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Bleeding risk and complications associated with percutaneous ultrasound-guided liver biopsy in cats

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Abstract

Objectives Liver biopsy is necessary for a diagnosis of liver disease; however, post-biopsy bleeding is a concern. The aim of this study was to describe the extent of bleeding and the occurrence of complications after percutaneous ultrasound-guided liver biopsy (PUGLB) in cats.

Methods The medical records of 30 cats that had a PUGLB were retrospectively reviewed. Using human guidelines, bleeding was classified as minor or major when the absolute change in packed cell volume (ΔPCV) was <0 and >–6% or ⩽–6%, respectively. Complications were defined as physiologic compromise necessitating an intervention, or death. The relationship between ΔPCV and the occurrence of complications and the signalment, initial PCV, coagulation parameters, serum liver enzymes and bilirubin, number of biopsies, histological diagnosis, ultrasound findings, radiologist experience, concurrent procedures and vitamin K administration were assessed using Fisher's exact test, ANOVA and Pearson's correlation coefficient, with a *P* value <0.05 considered significant.

Results All cats had a decrease in PCV after biopsy. The mean ΔPCV was –6.9% ± 4.1%. Minor and major bleeding occurred in 13/30 (43.3%) and 17/30 (56.7%) cats, respectively, and non-lethal bleeding complications occurred in 5/30 (16.7%). Cats with complications had a lower pre-biopsy PCV ($P < 0.003$). Major bleeding was more likely with a diagnosis of hepatic lipidosis ($P = 0.03$). There was no correlation between ΔPCV or complications and signalment, coagulation parameters, serum parameters, number of biopsies, ultrasound findings, radiologist experience, concurrent procedures and vitamin K administration.

Conclusions and relevance PUGLB is a relatively safe procedure in cats, although many cats have a subclinical decrease in PCV. As conventional coagulation tests did not predict complications or the magnitude of ΔPCV, there is a need for more sensitive indicators of bleeding risk in cats undergoing PUGLB.

Keywords: Liver; biopsy; ultrasound guided; bleeding

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Introduction

Percutaneous ultrasound-guided liver biopsy (PUGLB) is commonly performed to obtain a definitive diagnosis in cats with suspected hepatic disease.[1] The most frequent complication of PUGLB is hemorrhage.[1,2] The incidence of bleeding after PUGLB in the cat has not been well characterized. In one study of percutaneous ultrasound-guided biopsies of thoracic and abdominal organs in dogs and cats, the complication rate in cats was 10.5%.[3] Although there is insufficient information in that paper to determine the complication rate in cats undergoing PUGLB alone, 8/13 cats with major complications had liver

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biopsies.[3] In another, much smaller, study, no complications occurred in six cats that underwent PUGLB.[4] In a study examining 117 dogs and cats that had percutaneous ultrasound-guided biopsy of abdominal structures, major and minor complications occurred in 1.2% and 5.3% of animals, respectively; however, the complication rate from PUGLB alone in cats was not reported.[5] Thus, the body of literature on complications and bleeding risk after PUGLB in cats is limited and what is available is somewhat contradictory.

Risk factors for hemorrhage after PUGLB in cats are largely unknown. A single study examining blood loss following ultrasound-guided biopsies of abdominal and thoracic organs in cats found that pre-biopsy anemia and a greater number of needle passes were risk factors.[3] Risk factors for major hemorrhage after PUGLB in people include age (younger and older), body weight, female sex, more than three passes with the needle, cirrhosis, malignancy and pre-biopsy anemia.[6–12] Studies that determine blood loss following PUGLB in cats are needed.

Conventional plasma-based coagulation testing such as prothrombin time (PT), activated partial thromboplastin time (aPTT) and platelet count does not reliably predict bleeding risk after liver biopsy in humans.[12–15] Some evidence suggests that severe thrombocytopenia (<50,000/μl), moderate-to-severe prolongations in PT (>2.0-fold) and low fibrinogen levels (<60 mg/dl) predict bleeding in human patients with cirrhosis.[12–17] In cats undergoing percutaneous biopsy of thoracic and abdominal organs, low platelet count ($<80 \times 10^3$/μl) or an elevated aPTT (>1.5 × normal) were risk factors for bleeding complications.[3] No other studies have evaluated the role of conventional coagulation tests in predicting bleeding after PUGLB in cats.

