**­Title: Temporal Transitions In Fibrinolysis After Trauma: Adverse Outcome Is Principally Related To Late Hypofibrinolysis­­­­­**

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**Supplemental Fig. 1.** Flow diagram of the study cohort. NORMAL0, normal maximum lysis on admission; NORMAL24, normal maximum lysis at 24 hours; LOW0, low maximum lysis on admission; LOW24, low maximum lysis at 24 hours; HIGH0, high maximum lysis on admission; HIGH24, high maximum lysis at 24 hours.

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| **Supplemental Table 1.**  Characteristics and outcomes of the less frequent transition patterns in the non-tranexamic-acid-treated cohort | | | | | | | | | | |
|  | **LOW maximum lysis**  **on admission → HIGH maximum lysis at 24hr**  **(n = 4)** | | **HIGH maximum lysis**  **on admission → LOW maximum lysis at 24hr**  **(n = 4)** | | **NORMAL maximum lysis**  **on admission → HIGH maximum lysis at 24hr**  **(n = 8)** | | **HIGH maximum lysis on admission → NORMAL maximum lysis at 24hr**  **(n = 8)** | | **HIGH maximum lysis**  **on admission → HIGH maximum lysis at 24hr**  **(n = 2)** | |
| **ADMISSION CHARACTERISTICS** |  |  |  |  |  |  |  |  |  |  |
| Gender, male | 3 | (75) | 2 | (50) | 6 | (75) | 7 | (88) | 2 | (100) |
| Age, years | 40 | (27-51) | 32 | (23-47)) | 32 | (24-35) | 47 | (38-45) | 28 | (28-29) |
| Glasgow coma scale | 15 | (13-15) | 9 | (5-14) | 13 | (11-15) | 13 | (10-14) | 15 | (15-15) |
| SBP, mmHg | 119 | (100-138) | 82 | (72-91) | 127 | (117-139) | 134 | (89-143) | 146 | (131-160) |
| Base deficit, mEq·L-1 | 2.0 | (2.0-6.8) | 20.5 | (18.8-26.8) | 0.6 | (-1.0-3.8) | 5.4 | (0.8-9.9) | 0.9 | (0.0-0.9) |
| Prothrombin time ratio > 1.2 | 0 | (0) | 2 | (100) | 0 | (0) | 2 | (33) | 0 | (0) |
| EXTEM amplitude at 5 minutes, mm | 36 | (28-45) | 12 | (12-25) | 42 | (40-46) | 45 | (36-46) | 46 | (46-47) |
| EXTEM maximum lysis, % | 4 | (4-4) | 100 | (96-100) | 10 | (8-12) | 23 | (20-28) | 24 | (20-27) |
| **INJURY CHARACTERISTICS** |  |  |  |  |  |  |  |  |  |  |
| Blunt | 3 | (75) | 4 | (100) | 7 | (88) | 7 | (88) | 1 | (50) |
| Injury severity score | 26 | (21-28) | 32 | (29-38) | 25 | (11-30) | 35 | (20-39) | 17 | (10-23) |
| Severe head/neck injury | 2 | (50) | 1 | (25) | 5 | (63) | 2 | (25) | 0 | (0.0) |
| Severe chest injury | 2 | (50) | 3 | (75) | 3 | (38) | 7 | (88) | 1 | (50) |
| Severe abdominal injury | 1 | (25) | 0 | (0) | 0 | (0) | 2 | (25) | 0 | (0) |
| Severe extremity injury | 2 | (50) | 2 | (50) | 1 | (13) | 5 | (63) | 0 | (0) |
| **FLUID AND BLOOD PRODUCTS** |  |  |  |  |  |  |  |  |  |  |
| 24hr crystalloids, L | 4.1 | (3.6-4.3) | 5.8 | (2.9-8.3) | 2.1 | (1.3-3.9) | 4.7 | (3.3-4.9) | 2.0 | (2.0-2.0) |
| 24hr red blood cells, units | 1 | (0-3) | 21 | (5-42) | 0 | (0) | 3 | (0-11) | 0 | (0-0) |
| Massive transfusion | 0 | (0) | 2 | (50) | 0 | (0) | 2 | (25) | 0 | (0) |
| Any other blood product† | 1 | (25) | 4 | (100) | 0 | (0) | 4 | (50) | 0 | (0) |
| **OUTCOMES** |  |  |  |  |  |  |  |  |  |  |
| Venous thromboembolism | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) |
| Multi-organ dysfunction syndrome | 3 | (75) | 4 | (100) | 2 | (25) | 4 | (50) | 0 | (0) |
| Critical care length of stay, days | 5 | (2-8) | 10 | (5-18) | 3 | (2-7) | 10 | (3-15) | 0 | (0-0) |
| Total length of stay, days | 19 | (14-35) | 10 | (5-32) | 13 | (8-18) | 22 | (19-31) | 20 | (15-24) |
| Late mortality (beyond 24hr) | 1 | (25) | 3 | (75) | 1 | (13) | 0 | (0) | 0 | (0) |
| Data presented as median (interquartile range) or count (percentage).  †Fresh frozen plasma and/or platelets and/or cryoprecipitate.  LOW maximum lysis, EXTEM maximum lysis <5%; NORMAL maximum lysis, EXTEM maximum lysis 5-15%; HIGH maximum lysis, EXTEM maximum lysis >15%. | | | | | | | | | | |

