# Recent JVECCs Articles on Coagulation

(Aside from the curative guidelines)

Noelle Herrera

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WILEY

ORIGINAL STUDY

# Evaluation of point-of-care coagulation tests as alternatives to anti-Xa activity for monitoring the anticoagulant effects of rivaroxaban in healthy dogs

Alex M. Lynch BVSc(Hons), DACVECC[1] | Laura K. Ruterbories BS, VTS(LAM)[1] | Emily H. Griffith PhD[2] | Rita M. Hanel DVM, DACVIM, DACVECC[3] | Alyssa P. Stablein BS[4] | Marjory B. Brooks DVM, DACVIM[4]

[1] Department of Clinical Sciences, College of Veterinary Medicine, North Carolina State University, Raleigh, North Carolina

[2] Department of Statistics, North Carolina State University, Raleigh, North Carolina

[3] BluePearl Veterinary Partners, Tampa, Florida

[4] Comparative Coagulation Section, College of Veterinary Medicine, Cornell University, Ithaca, New York

# Background & Hypothesis

Gold standard for monitoring anticoagulant activity of rivaroxaban = rivaroxaban-specific anti-Xa activity

- Reference laboratory
- Time delay

Objective: To evaluate a panel of coagulation assays (PT, PTT, Rapid TEG, TG) for their potential utility in rivaroxaban monitoring as alternatives to the rivaroxaban-specific anti-Xa activity (RIVA).

Hypothesis: RapidTEG variables would correlate best with RIVA.

# Materials & Methods

Prospective experimental study using five healthy Beagles.

Each dog was administered ~1.8 mg/kg rivaroxaban PO SID for 2 consecutive days as part of a pharmacodynamic study.

Blood was collected from a jugular catheter for 48 hours and analyzed via PT, PTT, RapidTEG, and thrombin generation variables.

# Results

There was poor correlation between RIVA and the RapidTEG, with R time having the only statistically significant correlation ($r = 0.554$, $P < 0.0001$)

A stronger correlation was noted between TG variables and RIVA

- lag time (min) ($r = 0.827$, $P < 0.0001$)
- peak (nM) ($r = –0.752$, $P < 0.0001$)
- endogenous thrombin potential (nM · min) ($r = –0.762$, $P < 0.0001$).

Good correlation was also noted between RIVA and aPTT ($r = 0.772$, $P < 0.0001$)

PT correlated very strongly with RIVA ($r = 0.915$, $P < 0.0001$) and was the strongest correlation of all

# Discussion

However, most data points for RIVA and PT were clustered at lower levels.

- Only 18 of 140 data points are contained with the human therapeutic RIVA activity range of 150– 250 ng/mL.
- The correlation between PT and RIVA within this specific range was very weak

PT performed at a standardized laboratory

- Variability in machines and reagents (ex: warfarin)
- Desired degree of prolongation
- Dilute PT

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ORIGINAL STUDY

# In vitro effects of lactated Ringer's solution, hypertonic saline, hydroxyethyl starch, hypertonic saline/hydroxyethyl starch, and mannitol on thromboelastographic variables of canine whole blood

Adelina Chan BVSc, MVS, MANZCVS, DACVECC[1] | Dez Hughes BVSc, DACVECC[1,2] | Brett S. Tennent-Brown BVSc, MS, DACVIM, DACVECC[1,2] | Manuel Boller Dr med vet, MTR, DACVECC[1,2]

# Background & Hypothesis

Fluid therapy in hemorrhagic shock interferes with hemostasis

- Overconsumption and loss of coagulation factors through hemorrhage
- Commonly acidemic and hypothermic
- Incidence of coagulopathies in human trauma patients increased in proportion to the volume of isotonic crystalloid fluids received.
    - Coagulopathies  in >40%, >50%, and >70% of patients after 2, 3, and 4 L of fluids
- Hypotensive and hemostatic resuscitation
- Restricted fluid resuscitation reduced morbidity and mortality in people suffering from hemorrhagic shock secondary to trauma when compared to liberal fluid resuscitation.

# Background & Hypothesis

Hydroxyethyl starches (HES) can affect hemostasis

- impaired platelet adhesion and aggregation
- decreased circulating von Willebrand factor concentration and Factor VIII:C activity
- hyperfibrinolysis.
- impaired platelet function

Objective: to determine the effect of dilution of canine whole blood with clinically relevant doses of common IV fluids on TEG variables.

Hypothesis: In vitro dilution of canine whole blood will induce dose-dependent changes in TEG variables consistent with hypocoagulability.

# Materials & Methods

In-vitro experimental study using 22 healthy dogs

Citrated whole blood samples were then  diluted to mimic the effects of clinically relevant fluid doses to dogs with a presumed initial blood volume of 90mL/kg and estimated loss of 50% of their volume.

