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CLINICAL RESEARCH

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Outcomes and prognostic variables associated with right divisional hepatic lobectomies in 70 dogs

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Abstract

Objective: To determine the outcome and prognostic variables associated with survival and complications in dogs undergoing right divisional hepatic lobectomies.

Study design: Multi-institutional retrospective case series.

Animals: A total of 70 client-owned dogs with right divisional hepatic masses.

Methods: Medical records of dogs undergoing right divisional hepatic lobectomies and partial lobectomies from January 1, 2008 to January 1, 2022 were reviewed and key variables were extracted. Univariable logistic regression estimated effects of risk factors. Kaplan–Meier survival curves estimated overall survival times (OST) and median survival times (MST).

Results: Intraoperative complications occurred in 38/70 (54.3%) dogs. A total of 15 dogs (21.4%) required blood transfusions. No surgical method was

Abbreviations: HCC, hepatocellular carcinoma; HCA, hepatocellular adenoma; ICU, intensive care unit; MST, median survival time; OST, overall survival time; TA, thoracoabdominal.

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associated with intraoperative ($p = .566$), immediate postoperative ($p = .756$), or short-term complications ($p = .799$). Perioperative mortality risk was 2.9% and 30-day mortality risk was 12.1%. There were differences in survival based on the requirement for advanced hemodynamic support ($p = .004$). Hepatocellular carcinoma (HCC) was the most common diagnosis at 52.9%. The 1-, 2-, and 3-year survival rates for dogs with HCC were 77%, 55%, and 12%, respectively, with 35.3%, 48.8%, and 65.8% lost to follow-up at 1, 2, and 3 years.

Conclusion: Right divisional hepatic lobectomies were associated with a high intraoperative complication risk, with 21% of dogs requiring blood transfusions; however, no intraoperative deaths occurred. No surgical method was associated with greater risk of complications.

Clinical significance: Despite high intraoperative complication risks, right divisional lobectomy and partial lobectomy may carry a lower risk of perioperative mortality than previously considered.

1 | INTRODUCTION

Primary liver tumors account for 0.6%–1.3% of all canine neoplasms and hepatocellular carcinoma (HCC) is the most common primary liver tumor reported.[1,2] Hepatocellular carcinoma is classified as massive, nodular, or diffuse.[1,2] Massive HCC, described as a solitary mass originating from a single lobe, represents 61% of all canine HCC and is usually the only form amenable to surgical resection.[1,3] According to a study by Liptak et al., liver lobectomy is the recommended treatment for dogs with massive HCC.[3] The authors reported a median survival time (MST) of >1460 days and the tumor-related mortality risk was 15.4 times higher in dogs not treated with surgery.[3]

The liver is comprised of three divisions: left (left medial and lateral lobes), central (quadrate and right medial lobes), and right (right lateral and caudate/papillary processes of the caudate lobe) as described in Covey et al.[2,4] The left division comprises 44% of the hepatic volume, with the central and right divisions accounting for 28% each.[2,5] Various studies report left divisional masses to account for 58.1%–73% and central divisional masses to account for 19.5%–34.9% of all liver masses.[3,6–8] While the central and right divisions are roughly equal in volume, right divisional masses are consistently the least reported, accounting for 12.2%–20.6% of reported cases.[3,6–8]

Various methods have been described for performing liver lobectomies including stapling devices, vessel sealing devices, circumferential ligatures, and hilar resection, which is defined as blunt dissection of the hilus and ligation of individual vessels. Hilar resection has been associated with increased risk of intraoperative and short-term complications.[9,10] Lobectomies using a thoracoabdominal (TA) stapler are reportedly associated with reduced complications, with one study finding the use of a vessel sealing device, circumferential ligature, or hilar resection being 19 times more likely to have intraoperative complications and 4.4 times more likely to have postoperative complications compared to a TA stapler.[8,9]

Several studies to date have evaluated complication risks following lobectomy involving different hepatic divisions. A study assessing outcomes of central divisional lobectomies had a 37.7% intraoperative complication risk and 11.8% mortality risk.[9] One study including 18 dogs with right divisional hepatic lobectomies had a similar intraoperative complication risk of 33.3% and found no significant difference in risk of intraoperative complications between right and central divisional lobectomies.[8] This study also reported a 88% higher chance of intraoperative complications compared to left divisional lobectomies.[8] Another study including five right divisional lobectomies reported a 40% intraoperative mortality risk; however, both studies that assessed the right division had an overall low proportion of right divisional masses.[3,8] There are currently very few reports detailing complications and outcomes associated with right divisional hepatic lobectomies and none that solely focus on the right division.

