Comparison of computed tomography pulmonary angiography and point-of-care tests for pulmonary thromboembolism diagnosis in dogs

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OBJECTIVES: To evaluate the feasibility of CT pulmonary angiography for identification of naturally occurring pulmonary thromboembolism in dogs using predefined diagnostic criteria and to assess the ability of echocardiography, cardiac troponins, D-dimers and kaolin-activated thromboelastography to predict the presence of pulmonary thromboembolism in dogs.

METHODS: Twelve dogs with immune-mediated haemolytic anaemia and evidence of respiratory distress were prospectively evaluated. Dogs were sedated immediately before CT pulmonary angiography using intravenous butorphanol. Spiral CT pulmonary angiography was performed with a 16 detector-row CT scanner using a pressure injector to infuse contrast media through peripheral intravenous catheters. Pulmonary thromboembolism was diagnosed using predefined criteria. Contemporaneous tests included echocardiography, arterial blood gas analysis, kaolin-activated thromboelastography, D-dimers and cardiac troponins.

RESULTS: Based on predefined criteria, four dogs were classified as pulmonary thromboembolism positive, three dogs were suspected to have pulmonary thromboembolism and the remaining five dogs had negative scans. The four dogs identified with pulmonary thromboembolism all had discrete filling defects in main or lobar pulmonary arteries. None of the contemporaneous tests was discriminant for pulmonary thromboembolism diagnosis, although the small sample size was limiting.

CLINICAL SIGNIFICANCE: CT pulmonary angiography can be successfully performed in dogs under sedation, even in at-risk patients with respiratory distress and can both confirm and rule out pulmonary thromboembolism in dogs.

INTRODUCTION

Pulmonary thromboembolism (PTE) is the obstruction of the pulmonary artery or its branches by thrombi and is a major cause of morbidity and mortality in dogs with immune-mediated haemolytic anaemia (IMHA) (Reimer et al. 1999, Scott-Moncrieff et al. 2001). Dogs with IMHA are predisposed to PTE potentially because of an associated hypercoagulable state (Fenty et al. 2011, Goggs et al. 2012) that may result from increased intravascular tissue factor expression secondary to the marked inflammatory response that accompanies the disease (Pick et al. 2011, Kidd & Mackman 2013). There is also evidence of platelet activation in
dogs with IMHA (Weiss & Brazzell 2006). As such, both anticoagulants and antiplatelet agents are used to reduce PTE risk and manage thrombotic complications, but are often empirically prescribed due to difficulties with definitively identifying PTE ante mortem (Goggs et al. 2009).

In humans, rapid, multi-slice spiral computed tomography pulmonary angiography (CTPA) has been used to diagnose PTE (Fesmire et al. 2011). CTPA studies are obtained by simultaneous thoracic CT scanning and bolus injection of contrast media. Indicated contrast agents are rapidly infused through peripheral catheters using a pressure injector, linked electrically to the scanner to maximally enhance the pulmonary arteries (Habing et al. 2011). Oclusive or partial filling defects in pulmonary arteries are diagnostic for PTE (Wittram et al. 2004), while a normal CTPA study helps to rule out PTE as the cause of respiratory distress, unless the index of suspicion is very high (Torbicki et al. 2008). Multi-detector-row or multi-slice CT scanners are increasingly available in veterinary medicine and permit imaging of the whole thorax without the need for general anaesthesia. In dogs, multi-slice CT angiography has been used for experimental PTE studies (Takahashi et al. 2008), and to identify a descending aortic thrombus in a dog with spirocercosis (Kirberger & Zambelli 2007). CTPA has been used to investigate the incidence of PTE following non-cemented total hip arthroplasty in dogs, although no evidence of PTE was identified (Tidwell et al. 2007). CTPA has been successfully used to diagnose pulmonary embolism in dogs with naturally occurring heartworm disease (Jung et al. 2010).

