Clinical Controversy
Use of ACEI/ARBs in Patients with COVID-19

How the Controversy Began

A study conducted in Wuhan, China found that older patients (>65 years old) with comorbidities that included atherosclerotic cardiovascular disease (ASCVD) and Diabetes Mellitus were at an increased risk of death from pneumonia. A recent article published in *Lancet* suggested that human pathogenic coronaviruses bind to target cells through angiotensin-converting enzyme 2 (ACE2) and that ACE2 is increased in those who are treated with ACE inhibitors and Angiotensin Receptor Blockers (ARBs). Hence, the authors hypothesized that the increased ACE2 expression in this population would have an increased risk of developing coronavirus infection or worsen its prognosis.

Relationship between ACE Inhibitors/ARBs and ACE2

In 2002, Turner and colleagues determined through gene expression that ACE2 (also known as ACEH) does not hydrolyze bradykinin and is not inhibited by ACE inhibitors. Additionally, Tipnis and colleagues found that although predicted amino acid sequence was similar to ACE, ACE2 activity was not inhibited by captopril, lisinopril, or enalaprilat. Furthermore, a more recent article published by Kuster and colleagues in the *European Heart Journal*, suggested that although upregulation of ACE2 may be associated with higher risk of infections, it may not necessarily correlate with degree of infection. A mouse model of SARs-CoV infection suggested a protective role of ARBs on pulmonary injury. This was somewhat supported by a retrospective chart review of patients hospitalized with COVID-19 in China that showed, although not significant, patients who were prescribed ACEI/ARBs were associated with less severe cases than patients who were not on ACEI/ARBs.

Current Societal Guidelines Addressing the Use of ACEI/ARBs in COVID-19

On March 17, 2020, HFSA/ACC/AHA published a statement that reinforced the continual use of ACEI/ARBs for patients with heart failure, hypertension, or ischemic heart disease due to lack of evidence indicating increased risk of adverse outcomes related to COVID-19 associated with these drugs. The societal statement also advised to not add or remove any ACEI/ARBs beyond actions based on standard clinical practice.

A summary of statements from various clinical societies that encourages the continuous use of ACEI/ARBs can be found here.

Due to lack of clinical evidence linking the use of ACEI/ARBs with worsening COVID-19 infections and increased adverse events, ACEI/ARBs may be continued in patients with clear cardiac or renally related indications until further evidence suggests otherwise. Various clinical studies are underway evaluating outcomes of patients infected with COVID-19 who are also on ACEI/ARBs.

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