The objective of this study was to determine the outcome and prognostic variables associated with survival and complications in dogs undergoing right divisional hepatic lobectomies. We hypothesized that right divisional hepatic lobectomies would have a low perioperative mortality risk similar to central hepatic lobectomies as reported by Linden et al.[9] We also hypothesized based on anecdotal experience from multiple authors that, contrary to previously published information, there would be no difference in complications between the various surgical methods used to perform right divisional hepatic lobectomies.

2 | MATERIALS AND METHODS

2.1 | Study design

This was a multi-institutional, retrospective case series. Medical records were obtained from six contributing institutions including academic teaching hospitals and specialty hospitals between November 2008 and January 2022. Records were searched for dogs diagnosed with and surgically managed for masses of the right liver division. Data collected from the provided medical records included breed, sex, age, bodyweight, clinical signs at the time of diagnosis, preoperative diagnostics performed, date of surgical procedure, mass location and size, surgical method, use of intraoperative blood products and other interventional support (fluids, vasopressors), anesthetic duration, intraoperative complications, immediate postoperative complications (0–48 h), short-term postoperative complications (2–14 days), long-term postoperative complications (>14 days), histopathologic diagnosis, surgical margin evaluation, evidence of recurrence/progression of disease, date of last follow-up, and date and cause of death. Dogs with concurrent lobectomies of the central or left division were excluded.

Liver lobectomy was defined as complete when the entire liver lobe was excised or partial when a portion of the lobe was excised. Liver lobes were classified as right lateral, caudate (papillary process, caudate process, or unspecified process), or both. All procedures were performed or overseen by a board-certified surgeon or surgical oncology fellow. All cases had access to intensive care unit (ICU) care and various hospitals had board-certified anesthesiologists and criticalists available. Surgical method was defined as hilar resection (blunt dissection and ligation with suture or hemoclips), circumferential ligature, use of a stapling device, use of a vessel sealing device, or hybrid if two or more methods were used. Percentage of total blood volume lost was used to classify hemorrhage as mild (5%–15%), moderate (15%–30%), or major (30% or greater). Mass size was obtained from histopathology or surgery reports. For masses with only two dimensions provided, an estimated cubic size was calculated by multiplying these two dimensions by their mean value as performed in the study by Linden et al.[9] Duration of anesthesia was recorded from induction to extubation. Advanced hemodynamic support was classified as either fluid support (crystalloid or colloid fluids) or cardiovascular support (vasopressors or anticholinergics). Postoperative complications were classified according to the Clavien Dindo scale of surgical complications. Histopathologic margins were defined as complete, incomplete, or unknown when not reported. A minimum follow-up time was not utilized in this study. Hospital and referring veterinary clinic records were obtained and reviewed for date of last follow-up. Patient survival time was calculated from the date of surgery to the date of last follow-up or death.

2.2 | Statistical analysis

All analyses were performed using SAS 9.4 (SAS, Cary, North Carolina). A significance threshold of $p < .05$ was used. The assumptions of normality for age, weight, tumor size and anesthesia duration were confirmed via inspection of Q-Q plots, histograms, and skewness. Two-sided Wilson confidence intervals were calculated for binomial proportions.

Univariable logistic regression was used to estimate odds-ratios and test for the effects of risk factors on HCC diagnosis, recurrence, and complications. If quasi-separation was present Firth's bias-reduced penalized-logistic regressions were used. Log-likelihood *p*-values and odds ratios with profile-likelihood odds ratio confidence limits are reported.

Kaplan–Meier survival curves were constructed for overall survival times (OST) and used to estimate MST and 1-, 2- and 3-year survival probabilities. Log-rank tests were used to compare OST between categorical risk factors. Cox proportional hazards regression was used to test for the effect of continuous risk factors on OST and generate hazard ratios. Dogs were censored from survival analyses if they were alive at last follow-up. Survival analyses were run for all dogs and for HCC dogs separately.

Only risk factor groups with at least five dogs were included in inferential analyses. *p*-values were adjusted for multiple comparisons using the linear step-up false discovery method of Benjamini and Hochberg for each endpoint separately.

3 | RESULTS

3.1 | Signalment

A total of 70 client owned dogs met the inclusion criteria for this study. The median age at the time of surgery was 10.0 years (range: 2.0–16.0) and the median bodyweight was 16.3 kg (range: 4.0–52.0). There were 35 (50%) spayed female dogs, 34 (48.6%) castrated male dogs, and one (1.4%) intact male dog. The most common breeds represented were mixed breed (12), Beagle (5), Shih Tzu (5), Australian Shepherd (4), Dachshund (4), and Golden Retriever (4).

