

Use of ACE-I in a Patient with HFpEF and DM2

Matt Welzenbach PGY-2

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Story from the Frontline:

A woman in her 80s with a known history of DM2 and end-stage COPD with resultant pulmonary HTN presented for a routine follow up. She had recently been hospitalized at an outside hospital for shortness of breath and abdominal pain. Clinical evaluation and studies at that time were indicative of heart failure with a preserved ejection fraction (HFpEF). As a result, the patient's primary physician requested cardiology consultation to help in optimizing this patient's care.

At time of her follow up in her primary care clinic, she had already seen cardiology, who recommended starting an ACE inhibitor should her blood pressure allow. Given a normal blood pressure, an ACE inhibitor was started at low dose with plans to follow up in two weeks for a blood pressure check with BMP.

The patient was unable to make her 2-week appointment, and instead came back to clinic five weeks later. At that time, she was hypotensive with a small increase in her creatinine, and hyperkalemia. Fortunately, she suffered no consequences from her low blood pressure or lab abnormalities, and it was decided to stop her ACE-I completely.

Teachable Moment:

Currently there are no therapies that have been shown to reduce mortality in HFpEF. Few studies have been done that have looked at the relationship between ACE inhibitors and HFpEF. One study found no benefit with regard to mortality, although it did show improvements in functional class and the six-minute walk which were significant.ⁱ

This does not mean that ACE inhibitors play no role in the treatment of HFpEF. In fact, ACE inhibitors are crucial for treatment of many of the risk factors for HFpEF including hypertension and diabetes. It is known that ACE inhibitors can prevent progression of nephropathy in diabetic patients who have hypertension with or without a degree of microalbuminuria.ⁱⁱ This patient in question, while having diabetes, did not suffer from either hypertension or microalbuminuria. In this case specifically, there has been found no benefit of an ACE inhibitor as a primary preventative measure.ⁱⁱⁱ

Ultimately, there still may have been a role for an ACE inhibitor for this patient when taking into context that she had a degree of heart failure as well as diabetes. However, it is important to look at the clinical picture as a whole. Her other comorbidities included COPD, which was so bad that she was seeing palliative care. Taking into account that the effects of ACE inhibitors can take years to become apparent, the utility of this medication would be extremely limited. The concept of life expectancy versus lag-time to benefit becomes important here.^{iv} Given the overall poor life expectancy of this patient coupled with the lag-time to benefit for ACE inhibitors and the non-trivial side effects produced by these medications, treatment in this case specifically was likely avoidable.

ⁱ Cleland JG, Tendera M, Adamus J, et al. The perindopril in elderly people with chronic heart failure (PEP-CHF) study. *European Heart Journal*. 2006;27(19):2338. Epub 2006 Sep 8.

ⁱⁱ Patel A, MacMahon S, Chalmers J, et al. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the ADVANCE trial): a randomised controlled trial. *Lancet*. 2007;370(9590):829.

ⁱⁱⁱ Schrier RW, Estacio RO, Esler A, Mehler P. Effects of aggressive blood pressure control in normotensive type 2 diabetic patients on albuminuria, retinopathy and strokes. *Kidney International*. 2002;61(3):1086.

^{iv} Lee S, Leipzig R, Walter L. “When will it help?” Incorporating Lagtime to Benefit into Prevention Decisions for Older Adults. *Jama*. 2013 Dec 25; 310(24): 2609–2610.