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Acknowledgements

We wish to thank the medical roster and nurses from the Pediatric Intensive Care Unit of the Hospital General Universitario Gregorio Marañón for their collaboration in this study.

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2173-5727/
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Assessment of right atrial pressure with two-dimensional, Doppler and speckle tracking echocardiography in patients with acute right ventricular myocardial infarction.

Evalúación de la presión de la aurícula derecha con ecocardiografía bidimensional, Doppler y speckle tracking en pacientes con infarto agudo del ventriculo derecho

Dear Editor:

In patients with inferior myocardial infarction, right ventricular myocardial infarction (RDMI) can occur in up to 50% of cases. It is associated with higher in-hospital mortality rates.

Management of RDMI includes preload optimization and maintenance of atrio-ventricular synchrony. Preload optimization is a mainstay of treatment, but it is also a double-edged sword. High filling pressures in the right ventricle can worsen the performance of preload optimization and may lead to right ventricular dilatation and further dysfunction. On the other hand, insufficient preload is associated with low right cardiac output, hypotension and shock.

Right atrial pressure (RAP) is an essential component in the hemodynamic assessment of patients with RDMI. Unfortunately, RAP measurements are invasive and suffer from complications, and they are not always available to every patient. However, non-invasive evaluation of RAP is feasible with echocardiography and many techniques have been described. Even so, the usefulness of echocardiography in RAP assessment in patients with RDMI is uncertain.

The aim of this study was to assess whether echocardiography can accurately estimate RAP in patients with RDMI and predict increased RAP levels to guide management. The scope of the study was to assess the right ventricular function with comprehensive echocardiography and to measure the RAP with a central venous catheter.
In this study, patients with RVMI and elevated ST segment were analyzed. Consecutive cases were included from 2015 to 2016. Patients were required to satisfy a third universal definition of myocardial infarction (MI) and an ST-segment elevation of at least 0.1 mV in the V4R lead. The Cardiology Hospital Ethical Committee revised and approved the protocol, and all of the patients gave written informed consent to participate in the study.

We conducted comprehensive echocardiograms at the bedside immediately after admission. We analyzed the following echocardiographic parameters according to current international guidelines: tricuspid annular plane systolic excursion (TAPSE), tricuspid S wave velocity, global right ventricular longitudinal strain, free wall right ventricular longitudinal strain, right E/E ratio, right atrial area, inferior vena cava size and tricuspid regurgitation. We estimated right atrial pressure with the 3–8–15 mmHg approach and the 5–10–15–20 approach according to guidelines. In the first approach the RAP is 3 mmHg if inferior vena cava diameter is ≤21 mm and the diameter changes ≥50% with sniff; RAP is 15 mmHg if inferior vena cava diameter is >21 mm and the diameter changes <50% with sniff; if neither condition is satisfied the RAP is 8 mmHg. In the second approach the RAP is 5 mmHg if inferior vena cava diameter is ≤21 mm and the diameter changes ≥50% with sniff, if the diameter changes <50% RAP is 10 mmHg; RAP is 15 mmHg if inferior vena cava diameter is ≥21 mm but the diameter changes ≥50% with sniff, if the diameter changes <50% RAP is 20 mmHg. We measured parameters using the average of three consecutive beats in all cases. In cases of atrial fibrillation or atrioventricular block we used the average of five consecutive beats. Strain was analyzed offline with specific software (QLAB version 10.5, Philips Healthcare, Andover, MA, USA). Right ventricular longitudinal strain analyses consisted of a semi-automated process in which three points were selected: the tricuspid annular plane with the free wall and the interventricular septum, and the right ventricular (RV) apex. Right atrial strain analyses consisted of a similar process and three points were selected: the tricuspid annular plane with atrial lateral wall and interatrial septum, and the roof of the right atrium. We visually inspected the strain curves to ensure appropriate tracking. We defined global right ventricular longitudinal strain as the average of seven segments analyzed and free wall right ventricular longitudinal strain as the average of three free wall segments.

Just prior to the echocardiographic examination, we measured RAP with a central venous catheter as previously described in the literature. The RAP was measured for three times, and the average was reported in mmHg. We as investigators did not know RAP at either the time of examination or during the offline analysis. We defined increased RAP as being ≥13 mmHg.

For statistical analysis we compared groups using the Student’s t-test for independent groups. We used simple logistic regression and then we fit a multivariable logistic regression model with stepwise selection; the entry criteria were an association in the univariate analysis and a p value lower than 0.10, and the exit criterion was a p value higher than 0.05. We built a classification tree using the classification and regression tree (CRT) algorithm. We used SPSS version 22 (IBM, Chicago, IL, USA) and Stata 12 (StataCorp LP, College Station, TX, USA) for statistical analysis.

From 2015 to 2016, 460 patients had inferior MI and 106 patients fulfilled the right ventricular infarction criteria; 45 patients received a central venous catheter. Reliable RAP and complete echocardiographic was obtained for all of the 45 patients: age 68 ±10 years, male 71%, diabetes mellitus 58%, hypertension 76%, previous coronary artery disease 18%.

Based on univariate logistic regression, most of right heart echocardiographic variables predicted increased RAP. However, after the multivariate logistic regression, only the RAP assessment with the 3–8–15 mmHg approach and the right atrial area remained independent predictors of raised RAP.