Although in humans CTPA is the definitive test for PTE, other diagnostics are used to determine which patients require advanced imaging and for severity scoring to guide management. In humans presenting with compatible clinical signs but no prior thrombotic history, rapid quantitative D-dimer assays are performed prior to imaging (Wells et al. 2000, Huisman & Klok 2011). Where PTE is present, echocardiography and cardiac biomarkers including cardiac troponins can quantify the haemodynamic consequences of PTE and provide prognostic information. In humans with PTE, serum cardiac troponin values are highly correlated with cardiac myocyte injury, degree of cardiac dysfunction and with prognosis (Janata et al. 2003, Becattini et al. 2007). Typical echocardiographic findings in dogs with PTE include right ventricular (RV) dilatation, pulmonary arterial hypertension and paradoxical septal motion (Venco et al. 1998, Johnson et al. 1999). In humans with severe PTE, the RV apex is spared the hypokinesis that affects the remainder of the free wall. This apical sparing (the McConnell sign) is highly specific for PTE in humans, but has not been reported in dogs (McConnell et al. 1996). More recently, echocardiographic measurement of the tricuspid annular plane systolic excursion (TAPSE) and right ventricular myocardial performance index (TEI index) have been reported to be of value in humans with acute PTE (Park et al. 2008, Rydman et al. 2010, Park et al. 2012). To date, studies of D-dimers, cardiac troponins and echocardiography have not been carried out in dogs with PTE but might improve the initial assessment of PTE risk and provide prognostic information in known PTE cases.

The aims of this pilot study were therefore to evaluate the feasibility of CTPA for identification of naturally occurring PTE in dogs using predefined diagnostic criteria, and to evaluate the predictive ability of echocardiography, cardiac troponins, D-dimers and kaolin-activated thromboelastography (TEG) for canine PTE diagnosis.

**MATERIALS AND METHODS**

**Sample size**

A cohort of 12 dogs with IMHA was predetermined for this pilot study. Previous studies suggest 32 to 80% dogs with IMHA have postmortem evidence of PTE (Klein et al. 1989, Carr et al. 2002). It was therefore estimated that 4 to 10 dogs with IMHA and evidence of respiratory distress would have PTE detectable by CTPA and that this would provide sufficient positive and negative cases to evaluate the feasibility of CTPA for diagnosis of canine PTE.

**Animals**

Twelve client-owned dogs diagnosed with IMHA admitted to the Queen Mother Hospital for Animals, The Royal Veterinary College between November 2009 and January 2013 were prospectively evaluated. Written, informed owner consent was obtained at hospital admission. The diagnosis of IMHA was based on the presence of regenerative anaemia and at least one of the following: positive in-saline agglutination test, positive direct antibody (Coombs’) test or moderate-marked spherocytosis identified on peripheral blood smear examination by a board-certified clinical pathologist. Additional inclusion criteria were the combination of either tachypnoea (respiratory rate >20/min) or PaCO2<32 mmHg, plus either increased respiratory effort or hypoxaemia (SaO2<95% or PaO2<85 mmHg on room air or PaO2:FiO2 ratio of <400 mmHg on supplemental oxygen). Cases were ineligible if there was concurrent thrombocytopenia (<100×103/µL) or bodyweight <7·5 kg. Signalment, previous medical history and physical examination findings at admission were recorded.

**Ethics statement**

This study was approved by the institutional ethics and welfare committee (Ref: 20111133R). Case management was determined by the primary attending clinicians. To minimise risks associated with sedation, all cases were stabilised as appropriate prior to CTPA and flow-by oxygen provided during the procedure. To minimise risks associated with contrast material administration, dogs with known hypersensitivity to iodinated contrast agents were excluded. Fluid or electrolyte disorders were corrected prior to CTPA. In cases with renal insufficiency, fluid diuresis with physiologic saline following CTPA was at the primary clinician’s discretion.

**CTPA**

Dogs were sedated immediately before CTPA using a dose of 0·3 mg/kg butorphanol (Torbugesic 1%; Zoetis) intravenously and positioned in sternal recumbency. Spiral CT pulmonary
angiography was performed using a 16-slice CT scanner (Mx8000 IDT; Philips Healthcare). Initial precontrast survey CT scans of the thorax were performed with scan time <30 seconds. Boluses of 2 ml/kg (600 mg/kg) of 300 mg i/mL iohexol (Omnipaque 300; GE Healthcare) were then administered via peripheral intravenous catheters at 2 to 3 ml/s dependent on bodyweight using a pressure injector (Stellant; Medrad) with a maximum injection pressure of 150 psi. CT images were acquired immediately after the beginning of the contrast injection in order to capture the pulmonary artery phase. CT scan parameters were 120 kV, 150 to 250 mAs (dependent on patient size), 3 mm slice thickness, 1.5 mm increment, 0-688 pitch and sharp filter applied.

