

Understanding ACOS: some thoughts in the journey.

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ACOS (Asthma COPD Overlap Syndrome) has been a new nomenclature in the list of obstructive airway diseases. It means a situation where two diseases (asthma and COPD) have overlapped to share the features of both (1). The very recognition of such an entity clearly stands as a victory of the 'British hypothesis' that argues for a long time that asthma and COPD are two different diseases (2). With better understanding of the molecular mechanism of both the diseases (3, 4, 5), the pathophysiology of each of them appear distinct but the whole scenario has turned perhaps more enigmatic than before. The each of the diseases appears heterogeneous and understanding the phenotypes and sub-phenotypes has made it look difficult to translate the molecular knowledge to a perfect bedside practice. Moreover, there is a gray zone in the definition of obstruction and behaviour of reversibility (6, 7). Hence, one may tend to dump an airway obstruction showing anything short of COPD defining criteria ($FEV_1/FVC < 70\%$) or asthma defining reversibility (improvement in post bronchodilator FEV_1 as 200 ml 12 %), into the basket named ACOS.

The job appears simple theoretically but in real world the physicians are often confused. The lung function (and, of course, the symptoms) of an obstructive airway disease vary significantly from known and unknown reasons. The perception ability of the ailment or the symptoms may vary with same degree of obstruction and it may be difficult for a clinician to define a so called 'mild' exacerbation especially in 'mild' stage of a disease. Hence, it remains difficult to assess the quality of an airway disease historically.

In addition, it is not rare to see a patient shifting from lack of reversibility to a reversible disease in course of time and again shifting back to a reversible stage. Hence a patient diagnosed as 'ACOS' can slip into a diagnosis of 'asthma' or 'COPD' at different points of time in the course of illness. Defining the preconditions for performing a spirometry also

remains important in defining ACOS and one may need to see multiple spirometry results at intervals of days to weeks or so to define reversibility. Making it mandatory to have at least three features of both asthma and COPD from a list to make a diagnosis of overlap may have helped to overcome the confusion resulting from sole reliance on lung function, but this also needs examination and cross examination as a ACOS defining exercise.

There have been other problems too. Physicians come across patients who have either of the amount (> 200 ml) or the percentage ($> 12\%$) of reversibility critical for diagnosis of asthma but not the both together. With relatively better lung capacity (viz., $FEV_1 > 2.5$ litres) the absolute change of 200 ml may match even 6 or 7 % of relative reversibility. The reverse is true with poor lung capacity when significant reversibility by percentage (may be 25 to 30 %) can occur with even 100 ml of reversibility. The phenomenon keeps a physician perplexed regarding how to go ahead with treatment in a particular case; would they follow the COPD way or the asthma route.

Similarly again, a borderline reversibility situations may be fallacious as most of the time the patients receive some or other medication. We withhold them for a defined length of time to have their acute effects been washed out before performing spirometry but we cannot neutralize the chronic effects of medications. In real world practice, we can hardly find a truly treatment-naïve patient to assess the reversibility.

More than anything, the very concept of 'overlap' in defining ACOS ignores the 'mimics' The definition of ACOS does not include the patients who are basically 'COPD mimics'. These are 'asthmatic' patients historically but, on lung function behaviour they satisfy a diagnosis of 'COPD' consistently. These are the patients of chronic and poorly treated asthma with established remodelling. In the developing world, we find patients to receive

any anti-inflammatory drug often after decades of suffering and they behave more like COPD clinically and on spirometry. Unfortunately, the ACOS defining effort has put very little insight into this category of patients.

The definition of ACOS must have been evolving in the minds of our intelligentsia. The making of perfect definition appears difficult. Hence, despite the questions and doubts in mind, it must be an honest and jubilant welcome to ACOS as an entity showing the mixed qualities of asthma and COPD. We hope that in course of time, the cloud of confusion in understanding ACOS and the airway diseases as a whole will be far more clear.

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