3.2 | Clinical signs

The most common clinical signs were lethargy (23/70, 32.9%), hyporexia/anorexia (22/70, 31.4%), vomiting/regurgitation (13/70, 18.6%), and weight loss (11/70, 15.7%). A mass of the right liver division was an incidental finding in 21 dogs (21/70, 30%).

3.3 | Preoperative diagnostic tests

Preoperative bloodwork including serum biochemistry, hematology, coagulation panels, and blood typing were available in 61, 64, 35, and 19 dogs, respectively. Serum biochemistry abnormalities included increased alkaline phosphatase in 80.3% (49/61) of dogs (1212.4 U/L, range: 178–7634 U/L), increased alanine transferase in 67.2% (41/61) of dogs (777.0 U/L, range: 128–6629 U/L), and increased aspartate transaminase in 8.2% (5/61) of dogs (2157.6 U/L, range: 70–8256 U/L). Hematologic abnormalities included anemia in 29.7% (19/64) of dogs (30.4%, range: 13%–39.6%), thrombocytosis in 14.1% (9/64) of dogs (648.1 × 10^3/uL, range: 489–954 × 10^3/uL), thrombocytopenia in 12.5% (8/64) of dogs (115.1 × 10^3/uL, range: 4–219 × 10^3/uL), and leukocytosis in 12.5% (8/64) of dogs (29 × 10^3/uL, range: 19.5–66.9 × 10^3/uL). Coagulation abnormalities included a prolonged prothrombin time in 17.1% (6/35) of dogs (14.3 s, range: 8.1–22.5 s), prolonged partial thromboplastin time in 14.3% (5/35) of dogs (66.1 s, range: 14.8–> 200), and hyperfibrinogenemia in 48.6% (17/35) of dogs (418.9 mg/dL, range: 197–955 mg/dL). Five dogs were DEA 1.1 positive and 14 were DEA 1.1 negative. Preoperative imaging included abdominal ultrasound in 52 dogs and abdominal computed tomography (CT) in 39 dogs.

3.4 | Surgery

A ventral midline abdominal approach was performed in all dogs. A caudal sternotomy (8) was performed for some procedures at the discretion of the attending surgeon. A partial (17/70, 24.3%) or complete (49/70, 70%) liver lobectomy was performed depending on mass location and at the discretion of the attending surgeon; 4/70 (5.7%) were not specified (Table 1). Surgery involved the right lateral lobe in 31 dogs (44.3%), the caudate lobe in 31 dogs (44.3%) (20 caudate process (28.6%), 11 papillary process (15.7%)), and both lobes in eight dogs (11.4%) (Table 2). Six dogs were diagnosed with hemoperitoneum prior to surgery. A total of 14 dogs underwent concurrent procedures including splenectomy (6), gastrotomy (2), cholecystectomy (2), and one each of intestinal resection and anastomosis, nephrectomy, adrenalectomy, partial pancreatectomy, anal sacculectomy, and cystotomy. A liver mass was an incidental intraoperative finding in two of these cases for which one partial and one complete lobectomy were performed in addition to the partial pancreatectomy and intestinal resection and anastomosis respectively. Liver lobectomy was performed co-primarily in seven cases. One cholecystectomy was concurrently performed for a partial extra-hepatic biliary tract obstruction and the second for a gall bladder mucocele. One splenectomy was performed for a hemorrhaging mass in addition to a hemorrhaging liver mass. One anal sacculectomy was performed for a mass appreciated on physical examination. One splenectomy, nephrectomy, and adrenalectomy were each performed for an additional mass appreciated on imaging. Liver lobectomy was the primary procedure for all other cases.

Lobectomy methods included a stapling device (TA stapler, TA30-V3 and TA60-3.5 stapler cartridges; Medtronic Inc., Minneapolis, Minnesota) in 58.6% of dogs (41/70), a vessel sealing device (LigaSure; Medtronic Inc.) in 8.6% of dogs (6/70), circumferential ligature (2, 1, or 2–0 silk) in 15.7% of dogs (11/70), hilar resection in 2.9% of

TABLE 1 Distribution of liver lobectomy type and surgical method.

Surgical method	Partial lobectomy ($n = 17$)	Complete lobectomy ($n = 49$)	Unknown lobectomy degree ($n = 4$)
TA stapler	7	32	2
Vessel sealing device	4	2	0
Circumferential ligature	3	6	2
Hilar	N/a	2	0
Hybrid	3	6	0
Not specified	0	1	0

Abbreviation: TA, thoracoabdominal stapler.