The aim of this study was to describe the extent of bleeding and rate of complications after PUGLB in cats and, secondarily, to identify risk factors for bleeding tendencies.

Materials and methods

Medical records from the Foster Hospital for Small Animals at Cummings School of Veterinary Medicine at Tufts University between 2002 and 2015 were searched for cats that underwent PUGLB. Cats were included if they had a medical record available for review, a PUGLB performed, a pre-biopsy coagulation profile (PT, aPTT), a platelet count, a packed cell volume (PCV) that was obtained within 6 h of the PUGLB and at least one PCV that was obtained within 36 h post-biopsy. Cats were excluded if they had any treatments that may have significantly altered the PCV (eg, transfusion) or were given a drug that might alter hemostasis (non-steroidal anti-inflammatory medications, corticosteroids, heparin, clopidogrel, free fatty acids or hydroxylethyl starch).

Charts were reviewed for signalment, pre- and post-biopsy PCV, total solids, PT, aPTT, platelet count, serum liver enzymes (alanine aminotransferase [ALT], alkaline phosphatase [ALP], gamma glutamyl transpeptidase [GGT]), serum albumin, serum bilirubin, ultrasound findings (size, echogenicity, presence of nodules, ascites or a mass), expertise of the radiologist performing the PUGLB, biopsy needle type and size, number and adequacy of the biopsy samples, vitamin K administration, final histopathologic diagnosis, timing and extent of fluid administration, and additional procedures done.

As there are no established guidelines in veterinary medicine to classify the extent of post-procedural bleeding, we used definitions from the human literature.[18,19] The criteria chosen were defined for human patients on anti-hemostatic medications, but they have been extensively applied to assess bleeding in human patients with liver disease.[20–23] Under these guidelines major bleeding is defined as an absolute decrease in the hemoglobin of 2 g/dl. A fall in hemoglobin of 2 g/dl corresponds with a 6% or 6-point decrease in PCV; therefore, an absolute decrease in the PCV of 6% was used as a cut-off to define a major bleeding event. The absolute ($PCV_{pre} - PCV_{post}$) change in PCV and the relative (($PCV_{pre} - PC_{post}$/PCV_{pre})* 100) change in PCV (Δ PCV and RΔPCV, respectively) were calculated. For example, if the PCV dropped from 20% to 10% that is an absolute decrease of 10% and a relative decrease of 50%. The lowest PCV obtained within 36 h of liver biopsy was used as the post-PCV value. Cats with minor bleeding had a ΔPCV of <0 but >–6% and those with major bleeding had a ΔPCV of ⩽–6%.

Complications were defined independently from bleeding. Complications were defined as a physiologic compromise necessitating an intervention, or death. Medical records were reviewed to determine if an intervention (eg, resuscitative fluids or a blood transfusion) was needed owing to hemodynamic instability (increased heart rate, hypotension, depression).

A board-certified radiologist or a radiology resident performed the ultrasound and PUGLB. Only second- and third-year radiology residents under the guidance of a board-certified radiologist performed ultrasound-guided liver biopsies. Available ultrasonographic images and video clips (n = 28/30) were reviewed by a board-certified radiologist (DGP). Liver size was estimated based on radiographs taken at the time of PUGLB. If radiographs were not available, liver size was based on the ultrasound. Lesions more than or less than 3 cm were categorized as a mass or nodule, respectively. An 8–5 MHz convex transducer was used.

The biopsies were performed under anesthesia using an automated, double-spring-loaded biopsy instrument (BARD MAGNUM Biopsy Gun). Depending on liver size and the radiologists' assessment of a safe

window for biopsy, either an 18 or 16 G Tru-cut biopsy needle was used. Biopsies were usually procured from the left-sided hepatic lobes (however, the exact site of biopsy was not recorded in all cases and in some cases a nodule or mass was biopsied), after color Doppler evaluation to insure a safe location. At the end of the procedure, the biopsy site was ultrasonographically monitored for 2 mins for bleeding. Fluid seen between the liver lobes near the biopsy site post-biopsy was supportive of bleeding. In cats with ascites prior to PUGLB echogenic swirling seen after the liver biopsy was supportive of bleeding. If the ultrasound report did not specify hemorrhage post-biopsy and there was no effusion seen on the reviewed post-biopsy images it was assumed there was no hemorrhage seen.

