BEECROFT medicalbrief

VETERINARY SPECIALIST & REFERRAL HOSPITAL

★ August 2024 ★

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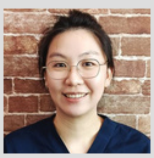

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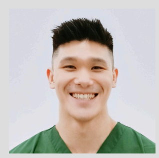

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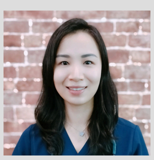

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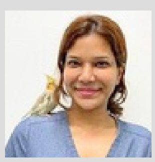

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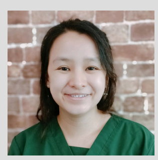

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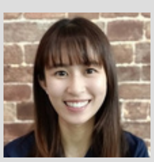

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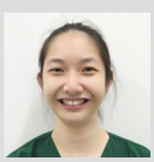

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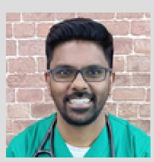

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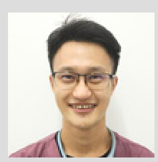

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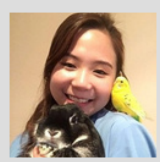

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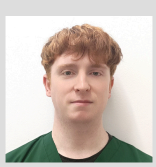

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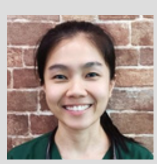

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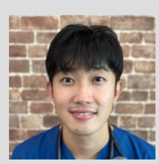

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SPINAL CORD DISEASES IN FRENCH BULLDOGS

By Dr Matthias le Chevoir
DVM, MANZCVS, DipECVN

The French Bulldog (FB), originating from France, has seen a substantial population increase in recent decades. Annual registrations in France have quadrupled over the past 15 years. In the United Kingdom, new registrations to the Kennel Club rose from 526 in 2006 to 14,607 in 2015. In North America, FBs were the sixth most popular breed in the United States in 2014 and the 9th in Canada in 2015. Although specific data for Singapore is unavailable, it is evident that FB numbers have surged significantly in the past five to ten years.

French Bulldogs' brachycephalic and chondrodystrophic conformations, due to selective inbreeding, have led to a high prevalence of various diseases, including several neurological conditions. While FBs are prone to certain brain diseases (e.g., meningoencephalitis of unknown origin, glioma), this article focuses on spinal cord disorders unique to the breed. In a veterinary hospital setting, 18.3% of FBs presented with neurological disorders.

Intervertebral disk extrusion was the most common (45.5%), followed by spinal arachnoid diverticulum (SAD) in 25 FBs (11.3%), and compressive vertebral malformation in 8.6% of the cases.

1. Intervertebral Disc Disease (IVDD)

(A) Reminders

Intervertebral disc disease (IVDD) is the predominant spinal neurological disorder in dogs. This debilitating condition can result in permanent paralysis, urinary and faecal incontinence, and in severe cases, death (due to ascending myelomalacia). Clinical signs of IVDD manifest from compression of the spinal cord within the vertebral canal.

Pathophysiology

Intervertebral disk disease (IVDD) arises from two types of known intervertebral disk degeneration.

In chondrodystrophic dogs, chondroid metaplasia is characterised by a loss of water content and an increase in collagen content, resulting in a loss of the disk's hydroelastic properties. By one year of age, 75 to 90% of the gelatinous nucleus pulposus in these breeds is transformed into hyaline cartilage. This transformation can lead to the mineralisation of the disk and tears in the annulus fibrosus due to damage from the mineralised nuclear material. This type of degeneration can result in intervertebral disk extrusion (IVDE), where the modified nucleus pulposus material herniates through the damaged annulus fibrosus. The extruded disk material can be dispersed or non-dispersed in the vertebral canal and appears irregular, brittle, grainy, sometimes plaster-like, and varies in colour from white-yellow to grey-yellow or grey-red if mixed with blood from a damaged venous sinus.

Conversely, fibroid metaplasia is characterised by fibroid collagenisation of the nucleus pulposus and degeneration of the annulus fibrosus, leading to intervertebral disk protrusion. In this condition, part of the nucleus pulposus shifts through a partially torn annulus fibrosus, causing a dorsal bulge of the intervertebral disk into the vertebral canal. This type of degeneration is more common in older, large, non-chondrodystrophic dogs.

Clinical presentation

The clinical signs of IVDE vary depending on the location of the IVDD and the severity of the spinal cord damage (compression, concussion, haemorrhage, secondary chemical lesions). In addition to neck or back pain, a range of upper motor neuron and lower motor neuron symptoms can occur. The severity of the clinical syndrome ranges from neck or back pain to complete paralysis with no pain sensation (refer to the Frankel modified score).

Diagnosis

Diagnosis requires advanced imaging, with MRI being superior to CT due to its superior parenchymal resolution. Radiography is not an acceptable diagnostic modality, as its accuracy is only 60%. Myelography improves diagnostic accuracy when radiography is the only available option, but it is considered suboptimal today.

Depending on the situation, CT (with or without myelogram) is an acceptable alternative to MRI in small dogs and chondrodystrophic breeds, as disk material is often mineralised and radiopaque in these breeds (see Fig. 1). However, CT is not ideal for older dogs with a history of disk extrusion, where distinguishing between old and recent extrusions is challenging. CT has the advantage of shorter acquisition time (a few minutes versus 45 to 90 minutes for MRI). MRI allows assessment of the hydration level of all intervertebral disks in the region, guiding the clinician in fenestration decisions, and enables evaluation of intramedullary changes, potentially adding prognostic value.

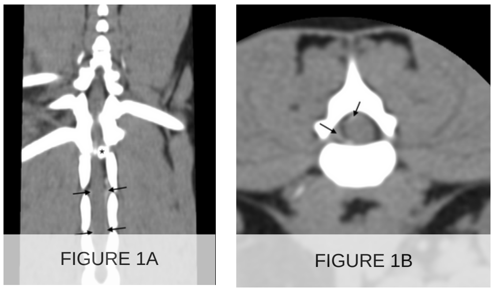

Figure 1. CT-scan images (without myelogram) at the level of the thoracolumbar junction of a 2-year-old French Bulldog presented for acute rapidly progressive hindlimb paralysis. A: dorsal view. Extradural radiopaque material extending on both sides of the spinal cord at from T13 to L2 (black arrows); likely a mixture of discal material and epidural haemorrhage. There is a radio-opaque extradural structure on the right side of the vertebral canal at the level of T13-L1 (black asterisk). This represents disk material from a previous extrusion. B: transverse view at the level of L1 showing the same extradural material made of dehydrated nuclear material and blood.