TABLE 2 Distribution of liver lobe(s) excised and surgical method.

Surgical method	Total cases	Right lateral (31)	Caudate (31)	Both (8)
TA stapler	41	19	18	4
Vessel sealing device	6	4	2	0
Circumferential ligature	11	3	7	1
Hilar	2	0	0	2
Hybrid	9	4	4	1
Not specified	1	1	0	0

Abbreviation: TA, thoracoabdominal.

dogs (2/70), and a hybrid of these methods in 12.9% of dogs (9/70). Hybrid procedures included hilar resection and vessel sealing device (5/9), stapler and vessel sealing device (2/9), and circumferential ligature and stapler (2/9).

Partial and complete liver lobectomies were performed of the right lateral (partial 6/17, complete 23/49), caudate (9/17, 20/49), and both right lateral and caudate lobes (2/17, 6/49), respectively. For the caudate lobe, 7/17 partial and 12/49 complete lobectomies were performed on the caudate process and 2/17 partial and 8/49 complete lobectomies were performed on the papillary process. A TA stapler was used for partial lobectomy in seven dogs (41.2%) and complete lobectomy in 32 dogs (65.3%). A vessel sealing device was used for partial lobectomy in four dogs (23.5%) and complete lobectomy in two dogs (4.1%). Circumferential ligature was used for partial lobectomy in three dogs (17.6%) and complete lobectomy in six dogs (12.2%). Hilar resection for complete lobectomy was performed in two dogs (4.1%). A hybrid of these methods was used for partial lobectomy in three dogs (17.6%) and for complete lobectomy in six dogs (12.2%). The method of surgical resection for complete lobectomy was not described in one case. Two complete right divisional lobectomies (right lateral and papillary and caudate processes) were performed.

Mass size was available for 38 dogs (38/70, 54.3%), all of which had histological diagnoses of either benign or malignant neoplasia including HCC (23), hepatocellular adenoma (HCA) (8), hemangiosarcoma (3), and one each of biliary adenoma, biliary cystadenoma, islet cell carcinoma, and histiocytic sarcoma. The median mass volume was 205.5 cm^3 (range: 3.4–3627 cm^3). The median tumor volume for HCC was 327.3 cm^3 (range: 3.4–3627.0 cm^3). The median tumor volume for HCA was 187.5 cm^3 (range: 26.3–2560.0 cm^3).

3.5 | Surgical complications and outcomes

Intraoperative complications were reported in 38/70 (54.3%) dogs. Surgical complications occurred in 28/70 (40%) dogs, hemorrhage being the most common with six experiencing mild hemorrhage, 17 experiencing moderate hemorrhage, and two experiencing major hemorrhage from injury to the caudal vena cava. The degree of hemorrhage was not specified for three cases; however, each required a blood transfusion, making it likely they experienced moderate to severe hemorrhage. Two dogs (2.8%) sustained damage to the caudal vena cava, both of which were successfully managed with placement of atraumatic vascular forceps and repair with monofilament absorbable suture material in a simple interrupted pattern. Anesthetic complications occurred in 23/70 (32.8%) dogs with cardiovascular abnormalities including arrhythmias and hypotension in 23 dogs and regurgitation in one dog (Table 3). The median anesthesia time was 170 min (range: 73–323 min). A total of 15 dogs (21.4%) required transfusions of either whole blood or packed red blood cells (Table 4). There was no association between receiving a blood transfusion and intraoperative ($p = .272$), immediate postoperative ($p = .268$), or short-term complications ($p = .790$). There was also no association between intraoperative complications and tumor size ($p = .866$). Advanced hemodynamic support was provided as necessary in the form of fluid support in 7/67 dogs (10.4%), cardiovascular support in 17/67 dogs (25.4%), and combined fluid and cardiovascular support in 13/67 dogs (19.4%). A total of 30 dogs did not require advanced hemodynamic support (44.8%). The necessity of advanced hemodynamic support was not associated with anesthetic time ($p = .390$). There was no association between intraoperative complications and the type of surgical method ($p = .566$), a partial versus complete liver lobectomy ($p = .272$), or the lobe(s) removed ($p = .272$).

Immediate postoperative complications (0–48 h) were reported in 19/70 dogs (27.1%) with nine dogs experiencing two complications and one dog experiencing three (Figure 1). Complications included anemia in 12 dogs, cardiovascular abnormalities (arrhythmias, coagulopathies, hypotension) in seven dogs, respiratory distress in five dogs, hepatic encephalopathy or neurologic signs in three dogs, and one dog each developing

TABLE 3 Intraoperative complications by surgical method.

