Difficulty with Diagnosis in ESRD patients

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Story from the Frontlines:

A woman in her 70s with end stage renal disease (ESRD) on dialysis, diabetes, hypertension, and COPD presented to the ED with chest pain. The pain had been present for several days, described as a "pressure" that was worse with exertion, located throughout her chest and did not radiate to her back or other areas. It was worse when she coughed and breathed deeply. She denied recent cough, fevers, chills, or sweats. She denied symptoms of heartburn or recent trauma. Her vital signs were normal. On exam, she appeared in no acute distress. Her heart exam was notable for a soft systolic murmur, no rubs, no JVD or peripheral edema. Her lungs were clear. Her chest pain was reproducible with palpation and with deep breaths. Her labs were notable for an initial troponin of 0.49. She was admitted to the hospital with subsequent two troponins at 6 hour intervals of 0.43 and 0.42 respectively. Her chest pain resolved on its own though because of her abnormal troponin level, coronary angiography was undertaken.

Teachable Moment:

The relationship between chronic kidney disease (CKD) and coronary artery disease (CAD) is well known. A 2011 meta-analysis including 10 cohorts of patients with risk factors for CKD including hypertension, diabetes or cardiovascular disease were examined to evaluate if CKD was an independent risk factor for CAD.[1] In total, they evaluated data from 266,975 patients. While there was no increased risk of all-cause mortality or cardiovascular mortality at glomerular filtration rates (GFR) of 60-105 mL/min, the hazard ratio for both outcomes at lower GFRs showed a linear progression with worsening renal function. Specifically, for cardiovascular mortality, the adjusted hazard ratios at GFR 60, 45, and 15 ml/min were 1.11, 1.73, and 3.08 respectively. CKD appears to be independently associated with death related to CAD, even in populations with other risk factors.

When patients with CKD do develop CAD, they are more likely to have worse outcomes. A study in 2004 evaluated 14,527 patients of whom there was a normal distribution around a mean GFR of 70.2 ml/min.[2] They found that for each 10-unit decrease in GFR under 81.0 ml/min, there was and incremental associated hazard ratio of 1.10 (95 percent confidence interval, 1.08 to 1.12; P<0.001) for death and nonfatal cardiovascular complications. This decreased survival is likely driven in part by worse outcomes from PCI and CABG. A 2002 study evaluated 5,237 patients who underwent PCI over a 6-year period.[3] They found that one year mortality increased with degree of renal insufficiency, with GFR >70, 50-69, 30-49, <30 ml/min, correlating with mortality rates of 1.5%, 3.6%, 7.8%, and 18.3%. Unsurprisingly, the mortality rate for ESRD patients was highest at 19.9%. In regard to CABG, a 2005 article in Circulation showed that patients with mild renal dysfunction, as defined by creatinine between 1.47 and 2.25 mg/dl had higher intra-operative, in-hospital and 3-year mortality.[4] Not only do patients with advanced kidney disease die more frequently when they have MIs, they are also at higher risk to die from the invasive interventions available to treat these conditions.

Given the risk of both cardiovascular disease and intervention related mortality in patients with CKD, the importance of appropriate diagnostic methods is paramount. A 2014 meta-analysis

evaluated the role of troponins in this population.[5] Though their 23 included studies were somewhat heterogeneous, they found that the sensitivity and specificity of troponin I ranged from 43% to 94% and 48% to 100% respectively while the sensitivity and specificity of troponin T ranged from 71% to 100% and 31% to 86% respectively. The increasingly popular high sensitivity troponins provided a new avenue to explore. A cross-sectional study in Europe looked at 1,514 patients who were evaluated for ACS with serial high sensitive troponins, of whom 25% had CKD. They found that high sensitivity troponins were more prevalent in CKD patients, with an overall sensitivity of 0.64 and specificity of 0.48.[6] A recent prospective study examined nearly 700 ESRD patients who presented with chest pain and dyspnea. While using a single high sensitivity troponin led to similarly poor diagnostic accuracy as previous studies, accuracy was significantly increased when a second troponin at 3 hours was drawn and used for analysis.[7]

Given both the high risk of CAD and of CAD related interventions in CKD patients, there must be caution in how to approach chest pain in this population. This caution should be further tempered with the knowledge that our typical diagnostic methods are less efficacious in these patients. Specifically, the use of troponins (either conventional or high sensitivity) must be incorporated judiciously into the management plan for patients. A small troponin rise should not be viewed in isolation and should not necessarily prompt immediate interventions. Given this patient's minor troponin elevation and chest pain more consistent with non-cardiac causes, more aggressive interventions could have likely been avoided.

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