Treatment

There are two main treatment modalities for intervertebral disk extrusion (IVDE): medical/conservative management and surgical decompression.

The cornerstone of medical management is cage or crate rest, with painkillers added as needed. The primary purpose of cage rest is to limit further extrusion of disk material at the site of the annular tear, thereby preventing further clinical deterioration. Limited spinal movements should allow the annulus to heal within four to six weeks. It is important to note that no drug, medication, or supplement has been proven to alter the outcome.

Surgical management involves opening the vertebral canal and removing the extradural compressive material, which may include disk material and sometimes epidural haemorrhage. For thoracolumbar IVDE, the main technique is hemilaminectomy and its variations (e.g., pediculectomy for ventral extradural material and mini-hemilaminectomy). Fenestration of at least the affected intervertebral disk should be standard practice, as it reduces the risk of relapse at the same site. Evidence suggests that adjacent disks should also be addressed in predisposed breeds and/or based on MRI features.

For cervical IVDE, the ventral slot technique is preferred, as the extrusion is typically ventral, and this approach is relatively atraumatic. In rare cases, cervical hemilaminectomy is required to remove very lateralised disk material. This approach is more challenging due to the need for extensive muscle elevation, management of the vertebral arteries, and handling of the scapula for more caudal IVDEs.

Outcomes vary between medical and surgical management, with surgical management generally being more successful and associated with faster improvement. However, the success rate of medical management remains surprisingly high, even for paralysed (grade 4) dogs.

Outcome and prognosis

The prognosis for intervertebral disk extrusion (IVDE) is generally favourable and is primarily dependent on the pre-operative clinical status. Patients lacking pain perception prior to decompression have a significantly worse prognosis: approximately 50% will regain the ability to walk if decompression occurs within 48 hours of pain sensation loss, and less than 5% if it occurs beyond this timeframe. Other factors influencing the outcome include the length of the intramedullary signal on MRI and the presence of myelin basic protein in the cerebrospinal fluid (CSF). Additionally, the longer the clinical signs persist before decompression and the higher the Frankel score, the longer the recovery period.

Interestingly, studies using immediate post-operative CT scans have shown that the success rate is not correlated with the amount of material left in the canal at the end of the procedure, suggesting that the bone defect created during surgery plays a crucial role in relieving compression. A positive outcome is defined as a return to ambulatory status (even with some residual ataxia) for non-ambulatory patients and resolution of back or neck pain for those presenting with only pain initially.

B) Intervertebral disk extrusion in French Bulldogs

French Bulldogs are predisposed to IVDE, a common condition among chondrodystrophic dogs. In one study, IVDEs accounted for 5.5% of all FB cases presented to the institution and 70.3% of all myelopathies. However, the characteristics of IVDE in FBs differ from those in other small breeds, particularly Dachshunds.

Neurolocalisation

In a retrospective study of over 300 FBs, the location of intervertebral disk extrusion (IVDE) was cervical in 39.8% of cases and thoracolumbar in 60.2%. Cervical intervertebral disk extrusions (C-IVDE) in FBs exclusively occur at the C2-C3, C3-C4, and C4-C5 intervertebral spaces, with C3-C4 being the most commonly affected. For thoracolumbar intervertebral disk extrusions (TL-IVDE), slightly over half of the cases involved the L2-L3, L3-L4, and L4-L5 intervertebral spaces, with L3-L4 being the most frequently affected. This data aligns with other studies showing that 54% and 58.8% of all FBs with IVDE are affected caudal to L1. This is distinct from many other small breeds predisposed to TL-IVDEs between the T11-T12 and L1-L2 intervertebral spaces.

Consequently, FBs are more likely than other breeds to present with a lower motor neuron syndrome (weak or abolished spinal reflexes) due to the more caudal location of the compressive disk material. The lumbosacral intumescence and the lower motor neurons in its grey matter are more likely to be damaged.

Clinical signs and grade

In FBs, the clinical grade (modified Frankel score) is significantly lower for cervical C-IVDE) compared to TL-IVDE), with grades ranging from 1-2 for cervical and 2-5 for thoracolumbar cases.

Several factors may explain this difference. First, in TL-IVDE cases, spinal cord compression often extends over two intervertebral spaces (19/28 cases), while it never extends beyond one space in C-IVDE cases (0/11, ref 1). Epidural haemorrhage partly accounts for this extension. The more extensive compression in TL-IVDE cases results in a greater compromise of blood flow along the spinal cord. Additionally, the relative diameter of the vertebral canal compared to the spinal cord is larger in the cervical region than in the thoracolumbar region. Consequently, the spinal cord in the cervical region is less often severely compressed. A recent study found that the degree of spinal cord compression in TL-IVDE is moderate in over half of the cases and severe in about a quarter, whereas it is never severe in C-IVDE cases. This difference in the spinal cord/vertebral canal ratio is a common anatomical feature in all dogs, leading to generally less severe neurological symptoms in cases of C-IVDE, regardless of breed.

Moreover, the more caudal location of TL-IVDEs causes more damage to the lumbosacral intumescence. Due to differential growth between the skeleton and the spinal cord, the L4-S3 spinal cord segments are not aligned with their corresponding vertebrae. Thus, an IVDE at L3-L4 can compress the L4, L5, or even L6 spinal cord segments, resulting in damage to the intumescence's grey matter, lower motor neuron signs and a more severe clinical syndrome.

Interestingly, a recent study noted that 13 of the 20 patients displaying cervical jerks as a clinical sign of C-IVDE were FBs, an observation consistent with the author's experience. French Bulldogs often exhibit neck jerks or myoclonus with IVDEs. Although this clinical sign is less prevalent, it is sometimes encountered in other breeds, such as Beagles.

Diagnosis

Magnetic Resonance Imaging (MRI) characteristics of IVDEs differ between the cervical and thoracolumbar regions. In the thoracolumbar vertebral canal, haemorrhage often accompanies the extruded disk material, leading to T2 hyperintensity on MRI sequences in TL-IVDE cases (see Fig. 2). In contrast, the MRI features of C-IVDE are more classic, showing a hypo-intense signal in both T2- and T1-weighted images.

