**Supplement Digital Content**

**Animal preparation and anesthesia**

All animals (German landrace pigs, male, weight [mean ± SD]: 41.3 ± 3.8 kg; age range: 3-4 months) were anesthetized in the morning of the experiment day by receiving the azaperone (4 mg kg-1,i.m.), atropine (0.1 mg kg-1,i.m.), and propofol (3 mg kg-1,i.v.), got orotracheal intubated and mechanical ventilation. All animals received intravenous maintenance fluid (crystalloid fluid; Sterofundin ISO®; 2 ml kg-1 h-1) before trauma induction and after trauma. Anesthesia and analgesia were maintained during the entire study period by utilizing isoflurane (1.2-1.4%) and fentanyl (3 µg kg-1 h-1). AS/3 device (Datex Ohmeda, Helsinki, Finland) was used to monitor all vital parameters (including blood temperature; arterial, central venous, and pulmonary arterial pressure; tail pulse oximetry; and ECG). Also, vital signs data were recorded based on blood sampling time points. According to the experiment protocol, arterial blood pressure was evaluated by right carotid artery cannulation with an 18 G catheter size, which also allowed for continuous collection of blood samples before and after rivaroxaban infusion. The jugular vein was implanted with two catheters for volume substitution and to monitor the pulmonary artery pressure. A midline laparotomy with cystostomy was performed.

**Coagulation-based tests and other blood variables**

Arterial blood gas analysis and electrolytes were measured after the infusion of rivaroxaban (0), and at 12, 30, 60, 120, 180, and 240 minutes post-injury. For animals dying before 240 minutes, the last assessment was performed immediately after death.

Blood gases were measured on a blood gas analyzer (ABL700 Flex®, Radiometer, Copenhagen, Denmark) using heparinized blood samples. Blood samples were collected in potassium-EDTA-anticoagulant tubes (1.9 mg/ml final concentration, Sarstedt, Nuembrecht, Germany) to measure hemoglobin and platelets utilizing the standard hematology analyzer (MEK-6108, Nihon Kohden, Rosbach, Germany). 3.2% sodium citrate (Sarstedt) and potassium-EDTA-anticoagulant (1.9 mg/ml final concentration, Sarstedt), respectively, were added to blood samples and centrifuged to obtain platelet-poor plasma for coagulation assays (including prothrombin time, D-dimer levels, fibrinogen levels) and measurement of plasma rivaroxaban concentration by standard laboratory methods using an ACL TOP550 analyzer (Instrumentation Laboratory, Werfen Group, Kirchheim, Germany).

**Whole-blood assays: Thromboelastometry**

Whole-blood thromboelastometry was performed on a ROTEM analyzer (Instrumentation Laboratory, Werfen Group, Kirchheim, Germany) according to the manufacturer’s instructions using blood samples collected in 3.2% sodium citrate. An extrinsically activated assay was measured by using the recombinant tissue factor (EXTEM). The parameters assessed were clotting time (CT, sec), and maximum clot firmness (MCF, mm).

**Thrombin generation**

Thrombin generation was measured in plasma using final concentrations of 5 pM tissue factor and 4 μM phospholipids on a Fluoroskan Ascent plate reader (Thermo Labsystems OY, Helsinki, Finland). Thrombinoscope software (version 4, Thrombinoscope BV) was used for thrombin generation curves to determine endogenous thrombin potential (ETP), lag time, and peak thrombin formation. Prolonged lag time values that the software could not detect were defined as having a value of 12 minutes for data analysis. The ELISA kit (Enzygnost® TAT micro, Siemens, Marburg, Germany) was used to quantify the thrombin-antithrombin, according to instructions from the manufacturer.