Statistical analysis

All the data were analyzed for normality using tests for kurtosis and skewness. Data are expressed as median and range (non-parametric) or mean ± SD (parametric). The signalment, results of pre-biopsy clinicopathologic testing, number of biopsies, parenteral administration of vitamin K, ultrasound findings (size, echogenicity and presence of ascites, mass or nodule), concurrent fine-needle aspiration (FNA) or cholecystocentesis, experience of the radiologist and duration of hospitalization were compared between cats with minor and major bleeding and cats with and without complications using an ANOVA and Fisher's exact test. Correlations were assessed using Pearson's correlation coefficient for continuous variables. A P value <0.05 was considered significant.

Results

The search identified 30 cats that fulfilled the inclusion criteria. The mean age at the time of biopsy was 10.1 years (range 2–16 years). There were 25 domestic shorthair cats and five purebred cats (three Maine Coons, one Norwegian Forest Cat and one Sphynx). Nineteen cats were male (63.3%) and 11 were female (36.7%). All cats were neutered.

All cats had a PCV within the 6 h prior to their biopsy, pre-biopsy coagulation testing and a biochemical profile. Selected parameters are summarized in Table 1. Pre-biopsy, 12/30 (40%) cats were anemic (PCV <30) and 4/30 (13.3%) had a mild thrombocytopenia. The PT and aPTT were prolonged in 9/30 (30%) and 2/30 (6.6%) cats, respectively. The median prolongation of PT was 1.15 times the upper limit of normal (ULN) (range 1.04–1.78) with only one cat having a prolongation greater than 1.5 times the ULN. The median prolongation of aPTT was 1.09-fold above the ULN (range 1.04–1.14).

Twenty nine of 30 cats (96.7%) had abnormalities on ultrasound. Eighteen of 30 (60%), 9/30 (30%) and 3/30 (10%) cats had a hyperechoic, normoechoic or hypoechoic liver, respectively. Assessment of liver size was only possible in 27 cats. Nineteen of 27 (70.4%) cats had hepatomegaly and 8/27 (29.6%) had a normal-sized liver. Nine cats (30%) had ascites seen prior to PUGLB. Four cats had a mass, two of which also had nodules and an additional six had at least one nodule

Nineteen of 30 (63.3%) cats received vitamin K 24 h prior to the biopsy at doses ranging from 0.5–1.0 mg/kg subcutaneously and at intervals ranging from every 12 h to once. All cats were briefly anesthetized for the procedure, with 26/30 (86.7%) cats receiving propofol alone or in combination with an opiate and/or benzodiazepine (PropoFlo 10 mg/ml; Abbot Laboratories). Two cats received only opiates and for two cats the type of sedation was not documented. Hepatic biopsy was performed by a board-certified radiologist in 10/30 (33.3%) cats and by a radiology resident in 20/30

Table 1 Selected clinical pathology parameters in cats prior to undergoing percutaneous ultrasound-guided liver biopsy (n = 30)

	Median (range)	Number of cats with increased blood parameter	Number of cats with decreased blood parameter	RI
PCV (%)	30 (20–39)	0	12	30–55
TS (g/dl)	7.1 (5.0–9.2)	3	3	6.0–8.4
PT (s)	11.6 (9.5–22.4)	9	0	6.9–12.6
aPTT (s)	14.8 (11–28.5)	2	3	11.5–25
Platelet (× 10^9/l)	300 (120–589)	0	4	180–640
Bilirubin (mg/dl)	1.3 (0.1–26.4)	19	0	0.1–0.3
ALT (IU)	248 (43–5334)	21	0	25–145
ALP (IU)	177 (8–1694)	21	0	10–79
Albumin (g/dl)	3.4 (1.7–4.1)	0	1	2.2–4.0

RI = reference interval; PCV = packed cell volume; TS = total solids; PT = prothrombin time; aPTT = activated partial thromboplastin time; ALT = alanine aminotransferase; ALP = alkaline phosphatase

(66.7%) cats. All cats but one had biopsies taken with an 18 G needle. Seventeen of 30 (56.7%) cats had two biopsies, 7/30 (23.3%) had three, 5/30 (16.7%) had one and 1/30 (3.3%) had four biopsies. Eighteen of 30 (60%) cats had concurrent FNA done, 11/30 (36.7%) of the liver, 3/30 (10%) of the spleen, one of the stomach, one hepatic lymph node, one of the liver and regional lymph node, and one of the liver and pancreas. Five of 30 cats (16.7%) had a cholecystocentesis.