A classification tree showed that the right atrium area can be used to further identify patients with a higher probability of having raised RAP after the use of the 3–8–15 mmHg approach; see Fig. 1.

In this study, the 3–8–15 mmHg approach and right atrium area exhibited the highest correlation with RAP and were predictors of increased RAP (Table 1).

We found that the 3–8–15 mmHg approach (the one recommended by current international guidelines) showed the highest correlation with invasively obtained RAP. However, we emphasize that because of the importance of preload in patients with RVMI, accurately assessing RAP is critical. It is extremely important because both a very low and a very high preload have deleterious effects on right ventricular performance.

In this study, the 3–8–15 mmHg approach was the best predictor of RAP. This is explained because there is strong evidence to support the fact that inferior vena cava size and collapse during inspiration are closely related to RAP.

Interestingly, novel echocardiographic parameters such strain were associated with RAP, but they did not improve reclassification after the 3–8–15 mmHg approach.
The classification tree shows that when a patient has a normal estimated RAP (3 or 8 mmHg in the 3–8–15 mmHg approach), most patients will have a normal RAP. Therefore, preload optimization with a higher intravascular volume might be indicated depending on the hemodynamic state at that precise moment. However, if the estimated RAP is high (15 mmHg in the 3–8–15 mmHg approach), the clinician would not administer more volume in order to avoid right ventricular dilatation and dysfunction. However, up to 20% of patients do not have increased RAP and might need higher intravascular volume. The assessment of right atrium area will help to confirm increased RAP. If the right atrium is enlarged or close to the maximum area, 100% of patients will have increased RAP and thus, no further intravascular volume would be necessary. However, if the right atrium area is normal, up to 60% of patients will have normal RAP, and preload optimization might be warranted depending on hemodynamic state.

We note that this is an observational study and thus is susceptible to bias. Variability in echocardiographic measures and sample size are other limitations.

In conclusion, the echocardiography can accurately estimate a raised RAP in patients with RVMI and guide fluid management in these high risk patients.

### Funding

No funding received for this study.

### Conflicts of interest

We declare that we have no conflicts of interest to declare, relevant to the content of this paper.

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Flow cytometry analysis of CD64, CD18, CD11a and CD11b in four children with Bordetella pertussis infection and admitted to critical care: New biomarkers?

Análisis mediante citometría de flujo de CD64, CD18, CD11a y CD11b en cuatro niños con infección grave por Bordetella pertussis: ¿Nuevos biomarcadores?

Dear Editor,

Pertussis, also known as "whooping cough," is a highly contagious acute respiratory illness caused by the gram-negative intracellular coccobacillus Bordetella pertussis. Prior to the vaccine introduction, the pertussis was a devastating illness. Nowadays, cyclical epidemics occur every two to five years and there has been a steady increase in reported cases with mortality occurring predominantly in young not vaccinated infants.

B. pertussis is transmitted via aerosolized respiratory droplets. The organism adheres to ciliated respiratory epithelial cells of the upper respiratory tract and nasopharynx. It promotes cellular attachment, causes local and systemic tissue damage and interferes with host defence mechanisms. Histopathological analysis from cases of fatal pertussis revealed intracellular organisms in alveolar macrophages as well as the ciliated respiratory epithelial cells. This may explain the prolonged duration of cough. The most notable systemic laboratory manifestation is lymphocytosis, which is caused by pertussis toxin. As an intracellular organism, the usual host defence patterns actuated in case of bacterial infection may associate a not typical response. The study by flow cytometry of this pattern through the expression of CD64, CD18, CD11b and CD11a in granulocytes could add useful data.

We study four children admitted to our pediatric critical care unit (PICU) from October 2015 to February 2016 because of B. pertussis infection (2 male, 2 female, mean age 48 ± 8 days, mean ± mean standard error). The patients were enrolled after obtaining a written informed consent. A blood sample was obtained at PICU admission to study the expression of CD64, CD18, CD11b and CD11a in granulocytes, using a BD FACS Canto II flow cytometer (Becton Dickinson, New York, USA). CD64 (clone 10.1), CD18 (clone CBR LFA-1/2), CD11b (clone CBRM1/5) and CD11a (clone HI111) monoclonal antibodies were from Biolegend, San Diego. Cells viability was confirmed by 7-AAD staining. The flow cytometer settings and samples were prepared according to the manufacturer’s instructions. Neutrophils, monocytes, and lymphocytes were identified on forward/side scatter dot-plot profiles and gated. The intensity of expression was measured as mean fluorescence intensity (MFI) and the positive cells were expressed as a percentage (Fig. 1). The patients were chronologically numbered. All of them were treated with azithromycin and received supportive treatment related with their needing. Respiratory support was the main problem in all of them. Blood cell counts and inflammatory biomarkers were obtained at the same time as flow cytometry (Table 1).

Patient one to three showed good clinical evolution, with PICU discharge after two-three weeks of admission (mean days of PICU admission 16 ± 6). Patient number four showed hemodynamic instability, coagulopathy and severe respiratory distress. Broad spectrum antibiotic was initiated and leukoreduction was done without improvement. Later, because of refractory hypoxemia despite aggressive approach, extracorporeal membrane oxygenation was initiated. The child died 48 h after PICU admission and later the bronchoaspirate cultures done were positive to Klebsiella pneumonia.

As known, in case of B. pertussis infection, the use of common biomarkers is not useful to anticipate clini-