**Table S1.** Hemodynamic variables.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Time points** | **Study Group** | **HR [min-1]** | **MAP (mmHg)** | **MPAP (mmHg)** | **Cardiac Output (L/min)** | **Lactate (mmol/L)** |
| Baseline | Control | 92 ± 4 | 65 ± 2 | 17 ± 2 | 4.2 ± 0.3 | 1.2 ± 0.6 |
|  | PCC 12.5 U/kg | 92 ± 3 | 66 ± 2 | 18 ± 1 | 4.3 ± 0.4 | 1.3 ± 0.4 |
|  | PCC 25 U/kg | 92 ± 6 | 63 ± 3 | 18 ± 2 | 3.8 ± 0.6 | 1.5 ± 0.5 |
|  | PCC 50 U/kg | 88 ± 4 | 68 ± 4 | 17 ± 2 | 4.2 ± 1.0 | 1.7 ± 0.5 |
|  | PCC 12.5 U/kg + tranexamic acid | 84 ± 8 | 67 ± 5 | 18 ± 3 | 4.5 ± 0.8 | 1.5 ± 0.4 |
|  | PCC 12.5 U/kg + tranexamic acid + fibrinogen | 86 ± 6 | 64 ± 3 | 17 ± 1 | 4.1 ± 0.7 | 1.1 ± 0.4 |
| After rivaroxaban infusion | Control | 91 ± 5 | 64 ± 3 | 17 ± 3 | 4.3 ± 0.4 | 1.6 ± 0.4 |
|  | PCC 12.5 U/kg | 92 ± 3 | 65 ± 2 | 18 ± 3 | 4.2 ± 0.3 | 1.8 ± 0.4 |
|  | PCC 25 U/kg | 91 ± 6 | 62 ± 3 | 17 ± 2 | 4.0 ± 0.5 | 1.7 ± 0.3 |
|  | PCC 50 U/kg | 90 ± 5 | 68 ± 4 | 17 ± 2 | 4.0 ± 0.7 | 2.0 ± 0.3 |
|  | PCC 12.5 U/kg + tranexamic acid | 84 ± 9 | 68 ± 5 | 19 ± 3 | 4.4 ± 0.7 | 1.8 ± 0.6 |
|  | PCC 12.5 U/kg + tranexamic acid + fibrinogen | 85 ± 8 | 67 ± 8 | 18 ± 3 | 4.1 ± 1.0 | 1.4 ± 0.5 |
| 12 minutes post-trauma | Control | 112 ± 9 | 42 ± 8 | 12 ± 3 | 4.0 ± 0.7 | 1.8 ± 0.4 |
|  | PCC 12.5 U/kg | 114 ± 9 | 42 ± 10 | 14 ± 3 | 3.7 ± 0.5 | 1.6 ± 0.4 |
|  | PCC 25 U/kg | 107 ± 7 | 40 ± 5 | 14 ± 3 | 3.6 ± 0.7 | 1.7 ± 0.4 |
|  | PCC 50 U/kg | 106 ± 12 | 45 ± 8§ | 14 ± 3 | 3.8 ± 0.8 | 2.0 ± 0.3 |
|  | PCC 12.5 U/kg + tranexamic acid | 97 ± 11 | 38 ± 6 | 13 ± 4 | 3.2 ± 0.9 | 1.7 ± 0.6 |
|  | PCC 12.5 U/kg + tranexamic acid + fibrinogen | 106 ± 19 | 46 ± 13§ | 16 ± 4 | 3.4 ± 0.8 | 1.4 ± 0.4 |
| 30 minutes post-trauma | Control | 127 ± 14 | 37 ± 4 | 11 ± 2 | 3.6 ± 0.4 | 2.9 ± 0.7 |
|  | PCC 12.5 U/kg | 125 ± 15 | 38 ± 9 | 13 ± 2 | 3.2 ± 0.8 | 2.3 ± 0.4 |
|  | PCC 25 U/kg | 108 ± 15 | 42 ± 7 | 13 ± 2 | 3.8 ± 0.6 | 2.7 ± 1.0 |
|  | PCC 50 U/kg | 107 ± 5† | 46 ± 5†¶§ | 13 ± 2 | 4.2 ± 0.8¶ | 2.7 ± 0.5 |
|  | PCC 12.5 U/kg + tranexamic acid | 116 ± 19 | 36 ± 7 | 11 ± 5 | 3.6 ± 0.5 | 2.8 ± 1.3 |
|  | PCC 12.5 U/kg+ tranexamic acid + fibrinogen | 110 ± 13 | 38 ± 12 | 13 ± 3 | 3.6 ± 0.7 | 2.1 ± 0.4 |
| 60 minutes post-trauma | Control | 130 ± 13 | 35 ± 6 | 12 ± 2 | 3.4 ± 0.7 | 4.5 ± 2.0 |
|  | PCC 12.5 U/kg | 130 ± 18 | 39 ± 3 | 13 ± 2 | 3.7 ± 0.4 | 3.1 ± 0.9 |
|  | PCC 25 U/kg | 105 ± 18†¶ | 47 ± 5† | 14 ± 3 | 4.2 ± 0.7 | 2.9 ± 1.5 |