**Criteria for PTE diagnosis**

The CTPA studies were reported by board-certified radiologists at the time of the scans. Images were subsequently blindly reviewed by two observers (LB, VLF) and predefined criteria applied for PTE diagnosis (Table 1). Initial imaging reports were then reviewed, any discrepancies evaluated and consensus on diagnoses reached.

**Echocardiography**

Echocardiographic examinations were performed by board-certified cardiologists or cardiology residents directly supervised by board-certified cardiologists, using a dedicated cardiac ultrasound machine (Vivid 7; GE Healthcare). All scans were subsequently reviewed (VLF) and a judgement was made regarding the presence or absence of the McConnell sign (apical sparing of right ventricular hypokinesis). Pulmonary artery (PA) pressures were estimated using spectral Doppler echocardiographic blood flow velocities of tricuspid and pulmonic insufficiency. The right ventricular Tei index and the tricuspid annular plane systolic excursion (TAPSE) normalised to aortic diameter were calculated from residual blood collected for annual health screening of dogs with indwelling IV catheters and for those receiving therapeutic heparin. Differences in contralateral arterial luminal density. Multi-focal alveolar pattern with no probable alternative diagnosis. Only one criterion in the positive category was necessary for that classification to be assigned. If none of these criteria were satisfied, then any one of the criteria in the suspicious category led to classification of the patient as suspicious for PTE. A negative diagnosis was only made when none of the criteria listed were satisfied.

**Table 1. A summary of the criteria used for diagnosis of pulmonary thromboembolism (PTE) by computed tomography pulmonary angiography (CTPA) in this study**

<table>
<thead>
<tr>
<th>PTE diagnosis</th>
<th>Criteria (only one required per category)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Complete pulmonary arterial occlusion.</td>
</tr>
<tr>
<td></td>
<td>Central intraluminal arterial filling defect(s) present.</td>
</tr>
<tr>
<td></td>
<td>Peripheral intraluminal arterial filling defect(s) present.</td>
</tr>
<tr>
<td>Suspicious</td>
<td>Luminal irregularities in central or peripheral pulmonary arteries.</td>
</tr>
<tr>
<td></td>
<td>Differences in contralateral arterial luminal density.</td>
</tr>
<tr>
<td></td>
<td>Multi-focal alveolar pattern with no probable alternative diagnosis.</td>
</tr>
<tr>
<td>Negative</td>
<td>None of the above.</td>
</tr>
</tbody>
</table>

**RESULTS**

Based on the predefined CTPA diagnostic criteria, four (33%) dogs were classified as positive for PTE, three (24%) dogs were suspected to have PTE and the remaining five (42%) dogs had negative CTPA scans. The four dogs with PTE definitively identified by CTPA all had discrete filling defects in main or lobar pulmonary arteries (Fig 1). Abnormalities present in the three dogs with scans classified as suspect included possible filling defects in smaller caudal lobe arteries (n=2), arterial size irregularities (n=1) and multi-focal alveolar infiltrates consistent with thromboembolic disease (n=2). Of the five dogs with negative
scans, one dog had evidence of cardiac enlargement and another
dog had evidence of atelectasis. In the three other dogs with neg-
avative CTPA scans an alternative diagnosis to explain the dog’s
respiratory distress was not identified.

Ten dogs underwent echocardiography; nine had evidence
of pulmonic regurgitation and six had tricuspid regurgitation.
TAPSE values and Tei indices were calculable in most patients
that underwent echocardiography. A subjective assessment
of right ventricular wall motion was made in all patients that
underwent echocardiography. Apical sparing of right ventricular
hypokinesis was subjectively identified in three patients, but
this finding did not correlate with CTPA diagnosis.

