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Chyle in the Wrong Place: Why Knowing the Target Matters

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Management of chylous effusions has remained a conundrum for many years; it is particularly challenging for nontraumatic causes owing to varied etiologies and complex underlying pathophysiologies. Nontraumatic causes account for 25–50% of chylous pleural effusions (1). Treatment options traditionally included treating the underlying cause, if one is identified, and conservative and surgical approaches, the latter being mainly ligation of the thoracic duct, carrying a mortality up to 10% (2). Since the groundbreaking work by Cope and colleagues in 1999 of using thoracic duct embolization (TDE) as an alternative to ligation of the thoracic duct (3), nonsurgical lymphatic interventions have been a particular focus of interest in changing the outlook of patients with persistent chylous effusions.

The key factor for treatment success in lymphatic interventions for chylous effusions is finding the exact abnormality in the lymphatic tract, which is in itself a complex and variable anatomical pathway. To put this in perspective, TDE success rates have been reported to be 52–78% in the presence of an abnormal thoracic duct and as low as 16% if the thoracic duct is anatomically normal (4). This suggests that there are other underpinning mechanisms, especially in cases of normal thoracic duct anatomy, for which a different targeted intervention is needed. To guide such treatment, advances in our understanding of imaging modalities are required to carefully delineate the precise underlying anatomical abnormality and thus increase the overall success of interventions. Invasive lymphangiography and now newer noninvasive imaging techniques (5) have not only improved our understanding of complex pathophysiology of these effusions but also paved the way for novel targeted interventions. One such intervention is image-guided interstitial lymphatic embolization (ILE), which uses a percutaneous approach to deliver an embolization agent into aberrant lymphatic vessels visualized on lymphangiogram (6). ILE is a promising technique, owing to its feasibility in targeting smaller lymphatic vessels that are too small for catheterization using standard techniques (7). This is a relatively new addition to the artillery of noninvasive techniques offering targeted treatment options for this complex disease.

In this issue of *AnnalsATS*, Gurevich and colleagues (pp. 756–762) present their experience using an algorithm-based approach to map out management plans for nontraumatic chylous effusions (8). The authors used novel dynamic contrast-enhanced magnetic resonance lymphangiography (DCMRL) to delineate primary site(s) of the lymphatic defect resulting in the clinical syndrome of chylous effusion and/or ascites (i.e., thoracic, retroperitoneal, or transdiaphragmatic), and this information subsequently guided a lymphatic intervention. A retrospective analysis was conducted of 52 patients, with chylothorax and/or chylopericardium, who were treated according to the underlying pathological abnormality as detected by DCMRL, with a 93% success rate in detection of an aberrant lymphatic pathway causing "true chylothorax."

The authors subdivided these patients into three distinct categories using DCMRL preintervention. A true chylous effusion with abnormal thoracic duct was treated with TDE; if additional retroperitoneal aberrant lymphatic channels were contributing, both TDE and ILE were performed. Chylous ascites leading to effusion due to abnormal transdiaphragmatic channels was managed with abdominal lymphatic channel embolization/pleurodesis/peritoneovenous shunts. The algorithm thus promoted a shift away from offering TDE to all patients in a nontargeted manner.

The authors should be congratulated on a carefully conducted study in a difficult-to-assess and often rare population, focusing on targeted management of chylous effusions based on distinct underlying mechanisms of these heterogenous cases. This algorithm has the potential to sow the seeds of a shift from a one-size-fits-all approach to more tailored management.

The study has distinct strengths, including the definition of discrete clinical groups using noninvasive imaging and the

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more rational and targeted use of ILE, with this combination potentially resulting in high success rates of treatment. The authors should again be congratulated on achieving this in a relatively rare disease, speaking to their expertise and experience in the management of chylothorax, from which the clinical community can learn valuable lessons. However, it should be noted that this is a retrospective study with a relatively small sample size, a mixed pediatric and adult population, and no comparator group. This is not a criticism, as such cases are complex and difficult to study because of their rare nature, but the cost and resource implications, as well as the 14.6% complication rate overall from multiple procedures, should be noted. Nevertheless, resolution of symptoms in 9.5 days after intervention in this selected study group, compared with total duration of debilitating symptoms in these patients of average 283 days at the time of recruitment into study, highlights the importance of timely targeted intervention. The required use of intranodal lymphangiography in three patients who were unable to undergo DCMRL also highlighted the need for flexible approaches and a multiskilled radiologist and physician team to approach this complex disease. This is reinforced by the fact that 94% of patients had failed conservative treatment for chylothorax before inclusion in the study, including nonfat diets, total parenteral nutrition, or octreotide, which highlights the need to pursue such treatment before consideration of this image-based approach.

How then should clinicians approach chylothorax cases in light of this evidence? This study has highlighted the potential for better phenotyping of patients who present with chyle in the wrong place using imaging to delineate the precise anatomical abnormality, and as such is a very welcome step forward in assessment and management of this often difficult-to-manage condition. Accepting that a clinical assessment of etiology, excluding common causes with specific treatment (e.g., lymphoma, trauma), and simple treatments (diet, octreotide) are still required, image-based phenotyping is very appealing as the next step in achieving clinical treatment success, especially for those patients who do not respond to standard treatment approaches. However, comparative data are now required to define the most efficacious and safest interventions in anatomically defined chylothorax. This study has provided the tools to conduct such studies, which, given the rare nature of chylothorax, are likely to need multicenter collaboration. ■

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

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Air Pollution and Child Lung Health: Critical Thresholds at Critical Times

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In September 2021, the World Health Organization (WHO) released updated global air quality guidelines (AQGs) for the first time since 2005. Incorporating a wealth of interim evidence demonstrating the adverse health effects of air pollution, the WHO tightened recommendations for target air pollution concentrations, including lowering the AQG for fine particulate matter (particulate matter ≤2.5 μm in aerodynamic diameter [$PM_{2.5}$]) from 10 μg/m^3 to 5 μg/m^3 (1). These updated guidelines not only emphasize the global urgency of improving air quality to prevent illness and death but also send the message that harmful effects occur even at lower concentrations of air pollution.

On the heels of these more stringent recommendations, in this issue of

AnnalsATS, Takebayashi and colleagues (pp. 763–772) investigated the association

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