| **Acute Hyperfibrinolysis after Burn Injury is Associated with Platelet Depletion and Increased Mortality** | **Saturday, November 10, 2018 7:30 – 7:45 am** |
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| **Objective:** | Upon completion of the lecture, attendees should be better prepared to:<br>▪ Describe how severe burn injury induces a pathologic acute phase response.<br>▪ Recognize that hyperfibrinolysis and thrombocytopenia are both associated with poor outcomes after burn |
| **Abstract:** | **Introduction:** Burn injury causes over 180,000 deaths worldwide every year and is associated with poor outcomes including trauma-induced coagulopathy (TIC), systemic inflammatory response syndrome (SIRS), poor tissue repair and death. Our overarching theory is that acute hyperfibrinolysis – the pathologic hyperactivation of plasminogen immediately after severe injury – is a critical event in the development of SIRS, TIC, and poor tissue repair. The pathomechanisms of this theory, however, are poorly defined (Figure 1). It is known that after severe trauma, platelet depletion predicts poor tissue repair, TIC and death. In this prospective study, we tested the hypothesis that acute hyperfibrinolysis after burn injury is associated with both platelet depletion and increased mortality.<br><br>**Methods**: Patients of any age presenting to our burn unit from 2016-2018 with ≥5% total body surface area burned (%TBSA) were included in this prospective cohort study. Blood samples were obtained on admission, and at 12 hrs, days 1, 2, 3, 5, and 7 post-injury. Admission plasmin-antiplasmin complex (PAPc; a biomarker of plasmin activation) levels were measured by ELISA. Multiple linear regression models were used to explore relationships between predictors of interest (PAPc, %TBSA, age, sex, mechanism of injury, and inhalation injury) and the percent drop in platelets from admission to nadir. Predictors that did not improve model fit based on ANOVA F tests for nested models were eliminated. Logistic regression was used to explore the relationship between PAPc and survival. Study protocol was approved by Vanderbilt IRB (#150751).<br><br>**Results**: 25 patients were included (Table 1). The linear regression model indicated PAPc and inhalation injury explained 70.5% of variance in percent drop in platelets. The interaction between PAPc and inhalation injury was also significant, demonstrating that the effect of PAPc on percent drop in platelets is moderated by the inhalation injury (Table 2; Figure 2). The logistic regression model indicated that for every one-unit change in PAPc concentration (ng/mL), there is a 6% increase in odds of death (Table 3; Figure 3). |

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| | **Conclusion**: In burn patients, the extent of acute hyperfibrinolysis as measured by PAPc predicts an effect on platelet depletion that is modulated by inhalation injury. One interpretation of these results is that acute hyperfibrinolysis may play a direct role in the pathophysiology of thrombocytopenia in burn patients, and that this process is different in lung tissue versus other soft tissues. Our findings also support previous work that has linked burn-associated thrombocytopenia to increased mortality, and suggest that hyperfibrinolysis may play a role in this association. Further studies that genetically and pharmacologically manipulate the fibrinolytic and inflammatory systems in animal models of burn injury are needed to test these hypotheses. An understanding of these connections has the potential to inform new uses of anti-fibrinolytic therapy in burn patients to prevent complications of hyperfibrinolysis. |
| **Disclosure:** | Patrick R. Keller – No Relevant Financial Relationships to Disclose<br>Breanne H.Y. Gibson – No Relevant Financial Relationships to Disclose<br>Bryan Keller – No Relevant Financial Relationships to Disclose<br>Matthew T. Duvernay – No Relevant Financial Relationships to Disclose<br>Emilie Amaro – No Relevant Financial Relationships to Disclose<br>Tanya Marvi – No Relevant Financial Relationships to Disclose<br>J. Blair Summitt – No Relevant Financial Relationships to Disclose<br>Jonathan G. Schoenecker – No Relevant Financial Relationships to Disclose |