Intramedullary T2 hyperintensity on MRI is significantly more common in TL-IVDE than in C-IVDE. This signal indicates intramedullary edema, haemorrhage, fibrosis (gliosis), and even early-stage myelomalacia.

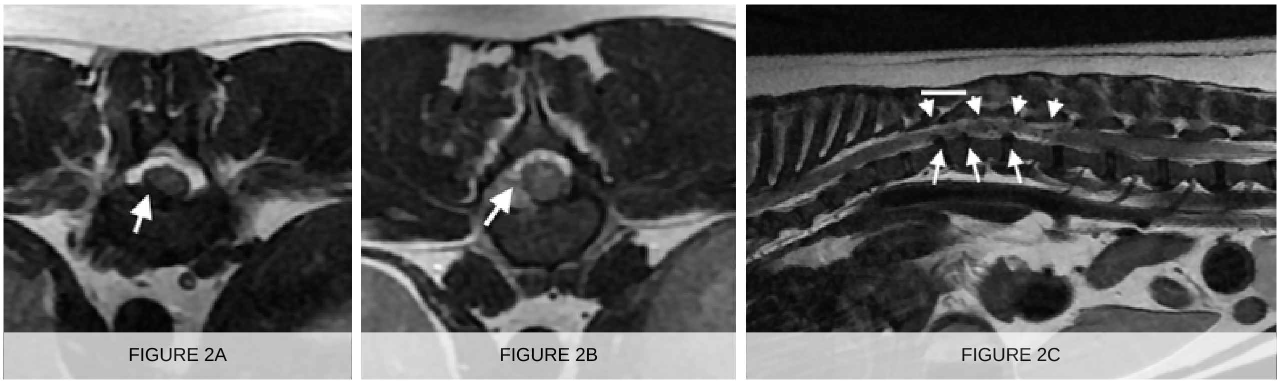

Figure 2. MR images of a 3-year-old French Bulldog presented for acute, rapidly progressive UMN hindlimb paralysis. A: right parasagittal T2W image at the level of the thoracolumbar vertebral column. There is extradural material of mixed T2 intensity extending from mid-T11 vertebra to the caudal aspect of L1 (white arrow). T11-T12, T12-T13, and T13-L1 intervertebral disk are bulging to an extent, making it impossible to tell which one has extruded (white arrows). All intervertebral disks are isointense to the grey matter when they should be hyperintense/white, illustrating global dehydration of all nuclei pulposus. B: T2 transverse images at the level of T13 showing the extradural material of mixed intensity on the right side of the vertebral canal (white arrow). C: T2 transverse images at the level of T12-T13 intervertebral disk, showing the dorsal aspect of the disk building out on the right ventral aspect of the canal. The disk material is continuous with the disk in place and hypointense (black) to the grey matter, meaning that it is probably an old extrusion or protrusion.

Surgical treatment

As mentioned above, cervical intervertebral disk extrusions (C-IVDEs) very rarely extend over a longer portion of the vertebral canal compared to TL-IVDEs. Cervical intervertebral disk extrusions always occupy one intervertebral space: specifically, 0.9 times the length of the C6 vertebra. In contrast, TL-IVDEs extend, on average, over a distance equal to 2.5 times the length of the L2 vertebra. This difference is likely due to the presence of associated haemorrhage in TL-IVDE cases. Disk-associated epidural haemorrhage, explained by disk material tearing the ventral venous plexus in the vertebral canal, is a common pathological feature of disk disease in the thoracolumbar area. It occurs in 66% of cases and is significantly more prevalent in FBs. Another study has shown that TL-IVDE is more often associated with epidural haemorrhage in FBs (41%) compared to Dachshunds (11%).

Given this, it is not surprising that most cases of C-IVDE require surgery at only one intervertebral space, typically using the ventral slot technique. However, the cervical lateral approach via hemilaminectomy is necessary to remove very lateralised disk material since the ventral slot does not allow direct access to the lateral aspects of the cervical canal. On the other hand, TL-IVDEs require hemilaminectomy extending over several intervertebral spaces, sometimes up to five. Interestingly, such a procedure rarely compromises the stability of the vertebral column.

Outcome and prognosis

Overall, there is no significant difference in outcome between cervical (C-IVDE) and thoracolumbar (TL-IVDE) intervertebral disk extrusions, but TL-IVDE cases graded as 5 have a poorer prognosis, especially when occurring between L1 and L4.

Some studies suggest that the length of changes in the spinal cord seen on imaging may have better prognostic value than the neurological status before surgery.

In clinical practice, due to the predisposition of French Bulldogs for epidural haemorrhage, it is advisable to recommend early decompression or very close monitoring, at the very least, rather than discharging for home medical management, when TL-IVDE is suspected in these dogs.

2. Others

(A) Vertebral malformations

Vertebral malformations typically involve abnormalities in the formation or fusion of vertebral ossification centres during embryonic or foetal development. Among these, malformations that result in kyphosis are particularly likely to cause neurological deficits. The terms hemivertebra and butterfly vertebra are commonly used interchangeably but are often misapplied. The primary malformations leading to wedge-shaped vertebrae and subsequent kyphosis on lateral views are dorsal hemivertebra (due to aplasia of the ventral part of the vertebral body) and ventral wedge-shaped vertebra (due to hypoplasia of the ventral part of the vertebral body).

While these issues can affect any breed, they are more prevalent in small breed dogs, especially brachycephalic screw-tail breeds like French Bulldogs, British Bulldogs, Pugs, and Boston Terriers. Interestingly, the screw tail shape in these breeds is believed to develop due to similar vertebral malformations observed in the thoracic region. The age at which these malformations present varies, with Pugs typically showing symptoms later in life.

In an important study detailing neurological issues in FBs, compressive vertebral malformation emerged as the third most common spinal disorder within the breed, affecting 19 out of 222 individuals (8.6%). Among these cases, seventeen dogs presented with hemivertebrae (89.5%, 95% CI 75.7–100%), often associated with significant kyphosis leading to spinal cord compression. The most commonly affected vertebrae were T6, T7, T8, and T10, and five FBs exhibited two or more malformations, a pattern frequently observed in such conditions. Interestingly, vertebral malformations causing kyphosis do not typically predispose FBs to intervertebral disk extrusion (IVDE) in the region of the malformed vertebrae but rather closer to the thoracolumbar junction. Conversely, scoliosis tends to predispose FBs to IVDE in the lumbar column. The reasons behind these predispositions remain unknown.

