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Cerebrovascular autoregulation is impaired during early-stage post-cardiac arrest syndrome

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***Abstract*— Using a rodent cardiac arrest (CA) model, we interrogated cerebrovascular autoregulation before and after CA. Autoregulation was quantified using a metric dubbed "the cerebrovascular autoregulation index" or CVARx, akin to the clinically used surrogate cerebrovascular oxygenation index or COx. CVARx was defined as Spearman's correlation coefficient between cerebral blood flow (CBF) and mean arterial pressure (MAP) using a 5-minute sliding window. A higher CVARx depicts a tighter correlation between CBF and MAP and indicates impaired autoregulation. We found low CVARx levels (-0.17 ± 0.60) pre-CA, indicating intact cerebrovascular autoregulation. In contrast, CVARx values were significantly higher (0.63±0.46, p=0.01) in the aftermath of resuscitation from CA, illustrating impaired cerebrovascular autoregulation. Our preclinical quantifications characterize the vascular dysfunction associated with post-CA syndrome during its earliest stages. Our findings on CVARx may help elucidate the pathological basis for employing COx, the clinically used index for autoregulation assessment, as the brain's oxygenation status is closely guided by its blood flow levels.**

I. INTRODUCTION

Cardiac arrest (CA) creates an abrupt loss of systemic circulation, halting oxygen delivery to the brain. CA is often fatal, and even in instances of resuscitation, inflicts brain injury. Impaired cerebrovascular autoregulation, i.e., the disintegration of the brain's ability to maintain a steady level of blood flow despite blood pressure variations, is a hallmark of the post-cardiac arrest syndrome [1]. With its clinically measured surrogate cerebrovascular oxygenation index (COx), quantification of autoregulation has immense potential for calibrating therapeutic interventions post-resuscitation.

II. METHODS

Six male Wistar rats (399 ± 18 g) underwent an asphyxia cardiac arrest (CA) protocol [2]. Asphyxia durations were chosen as 5 or 7 minutes (n = 3) to model a range of pathologic insults. Cerebral blood flow (CBF) was measured via laser speckle contrast imaging using a miniature microscope [3]. Mean arterial pressure (MAP) was recorded via femoral artery cannulation. CBF and MAP were computed at 10s steps. Cerebrovascular autoregulation index (CVARx), defined as the Spearman's correlation coefficient between CBF and MAP, was computed via a 5-minute window (1-minute steps) for 15-minute pre-CA baseline and 30-minute post-return of spontaneous circulation (ROSC) durations. Comparisons were performed with a two-way ANOVA test (p = 0.01).

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III. RESULTS

Fig. 1 shows a representative example of CBF and MAP fluctuations during the CA protocol. These illustrate the tight CBF and MAP correlation during the early post-ROSC period, and the lack thereof at baseline. Early-stage post-ROSC CVARx were significantly higher (0.63±0.46) than their baseline counterparts (-0.17 ± 0.60), indicating dysfunction of cerebrovascular autoregulation even in the aftermath of successful resuscitation.

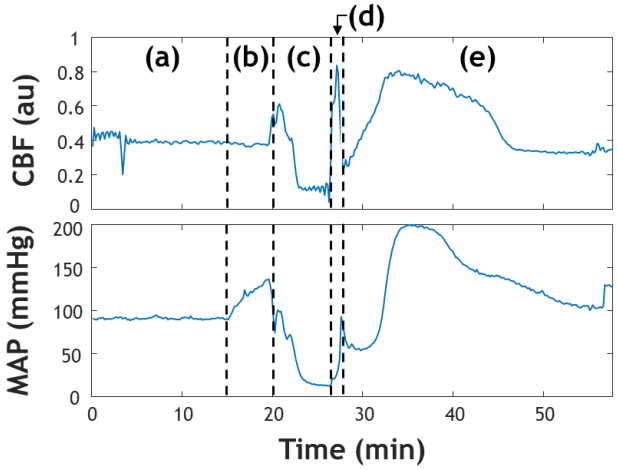

Fig. 1. CBF (top) and MAP (bottom) time series for the CA protocol consisting of: (a) baseline, (b) anesthesia washout, (c) asphyxia, (d) CPR, and (e) post-ROSC phases.

IV. DISCUSSION & CONCLUSION

Our findings agree with previous work by Crouzet et al [4], where CBF and MAP were found to be "uncoupled" immediately post-ROSC. However, their findings relied on a single correlation computation using the entire, e.g., ~30 minutes early post-ROSC window, which is not amenable for real-time assessment. In contrast, our 5-minute CVARx computations offer the potential for real-time therapeutic intervention. Further characterization of CVARx, its relation to COx, neurological outcomes and histopathology could provide invaluable insights.

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