**Table 1.**

*Patient Characteristics on Admission*

| Variables | n (%) |
|---|---|
| Total no. patients | 25 (100) |
| TBSA burn, % | |
| 5-20 | 11 (44) |
| 21-40 | 12 (48) |
| >40 | 2 (8) |
| Age, y | |
| <18 | 2 (8) |
| 18-40 | 10 (40) |
| 41-65 | 8 (32) |
| >65 | 5 (20) |
| Sex | |
| M | 18 (72) |
| F | 7 (28) |

**Table 1, cont.**

| Variables | n (%) |
|---|---|
| Mechanism of Injury | |
| Flame related | 20 (80) |
| Scald | 4 (16) |
| Other | 1 (4) |
| Inhalation injury | |
| Yes | 10 (40) |
| No | 15 (60) |
| Survived | |
| Yes | 21 (84) |
| No | 4 (16) |

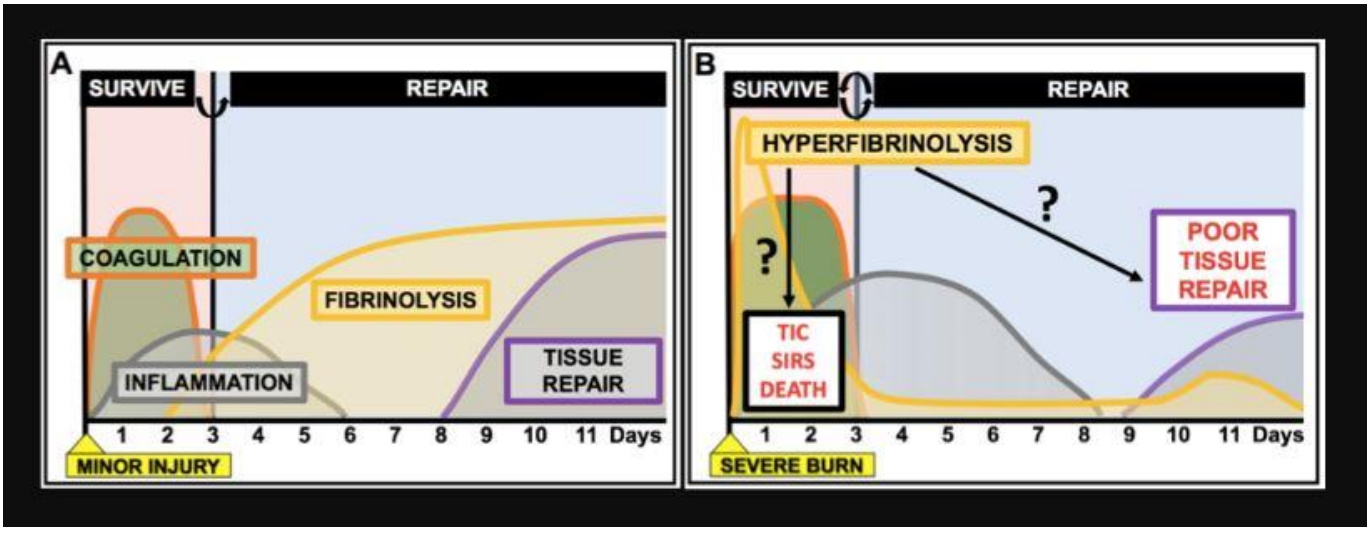

**Table 2.**

*Results of Multiple Linear Regression Model for % Plt Drop*

| Covariate | B | SE (B) | Sig |
|---|---|---|---|
| (Intercept) | -10.70 | 7.09 | .153 |
| PAPc | 5.74 | 1.58 | .003 |
| Inhalation Injury | 39.14 | 9.76 | .001 |
| PAPc x Inhalation Injury | -4.86 | 1.62 | .010 |

$R^2$ (adjusted) = .705 ($p < .001$)