It is crucial for clinicians to understand that most vertebral malformations identified in FBs are incidental findings. Two studies have shown that 64.7% and 80.7% of clinically normal groups of French Bulldogs, British Bulldogs, and Pugs carry at least one vertebral malformation. Several authors have proposed using the severity of the dorsal curvature angle of the vertebral column in kyphotic dogs to differentiate between significant malformations and incidental findings. The Cobb angle, which measures the curvature of kyphosis, is a useful tool for this purpose. A Cobb angle exceeding 34.5 degrees has demonstrated the highest combined sensitivity and specificity in distinguishing between affected and unaffected dogs.

Radiography is valuable for assessing bony malformations and measuring the Cobb angle, which evaluates the severity of spinal curvature. Myelography provides insights into spinal cord compression. However, MRI is the preferred imaging modality due to its superior parenchymal resolution (see Fig. 3). T1-weighted MRI images offer detailed bone information. Additionally, CT scans excel in bone definition and are indispensable for surgical planning. It enables 3D reconstruction of the vertebral column and facilitates the creation of 3D models or printed guides for accurate screw placement during surgery (see Fig. 4).

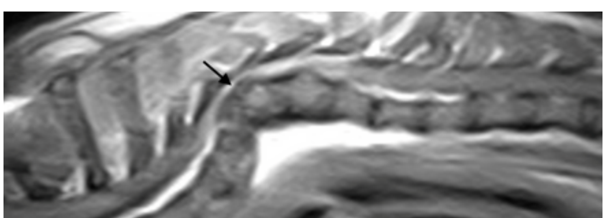

FIGURE 3

Figure 3. Image of a 3-year-old French Bulldog with T6 (dorsal hemivertebra. Low field sagittal T2 weighted MR images resulting in severe kyphosis and spinal compression. The black arrow shows the severely reduced vertebral canal diameter.

FIGURE 4

Figure 4. 3D reconstruction from CT-scan images of a 2-year-old French Bulldog with a T7 hemivertebra (truly dorsal wedge vertebra; black asterisk) causing kyphosis.

Medical management of vertebral malformations in dogs is typically empirical and involves several key approaches. Exercise restriction is crucial, along with the administration of painkillers when hyperesthesia is present. For dogs experiencing motor dysfunction, anti-inflammatory doses of prednisolone are often prescribed. Anecdotal evidence suggests that prednisolone may be more effective than non-steroidal anti-inflammatory medications in dogs with motor dysfunction.

Surgery is generally not recommended before the age of 9 months, although there are rare cases where young patients remain clinically stable or even show improvement without surgical intervention. Surgical management of clinically significant vertebral malformations in dogs is an area with limited literature compared to human medicine, where sagittal realignment is a primary objective due to bipedal posture. In dogs, the main surgical goals typically focus on relieving spinal cord compression and stabilising the vertebral column. While no single treatment has proven superior over others due to the lack of extensive literature, two main surgical techniques are commonly considered. The less invasive approach is "spinal stapling," where the surgeon uses shaped rods aligned to the curvature of the vertebral column and secures them to the spinous processes with surgical wire. The more complex technique involves placing pins or screws into the malformed vertebral bodies, followed by embedding them in polymethyl methacrylate (see Fig. 5). This method is challenging due to the abnormal shape of the vertebrae, but advancements such as patient-specific 3D-printed guides have enhanced its precision and effectiveness in recent years. There remains debate among clinicians on whether to perform decompression of the spinal cord (via dorsal laminectomy or hemilaminectomy) prior to stabilisation.

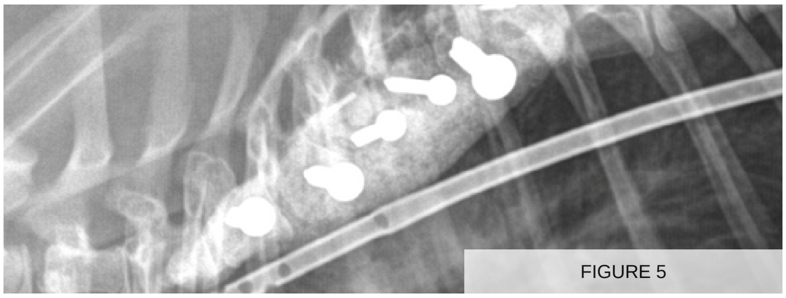

FIGURE 5

Figure 5. Post-operative lateral radiographic image of the thoracic vertebral column of a dog with a clinically significant wedge shape vertebra surgically stabilised with a combination of screws and polymethyl methacrylate.

Some advocate for a hemilaminectomy to visualise the spinal cord before proceeding with vertebral stabilisation. Overall, barring surgical complications, the majority of dogs experience maintenance or improvement in neurological status following stabilisation surgery.

(B) Spinal arachnoid diverticulum

Spinal Arachnoid Diverticulum (SAD) refers to a localised dilation of the subarachnoid space that leads to compression of the spinal cord. Previously referred to as a subarachnoid cyst, the term diverticulum is now preferred due to the absence of a complete lining in the dilated space. Spinal Arachnoid Diverticulae can occur in either the cervical or thoracolumbar regions of the spine. There is a notable predisposition for large breed dogs to develop cervical SADs, whereas small breed dogs, particularly Pugs and French Bulldogs, are predisposed to thoracolumbar SADs. Additionally, males appear to be predisposed regardless of the location of the SAD. Clinical signs related to SADs can manifest in dogs of all ages, with one study indicating a median age of 36 months at presentation, although there is a potential shift towards older patients for thoracolumbar SADs, with a median age reported as 6.2 years in another study. Notably, French Bulldogs tend to present with SAD-related clinical signs at a younger age compared to Pugs.

Various causes have been proposed for SAD in dogs, including hereditary and congenital factors, biomechanical stresses, and concurrent or prior spinal disorders such as intervertebral disk extrusions or inflammatory conditions like meningo-myelitis. The overrepresentation of certain breeds suggests a potential hereditary or congenital component to SAD development. Additionally, adjacent extradural spinal cord issues are often associated with SADs, suggesting that pia-arachnoid adhesions may play a role. These adhesions can result from previous surgeries, trauma, tumours, or conditions causing vertebral instability. Spinal Arachnoid Diverticulae predominantly occur in the dorsal part of the spinal cord, as observed in 83.2% of cases in one study. Thoracolumbar SADs are typically located between the T9 and L1 vertebral levels.

