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LETTER TO THE EDITOR

The Predictive Accuracy of High Sensitivity Cardiac Troponin I in Neonatal Encephalopathy

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In the last 20 years, researchers worldwide have focused on the use of different serum biomarkers for prognostication and staging of neonatal encephalopathy (NE). Among these, cardiac troponin I is certainly one of the most established and validated serum markers for detecting myocardial ischemic injury following NE and for the prediction of different short and long-term outcomes [1].

NE occurs unexpectedly following an otherwise uneventful pregnancy; 20 to 25% of the affected infants die in the first few days after birth and up to 75% of the survivors may develop significant life-long disabilities despite the introduction of therapeutic hypothermia in the clinical practice [2]. The incidence of NE is 1 to 2 per 1,000 live births in developed countries although the incidence is ten times higher in low- and middle-income countries [3].

Currently there is a concerted effort from the research community to find a point-of-care test which can assist clinicians in identifying the high-risk encephalopathic infants who are more likely to have long term neurodisabilities. High-sensitivity assays can successfully detect extremely low concentrations of troponin I and therefore have the potential to increase the specificity and accuracy of this biomarker. However, at the moment, there is no study which has assessed the prognostic ac-

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Table 1. Demographic and clinical characteristics of the patients.

n	92
Female gender	37 (40)
Gestational age (weeks)	39 (38 - 40)
Birth weight (g)	3,182 (3,012 - 3,622)
Apgar 10 min	6 (4 - 7)
Need for inotropic support	60 (65)
Seizures	59 (64)
Invasive ventilation	74 (80)
Adverse outcome	48 (52)

Data as median (range) or n (%).

curacy of high sensitivity cardiac troponin I in NE and, therefore, there are no diagnostic thresholds for high-sensitivity cardiac troponins in these patients.

We retrospectively reviewed the data from all the neonates with NE who fulfilled the criteria for therapeutic hypothermia and were admitted to the Department of Neonatology of Monaldi Hospital between August 2014 and February 2019. The Monaldi Hospital Ethical Committee approved the study. Cardiac troponin I concentrations were measured (Dimension vista 500, SIEMENS) within 12 hours of birth and compared with the neurodevelopmental outcome assessed with the Bayley Scales of Infant Development at 2 years. Adverse outcome was defined as death or moderate-severe disability. Area under the curve was obtained from receiver operating characteristic (ROC) curves to assess the most suitable troponin I cutoff value for adverse neurodevelopmental outcome.

Overall 124 neonates were admitted with NE in the study period of which 92 neonates (69 moderate and 23 severe) had the neurodevelopmental data available for the analysis. Table 1 shows the characteristics of the infants. Babies with severe NE had significantly higher troponin I values when compared with those with moderate NE (0.12 ± 0.25 versus 0.65 ± 0.77, $p < 0.05$ Mann-Whitney *U* test). ROC curve analysis showed that the most suitable high sensitivity cardiac troponin I cutoff value for adverse neurodevelopmental outcome was 0.17 µg/L (area under the curve (AUC) 0.82, 95% CI 0.72 to 0.91) (Figure 1) with a sensitivity of 71% (95% confidential interval (CI: 56 to 83%), specificity of 88% (95% CI: 74 to 96%), positive predictive value 87% (95% CI: 74 to 94%), and negative predictive value of 72% (95% CI: 62 to 80%).

This represents the first report on the prognostic accuracy of high sensitivity cardiac troponin I in NE. We found that high sensitivity cardiac troponin I had a higher specificity and positive predictive value when compared with what was previously reported with non-high sensitivity cardiac troponin I [4]. Moreover, our data show that cardiac troponin I can also be successfully used for severity stratification of NE.

Previous research showed that cardiac troponin I resulting within 24 hours after birth had a significant predictive value for assessing mortality in neonates with birth asphyxia, although there was no statistically significant correlation between cardiac troponin I concentrations and traditional markers of asphyxia. More recently, Jiang Li et al. assessed the use of high sensitivity cardiac troponin I in the early diagnosis of myocardial injury following neonatal asphyxia [5]. The authors showed that high sensitivity cardiac troponin I had sensitivity and specificity for asphyxia-induced myocardial injury of 55.6% and 95.5%, respectively. The accuracy of high sensitivity cardiac troponin I (AUC 77.5%) was higher than CK-MB (AUC 0.672), myoglobin (AUC 0.653), and BNP (AUC 0.578). Nevertheless, these studies did not examine long-term outcomes.

Magnetic resonance imaging and spectroscopy have been recently reported to be highly predictive of neurodevelopmental outcomes [6,7]. However, their use is held back by the inability to perform a scan as soon as possible after birth. Inevitably, clinicians must make treatment decisions before this information is available. The use of blood biomarkers like troponin can represent the way forward. Our data suggest the prognostic potential of cardiac troponin I, which may be important for families and clinicians, especially when deciding about neuroprotective interventions and long-term treatment plans. However, given the retrospective design and the small sample size of the present study, further data are required to confirm the prognostic accuracy of high sensitivity cardiac troponin I.

Declaration of Interest:

All authors declare that they have no conflict of interest.

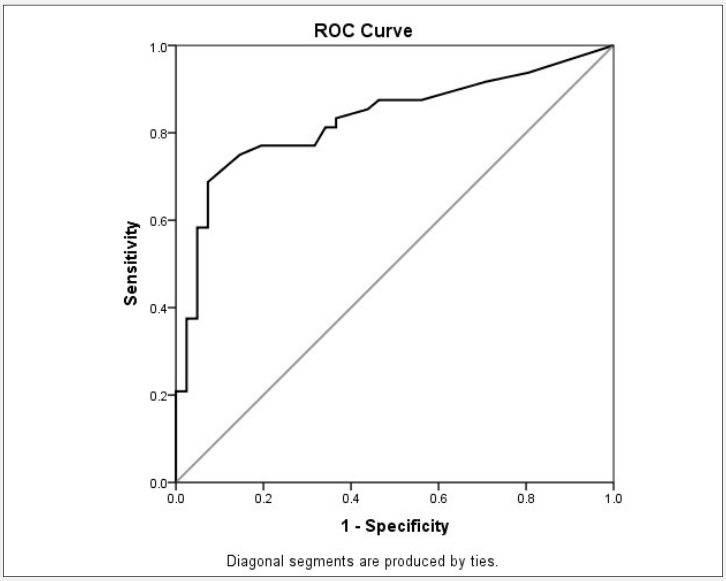

Figure 1. Receiver operating characteristic (ROC) curve shows the predictive accuracy of high sensitivity cardiac troponin I (black line) together with reference line (grey line).

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