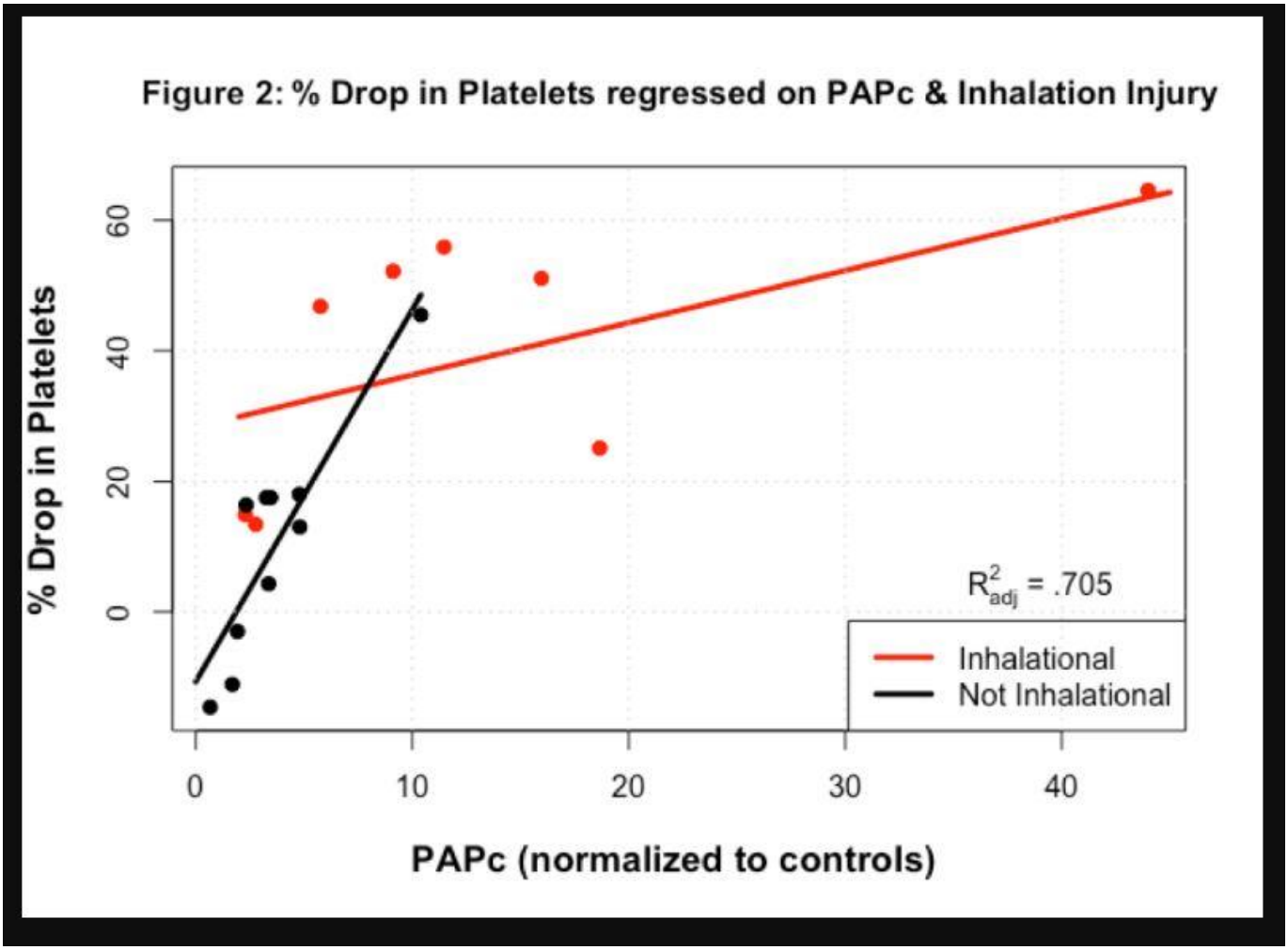

**Table 3.**

*Results of Logistic Regression Model for Survival*

| Covariate | B | SE (B) | exp(B) | Sig |
|---|---|---|---|---|
| (Intercept) | -3.12 | 1.01 | 0.04 | .002 |
| PAPc | 0.06 | 0.03 | 1.06 | .048 |

**Figure 3: Box Plot of PAPc vs Survival**