Additional clinicopathologic data collected from the 12 dogs is
summarised in Table 2. All blood samples were collected within 4
hours of the CTPA scan being performed. Correlations between
clinicopathologic variables and CTPA diagnosis were assessed
by visual inspection of scatterplots (Fig 2), but no variable was
clearly discriminant for CTPA diagnosis. In terms of outcome,
seven dogs survived to discharge, three dogs were euthanised
and two dogs died. The non-survivors were evenly distributed across
the three CTPA diagnosis groups. None of the cardiopulmonary
variables (arterial blood-gases, echocardiographic indices, car-
diac troponins) assessed were significantly different between the
survivors and the non-survivors. Of the coagulation parameters
measured, the kaolin-TEG variables were most associated with
outcome, although only the R time of non-survivors was signifi-
cantly longer than in survivors (P=0.0235, unpaired Student’s t
test; Fig 3).

**DISCUSSION**

This study describes the use of CTPA to establish definitive
antemortem diagnoses of naturally occurring PTE in dogs with
IMHA. Using CTPA, PTE was confirmed in 33% dogs and either
confirmed or suspected in 58% of dogs with IMHA and respira-
tory distress, values consistent with previous postmortem reports
of similar populations (Klein et al. 1989, Carr et al. 2002). These
findings support the assertion that PTE is common in these dogs,
and that CTPA is useful for confirming the diagnosis.

The present study is based on the premise that CTPA repre-
sents the best available technique for the identification of PTE
in dogs. CTPA is recommended for diagnosis of massive PTE
in humans (Torbicki et al. 2008) and for investigation of those
with appropriate clinical probability scores. No studies in dogs
have yet compared CTPA with more established techniques
such as ventilation/perfusion (V/Q) scanning or selective angi-
ography, or sought to incorporate probability assessments into
clinical decision making. There are several potential advantages
of CTPA over these tests which are less widely available, require
more involved radiation management protocols or necessitate
invasive pulmonary artery catheter placement. It is not yet clear
that the benefits and diagnostic capabilities of CTPA in humans
will directly translate to dogs, particularly given the inherently
different anatomy and patient size. Work establishing multi-slice
CTPA protocols including those for bolus-tracking studies has
recently been published, paving the way for greater use of CTPA
in dogs (Drees et al. 2011, Cassel et al. 2013).

Where PTE was suspected rather than confirmed, multiple
small emboli may have been present in mainstem vessels or
emboli present only in subsegmental vessels impairing diagno-
sic ability. In humans, the two major causes of indeterminate
CTPA scans are motion artefacts and poor contrast enhance-
ment (Jones & Wittram 2005). Both are possible using a
sedated CTPA protocol in dogs given that breath holding to
minimise motion artefact and to improve lung aeration can-
not be achieved. These potential issues must be considered
when undertaking and interpreting CTPA scans. Repeat scans
or reconstructions with narrower slices might enable definitive
identification or exclusion.
Table 2. A summary of the clinicopathologic data from the 12 dogs stratified by computed tomography pulmonary angiography (CTPA) diagnosis

