Here we report performance characteristics of this novel biomarker panel. We recently reported data from two multi-center studies of 728 (Sapphire) Diabetes mellitus (DM) and chronic kidney disease (CKD) are both risk factors for AKI and possible confounders for biomarkers. We recently reported data from two multi-center studies of 728 (Sapphire) and 408 (Topaz) critically ill patients where a panel of urinary tissue inhibitor of metalloproteinases-2 (TIMP2) and insulin-like growth factor-binding protein 7 (IGFBP7), both markers of cell cycle arrest, were validated for risk stratification for moderate to severe AKI (KDIGO stages 2 and 3). Here we report performance characteristics of this novel biomarker panel ([TIMP2][IGFBP7]) in patients with a variety of comorbidities, including DM, CKD, or both.

**RESULTS**

In the overall cohort, 139 patients (12.3%) developed moderate to severe AKI within 12 hours. There were 326 patients with DM, 97 patients with CKD, and 50 patients with both. Patient demographics between the Sapphire and Topaz studies were similar. The area under the ROC curve was 0.83 (95%CI 0.77-0.89), 0.91 (95%CI 0.85-0.97), and 0.89 (95%CI 0.80-0.99), respectively, for patients with DM, CKD, and both DM and CKD. The RR for AKI above the 0.3 cutoff was 13 (95%CI 4-40), 32 (95%CI 2-530), and 22 (95%CI 1-361), respectively, for patients with DM, CKD, and both DM and CKD.

**CONCLUSIONS**

Cell cycle arrest markers have emerged as important tools in the prediction of moderate to severe AKI. Because a variety of stress states can contribute to cell cycle arrest, it is important to examine the influence of comorbidities on the test characteristics of these markers. Urinary [TIMP2][IGFBP7] levels remained similar to levels in healthy subjects (mean=0.3) in all comorbidity subgroups among patients who did not develop AKI.

The performance of urinary [TIMP2][IGFBP7] levels for AKI risk remained high in both the DM (Figure 1) and CKD (Figure 2) subgroups as demonstrated by AUC values above 0.80. These findings are consistent with test characteristics in the overall population and are similar to or better than the test characteristics reported for other AKI biomarkers.

Of particular note, in the CKD group urinary [TIMP2][IGFBP7] performed better than the general population, with AUC exceeding 0.90 (Figure 3). This is important because CKD patients are at higher risk for developing AKI, yet other AKI biomarkers are noted to perform poorly in this population.

**REFERENCES**