The clinical signs observed in dogs with SAD primarily reflect the compressive effects of the condition. The most common manifestation is spinal ataxia, which is nearly universal among affected dogs. Hypermetria, attributed to the dorsal location of the diverticulum and compression of the spinocerebellar tracts, occurs in just over 20% of cases.

Spinal hyperaesthesia is present in fewer than 20% of cases. Other signs such as paresis, and urinary or faecal incontinence are rare occurrences. The clinical syndrome associated with SAD is typically progressive, indicating a worsening of symptoms over time.

The diagnosis of SAD can be established using myelography, CT scan, or MRI. On myelograms or CT-myelograms, SAD typically appears as a gradual dilation of the subarachnoid space, culminating in a characteristic teardrop shape filled with contrast medium. In some cases, it may present simply as a blockage of the contrast column. However, MRI is the preferred diagnostic modality for SAD due to its superior anatomical resolution and ability to detect concurrent conditions, such as syringomyelia. On MRI, SAD exhibits a teardrop shape, appearing hyperintense on T2-weighted and FLAIR images, and hypointense on T1-weighted images (see Fig. 6). The use of HASTE sequences enhances the sensitivity of MRI in diagnosing SAD. Notably, MRI allows for the identification of associated syringomyelia, which is found in up to 50% of cases.

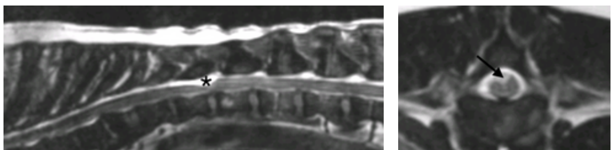
FIGURE 6A FIGURE 6B

Figure 6. T2-weighted MR images of a 5-year-old French Bulldog presenting for a 2-month history of moderate hindlimb upper motor neuron ataxia. A: sagittal view showing a dorsal subarachnoid diverticulum (black asterisk) at the level of T9-T10 in the form of a dilation of the subarachnoid space. B: transverse view at the level of the diverticulum (black arrow).

More generally, an adjacent concurrent spinal cord disease is identified in approximately 25% of SAD cases, with FBs being overrepresented in this category. Vertebral malformations and intervertebral disk disease are the most commonly associated spinal disorders.

Medical treatment of SAD is empirical, focusing on reducing cerebrospinal fluid (CSF) flow and accumulation and addressing subsequent spinal cord inflammation. Although no studies have clearly established the benefits of medical management alone, one study has compared it to surgical treatment. Prednisolone is the preferred treatment, with various regimens employed. In this study, only 26% of dogs showed improvement with medical management. Some practitioners also use omeprazole, a proton-pump inhibitor thought to reduce CSF production, though this application remains empirical.

Surgical management is generally preferred for SAD with studies indicating a positive outcome at the 1- to 2-year mark regarding gait and urinary continence. Various surgical techniques have been described, including durotomy, durectomy, diverticulum fenestration, dural marsupialisation, and vertebral stabilisation. Among these, marsupialisation and durectomy are the preferred techniques. The practice of dissecting leptomeningeal adhesions during durectomy or marsupialisation is debated, with no definitive evidence supporting its necessity. Stabilisation of adjacent vertebral instability or malformation can contribute to a positive outcome, particularly in breeds like Pugs and French Bulldogs, which are prone to such instability. The recurrence rate for SAD is approximately 20%, with a median time to recurrence of around 20 months.

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Nadine completed her rotating small animal internship at the Royal Veterinary College, followed by an Emergency and Critical Care internship at the University of Edinburgh. She subsequently completed a 3 year Emergency and Critical Care residency at RVC subsequently, and took on her board exams in 2023 to become a Diplomate of both the American and European Colleges of Veterinary Emergency and Critical Care.

Nadine enjoys all aspects of Emergency and Critical Care (ECC) and she is especially interested in the management of trauma patients, sepsis, acute kidney injury, as well as the use of extracorporeal therapies and transfusion medicine.

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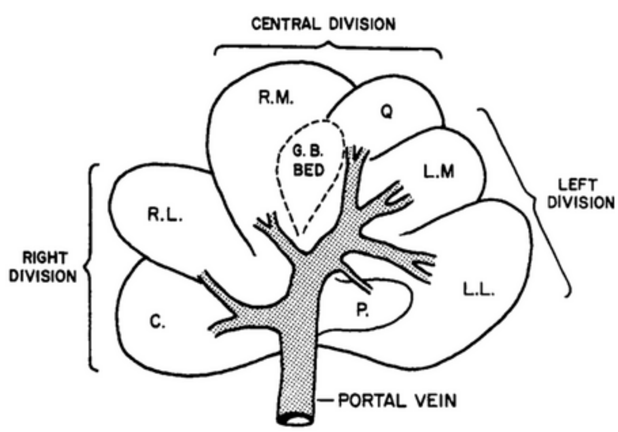
SURGICAL MANAGEMENT OF MASSIVE HEPATOCELLULAR CARCINOMA (HCC) IN DOGS

By Dr Hana Kurnianta, BSc (NUS Life Sciences), BVSc (Massey)

THE LIVER

The liver lobes were classified into three divisions[2-4]:

- Right division (right lateral lobe, caudate),
- Central division (right medial, quadrate),
- Left division (left medial, left lateral). In Sleight and Thomford, the papillary process of the caudate lobe was considered part of the left division, due to its blood supply.[3]



Drawing showing the three major divisions of the canine liver lobes. Image adapted from Sleight and Thomford et al.