<table>
<thead>
<tr>
<th>Case</th>
<th>CTPA Dx</th>
<th>RR (bpm)</th>
<th>pH</th>
<th>PaO2 (mmHg)</th>
<th>PaCO2 (mmHg)</th>
<th>A-a (mmHg)</th>
<th>PaO2:FiO2 (%)</th>
<th>D-dim (ng/ml)</th>
<th>R (min)</th>
<th>K (min)</th>
<th>Alpha (%)</th>
<th>MA (mm)</th>
<th>cTnl (ng/ml)</th>
<th>Tei index</th>
<th>Apical sparing</th>
<th>PEP/RVET PR vel (m/s)</th>
<th>TR vel (m/s)</th>
<th>TAPSE (mm)</th>
<th>TAPSE/Ao</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-8 y MC Giant schnauzer</td>
<td>+ve 28</td>
<td>7·385</td>
<td>58·6</td>
<td>27·4</td>
<td>55·5</td>
<td>279·0</td>
<td>88</td>
<td>500 to 1000</td>
<td>8·9</td>
<td>3·6</td>
<td>46·1</td>
<td>54·1</td>
<td>0·74</td>
<td>No</td>
<td>0·282</td>
<td>—</td>
<td>0·319</td>
<td>0·154 to 4·05</td>
<td>12·4</td>
<td>0·44 Euthanised</td>
</tr>
<tr>
<td>7-2 y FS Irish setter</td>
<td>+ve 48</td>
<td>7·455</td>
<td>87·7</td>
<td>26·8</td>
<td>26·8</td>
<td>417·6</td>
<td>97·7</td>
<td>5·3</td>
<td>1·6</td>
<td>66·4</td>
<td>54·2</td>
<td>17·6</td>
<td>0·15 Yes</td>
<td>0·158</td>
<td>1·67</td>
<td>2·9</td>
<td>20·0</td>
<td>0·88 Discharged</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 y MC Maltese</td>
<td>+ve P+</td>
<td>1·6</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-5 y MC GSD</td>
<td>+ve 38</td>
<td>7·416</td>
<td>132·2</td>
<td>16·5</td>
<td>1·1</td>
<td>629·5</td>
<td>99·3</td>
<td>7</td>
<td>2·4</td>
<td>65·3</td>
<td>70·1</td>
<td>1·6</td>
<td>0·28 No</td>
<td>0·153</td>
<td>1·7</td>
<td>—</td>
<td>43·0</td>
<td>1·74 Discharged</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-1 y ME Cocker spaniel</td>
<td>Susp.</td>
<td>7·414</td>
<td>83·9</td>
<td>36·3</td>
<td></td>
<td>209·8</td>
<td>94·6</td>
<td>&gt;2000</td>
<td>4</td>
<td>1·1</td>
<td>73·9</td>
<td>59·6</td>
<td>53·8</td>
<td>No</td>
<td>0·93</td>
<td>2·91</td>
<td>20·0</td>
<td>1·00 Discharged</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-2 y MC Miniature Dachshund</td>
<td>Susp.</td>
<td>48</td>
<td>7·393</td>
<td>54·5</td>
<td>22·4</td>
<td>66·3</td>
<td>259·5</td>
<td>87·6</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>10-8 y FS Cocker spaniel</td>
<td>Susp.</td>
<td>42</td>
<td>7·41</td>
<td>71·4</td>
<td>17·6</td>
<td>54·8</td>
<td>340·0</td>
<td>94·7</td>
<td>1000 to 2000</td>
<td>2·8</td>
<td>0·8</td>
<td>79·5</td>
<td>77·7</td>
<td>1·4</td>
<td>0·2 Yes</td>
<td>0·231</td>
<td>1·15</td>
<td>3·36</td>
<td>15·2</td>
<td>0·97 Discharged</td>
</tr>
<tr>
<td>4 y FS ESS</td>
<td>−ve</td>
<td>7·358</td>
<td>217·5</td>
<td>27·4</td>
<td></td>
<td>543·8</td>
<td>99·8</td>
<td>0·33</td>
<td>No</td>
<td>1·02</td>
<td>21·9</td>
<td>1·15 Euthanised</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 y FS Cairn terrier</td>
<td>−ve</td>
<td>30</td>
<td>7·479</td>
<td>123·8</td>
<td>19·6</td>
<td>1·1</td>
<td>589·5</td>
<td>96·6</td>
<td>7·5</td>
<td>3·5</td>
<td>52</td>
<td>66·9</td>
<td>7·8</td>
<td>0·1 No</td>
<td>0·138</td>
<td>1·22</td>
<td>2·84</td>
<td>10·0</td>
<td>0·78 Discharged</td>
<td></td>
</tr>
<tr>
<td>10-8 y MC Keeshond</td>
<td>−ve</td>
<td>20</td>
<td>7·454</td>
<td>86·3</td>
<td>21·1</td>
<td>33·4</td>
<td>411·0</td>
<td>96·5</td>
<td>500 to 1000</td>
<td>4</td>
<td>1</td>
<td>76</td>
<td>70·5</td>
<td>5·1</td>
<td>0·15 No</td>
<td>0·172</td>
<td>1·85</td>
<td>—</td>
<td>Discharged</td>
<td></td>
</tr>
<tr>
<td>5-8 y FS Tibetan spaniel</td>
<td>−ve</td>
<td>16</td>
<td>96*</td>
<td>&gt;2000</td>
<td>3·7</td>
<td>0·8</td>
<td>81·3</td>
<td>78·3</td>
<td>0·25</td>
<td>0·12 No</td>
<td>0·130</td>
<td>1·38</td>
<td>—</td>
<td>23·3</td>
<td>1·70 Discharged</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-1 y FS Maltese</td>
<td>−ve</td>
<td>72</td>
<td>7·406</td>
<td>98·2</td>
<td>25·5</td>
<td>20·2</td>
<td>467·6</td>
<td>98</td>
<td>500 to 1000</td>
<td>8·5</td>
<td>2·2</td>
<td>58·6</td>
<td>63·6</td>
<td>0·91</td>
<td>0·25 Yes</td>
<td>0·109</td>
<td>1·44</td>
<td>4·05</td>
<td>11</td>
<td>0·61 Euthanised</td>
</tr>
</tbody>
</table>