Twenty-four cats received intravenous fluids prior to the liver biopsy. Cats were on fluids for a minimum of 18 h and up to 4 days prior to the biopsy. Cats were on a variety of fluid rates that ranged between 35 ml/kg/day to 72 ml/kg/day at the time of the liver biopsy. The mean fluid rate was 53 ± 9.4 ml/kg/day. All cats were deemed to be euhydrated and stable prior to their liver biopsy. None of the cats were given intravenous fluids during anesthesia for their liver biopsy.

All cats had a decrease in PCV after biopsy and an additional 14 cats became anemic post-biopsy (Table 2). Mean ΔPCV was −6.9% ± 4.1%. Mean RΔPCV was 23.4% ± 12.9%. Minor and major bleeding occurred in 13/30 (43.3%) and 17/30 (56.7%) cats, respectively. The mean ΔPCV in cats with minor and major bleeding was −3.4% ± 1.9% and −10% ± 2.5%, and the mean RΔPCV in cats with minor and major bleeding was 12.0% ± 6.9% and 31% ± 9.9. The median time post-biopsy to the lowest PCV in cats with minor and major bleeding was 2 h (range 1–9 h) and 10 h (range 1–24 h), respectively.

We looked for factors that might be associated with bleeding (Table 3). There was no significant difference in the incidence of PT prolongation in cats with minor (3/13 [23%]) and major bleeding (6/17 [35%]). Similarly, there was no significant difference in the incidence of aPTT prolongation in cats with minor (1/13 [7.7%]) and major bleeding (1/17 [5.9%]). Three of four cats with thrombocytopenia had minor bleeding and one had major bleeding. Platelet count was significantly higher in cats with major bleeding compared with cats with minor bleeding ($P = 0.006$) and ΔPCV was moderately positively correlated with platelet count ($r = 0.47$; $P = 0.009$), although none of the cats had a thrombocytosis.

Twelve of 17 (70.6%) cats with major bleeding had a hyperehoic liver, 3/17 (17.6%) had normal echogencity and 2/17 (11.8%) had a hypoechoic liver. Ten of 17 (58.8%) cats with major bleeding had hepatomegaly and 6/17 (35.3%) had a normal-sized liver (liver size not available in one cat). Nine of 17 (52.9%) cats with major bleeding had a mass or nodules seen on ultrasound. Four of five cats that had concurrent cholecytocentesis

Table 2 Mean pre- and post-biopsy packed cell volume (PCV) in the cats with and without complications

	All cats (n = 30)	No complications (n = 25)	Complications (n = 5)
Pre-biopsy PCV (%)	30.4 ± 5.7	31.8 ± 5.0	23.8 ± 4.3*
Post-biopsy PCV (%)	23.5 ± 5.8†	24.9 ± 5.1†	16.8 ± 4.7*†

*Significantly different than PCV in cats with no complications ($P < 0.005$)
†Significantly different than pre-biopsy PCV ($P < 0.003$)

Table 3 Selected clinical parameters in cats with minor and major bleeding after percutaneous ultrasound-guided liver biopsy

Parameter	Minor bleeding*	Major bleeding†	*P* value	RI
PT (fold increase)	0.94 (0.76–1.13)	0.96 (0.87–1.78)	1.0	NA
aPTT (fold increase)	0.62 (0.37–1.14)	0.62 (0.38–0.89)	0.98	NA
PCV (%)	29.6 ± 5.9	31.0 ± 5.6	0.52	30–55
Total solids (g/dl)	7.1 ± 1.1	7.1 ± 1.2	0.98	6.0–8.4
Platelets (× 10^9/l)	237 ± 76	354 ± 125	0.006	180–640
Bilirubin (mg/dl)	5.1 ± 7.6	3.9 ± 4.8	0.61	0.1–0.3
ALT (IU)	836 ± 1506	292 ± 273	0.16	25–145
ALP (IU)	440 ± 570	202 ± 196	0.12	10–79
Albumin	3.3 ± 0.6	3.8 ± 4.3	0.71	2.2–4.0
Duration of hospitalization	5 (2–14)	2 (1–6)	0.001	NA
Number of biopsies obtained	2.0 ± 0.58	2.2 ± 0.81	0.78	NA