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| **Supplemental Table 2. Univariable and multivariable logistic regression analysis of fibrinolysis states and other factors associated with the development of multi-organ dysfunction syndrome** | | | | | | | | | |
|  | **Odds ratio** | | **p value** | **Adjusted odds ratio** | | **p value** | **Adjusted odds ratio** | | **p value** |
| Age | 1.04 | (1.02-1.05) | <0.001 | - | - | - | 1.04 | (1.02-1.06) | <0.001 |
| Gender, male | 1.03 | (0.55-1.91) | 0.931 | - | - | - | 1.90 | (0.81-4.46) | 0.138 |
| Base deficit, mEq·L-1 | 1.13 | (1.06-1.20) | <0.001 | - | - | - | 1.09 | (1.00-1.18) | 0.047 |
| Injury severity score | 1.10 | (1.07-1.12) | <0.001 | - | - | - | 1.06 | (1.03-1.09) | <0.001 |
| Severe traumatic brain injury | 9.92 | (5.90-16.70) | <0.001 | - | - | - | 7.39 | (3.86-14.16) | <0.001 |
| 24hr crystalloids, L | 1.31 | (1.17-1.47) | <0.001 | - | - | - | 1.30 | (1.11-1.53) | 0.001 |
| LOW maximum lysis on admission | 2.88 | (1.84-4.52) | <0.001 | 2.12 | (1.31-3.44) | 0.002 | 1.59 | (0.87-2.93) | 0.134 |
| LOW maximum lysis at 24 hours | 5.28 | (2.82-9.79) | <0.001 | 3.89 | (2.03-7.47) | <0.001 | 3.54 | (1.55-8.06) | 0.003 |
| Complete data available for 97% (360/372) of the patients. Cramer’s V for admission and 24hr maximum lysis = 0.34. 64.5 positive events per variable and variance inflation factor = 1.07 for the multivariable model with no confounding variables included. 16.1 positive events per variable, admission maximum lysis variance inflation factor = 1.07 and 24hr maximum lysis variance inflation factor = 1.10 for the multivariable model with confounding variables included. NORMAL maximum lysis was used as a reference category. LOW maximum lysis, EXTEM maximum lysis <5%; NORMAL maximum lysis, EXTEM maximum lysis 5-15%. | | | | | | | | | |

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| **Supplemental Table 3.**  Characteristics and outcomes according to the timing of the empiric administration of tranexamic acid in patients who required the activation of the major haemorrhage protocol | | | | | | |
|  | **No tranexamic acid**  **(n= 79)** | | **Tranexamic acid administered before admission sample (n = 195)** | | **Tranexamic acid administered after admission sample (n = 41)** | |
| **ADMISSION CHARACTERISTICS** |  |  |  |  |  |  |
| Gender, male | 58 | (73) | 140 | (72) | 34 | (83) |
| Age, years | 37 | (24-53) | 34 | (25-52) | 35 | (27-52) |
| Glasgow coma scale | 13 | (7-14) | 11 | (3-14) | 14 | (12-15) |
| SBP, mmHg | 107 | (83-126) | 98 | (74-123) | 87 | (69-108)\* |
| Base deficit, mEq·L-1 | 7.1 | (3.7-11.1) | 8.5 | (4.4-16.7) | 6.3 | (3.6-13.0) |
| Prothrombin time ratio > 1.2 | 22 | (33) | 61 | (39) | 8 | (24) |
| EXTEM amplitude at 5 minutes, mm | 38 | (30-46) | 36 | (30-44) | 39 | (33-43) |
| EXTEM maximum lysis, % | 6 | (4-13) | 3 | (1-5)\*\*\* | 5 | (3-11) |
| Tranexamic acid infusion | - | - | 50 | (30) | 10 | (27) |
| **INJURY CHARACTERISTICS** |  |  |  |  |  |  |
| Blunt | 62 | (79) | 148 | (76) | 24 | (59) |
| Injury severity score | 29 | (22-38) | 30 | (22-43) | 26 | (17-38) |
| Severe head/neck injury | 25 | (36) | 73 | (38) | 9 | (23) |
| Severe chest injury | 55 | (71) | 127 | (67) | 25 | (63) |
| Severe abdominal injury | 20 | (26) | 58 | (31) | 14 | (35) |
| Severe extremity injury | 41 | (53) | 99 | (52) | 14 | (35) |
| **FLUID AND BLOOD PRODUCTS** |  |  |  |  |  |  |
| 24hr crystalloids, L | 3.3 | (1.5-5.1) | 3.3 | (1.9-4.4) | 3.0 | (2.0-4.2) |
| 24hr red blood cells, units | 6 | (4-10) | 6 | (3-10) | 6 | (4-9) |
| Massive transfusion | 23 | (30) | 51 | (26) | 10 | (24) |
| Any other blood product† | 59 | (76) | 160 | (83) | 34 | (83) |
| **OUTCOMES** |  |  |  |  |  |  |
| Venous thromboembolism | 0 | (0) | 11 | (6) | 4 | (10)\* |
| Multi-organ dysfunction syndrome | 34 | (61) | 131 | (78)\* | 28 | (74) |
| Critical care length of stay, days | 3 | (0-11) | 6 | (2-15)\*\* | 5 | (3-16) |
| Total length of stay, days | 9 | (1-24) | 20 | (6-41)\*\* | 14 | (6-38) |
| Early mortality (within 24hr) | 23 | (29) | 28 | (14)\* | 3 | (7)\* |
| Late mortality (beyond 24hr) | 8 | (10) | 27 | (14) | 8 | (20) |
| Overall in-hospital mortality | 31 | (39) | 55 | (28) | 11 | (27) |
| Data presented as median (interquartile range) or count (percentage).  For 10 patients, it was not possible to clarify whether tranexamic acid had been administered before or after the baseline sample.  \* p<0.05; \*\* p<0.01; \*\*\* p<0.001; when compared to No tranexamic acid. Bonferroni correction was applied for 2 comparisons.  †Fresh frozen plasma and/or platelets and/or cryoprecipitate. | | | | | | |