A normal liver can regenerate itself after resection or injury.[1] It has been reported that removal of up to 70% of the liver tissue can be tolerated.[1] The liver will start regenerating within hours and peak in about three days, but full regeneration may take up to 6-10 weeks.[1] In dogs, the right lateral and caudate lobes make up approximately 28% of the liver, the right medial and quadrate lobes make up approximately 28%, and the left lateral and medial lobes make up the remaining 44%.[1]

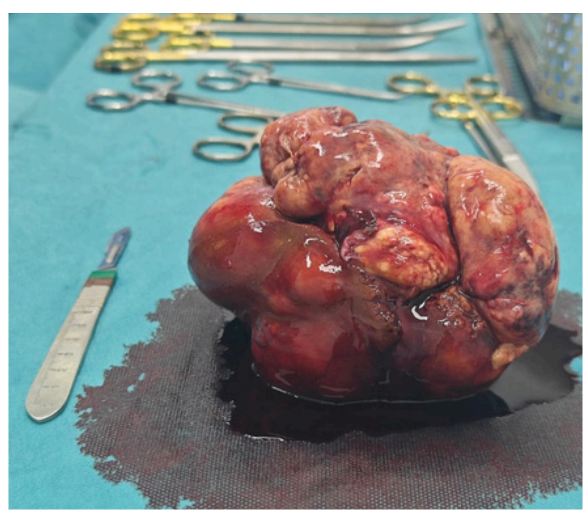
HEPATOCELLULAR CARCINOMA (HCC)

Primary hepatic neoplasia is rare in dogs, documented in 0.6-1.5% of all canine neoplasms.[5] Metastatic liver neoplasia is more commonly diagnosed than primary hepatic neoplasia in dogs.[5] Hepatocellular carcinoma (HCC) is the most commonly diagnosed primary liver tumour, accounting for 50-77% of primary liver tumours in dogs.[1,6,7]

There are different types of hepatic neoplasm based on gross morphology[6]:

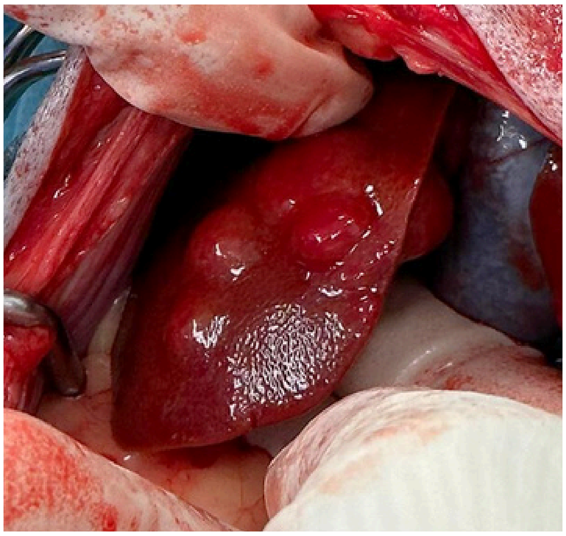
- *Massive type*

  One large solitary mass is observed in one of the liver lobes. There may or may not be involvement in other lobes.[8] The majority of HCC has the massive form, reported to be 61%. It was also reported that 66% of the massive type of HCC was found in the left lateral lobe.[8]

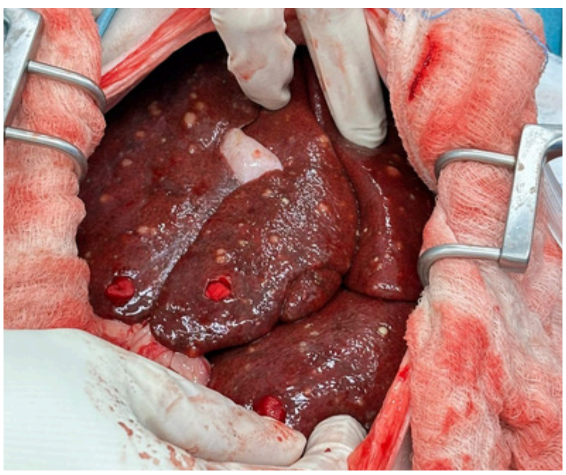


- *Nodular type*

  In this type, there are discrete nodules of various sizes in several lobes of the liver.[6] Nodular type accounts for 29% of all HCC.[7,8]



- *Diffuse type*
  Hepatic neoplasia of this type shows the entire or part of the liver permeated with neoplastic cells.[6] This type is found in 10% of all HCC.[7,8]



A study evaluating necropsy findings of dogs reported a metastatic rate of 61% for dogs with HCC, with lymph nodes and lungs being the most common location of metastasis.[6,8] The same paper reported a 36.6% metastatic rate in dogs with massive HCC.[8] More recent papers reported a lower metastatic rate in dogs with massive HCC. Liptak et al reported a 4.8% metastatic rate for massive HCC. A low local tumour recurrence rate was also reported for massive HCC.[7,9]

IMAGING

Radiographs

The presence of space-occupying lesions in the cranial abdomen area may be suggestive of a liver mass,[1] but often not specific for a hepatic mass.[5] It is also difficult to evaluate the extent of the mass with surrounding structures on radiographs.[1]

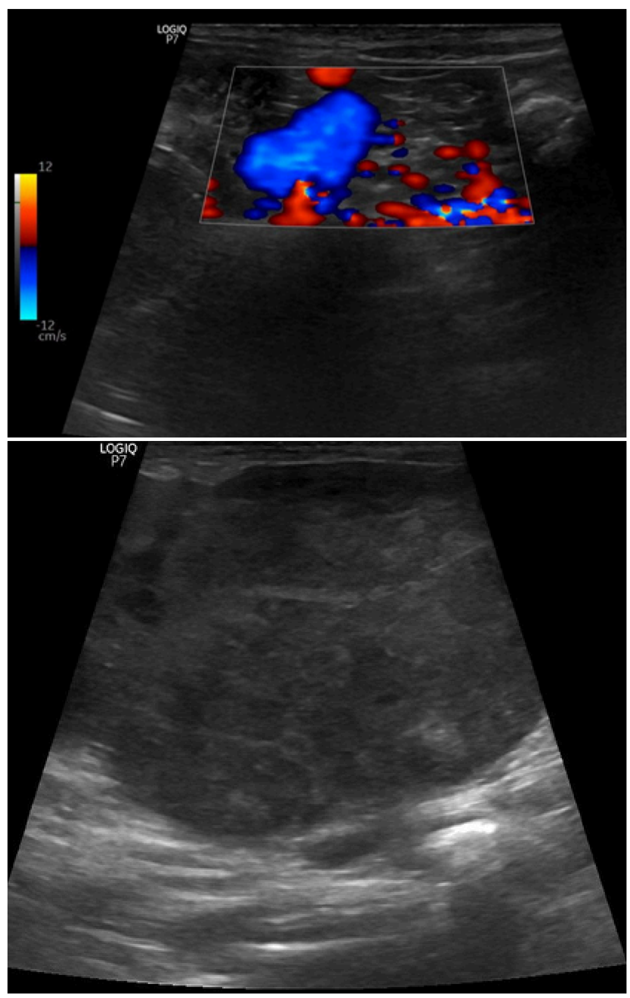
Three-view thoracic radiographs, however, can be useful to evaluate any evidence of pulmonary metastasis to the lungs.[5]

Ultrasound

Abdominal ultrasound is useful to identify the presence and type of hepatic mass.[5] Liptak et al found that the presence of solitary hepatic mass was able to be identified in 93.5% of the dogs.