Data are median (range) or mean ± SD
*Minor bleeding defined as an absolute change in packed cell volume (PCV) <0 and >–6%
†Major bleeding defined as an absolute change in PCV ⩽–6%
RI = reference interval; PT = prothrombin time; NA = not available; aPTT = activated partial thromboplastin time; ALT = alanine aminotransferase; ALP = alkaline phosphatase

had major bleeding, one of which also had a complication. Nine of 30 cats had ascites prior to the liver biopsy, 5/9 (55.5%) of which had major bleeding. Bleeding was seen ultrasonographically at the time of biopsy in 17/30 (56.7%) cats after PUGLB, 9/17 (53%) of which had major bleeding and 3/17 (17.6%) of which had complications.

There was no significant association between the severity of bleeding and pre-biopsy PCV, coagulation parameters (PT and aPTT), serum bilirubin or serum liver enzymes (Table 2). In addition, signalment, number of biopsies obtained, ultrasound changes (size, mass, nodule, echogenicity, ascites, visualization of bleeding post-procedure), administration of vitamin K, concurrent FNA, cholecystocentesis or the experience of the radiologist performing the biopsy were not associated with bleeding. Cats with minor bleeding were hospitalized for a significantly longer duration than cats with major bleeding ($P = 0.001$; Table 1).

Complications occurred in 5/30 (16.7%) cats. A transfusion or resuscitative fluids were required in three and two cats, respectively. Two cats that needed a transfusion had major bleeding with a decrease in PCV from 20% to 10% and 23% to 16%, whereas the third cat had a minor bleed, with a drop from 20% to 17%. Both cats that required resuscitative fluids had major bleeds with decreases in PCV from 26% to 18% and 30% to 23%. The latter cat also had a vagal reaction (bradycardia and respiratory arrest) post-PUGLB and cholecystocentesis and responded to anti-cholinergics, supplemental oxygen and fluid administration.

The ΔPCV and RΔPCV in cats with and without complications were similar (ΔPCV −7.0% ± 2.3% and −6.8% ± 4.2%, respectively; RΔPCV 29.8% ± 11.6% and 21.4% ± 13.2%, respectively). The pre-biopsy and post-biopsy PCVs, however, were significantly lower in cats with complications compared with cats with no complications ($P < 0.005$; Table 2).

There was no significant differences between cats with and without complications with regard to signalment, coagulation parameters, serum bilirubin, serum liver enzymes, ultrasound findings, vitamin K administration, experience of the radiologist, concurrent FNA or cholecystocentesis, number of liver biopsies or duration of hospitalization.

Hepatic biopsy samples were deemed adequate by a board-certified veterinary pathologist to make a morphologic histopathologic diagnosis in 29/30 (96.7%) cases. The primary diagnoses were: cholangitis in 10/30 (33.3%), lipidosis in 8/30 (26.7%) and neoplasia in 7/30 (23.3%); acute necrosis, eosinophilic vasculitis and biliary cirrhosis in one cat each, and the remaining two cats were non-diagnostic and normal. Three cats with inflammatory disease also had moderate-to-severe lipidosis. Cats with lipidosis (n = 11) had a greater RΔPCV than cats without lipidosis ($P = 0.03$), but cats with and without lipidosis had a similar incidence of complications ($P = 0.16$). Cats with lipidosis were also more likely to have a prolongation of PT (n = 6/11) than non-lipidotic cats (n = 3/19; $P = 0.025$).

Discussion

In this study, PUGLB in cats was associated with a moderate risk of complications (16.7%) and a high rate of clinically silent major bleeding (56.7%). Major bleeding was more likely in cats with a histopathological diagnosis of hepatic lipidosis and complications were more common in cats with pre-biopsy anemia. Conventional indicators of hypocoagulability (platelet count, PT and aPTT) did not predict the occurrence of complications or the magnitude of change in PCV post-biopsy.