Aa Alveolar-arterial oxygen difference, SaO2 Arterial oxygen saturation, PaO2 Arterial partial pressure of oxygen, cTnl Cardiac troponin I, K Clot formation time, Alpha Clot formation angle, D-Dim D-dimers, Dx Diagnosis, ESS English springer spaniel, FE Female entire, FS Female spayed, RO Fraction of inspired oxygen, MC Male castrated, ME Male entire, MA Maximum amplitude, PEP/RVET Pre-ejection period/right ventricular ejection time, PTE Pulmonary thromboembolism, PR vel Pulmonic regurgitation velocity, R Reaction time, RR Respiratory rate, Susp. Suspicious, TAPSE/Ao TAPSE normalised to aortic diameter, Tei Tei index, TAPSE Tricuspid annular plane systolic excursion, TR vel Tricuspid regurgitation velocity
*Reference interval from (Teshima et al. 2006)
†Reference interval from (Baumwart et al. 2005)
FIG 2. Scatterplots of clinicopathologic and cardiopulmonary parameters stratified by CT pulmonary angiography (CTPA) diagnosis including (A) Kaolin-activation thromboelastography maximum amplitude; (B) \( \text{PaO}_2 : \text{FiO}_2 \) ratio from arterial blood gas analyses; (C) cardiac troponin I values and (D) pre-ejection period/right ventricular ejection time (PEP/RVET) values. Solid horizontal lines represent the median value. Grey shaded areas between dotted lines represent normal reference intervals.

FIG 3. Scatterplots of the four principle thromboelastography variables, reaction time (R), clot formation time (K), clot formation angle (alpha) and maximum amplitude (MA) stratified by outcome. Solid horizontal lines represent the median value. Grey shaded areas between dotted lines represent normal reference intervals.
The cause of respiratory distress in the dogs with negative CTPA scans is unclear. In humans, multi-slice CTPA has a low false-negative rate (sensitivity 83 to 100%) (Cronin et al. 2008). Sensitivity is lower when emboli are confined to subsegmental vessels (Goodman et al. 1995), although multi-slice scans have improved detection rates in humans (Ghaye 2007), particularly as slice thickness is reduced (Jung et al. 2011). If these three dogs were truly PTE-negative, then non-respiratory causes of tachypnoea including reduced blood oxygen content, metabolic acidosis, pain, anxiety and medications such as glucocorticoids are all plausible causes in dogs with IMHA (Hall & Lee 2009).

Surprisingly, no clinicopathologic variable assessed reliably related to the CTPA diagnosis. For instance, two dogs with definitively identified PTE had a PaO2:FiO2 ratio above 400 mmHg. Similarly, two dogs without CTPA evidence of PTE had cTnI values above 5 ng/mL (reference value <0.23 ng/mL). This may suggest these diagnostic tests are of limited value for PTE diagnosis in dogs, although the small sample size limits the ability to draw definitive conclusions. Each parameter assessed has distinct sensitivity and specificity characteristics and diverse causes of false-positive or false-negative results. For example, oxygenation impairment is related to pulmonary vascular compromise, thus PTE might be clearly visible on CTPA but have limited impact on PaO2:FiO2 ratio (McIntyre & Sasahara 1971). Myocardial hypoxia or dysfunction can occur in IMHA and might have been responsible for increased cTnI values in dogs with negative CTPA scans (Prosek & Ettinger 2010). Timing of measurement in relation to the PTE event is also important for certain parameters. D-dimers should be measured within 1 to 2 hours of the suspected event because they peak rapidly after PTE and decline to reference values within 24 hours (Ben et al. 2007). In contrast, early measurement of cardiac troponins can lead to false-negative findings in PTE (Ferrari et al. 2012). This study was based on the premise that CTPA represents the optimal diagnostic method for PTE diagnosis in dogs and therefore compared the performance of other diagnostics to it. This assumption may not be true for all cases, however, which might explain why some dogs with negative CTPA scans had high cTnI values for instance. Further evaluation of both CTPA and the point-of-care tests for identification of PTE in dogs is clearly necessary before firm conclusions about their value in PTE diagnosis can be drawn.

