an impact on the normal local environment, also potentially by altering the normal motion and finally predisposing the development of bacteria, as it could have happened with any other spine surgery and not necessarily because of the presence of the synthetic material.56,57 Indeed, all cases improved after a relatively short course of antibiotics, without the need to remove the implants and none showed signs of relapse. Subsidence was rarer and of milder degree in DS cases than those in PD dogs and, more important, none of the DS cases developed severe subsidence, which seems to be more often related to early and severe neurological deterioration. Repeat MRI in the DS cases with subsidence did not show relevant new or relapse of cord compression, possibly because of the mild vertebral collapse. We hypothesized that the most common cause for subsidence in these cases was linked to the screw rupture, like witnessed in three cases. The breaking of the screws, even if rare, could be caused by the choice of a too small screw diameters and/or by an anomalous angulation of the screws, possibly in association with an excessive physical activity of the patient, especially in the first weeks or months after surgery.

A major disadvantage of DS technique as described here is the long time of the operation, especially if two adjacent sites needed to be stabilized, both ventrally and dorsally. However, this time may be reduced with experience; the mean time reported in this case series is influenced by longer duration for the initially treated cases. Both PD and DS techniques had very low to none intraoperative complication rate and short hospital stay; so they were both considered two safe procedures to treat CSM dogs, though a longer learning curve is required with the DS surgery, whereas the PD implantation was relatively easy.

We should disclose that despite results indicating superiority of DS over PD in multinomial model,

we were unable to find strong evidence against the null hypothesis that PD=DS with the current sample size. This was due to the small number of cases and wider population is necessary to confirm these preliminary results, which however support the evidence that distraction-stabilization technique as described here represents a valuable option to treat CCSM dogs. Despite some minor complication such as discospondylitis and/or screw rupture, it was deemed superior than the prosthetic disc currently available in veterinary neurosurgery, leading to a better short and long term clinical and radiographic outcome.