In addition, ultrasound can also assess the size and location.[5] Ultrasound is more likely to accurately localise focal hepatic lesions compared to diffuse or multifocal hepatic lesions.[4] It was shown that ultrasound is also more likely to correctly identify liver masses located within the right and left division of the liver, compared to central division masses.[4] One study reported that ultrasound correctly localised 51.8%[4] of solitary liver masses, while another study found a higher accuracy rate of 74%[10] for the same task. It should be noted that factors such as operator skill, experience and equipment could affect the accuracy of lesion localisation via ultrasound.[4]

Ultrasound is more useful than radiographs in evaluating the relationship of the liver mass with surrounding structures.[5] However, in massive HCC, due to its large size, it may be difficult to differentiate between impingement and invasion of surrounding structures, and proximity of vital vascular structures such as the[7] caudal vena cava.



Abdominal ultrasounds of a four-year old female Golden Retriever.

Advanced Imaging

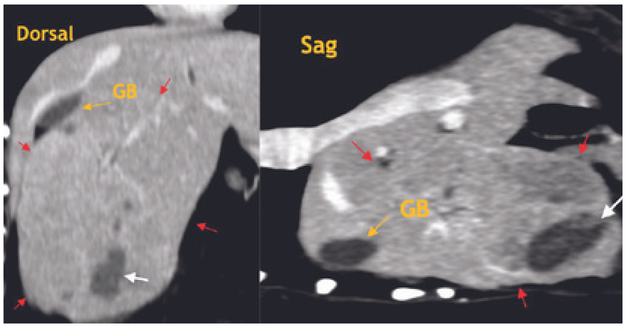
In humans, advanced imaging such as Computed Tomography (CT) scan or Magnetic Resonance Imaging (MRI) are routinely used as they can provide better information on the relationship of the hepatic mass with other anatomic structures.[7]

Moyer et al found a 90% agreement rate with ultrasound or CT scan with surgery, with regards to location of the tumour and presence of metastasis.[11] Another paper reported that ultrasound and CT scans could correctly predict the location of the liver masses in 74% and 84% of dogs in the study respectively.[10] Liptak et al found similar accuracy for both CT scan and ultrasound. CT scan, however, remains superior for differentiation between the underlying pathology of identified hepatic masses.[11]

Similar to ultrasound, CT scan also has lower sensitivity in localising mass located in the central and right division, compared to those in the left division.[10]

Advanced imaging may be recommended especially if the liver mass is suspected to be in the right or central division of the liver, due to the increased risk associated with surgery of these locations.[7] The association between tumour location and risk of complications will be discussed further in the section below.

CT scan is also useful for staging, as it has been reported to be more sensitive in detecting pulmonary nodules, especially in large and giant breed dogs.[12] In humans, CT is considered the gold standard for detecting pulmonary nodules due to its ability to detect small nodules with greater frequency than radiographs.[12]



Red arrows indicates a liver mass found in a 13-year-old male Siberian Husky.

SURGERY AND COMPLICATIONS

Surgical resection is the mainstay treatment for massive type, solitary liver tumours in dogs.[9,10] There are a few different techniques that can be used to perform complete or partial liver lobectomies, including hilar resection, preformed suture loops, surgical staplers, and vascular sealing devices.[9] The location of the tumour within the hepatic lobe influences the chosen method of dissection.[9] Linden et al reported no association between tumour size and intraoperative surgical complications.[9]

The most common complication of hepatic surgery reported was haemorrhage[7,13,14] which can potentially be life-threatening.[2] The liver produces coagulation factors and hence, underlying hepatic disease can increase the risk of haemorrhage in dogs undergoing hepatic surgery.[2] Therefore, evaluating APTT/PT prior to performing surgery is highly recommended.[2] It is worth noting that the results of preoperative coagulation testing may not accurately reflect the risk of intraoperative or postoperative haemorrhage in all cases.[2]

Liptak et al reported a 28.6% surgical complication rate for liver lobectomy for HCC, with haemorrhage being the most common complication.[7] The same paper reported an intraoperative mortality rate of 4.8% due to exsanguination.[7] Other reported complications associated with hepatic surgeries include hypotension,[9,11] extrahepatic biliary system injury,[9] vascular compromise to adjacent liver lobes, transient hypoglycaemia and reduced hepatic function.[5,7]

Tumour location affects the feasibility of resection and the likelihood of complications. Surgery involving the left division of the liver is usually technically simpler than other divisions,[9] as the left division is clearly demarcated from the central division.[2]

On the contrary, the lobes of the right and central divisions are fused to a certain degree. This poses more difficulty while trying to isolate the vascular pedicle during liver lobectomy in these divisions. The right and central divisions are also more adhered to the caudal vena cava, creating further surgical challenges. Liptak et al reported the intraoperative mortality rate involving right division to be 40%, due to haemorrhage as a result of trauma to the caudal vena cava. Similarly, Linden et al reported 37.7% of intraoperative complications in central division liver lobectomies, most commonly consisting of haemorrhage and a few due to injury to the extrahepatic biliary system.

In a retrospective study by Hanson et al, they found that 17% of dogs undergoing liver lobectomy required blood transfusion. No significant differences in techniques used between dogs requiring versus not requiring a transfusion.[14] The study found a significantly higher mortality rate within the group of dogs requiring transfusion – 27% of dogs requiring transfusion failed to survive to hospital discharge. Another paper by Moyer et al reported a 9% transfusion rate in dogs with HCC undergoing surgical liver biopsy procedures. In contrast to the study by Hansen et al, the findings did not show a higher mortality rate in the group needing transfusion.[11]

A paper by Linden et al evaluated the outcome of central division hepatic lobectomies in dogs.[9] The study reported an 11% perioperative mortality rate.[9] A higher number (31%) of the dogs in this study required transfusion.[9]

The higher transfusion rate may reflect the greater technical challenge associated with central division lobectomy, as hepatic veins of the central division are short, wide, and covered in hepatic parenchyma.[9]

Complications were more common when hilar resection was performed during lobectomy of the central division, as more extensive resection is required when removing tumours near the hilus.[9] This can result in substantial haemorrhage.[9] Hence, it is ideal to prepare blood products especially when planning for surgeries involving the central division of the liver.[9]