All cats in the current study had post-biopsy decreases in PCV (mean ΔPCV −6.9%) such that 26/30 (86.7%) were anemic (PCV <30%) post-PUGLB (mean post-biopsy PCV 23.5 ± 5.8%). Bleeding from the biopsy site may have contributed to this fall in PCV. Other factors could have contributed to the anemia, such as the inclusion of small-sized cats with an overall smaller blood volume, which makes them more prone to iatrogenic anemia from blood sampling; dilution from intravenous fluids; anesthesia; and/or the fact that feline red blood cells (RBCs) are very sensitive to oxidant damage.

Three previous studies in cats showed a significant decrease in PCV following sedation with ketamine, either as a sole agent or given in combination with midazolam and buprenorphine.[24–26] In another study in cats, ketamine administered subcutaneously as a sole agent did not cause a significant decrease in PCV.[27] Two studies evaluating the effects of propofol in cats also showed a decrease in PCV.[28,29] General anesthesia may cause a decrease in PCV, either by suppressing the release of catecholamines, which are responsible for splenic contraction in cats, or by inducing smooth muscle relaxation, therefore resulting in RBC sequestration within organs. Propofol can increase oxidative stress in feline RBCs; however, it typically occurs when propofol is administered repeatedly.[28,30] A study of one-time use of propofol in cats with hepatic lipidosis showed no effect on the need for blood product support; however, PCV was not monitored, so asymptomatic decreases in PCV could have occurred.[31] As the lowest PCVs in the current study were seen 2 and 10 h post-procedure in minor and major bleeds, respectively, it is probable that the physiologic effect of anesthesia had worn off and measured PCV at those time points was a true reflection of circulating RBC volume.

Major bleeding occurred in 56.7% of cats in this study. The mean ΔPCV in cats with major bleeding was −10%. This degree of blood loss is similar to that seen in the Bigge et al study in which cats underwent ultrasound-guided biopsy of various thoracic and abdominal structures (−8.0%).[3] A histopathologic diagnosis of

hepatic lipidosis was a risk factor for major bleeding. Bleeding after invasive procedures in cats with lipidosis could reflect more severe coagulation derangements in these cats. In this study cats with lipidosis were more likely to have prolongations in PT than cats with other liver disorders. Previous studies have also demonstrated a high incidence of prolongations in PT and aPTT, Factor XIII deficiency and hypofibrinogenemia in lipidotic cats, all of which would predispose to bleeding complications.[2,32–34] Alternatively, increased bleeding may be associated with the friable nature of lipidotic livers and/or due to the hyperechoic appearance of the lipidotic liver, which limits the visualization of the needle tip during the procedure.

In our study, the platelet count was significantly higher in cats with major bleeding compared with cats with minor bleeding, although platelet counts in both groups were in the normal range. The ΔPCV was also positively correlated with platelet count. These paradoxical associations were unexpected. They might be explained if higher platelet counts in cats reflected the presence of platelet function abnormalities. Platelet function has not been evaluated in cats with liver disease. The relationship between platelet number, function and hemorrhagic tendencies in cats with liver disease will require further investigation.

The complication rate after PUGLB in this study (16.7%) was higher than that seen in a previous study of ultrasound-guided biopsy of abdominal and thoracic organs in cats (10.5% [n = 13/124]).[3] In that study the complication rate with liver biopsy alone was not calculated, but 8/13 major complications occurred after liver biopsy.[3] In humans, complications after PUGLB occur, on average, in 0.4% and 2.0% of adults and children, respectively.[10–12] In a preliminary study in dogs undergoing PUGLB the complications rate was 1.9%.[35] Thus, evidence suggests that cats with hepatic disease may have a higher risk of complications following PUGLB than dogs or humans.

The only risk factor identified for complications following PUGLB in cats was pre-biopsy anemia. Similarly, in a study of ultrasound-guided biopsy of thoracic and abdominal structures in cats, the mean pre-biospy PCV was lower in cats with major complications than in cats with no complications.[3] Anemia worsens hemorrhagic tendencies in people with liver dysfunction by producing a reversible platelet dysfunction. This dysfunction is related to decreased platelet deposition on the subendothelium secondary to the altered flow dynamics that accompanies low red blood cell volume.[36,37] Thus, it seems prudent that clinicians are prepared to rescue anemic cats undergoing PUGLB from hemorrhagic tendencies.