There were five non-survivors in this study. Three dogs were euthanised due to the severity of the underlying disease, failure to respond to therapy and the development of complications including PTE and anuric kidney failure. One dog with suspected PTE suffered respiratory arrest and died but necropsy was not performed in that case. Necropsy was performed in three cases (2 positive for PTE and 1 negative for PTE). In both cases where PTE was diagnosed by CTPA antemortem, PTE was identified postmortem. No PTE was identified in the dog with negative CTPA, which was euthanised due to development of acute kidney injury.

Few of the variables measured were associated with outcome, although this study was not designed to assess outcome in these dogs. None of the cardiopulmonary variables were useful for outcome stratification. The association between the four TEG variables and outcome in this study was consistent with previous studies of IMHA, wherein dogs with "relative hypercoagulability" were less likely to survive than those with hypercoagulable tracings (Sinnott & Otto 2009, Goggs et al. 2012). The lack of correlation between CTPA results and outcome in these patients is noteworthy and is most likely explained by the low case numbers. The argument for definitively diagnosing PTE with CTPA is to enable administration of specific treatment to dogs with thromboembolic disease, such as antithrombotic therapies or supportive medications including sildenafil, which may improve outcome. Definitive PTE diagnosis is a requisite for interventional clinical trials, which in humans have identified potentially beneficial interventions for PTE such as tirofiban and low-dose thrombolysis (Büller et al. 2012, Sharifi et al. 2013). Such studies in dogs are not currently available, but might be possible once PTE can be routinely diagnosed.

It is recognised that this study has limitations. This investigation was designed as a pilot study, with a small planned enrollment, but clearly represents a small sample of the dogs treated at the institution. All dogs in this study were deemed high-risk for PTE. Although this increased the pretest probability of PTE, it did enable evaluation of the feasibility of CTPA for PTE diagnosis in dogs. The study was also limited by the lack of a gold-standard against which to compare CTPA. V/Q scintigraphy and selective pulmonary angiography have previously been used for PTE diagnosis in dogs (Suter 1984, Bunch et al. 1989, Johnson et al. 1999), but V/Q scanning was not available and selective pulmonary angiography is an invasive and potentially high-risk procedure in unstable cases.

This study was undertaken prospectively to maximise the completeness of data collection. Despite this precaution, some data are missing. In two cases the omission of data was due to deterioration in the dog’s condition. The missing data limit the ability to evaluate the predictive ability of non-imaging diagnostic tests for the presence of PTE; however, this study does provide a clear basis for future, larger studies in this area.

In summary, the feasibility of CTPA for identification of naturally occurring PTE in dogs has been established and that CTPA can be successfully performed under sedation, even in cases with respiratory distress, has been demonstrated. This study also shows that CTPA can both confirm and rule out PTE in major pulmonary arteries in these cases. Although few of the other diagnostic tests for PTE correlated with CTPA in this study, larger studies of this and other populations can now be undertaken using the protocols established here to more fully assess their diagnostic potential.

**Conflict of interest**

This work was funded by a Clinical Research Project Award (05-10) from Petsavers, British Small Animal Veterinary Association. During manuscript preparation, RG was supported by a Clinical Research Project Award (05-10) from Petsavers, British Small Animal Veterinary Association. During manuscript preparation, RG was supported by a Clinical Research Project Award (05-10) from Petsavers, British Small Animal Veterinary Association. During manuscript preparation, RG was supported by a Clinical Research Project Award (05-10) from Petsavers, British Small Animal Veterinary Association.

**References**


References
SUPPORTING INFORMATION
The following supporting information is available for this article:
Table S1. Summary historical, physical examination, diagnostic, clinicopathologic and treatment data for the 12 dogs with IMHA included in this study.