Surgical method	Total cases	Hemorrhage	Cardiovascular	Injury to surrounding structures	Regurgitation
TA stapler	41	16	12	0	0
Vessel sealing device	6	3	3	0	0
Circumferential ligature	11	2	1	1	0
Hilar	2	2	0	1	0
Hybrid	9	5	6	0	0
Not specified	1	1	1	0	1

Abbreviation: TA, thoracoabdominal.

TABLE 4 Blood transfusions by surgical method.

Surgical method	Total cases	Blood transfusion
TA stapler	41	7
Vessel sealing device	6	1
Circumferential ligature	11	2
Hilar	2	0
Hybrid	9	4
Not specified	1	1

Abbreviation: TA, thoracoabdominal.

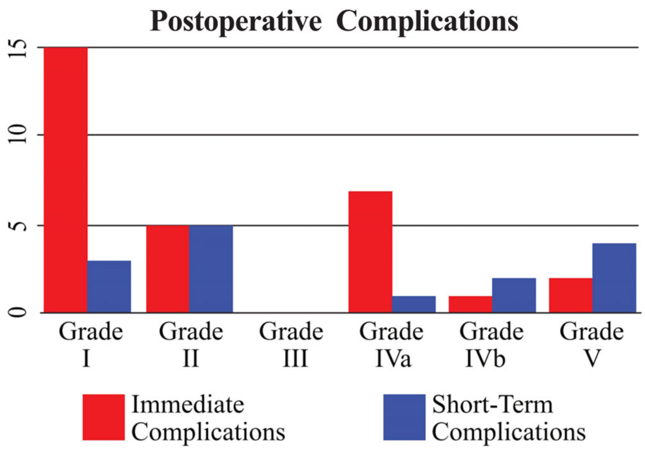

FIGURE 1 Bar graph depicting the number of immediate (red) and short-term (blue) postoperative complications according to the Clavien Dindo scale of surgical complications.

hyperglycemia, azotemia, and icterus. Two of these complications resulted from additional procedures including hyperglycemia following partial pancreatectomy and icterus following cholecystectomy. Advanced hemodynamic support was not associated with immediate postoperative complications ($p = .268$). Two patients died during the immediate postoperative period. One dog died from suspected disseminated intravascular coagulation (DIC) the day after surgery and the other was euthanized the day after surgery for suspected multiple organ dysfunction syndrome (MODS). Both dogs received a blood transfusion, and a hemolytic transfusion reaction was suspected in the dog with MODS as hemolysis and foci of splenic and adrenal necrosis were appreciated on necropsy. There was no association between immediate postoperative complications and the type of surgical method ($p = .756$), a partial versus complete liver lobectomy ($p = .326$), or the lobe(s) removed ($p = .196$).

Short-term postoperative complications were reported in 15/64 dogs (23.4%). Four dogs were lost to follow-up in the short-term period. Eight dogs developed a surgical site infection, three developed a seroma, two developed septic peritonitis, and one dog each developed aspiration pneumonia and a perforated gastrointestinal ulcer. Septic peritonitis following intestinal resection and anastomosis was the only complication resulting from an additional procedure. Advanced hemodynamic support with combined fluid and cardiovascular support was associated with short-term complications increasing odds by 17 times ($p = .029$, OR 17.3, 95% CI: 3.5–112) compared to dogs that did not require hemodynamic support. Four dogs died within the short-term period. Two died from complications attributed to additional procedures performed, including the intestinal resection and anastomosis from septic peritonitis on day 4 and suspected DIC secondary to biliary disease (concurrent cholecystectomy performed) on day 6 postoperatively. One dog with a concurrent splenectomy was euthanized for septic peritonitis on day 7 postoperatively. The last dog had a perforated gastrointestinal ulcer suspected to be secondary to nonsteroidal anti-inflammatory use and was euthanized day 3 postoperatively. There was no association between short-term complications and the type of surgical method ($p = .799$), a partial versus complete liver lobectomy ($p = .790$), or the lobe(s) removed ($p = .790$).

Long-term complications occurred in two dogs, both of which were fatal. One dog died from suspected DIC 28 days postoperatively and one dog diagnosed with chronic hepatitis died 29 days postoperatively from liver failure. No additional dogs were lost to follow-up 30 days following surgery. A total of 15 dogs were lost to follow-up 6 months postoperatively. There was a perioperative mortality risk of 2/70 (2.9%) and an overall mortality risk of 6/66 (9.1%) at 2 weeks and 8/66 (12.1%) at 30 days.