Cats with complications had a lower mean pre- and post-biopsy PCV (23.8% and 16.8%, respectively) than cats without complications (31.8% and 24.9%, respectively); however, there was no difference in the ΔPCV and RΔPCV in these two populations of cats. Thus, it may be the absolute PCV and/or other factors, such as the presence of systemic inflammatory response syndrome, sepsis or pain, which trigger the physiologic response necessitating transfusion or fluid therapy, rather than the ΔPCV. Owing to the retrospective nature of this study it was difficult to discern from the record the exact clinical reasoning that led to the decision to intervene.

Although many cats were anemic (86.6%) post-biopsy only a small percentage (16.7%) required intervention. Thus, anemia in many cats appeared to be asymptomatic. Nonetheless, there could have been effects on morbidity and mortality that were undetected. Anemia is a risk factor for mortality in cats with hepatic lipidosis and contributes to increased time in the hospital and cost.[34] In dogs, anemia is associated with shorter survival times.[38–40] Although the current study actually showed that cats with major bleeding had shorter hospitalization than cats with less bleeding, this needs to be evaluated in the light of overall survival of the cats, which was beyond the scope of this retrospective study. Further prospective studies exploring the possible morbidity and mortality associated with the development of post-PUGLB anemia in cats with liver disease are warranted.

Prolongations in PT and aPTT were not risk factors for major bleeding or complications. This is in contrast to a previous study, which showed that cats with a aPTT >1.5 times normal had an increase in complications following ultrasound-guided biopsy of various thoracic and abdominal structures.[3] The reason for the difference could be the small number of cats in the current study that had an elevated aPTT (n = 2). Alternatively, the poor correlation between PT and aPTT with clinical bleeding could be owing to the failure of these tests to measure the complex coagulation abnormalities that exist in liver disease. These abnormalities involve not only pro-coagulants, but also the changes in the vascular endothelium, the fibrinolytic system and in anti-coagulant activity.[2,14] Prospective studies looking at a more extensive array of coagulation parameters, including fibrinogen, factor analysis and thromboelastography, in cats undergoing PUGLB are necessary.

Given the moderate risk of complications and major bleeding in this study, standards are needed for monitoring cats post-PUGLB. None currently exist. As the current study and that of Bigge et al suggest that major bleeding complications can occur, on average, 10–11 h and up to 18–24 h post-biopsy, cats should be monitored for up to 24 h post-PUGLB for signs of decompensation.[3] In order to determine the best post-biopsy monitoring guidelines, prospective studies are needed in which cats are subjected to more thorough post-biopsy monitoring, including serial blood pressure, heart rate, temperature and

measurement of blood lactate, as well as PCV, to detect subtle changes in clinical status. In addition, a study evaluating the usefulness of serial post-biopsy ultrasound to detect evidence of occult hemorrhage is needed.

Limitations of this study include the retrospective design, small sample size, failure to control for fluid rate, limited assessment of coagulation and the fact that it was carried out in a single academic center. The small sample size may have limited our ability to detect small differences between cats with major and minor bleeding and cats with and without complications (type II error). Post-hoc analysis showed that the study was powered to find differences in cats with major and minor bleeding or in cats with and without complications for all parameters except for serum bilirubin, ALT and ALP. As it was difficult to discern the total intravenous fluids administered between the biopsy and the post-biopsy hematocrit from the medical records, it was hard to estimate the influence of hemodilution on post-biopsy PCV. There was limited assessment of coagulation (only platelet count, PT and aPTT were inclusion criteria) in the current study and other indices of coagulation such as thromboelastography or factor analysis may predict the incidence of bleeding or complications. In addition, very few cats had serious alterations in coagulation status, likely reflecting clinician bias in deciding to pursue PUGLB.

Larger, prospective multi-institutional studies where the influence of post-biopsy fluid administration and blood collection can be controlled, the effects of different biopsy protocols evaluated and broader assessment of coagulation performed are necessary.

Conclusions

PUGLB is associated with a moderate rate of complications and high rate of major bleeding in cats, although neither were linked to high morbidity or mortality in this study. The need for possible rescue therapy post-PUGLB should be considered in cats with pre-biopsy anemia or a presumptive diagnosis of hepatic lipidosis. There is a poor correlation between conventional coagulation tests and either bleeding severity or the occurrence of complications.

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