Abnormal Spirometry in Congenital Heart Disease:

Where Do We Go From Here?

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“But the gods, foreknowing that the palpitation of the heart in the expectation of danger and the swelling…of passion was caused by fire, formed… as a supporter to the heart the lung….as a soft spring, that, when passion was ripe within, the heart, beating against a yielding body, might be cooled and suffer less, and might…join with passion in the service of reason.”

Timaeus, Plato

The close relationship between the heart and lungs has been appreciated for over 2,000 years, though the functions of each organ and their connection were misunderstood. While Plato’s assertion that the lungs’ purpose is to support the heart may be considered an early case of cardiac chauvinism, his description of their close interaction aligns with our current understanding. Not only is efficient cardiopulmonary coupling critical to support tissue metabolic demands at rest and with effort, but cardiac and pulmonary development are also intertwined. Cardiac dysfunction produces readily appreciated and dynamic effects on measured pulmonary function; the converse is equally true. As the electrocardiogram is affected by pulmonary disease, spirometry provides a window on cardiac function. Hutchinson’s description of spirometry and the divisions of thoracic volume in the mid-19th century had been applied to patients with heart disease by the early-20th century and it was quickly clear that heart disease was associated with abnormal vital capacity. These relationships have been explored extensively in acquired heart and lung disease, but investigation in congenital heart disease has generally been limited to small series. In this issue of Circulation Alonso-Gonzalez, Borgia and colleagues present data on spirometry from a large cohort of adults with congenital heart disease. The authors report two major findings. First, there is a high prevalence of markedly abnormal forced vital capacity (FVC) in this population. Second, reduced FVC is associated with increased mortality.
Diverse pulmonary vascular and parenchymal abnormalities, including the presence of low vital capacity, are common among patients with various congenital heart defects and correlate with exercise capacity. 6, 7 While the current report includes a large number of patients, available pulmonary function data are limited to simple spirometry without information on lung volumes or diffusing capacity, which limits mechanistic inference. Previous reports demonstrate that the pattern of pulmonary function abnormalities and underlying mechanisms may vary between defects and at different stages of disease and repair. With that caveat, potential etiologies include several variables included in the authors’ analysis such as scoliosis, prior sternotomy or thoracotomy, and diaphragmatic dysfunction. The strong association between these factors and reduced FVC does not entirely account for the prevalence of low FVC. Data from children and adolescents with unrepaired congenital heart disease without scoliosis or apparent lung disease also found a high prevalence of abnormal lung function.8 This suggests that other, more generally applicable reasons for the very high prevalence of low FVC exist in this population.

Alveolar size and number continue to increase for several years after birth. Various insults early in life, such as diaphragmatic hernia or pulmonary hypoperfusion, impair normal development.9 Presumably, events during early life in patients with congenital heart disease such as surgical intervention, large chronic pleural effusion, malnutrition, mechanical ventilation, or transient diaphragmatic dysfunction may have unappreciated effects on pulmonary development. Other clinical interventions, such as exercise restriction, also may blunt alveolar growth. Physical activity in early life may translate into differences in FEV1 and FVC,10, 11 and there is a real, though modest, effect of physical activity on spirometric volumes in adults.12

More recently, investigators have reported data supporting a potential relationship between fetal
factors as assessed by birth weight and gestational age at birth, and other early post-natal (e.g., breast feeding) and measures of lung function.\textsuperscript{13} This has direct implications for congenital heart disease. Changes in clinical practice, unrelated to lung considerations, such as avoiding exercise restriction and breast-feeding infants with congenital heart disease, could presumably impact pulmonary parenchymal development.\textsuperscript{14} In light of practice variation and secular trends in management, investigation of spirometry in children and young adults with similar defects but who have had heterogeneous care may help tease out the most important contributors to abnormal spirometry.

The reported association between abnormal spirometry and mortality, in conjunction with previous reports relating abnormal FVC to lower aerobic capacity,\textsuperscript{6} lends importance to the high prevalence of low FVC in this population. While this is the first report to specifically highlight this connection among adults with congenital heart disease, numerous studies have reported an association between spirometric variables (e.g., slow vital capacity, FEV\textsubscript{1} and FVC) and overall and cardiovascular mortality in both patients with acquired heart disease and in the general population, independent of tobacco use or clinical lung disease.\textsuperscript{15,16}

The relationship between abnormal spirometry and mortality in acquired adult heart disease and in the general population cannot be attributed to scoliosis or prior thoracic surgery, and it is difficult to suggest that these patients have anything approaching the gross early pulmonary perfusion abnormalities seen in a subset of congenital heart defects. Subclinical pulmonary congestion may partly explain the relationship between low FVC and assorted cardiovascular events, though measurement of abnormal spirometry may predate clinical events by years. Others have suggested that mild parenchymal lung disease is associated with an increased inflammatory state, resulting in higher cardiovascular risk.\textsuperscript{16} Two other potential
mechanisms, discussed briefly above, are more readily applicable to both congenital heart disease and acquired heart disease in adults. The first is the “Barker hypothesis” relating the fetal and infant environment to the risk of adulthood chronic diseases and adverse outcomes in later life.\textsuperscript{17, 18} While the burden and timing vary by defect type and severity, patients with congenital heart disease have a less favorable fetal and early post-natal environment than the average person. In this context, reduced lung size and vital capacity may be an indicator of distant fetal and early post-natal events. A second possible cause is a less physically active childhood (and to a lesser degree adulthood) which could result in both lower FVC via effects on lung development and increased mortality in the general population as well as in patients with congenital heart disease because of the many detrimental consequences of low physical activity. While both hypothetical mechanisms would assign low FVC a non-causal role, they would allow for potential intervention to improve outcomes. In this context, it is plausible that FVC could find a useful function as an intermediate marker to assess the medium-term effects of interventions. 

As suggested by the authors, the current findings could allow clinicians to better risk-stratify adults with congenital heart defects. The limited use of spirometry in guiding the clinical care of acquired heart disease provides a less than hopeful example, however. The well documented equivalent relationship between spirometry and mortality in the general population and among patients with acquired heart failure remains little more than an interesting epidemiologic observation. Measurements of vital capacity, given its inverse relationship to engorgement of the lungs, were, 70 years ago, “…considered indispensable in cases of heart disease,” but this certainly is no longer the case in clinical practice.\textsuperscript{19} The most important obstacle to applying these findings to patients is that abnormal spirometry is a risk marker which
does not suggest any specific intervention. What should a clinician do for an adult with congenital heart disease and low FVC? Until we answer that question, it is difficult to see a meaningful role for spirometry in the clinical care of adults with congenital heart defects.

Translation of the current observations to a clinically useful tool will therefore require two related avenues of further investigation. First, the underlying pathophysiology of abnormal spirometry in this population needs to be defined, along with its causal relationship relative to adverse outcomes. FVC has limited specificity for restrictive lung disease, and the contributions of reduced total lung capacity, diaphragmatic weakness, and other contributors including early developmental factors remain to be defined. Second, if the underlying mechanisms are potentially modifiable the efficacy of specific interventions, such as inspiratory muscle training, should be tested prospectively. The current data, taken in context of a prior literature, provides several clinically relevant testable hypotheses. In the current era, congenital heart disease represents an unnatural experiment with enormous heterogeneity in initial anatomy and subsequent care. While this heterogeneity often frustrates generalizable research, it may alternatively be seen as providing an opportunity to define novel mechanisms and interventions, with implications not only for management of congenital heart disease but also with potential significance for the larger population of patients with acquired heart disease.

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**References:**


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