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### Letter to the Editor

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# Plasmatic NT-proBNP could help to select cases for screening echocardiography in healthy infants with Respiratory Syncytial Virus infection

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### Abstract

In Respiratory Syncytial Virus infection, the early identification of infants at risk for severe disease in order to potentially decrease morbidity could be considered a major goal. Current guidelines recommend only clinical observation for this purpose in infants without known comorbidities. However, recent evidence shows that the presence of pulmonary hypertension in this population is a relevant risk factor for the development of a severe illness, even in healthy infants. The determination of plasmatic NT-proBNP levels could help to identify those cases that benefit of echocardiographic screening to detect pulmonary hypertension in this population during hospitalization.

We read with great interest the article by Kimora et al.<sup>1</sup> In this retrospective study, they found pulmonary hypertension detected by echocardiography in approximately 17% of cases of Respiratory Syncytial Virus infection without any comorbidity. They concluded that routine echocardiography is not warranted for previously healthy and hemodynamically stable infants. Although we agree with the authors on most aspects of their study, there are a few points that we think merit some discussion.

In the absence of any effective therapy for Respiratory Syncytial Virus infection, early identification of infants at the risk of developing a severe form of disease is considered a major goal in order to potentially decrease morbidity. Interestingly, nearly half of the children needing ICU admission are healthy prior to the clinical event.<sup>2</sup> At this moment, outcome prediction in this population is usually based only on clinical scores, but the identification of novel biomarkers and point-of-care echography parameters with adequate predictive value for disease severity is an area of increasing research interest.<sup>3</sup> Recently, we have reported a prospective cohort study including 93 previously healthy infants admitted with Respiratory Syncytial Virus infection,<sup>4</sup> with a similar incidence (22%) of pulmonary hypertension than Kimora et al. Remarkably, we performed the echocardiogram at the time of admission in hemodynamically stable infants with no respiratory support, highlighting that pulmonary hypertension could be present even at early stages of the disease. Also, those patients with pulmonary hypertension in the subgroup with impaired gas exchange presented a worst outcome in terms of ICU admission, time of supplemental oxygen, and hospitalization length of stay. This highlights the relevance to early detection of pulmonary hypertension in order to identify high-risk patients, even in healthy infants. Another interesting finding of our study was that plasmatic NT-proBNP (determined by the electrochemiluminescent immunoassay kit ElecSys 2010, Roche Diagnostics, Barcelona, Spain) resulted an accurate biomarker for pulmonary hypertension (area under the receiver operating characteristic curve of 0.932; estimated optimal cut-off value of 1345 pg/ml (Sensitivity 0.86, Specificity 0.89, Positive predictive value 0.70, Negative predictive value 0.95)) and subsequent outcomes in this population. Also, we recently observed in a small cohort of 50 healthy infants with bronchiolitis that increased right ventricular pressures are associated with left ventricular dysfunction (assessed by Doppler-Tissue imaging derived TEI index), and that the addition of plasmatic NT-proBNP > 1500 pg/ml to the traditional clinical assessment enhances the early detection of those cases that will develop a severe illness.5

We agree with the authors that obtaining an echocardiogram in every patient admitted with Respiratory Syncytial Virus bronchiolitis would mean significant cost and resource burden. However, we think that the development of new bedside scores, including NT-proBNPplasmatic levels and maybe point-of-care echocardiography (that would preclude a standard examination if normal), could improve the predictive value of current clinical scores in order to identify high-risk patients, even in healthy infants. Specifically, NT-proBNP could be used to screen which patients will benefit from an echocardiogram, a closely motorization during the hospitalization, or maybe an early respiratory support. Larger multicentre cohort studies that validate our findings will provide evidence of what should be recommended routinely.

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### Conflict of Interest. None.

### References

 Kimura D, McNamara IF, Wang J, Fowke JH, West AN, Philip R. Pulmonary hypertension during respiratory syncytial virus bronchiolitis: a risk factor for severity of illness. Cardiol Young 2019 May 20; 20: 1–5.

- Ghazaly M, Nadel S. Characteristics of children admitted to intensive care with acute bronchiolitis. Eur J Pediatr 2018 Jun; 177(6): 913–920.
- Brown PM, Schneeberger DL, Piedimonte G. Biomarkers of respiratory syncytial virus (RSV) infection: specific neutrophil and cytokine levels provide increased accuracy in predicting disease severity. Paediatr Respir Rev 2015 Sep; 16(4): 232–240.
- Rodriguez-Gonzalez M, Benavente Fernández I, Castellano-Martinez A, Lechuga-Sancho AM, Lubián-López SP. NT-proBNP plasma levels as biomarkers for pulmonary hypertension in healthy infants with respiratory syncytial virus infection. Biomarkers Med 2019 Jun 3; 2017(3): 7074508.
- Rodriguez-Gonzalez M, Perez-Reviriego AA, Castellano-Martinez A, Lubian-Lopez S, Benavente-Fernandez I. Left ventricular dysfunction and plasmatic NT-proBNP are associated with adverse evolution in respiratory syncytial virus bronchiolitis. Diagnostics 2019; 9(3): pii: E85.