- 8% dilution = 4mLs/kg fluid bolus; 16% = 8mLs/kg, 33% = 16mLs/kg, and 66% = 32mLs/kg

3.4% HTS at 8% dilution

7% HTS at 8% dilution

20% mannitol at 8% and 16% dilutions

# Materials & Methods

Hydroxyethyl starch 130/0.4 (HES 130/0.4) at 16% dilution

LRS at 16%, 33%, and 66% dilutions

HTS 7-HES 130/0.4 at a volume: volume of 1:2 at 25% (4mLs/kg HTS 7, 8mLs/kg HES) and 50% dilutions (8, 16)

Kaolin-activated TEG analysis was concurrently performed on diluted and control (undiluted) samples followed by measurement of platelet and fibrinogen concentration.

# Results

LRS reduced $\alpha$ angle and MA at both 33% (P = 0.009 and P = 0.011, respectively) and 66% dilution (P < 0.001 and P < 0.001, respectively)

- Prolonged K time at 66% dilution (P = 0.003).
- At 16% dilution, HTS 3.4, prolonged R time (P = 0.007)

Mannitol prolonged K time (P=0.006), reduced $\alpha$ angle (P<0.001), MA (P=0.046), and LY60 (P=0.015)

At 8% dilution, HTS 7 prolonged R time (P = 0.009) and reduced MA (P = 0.015), while all measured TEG variables were altered at the 16% dilution (P < 0.01 for all variables).

HES 130/0.4 reduced $\alpha$ angle (P = 0.031) and MA (P = 0.001) and increased LY60 (P < 0.001) at 16% dilution.

Comparing different fluid types, HES 130/0.4 and HTS 3.4 had no to minor, mannitol intermediate, and HTS 7 profound effects on TEG variables (P < 0.05) when compared to LRS at the same dilution

# Discussion

In vitro dilution of canine whole blood with commonly used IV fluids leads to thromboelastographic changes consistent with hypocoagulability in a dose dependent manner for all fluid types tested.

- Larger the fluid volume dilution, the greater magnitude of change to coagulation

High tonicity of the dilution fluid, such as with HTS 7, resulted in further compromise of coagulation.

- Different fluids of comparable osmolarity did not have identical effects on coagulation suggesting additional, non osmolarity dependent mechanisms

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ORIGINAL STUDY

# Multicenter investigation of hemostatic dysfunction in 15 dogs with acute pancreatitis

Lindsey Nielsen DVM, DACVECC[1] | Jennifer Holm DVM, DACVECC[1] | Elizabeth Rozanski DVM, DACVIM, DACVECC[2] | Dawn Meola BS[2] | Lori Lyn Price MAS[3,4] | Armelle de Laforcade DVM, DACVECC[2]

# Background & Hypothesis

Acute pancreatitis results in systemic activation of coagulation and inflammatory cascades -> microthrombi

- Necropsy of dogs with fatal acute pancreatitis: 40% had thrombotic complications and 75% had thrombi affecting multiple organs

In people with acute pancreatitis, an increase in D-dimers correlates with disease severity and mortality rate

Objective: To characterize hemostatic profiles in dogs with acute pancreatitis

Hypothesis: Dogs with acute pancreatitis will have laboratory evidence of hypercoagulability

# Materials & Methods

Prospective observational study using 15 dogs with pancreatitis

Blood samples were collected at the time of diagnosis for measurement of platelet count, PCV, kaolin-activated TEG, D-dimer concentrations, coagulation profiles, fibrinogen concentration, vWF, and AT activity.

# Results

Thirteen dogs survived to discharge, one dog died, and one dog was euthanized.

All dogs with acute pancreatitis were hypercoagulable on TEG analysis with a higher MA and $\alpha$-angle and shorter R and K times.

Dogs with AP had significantly higher D-dimers (1,144 $\mu$g/L vs 251 $\mu$g/L, P=0.001), fibrinogen (837 vs 232 mg/dL; P < 0.001), and von Willebrand factor (92.9% vs 65.1%; P = 0.02) as well as significantly lower antithrombin (85.7% vs 120%; P < 0.001) and prothrombin time values (3.8 vs 7.6 sec; P < 0.001) than reference intervals.

There was no difference in PTT of dogs with acute pancreatitis vs reference intervals.

There was no associated with platelet count or PCV and the TEG parameters.

# Discussion

Dogs with acute pancreatitis were documented to have hypercoagulability in vivo.

Additional studies are needed to compare these to healthy dogs and across multiple time points to determine if there are significant changes over time.

- TEG may be useful for monitoring response to therapy and guiding therapeutic interventions.