Additionally, hilar resection of tumours involving the central division also often requires en bloc removal of the entire central division and concurrent cholecystectomy due to the shared vascular supply of the right medial and quadrate liver lobe.[9]

PROGNOSIS

Prognosis is good for massive HCC as they are reported to have relatively nonaggressive behaviour, and surgical resection is often possible.[5,11] Surgery is the treatment of choice for massive hepatocellular carcinoma, as surgical excision offers long-term survival time.[7] The nodular and diffuse types of HCC have a worse prognosis than the massive type.[5,11] Nodular and diffuse types usually involve multiple lobes and are not amenable to surgical resection.[7] The poorer prognosis of nodular and diffuse types could also be associated with the presumed increase of hepatic function compromise in the nodular and diffuse forms.[11]

Reported median survival time (MST) with surgery is between 707 days[15] to more than 1,460 days (more than four years).[7] The paper found that disease-related deaths were 15.4 times more frequent in dogs managed conservatively, compared with dogs managed surgically.[7] MST is significantly shorter without surgical intervention.[7] MST without surgery is less than one year (270 days).[7]

There are conflicting results regarding the association between survival time and histopathological margins.

Matsuyama et al found a difference in the survival time of patients with complete and incomplete margins.[16] Other papers do not show a significant difference in survival times.[7,9,11,15] Despite the significant difference in survival time, the median overall survival time is still within years: 765 days (>two years) for incomplete margins and 1,836 days for complete margins.[16] Matsuyama et al also found that complete margins were more frequently achieved from samples from the left division, than the right or central divisions.[16]

Linden et al reported higher surgical complication rates pertaining to the central division.[9] Considering that a long survival time still can be achieved without completely removing the tumour, debulking of the central division may be considered if a more aggressive surgery is likely to put the patient's life at risk.[11]

The distant metastatic rate for massive HCC has been reported to be between 0-37%.[13] The effect of HCC appears to be due to its space-occupying lesion effect, hepatic dysfunction secondary to local invasion, or spontaneous rupture leading to hemoabdomen.[11,15] Liver mass rupture is the second most common cause of spontaneous hemoabdomen, accounting for 13-18% of the causes in dogs.[15] Well-differentiated HCC was the most frequent lesion (36%) in cases of hemoabdomen due to ruptured liver mass.[15] Hemoabdomen is often associated with rupturing of the spleen,[15] but it is important to keep liver mass as one of the potential differential diagnoses, especially in patients with a history of having a hepatic mass.

MONITORING AND FOLLOW-UP AFTER SURGERY

The local recurrence rate after mass removal for massive HCC has been reported to be low (0-27%).[7,9,13] A case-control study by Lapsley et al aimed to further explore the time to local recurrence, risk factors for local recurrence, and outcome following recurrence for a single massive HCC after surgical excision.[13]

In this study, the median time to develop local recurrence is one year from surgery.[13] Median survival time was not significantly different in dogs that developed recurrence and those that did not develop recurrence – 851 days vs 970 days.[13] There was also no significant difference in survival time for those undergoing additional treatment at the time of recurrence, however, overall survival trended toward being longer for those who had additional treatment.[13] Reported treatment for recurrence includes surgery and medical management (chemotherapy, liver supplementation, supportive gastrointestinal medications, analgesics).[13] Therefore, if recurrence is suspected or identified and further intervention is possible, treatment is strongly encouraged.[13] Longer overall survival has been shown in humans with HCC recurrence who undergo treatment.[13]

In this paper, risk factors for the development of recurrence were not identified.[13] However, the study found that many of the dogs with identified tumour recurrence had ALT and ALP elevations respectively.[13] In 25% of patients with recurrent disease, the elevation of liver enzymes prompted the initial workup.[13] Liver enzyme monitoring could act as a non-invasive surveillance tool to monitor recurrence,[13] and to consider further workup if there is evidence of an increasing trend in patient's liver enzymes. Ultrasound is a widely available, non-invasive and relatively cost-effective modality that can be used during routine surveillance as well.[13]

In humans with HCC, routine surveillance consists of ultrasound and biomarker testing every three to six months.[13] In veterinary medicine, liver enzyme monitoring and abdominal imaging every three to six months could be considered. Tumour recurrence is more likely to be detected earlier in dogs who had routine surveillance.[13] Routine surveillance is recommended in dogs and should extend beyond one year after surgery.[13]

CONCLUSION

In general, the prognosis of patients with massive HCC undergoing surgical treatment is good. Surgical management remains the mainstay of treatment for dogs with HCC and should be recommended whenever possible. Imaging prior to surgery is beneficial for surgical planning and preparation for anticipated complications. Preparation for transfusion should be considered especially in surgeries involving the central or right divisions of the liver. After surgery, it is recommended to continue surveillance at least bi-annually and extend surveillance beyond one year post-surgery. Further treatment should be considered if evidence of recurrence is observed.

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Having completed a master's degree and Surgical Residency at Virginia Tech, he did a 12-month Fellowship in Cardiac Surgery and Surgical Oncology before starting one of the busiest surgical referral practices in the Washington DC area.

Dr Charles served on the Board of Directors and as Program Chair for the District of Columbia Academy of Veterinary Medicine in Washington DC. He has published dozens of scientific articles, abstracts, patents, proceedings, and book chapters on topics of surgery and surgical oncology. With his years of experience, he has trained innumerable interns and surgical residents.

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UPDATES & announcements

VETERINARY CE LUNCHEON

Beecroft's upcoming Vets' Continuing Education Luncheon is scheduled for brunch on 17 November 2024. More details will be sent to you via an email invitation and shared on our website and social media. We look forward to sharing knowledge and fostering collaboration with you.

BEECROFT'S REFERRAL SERVICES

Beecroft's website now offers online request forms for PennHip and Outpatient Lab services. Scan the QR code on the left to access the online forms or visit our website directly: *https://beecroft.com.sg/for-veterinarians*

HELP US IMPROVE OUR SERVICES

As part of our ongoing efforts to enhance patient care and referral services, we invite you to share your thoughts and experiences with us. We would be grateful if you could complete a brief online survey to help us understand our strengths and identify areas for improvement, allowing us to better support you and your patients.

BEECROFT
ANIMAL SPECIALIST & EMERGENCY HOSPITAL

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