3.6 | Histopathologic diagnosis

Histopathologic reports were available for all resected liver masses. The most common diagnosis was hepatocellular carcinoma (HCC) in 37 dogs (52.9%), followed by hepatocellular adenoma (HCA) in 14 dogs (20%), hemangiosarcoma in five dogs (7.1%), and one each of biliary adenoma, biliary cystadenoma, combined hepatocellular and cholangiocarcinoma, nodular hyperplasia, vacuolar hepatopathy, hepatic abscess, lymphoma, neuroendocrine tumor, islet cell carcinoma, unspecified round cell tumor, histiocytic sarcoma, unspecified sarcoma, unspecified carcinoma, and chronic hepatitis with fibrosis. The median age of dogs diagnosed with HCC was 10.4 years (range: 7.0–14.0). The odds of having HCC versus HCA were not affected by sex ($p = .624$), age ($p = .271$), or weight ($p = .608$).

Histopathologic margins were available for 36 of 37 dogs diagnosed with HCC. Margins were recorded as complete in 23 dogs (63.9%) and incomplete in 13 dogs (36.1%). The overall recurrence risk for dogs with HCC was 17.6% (6/34). The HCC recurrence risk was 2/22 (9.1%) for dogs with complete margins and 4/11 (36.4%) for those with incomplete margins. There was no difference in OST for dogs with HCC with complete vs. incomplete margins, which were 741 days and 742 days, respectively ($p = .697$).

3.7 | Clinical outcome

The median time to last follow-up was 221 days (interquartile range: 72–569.5, range: 1–1649 days). At the time of last follow-up, 34 dogs were deceased and the remaining 36 were censored according to their last known contact. At the end of the study, five dogs were still alive within 1 year of surgery, three dogs within 2 years of surgery, and one dog within 3 years of surgery. A total of 15 (27.2%), 18 (35.3%), 21 (48.8%), and 25 (65.8%) dogs were lost to follow-up 6-months, 1, 2, and 3 years postoperatively, respectively. There was no difference in survival time between dogs with increased ALP ($p = .139$) or ALT ($p = .754$) and those without. There were differences in survival time based on the requirement for advanced hemodynamic support ($p = .004$). The MST for dogs requiring cardiovascular support, fluid support, and combined fluid and cardiovascular support were 741, 505, and 159 days, respectively. Dogs that did not need additional intervention had an MST of 829 days. The MST for dogs diagnosed with HCC was 741 days; however, this was not censored for cause of death as only 4/15 (26.7%) dogs died from progressive HCC (Figure 2). One-, 2- and 3-year survival rates (95% CI) were 77%, 55% and 12%, respectively. No other variables were significantly associated with survival time.

4 | DISCUSSION

The objective of this retrospective study was to describe the outcome and prognostic variables associated with survival and complications of right divisional hepatic lobectomies. The perioperative mortality risk (2.9%) was low as hypothesized and was lower than previously reported risks of 4.8%–11.9% for right and central divisional resections.[3,6,8,9] There were also no instances of intraoperative mortality. This is a unique finding in such a large population as previous studies with fewer cases have reported right divisional hepatectomy intraoperative mortality risks ranging from 5.6% to 40%, with all deaths resulting from iatrogenic damage to the caudal vena cava and exsanguination.[3,8] Direct comparison should be made cautiously, however, as none of the comparing studies included the papillary process of the caudate lobe in the right division as described by Covey et al., whereas this study did. If the papillary process was not included, 11 dogs would have been removed from analysis; however, this would not have impacted intraoperative or perioperative mortality, as all 11 dogs survived. These differences in intra- and perioperative mortality may be partially linked to different proportions of partial and complete lobectomies. In the present study, 17 partial (25.7%) and 49 complete lobectomies were reported. In one study, all five lobectomies were complete, and the other had 26 partial (21.0%) and 98 complete lobectomies amongst all three liver divisions, but did not specify per division.[3,8] The study reported here did, however, have fewer partial lobectomies than the central divisional study which had 24 (39.3%) partial and 37 complete lobectomies.[9] The lack of intraoperative death represented in this study may also be attributable to the more common and widespread use of preoperative CT imaging. The use of preoperative CTs allows the surgeon to determine the proximity of the mass to the caudal vena cava or portal vein and whether a mass is operable. This provides better insight to vascular proximity for planning and may filter out dogs with larger, more complex or inoperable masses from going to surgery, thus decreasing the risk of iatrogenic hemorrhage resulting in death. As