|  | PCC 50 U/kg | 103 ± 9†¶§ | 48 ± 5†¶§ | 14 ± 2 | 4.2 ± 0.6 | 3.0 ± 0.9 |
|  | PCC 12.5 U/kg + tranexamic acid | 122 ± 28 | 39 ± 6 | 11 ± 5 | 4.0 ± 0.5 | 3.8 ± 2.1 |
|  | PCC 12.5 U/kg + tranexamic acid + fibrinogen | 104 ± 11†¶ | 43 ± 9 | 14 ± 2 | 3.7 ± 0.7 | 3.0 ± 1.1 |
| 120 minutes post-trauma | Control | 147 ± 24\* | 33 ± 4 | 12 ± 1 | 3.1 ± 0.8 | 5.6 ± 2.6 |
|  | PCC 12.5 U/kg | 121 ± 17 | 39 ± 4 | 13 ± 3 | 3.3 ± 0.3 | 3.6 ± 1.2† |
|  | PCC 25 U/kg | 102 ± 21 | 48 ± 4†¶§ | 14 ± 2 | 4.0 ± 0.5 | 2.1 ± 1.2†¶ |
|  | PCC 50 U/kg | 100 ± 9¶ | 48 ± 4†¶§ | 14 ± 1 | 4.2 ± 0.7† | 2.4 ± 0.8† |
|  | PCC 12.5 U/kg + tranexamic acid | 116 ± 19 | 35 ± 5 | 11 ± 3 | 3.7 ± 0.7 | 3.8 ± 2.6 |
|  | PCC 12.5 U/kg + tranexamic acid+ fibrinogen | 105 ± 14 | 45 ± 6†§ | 14 ± 2 | 4.4 ± 1.2†¶ | 3.1 ± 1.3† |
| 180 minutes post-trauma | Control | 144 ± 5\* | 26 ± 5 | 12 ± 4 | 2.1 ± 0.5 | 7.8 ± 2.8\* |
|  | PCC 12.5 U/kg | 124 ± 20 | 37 ± 4† | 13 ± 3 | 3.0 ± 0.5 | 4.2 ± 1.6 |
|  | PCC 25 U/kg | 95 ± 16¶ | 48 ± 3†¶§ | 15 ± 2 | 4.0 ± 0.3†¶ | 1.8 ± 0.8¶§ |
|  | PCC 50 U/kg | 97 ± 8¶ | 48 ± 3†¶§ | 13 ± 1 | 3.8 ± 0.7† | 1.8 ± 0.3¶§ |
|  | PCC 12.5 U/kg + tranexamic acid | 112 ± 14 | 35 ± 5 | 11 ± 2 | 3.9 ± 0.9† | 4.4 ± 3.6 |
|  | PCC 12.5 U/kg + tranexamic acid+ fibrinogen | 108 ± 17 | 47 ± 6†¶§ | 15 ± 3 | 3.8 ± 0.5† | 2.5 ± 1.4 |
| 240 minutes post-trauma | Control | 141 | 17 | 11 | 1.5 | 7.2 |
|  | PCC 12.5 U/kg | 115 ± 7 | 35 ± 5 | 15 ± 3 | 2.8 ± 0.6 | 4.9 ± 1.8 |
|  | PCC 25 U/kg | 98 ± 15¶ | 48 ± 3¶ | 15 ± 2 | 3.9 ± 0.5¶ | 1.4 ± 0.6¶§ |
|  | PCC 50 U/kg | 99 ± 11¶ | 48 ± 5¶ | 13 ± 1 | 3.9 ± 0.7¶ | 1.4 ± 0.2¶§ |
|  | PCC 12.5 U/kg + tranexamic acid | 119 ± 18 | 41 ± 5 | 12 ± 3 | 4.7 ± 0.9¶ | 4.0 ± 5.3 |
|  | PCC 12.5 U/kg + tranexamic acid + fibrinogen | 111 ± 24 | 47 ± 7¶ | 16 ± 3 | 3.9 ± 0.6¶ | 2.1 ± 1.3¶§ |

Data are shown as mean ± standard deviation.

Initially, n=8 per group; in the control group, n=7 at 120 minutes, n=5 at 180 minutes, and n=1 at 240 minutes after trauma. In the PCC 12.5 U/kg plus tranexamic acid group, n=7 at 120 minutes and n=5 at 240 minutes after trauma.

HR=heart rate; MAP=mean arterial pressure; MPAP=mean pulmonary arterial pressure; PCC=prothrombin complex concentrate; Tranexamic acid = 20 mg/kg; Fibrinogen = 80 mg/kg.

\*P<0.05 vs. all other groups, †P<0.05 vs. control, ¶P<0.05 vs. PCC 12.5 U/kg, §P<0.05 vs. PCC 12.5 U/kg plus tranexamic acid.