Contrast-enhanced Magnetic Resonance Imaging Does Not Detect a Progression in Lung Morphological Score in Preschool Children with Cystic Fibrosis

To the Editor:

We have read with interest the study by Stahl and colleagues about the use of lung magnetic resonance imaging (MRI) in preschool children with cystic fibrosis from 0 to 4 years of age (1). Using multiple comparison statistical tests across patients from 0 to 4 years of age, the authors concluded that MRI could allow early detection of modifications over time, which were ascribed to the progression of the lung disease. However, two major limitations are not discussed in the text.

First, the authors provide an overall *P* value of multiple comparison analyses in the main manuscript. However, a more extensive description of how these statistical tests were obtained was made available in Tables E7 and E8 in their online supplement. Interestingly, there was no difference in any of their biomarker analyses from 1 to 4 years of age (Table E7). All statistical tests in those preschool children between 1 and 4 years of age found no significant longitudinal variation over that time.

The only differences were found when comparing the patients at 1–4 years of age with the patients at 0 years of age. This finding deserves some comment, as it is not discussed as a major limitation of the study. Indeed, at 0 years of age, only 20 out of 48 (41%) patients could undergo a contrast material injection because of ethical issues. Conversely, 91–100% had a contrast-enhanced MRI scan between 1 and 4 years, using an additional gadolinium chelate injection ($P < 0.001$). It is common knowledge that non–contrast-enhanced and contrast-enhanced MRI are noncomparable imaging modalities (2–4). As expected, an injection of contrast MRI does increase the visibility of morphological abnormalities using lung MRI, most notably wall thickening and bronchiectasis (2–4).

Second, there is another major limitation of this study. The comparisons were made using a repeated measure ANOVA. The statistical requirement of this test is to be performed in the same subjects over time. In Table E7, it looks like the comparisons were made in heterogeneously distributed patient groups, with various and different patients per group. This is confirmed and well documented in Table E8 of the article, demonstrating that the study groups at 0 to 4 years were composed of different children. Notably, there are 6 out of 48 (12%) children with late cystic fibrosis diagnosis at 0 years, versus 13 out of 35 (37%) children with late cystic fibrosis diagnosis at 4 years ($P < 0.001$). Conversely, there were 22 out of 48 children with ne8wborn screening (NBS) at 0 years (45%) versus 8 out of 35 children with NBS at 4 years (22%) ($P = 0.03$). Of note, two-thirds of the NBS population was not clinically stable enough to perform the lung MRI procedure, which contradicts the statement of a good clinical condition. Therefore, Figures 1 and 3 of the main article are reporting means and SDs from noncomparable and different patients (Table E8). Thus, Figures 1 and 3 do not correspond to longitudinal data from the same patients over time (Table E8).

To conclude, the lack of any variation in contrast-enhanced MRI from 1 to 4 years of age does not seem convincing data to promote the use of general anesthesia with contrast material injection once a year, in this age range. Regarding its use in newborns at 0 years to support NBS, a study that would not compare non–contrast-enhanced versus contrast-enhanced MRI would be appropriate. Indeed, better MRI visibility of wall thickening/bronchiectasis and morphology, thanks to a contrast material injection, is an expected finding. Also, a longitudinal study with comparison tests performed within the same patients over time is still lacking. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Reply to Dournes *et al.*

From the Authors:

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