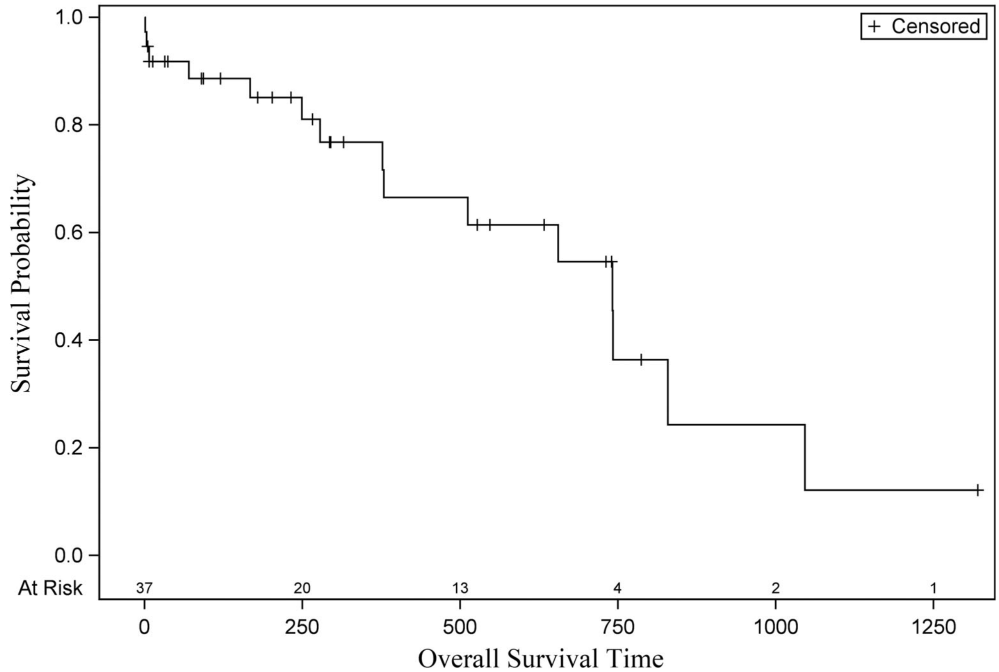

FIGURE 2 Kaplan–Meier curve depicting overall survival time (OST) for dogs diagnosed with hepatocellular carcinoma ($n = 37$). Numbers listed above the x-axis represent dogs diagnosed with hepatocellular carcinoma that were still alive at each time point (days). Dogs still alive at the conclusion of the study were censored (+) according to last follow-up.

31 dogs did not have a preoperative CT in this study, other considerations for the lack of intraoperative death include advances in surgical instrumentation, such as vessel sealing devices, or techniques like caudal sternotomy to improve exposure and manipulation for right divisional masses.

Similar to other studies, the most common intraoperative complications encountered were hemorrhage and cardiovascular abnormalities such as hypotension and arrhythmias. The surgical complication risk of 40.0% of this study was higher than previous reports, and 15 dogs (21.4%) required transfusions.[3,8,9] These rates clearly emphasize the level of difficulty and risk associated with right divisional hepatic lobectomies. Historically, this division has a higher mortality risk compared to resections of other divisions, often resulting from marked intraoperative hemorrhage.[3] This is due to the close association between the caudal vena cava and the right hepatic division; the caudate lobe in particular.[3] In addition, the right division is anatomically challenging to approach due to its craniodorsal location within the abdominal cavity, often requiring surrounding retraction for visualization and manipulation.[2,11] Equipment like TA staplers and vessel sealing devices are helpful for liver mass resection; however, space for instrument manipulation and visualization, which is important to ensure surrounding structures are not included, can easily be impaired by a large mass. It has been suggested that right and central divisional lobectomies pose similar technical challenges, as damage to the caudal vena cava has been reported in both procedures.[8,9] When compared in a previous study, there was no significant difference between right and central divisional resection in regard to risk of intraoperative complications, short-term complications, and requirements for blood transfusions.[8]

Advanced hemodynamic support with both fluid and cardiovascular support was associated with short-term complications ($p = .001$) increasing odds by 17 times. Short-term complications included eight surgical site infections, three seromas, two septic abdomens, and four deaths. Hypotension was a predominant intraoperative occurrence necessitating fluid and cardiovascular support. At the cellular level, hypotension leads to decreased oxygen and nutrient availability, which can negatively impact wound healing and increase the risk of infection.[12,13] It is possible that hypotensive dogs who required multimodal intervention experienced longer periods of hypotension and decreased perfusion due to lack of resolution with the first therapy, thus potentially increasing their susceptibility to the development of surgical site infections. There were also differences in survival time for dogs requiring advanced hemodynamic support ($p = .004$). Those receiving multimodal blood pressure support had the shortest MST, followed by those receiving fluid support, then those receiving cardiovascular support. It is suspected that multimodal support was associated with shorter survival because multiple dogs (7/13) receiving combined support experienced higher degrees of hemorrhage, likely from more extensive dissection around larger tumors with more advanced disease. It is also possible that dogs with more aggressive disease (hemangiosarcoma) experienced shorter survival not only due to an accompanying poor prognosis, but also because they were more likely to require multimodal hemodynamic support, as 3/5 dogs in this study did.

