Clinical Practice Statement:

What is the Emergency Department Management of Patients with Angioedema Secondary to an ACE-inhibitor?
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Angiotensin-converting-enzyme (ACE) inhibitors are one of the most commonly prescribed antihypertensive medications worldwide. A known adverse effect of ACE-inhibitors is angioedema, characterized by the abrupt onset of non-pitting, non-pruritic swelling that involves the reticular dermis, subcutaneous, and submucosal layers. Lesions are typically asymmetric in distribution, well defined, and located in non-dependent areas. Angioedema is a potentially life-threatening condition, as laryngeal swelling can rapidly lead to complete airway obstruction and death. Since the majority of patients with the acute onset of angioedema present to an emergency department (ED), it is crucial for the emergency physician to be expert at diagnosing and evaluating patients with ACE-inhibitor angioedema.

The current literature on ACE-inhibitor angioedema is primarily limited to retrospective reviews, case series, and case reports. Based upon this review of the literature, ACE-inhibitor angioedema should be considered in any ED patient presenting with asymmetric swelling of the lips, tongue, floor of the mouth, face, neck or eyelids. Patients with angioedema who present with respiratory distress, stridor, or drooling should be assumed to have laryngeal edema and emergently intubated. Patients who are not in extremis but report odynophagia, dyspnea, dysphonia, hoarseness, or dysphagia may have significant laryngeal edema and should undergo fiberoptic examination in the ED.

Patients with angioedema are often treated with medications, namely epinephrine, antihistamines, or corticosteroids. Although the exact mechanism

has not been fully elucidated, it is believed that ACE-inhibitor angioedema is not mediated by degranulation of mast cells and basophils. As a result, medications commonly used to treat allergic emergencies may not be efficacious for ACE-inhibitor angioedema. There is currently insufficient evidence to recommend for, or against, the routine administration of epinephrine, antihistamines, or corticosteroids in the ED management of patients with ACE-inhibitor angioedema. While there is a paucity of literature on medication efficacy, there are no reports detailing adverse events in patients receiving these medications. When deciding whether to administer these medications, the emergency physician must continue to incorporate their clinical experience along with the potential adverse effects of these medications on the individual patient. Icatibant, a bradykinin receptor antagonist, is currently under review by the US Food and Drug Administration. In several Phase 3 trials, Icatibant has demonstrated improved results when used for the patient with hereditary angioedema. It currently has orphan drug status in the US and has been approved and utilized in the European Union for the treatment of hereditary angioedema. It has also been shown to be beneficial in those patients with ACE induced angioedema.

Determining whether to admit, observe, or discharge the ED patient with angioedema can be challenging. Intubated patients and those with laryngeal edema (involvement of the true vocal cords, false vocal cords, arytenoids, aryepiglottic folds, or epiglottis) on fiberoptic examination should be admitted to an intensive care unit. Patients with a prior history of angioedema, tongue or floor of the mouth edema, pharyngeal edema (palate or uvula), or those with progression of symptoms in the ED should be admitted to a monitored bed. Those with isolated swelling of the lips or face can be observed in the ED. There is currently no well defined period of ED observation. Regardless of patient disposition, any patient presenting with suspected ACE-inhibitor induced angioedema needs to be counseled to discontinue usage of this medication.