Massive HCC was the most common diagnosis in this study at 52.9%. The MST for dogs diagnosed with HCC was 741 days (range: 1–1648) which is lower than the previously reported MST of >913 days for dogs with right divisional tumors.[3] The present study includes a larger population of 37 dogs diagnosed with HCC compared to five dogs in the previous report; however, the MST in this study could not be censored for disease specific death due to limited case numbers.[3] Possible recurrence was noted in six dogs (17.6%) on imaging, four of which had incomplete margins and two of which had complete margins. Multiple studies have assessed whether completeness of resection has any effect on recurrence or survival and have provided mixed results.[3,9,14,15,16] One study by Matsuyama et al.[14] indicated incomplete resection decreased progression free interval and overall survival, while other studies have not identified an impact of incomplete resection on recurrence and survival.[3,9,15,16] When comparing complete and incomplete margins in this study, there was no difference in OST. Given the average age of 10.4 years at the time of HCC diagnosis, the slow growing nature of this disease may result in death from other causes before the impact of incomplete margin status can be appreciated.

There are many methods to perform hepatic lobectomies including staplers, vessel sealing devices, circumferential ligatures or preformed loops, hilar resection, or any combination of the previous. In this study, no surgical method was associated with a greater risk for intraoperative, immediate postoperative, or short-term complications. The most common technique utilized in this study was the TA stapler (58.6%). This technique is associated with shorter procedure times and may provide additional hemostasis by crushing hepatic parenchyma.[9,17] Surgical resection was often performed with a combination of methods in this study, necessitating the hybrid category. Some hybrid cases utilizing the stapler noted residual hemorrhage along the staple line, requiring additional methods such as a vessel sealing device or circumferential ligations to achieve hemostasis. Another common hybrid combination was hilar resection and a vessel sealing device.

The limitations of this study were those commonly encountered in multi-institutional retrospective studies. Medical records were sometimes incomplete or lacking detail. There was no standardization of preoperative diagnostics, surgical procedures, anesthetic protocols or intervention, postoperative care, or follow-up. With a disproportionate distribution amongst surgical methods and varying combinations of surgical procedures (hybrids), it was difficult to assess and compare complication risks. A prospective study limiting hepatectomies to a single method or an even distribution amongst method groups would be beneficial to determine if any method is more associated with complications. Lastly, the recurrence risk of HCC may be underrepresented due to patients lost to follow-up.

In summary, the perioperative mortality risk for dogs undergoing right divisional hepatic lobectomy was lower than reported in previous studies. There were no intraoperative deaths; however, the surgical complication risk (40.0%) was higher compared to earlier studies. Hemorrhage was the most frequent complication and 21% of dogs required a blood transfusion. Advanced hemodynamic support was significantly associated with short-term complications as well as MST. There was no association between complications and the type of surgical method, lobe(s) removed, or mass size.

AUTHOR CONTRIBUTIONS

Foster HD, DVM: Study design, data collection, organization, and interpretation, and manuscript drafting, review, and approval. Matz BM, DVM, MS, DACVS (Small Animal), ACVS Fellow Surgical Oncology: Study conception, study design, data interpretation, and manuscript review and approval. Grimes JA, DVM, MS, DACVS (Small Animal): Data acquisition and manuscript review and approval. Thieman Mankin KM, DVM, MS, DACVS (Small Animal): Data acquisition and manuscript review and approval. Vinayak A, DVM, DACVS (Small Animal), ACVS Fellow Surgical Oncology: Data acquisition and manuscript review and approval. Liptak JM, BVSc, MVetClinStud, FANZCVSc, DACVS (Small Animal), DECVS, ACVS Founding Fellow Surgical Oncology, ACVS Founding Fellow Oral and Maxillofacial Surgery: Data acquisition and manuscript review and approval. Linden DS, DVM, MS, DACVS (Small Animal), ACVS Fellow Surgical Oncology: Data acquisition, data interpretation, and manuscript review and approval. Kennedy EJ, DVM: Data acquisition and manuscript drafting, review and approval. Korchek KA, DVM: Data acquisition and manuscript review and approval. Kim WS, DVM: Data acquisition and manuscript review and approval.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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