**Supplementary Online Content**

**TIMP-2•IGFBP7 Biomarker Panel Accurately Predicts Acute Kidney Injury In High Risk Surgical Patients**

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**eTable 1. Baseline characteristics and primary results comparing the Sapphire and Topaz surgical cohorts.**

|  | Sapphire | Topaz | P-value |
| --- | --- | --- | --- |
| All patients | 247 | 128 |   |
| Male | 168 (68%) | 74 (58%) | 0.05 |
| Age (years)\* | 64 (14) | 64 (15) | 0.98 |
| Body Mass Index (kg/m²)† | 27 (24-31) | 28 (25-32) | 0.09 |
| Race |  |  | 0.04 |
|  Black | 32 (13%) | 16 (13%) |   |
|  White | 196 (79%) | 110 (86%) |   |
|  Other/Unknown | 19 (8%) | 2 (2%) |   |
| Medical History |  |  |   |
|  Chronic Kidney Disease | 29 (12%) | 11 (9%) | 0.38 |
|  Diabetes Mellitus | 76 (31%) | 25 (20%) | 0.02 |
|  Congestive Heart Failure | 42 (17%) | 19 (15%) | 0.66 |
|  Coronary Artery Disease | 99 (40%) | 46 (36%) | 0.50 |
|  Hypertension | 160 (65%) | 86 (67%) | 0.73 |
|  Chronic Obstructive Pulmonary Disease | 49 (20%) | 27 (21%) | 0.79 |
|  Cancer | 67 (27%) | 36 (28%) | 0.90 |
|  Liver Disease | 13 (5%) | 5 (4%) | 0.62 |
| Acute Exposures and Susceptibilities |  |  |   |
|  Sepsis | 27 (11%) | 17 (13%) | 0.50 |
|  Radiocontrast Agents | 71 (29%) | 43 (34%) | 0.35 |
|  Nephrotoxic Drugs | 183 (74%) | 112 (88%) | 0.002 |
|  Hematocrit < 30% | 147 (60%) | 72 (56%) | 0.58 |
|  Non-Renal Apache III† | 57 (41-79) | 58 (46-76) | 0.49 |
| Surgery Subgroup |  |  |  |
|  Cardiothoracic Surgery | 105 (43%) | 55 (43%) | >0.99 |
|  Emergent Surgery | 54 (22%) | 47 (37%) | 0.003 |
| Time from ICU admission to biomarker sample collection (h)† | 15 (5-20) | 14 (3-20) | 0.32 |
| Enrollment Serum Creatinine (mg/dL)†,‡ | 0.9 (0.7-1.3) | 0.9 (0.7-1.1) | 0.73 |
| AKI (KDIGO stage 2-3) | 19 (7.7%) | 16 (12.5%) | 0.14 |
| [TIMP-2]•[IGFBP7] AUC (95% CI) for AKI within 12 h | 0.80(0.69-0.92) | 0.88(0.81-0.96) | 0.25 |

\*Average (standard deviation)

†Median (interquartile range)

‡Hospital value taken closest to the time of enrollment

**eTable 2. Operating characteristics for varying [TIMP-2]•[IGFBP7] cutoff values**

Operating characteristics with 95% confidence intervals for the [TIMP-2]•[IGFBP7] test for moderate-severe AKI within 12 hours in all surgical patients.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Cutoff**((ng/ml)2/1000) | **Sensitivity,****%** | **Specificity,****%** | **Negative Predictive Value, %** | **Positive Predictive Value, %** | **Negative Likelihood Ratio** | **Positive Likelihood Ratio** |
| 0.1 | 100(90-100) | 21(16-25) | 100(95-100) | 11(11-12) | 0(0-0.48) | 1.26(1.2-1.33) |
| 0.2 | 91(80-100) | 35(30-40) | 98(94-100) | 13(11-14) | 0.24(0-0.6) | 1.41(1.19-1.58) |
| 0.3 | 89(77-97) | 49(43-54) | 98(95-99) | 15(13-17) | 0.24(0.06-0.49) | 1.72(1.44-2.01) |
| 0.4 | 89(77-97) | 57(52-62) | 98(96-100) | 18(15-20) | 0.20(0.05-0.43) | 2.06(1.7-2.47) |
| 0.5 | 86(74-97) | 65(59-70) | 98(96-100) | 20(17-23) | 0.22(0.04-0.42) | 2.43(1.96-2.96) |
| 0.6 | 86(74-97) | 72(67-76) | 98(96-100) | 24(20-28) | 0.20(0.04-0.38) | 3.07(2.45-3.77) |
| 0.7 | 80(66-91) | 76(71-80) | 97(96-99) | 25(21-30) | 0.26(0.11-0.46) | 3.28(2.52-4.07) |
| 0.8 | 74(57-89) | 78(73-82) | 97(95-99) | 26(20-31) | 0.33(0.15-0.55) | 3.37(2.49-4.36) |
| 0.9 | 71(54-86) | 81(76-85) | 96(95-98) | 28(22-34) | 0.35(0.17-0.55) | 3.74(2.71-5.02) |
| 1.0 | 69(52-83) | 84(80-87) | 96(94-98) | 30(24-38) | 0.37(0.2-0.57) | 4.24(3.02-5.87) |
| 1.1 | 69(52-83) | 86(81-89) | 96(95-98) | 33(26-41) | 0.37(0.2-0.55) | 4.76(3.41-6.8) |
| 1.2 | 66(49-83) | 87(84-90) | 96(94-98) | 34(26-43) | 0.39(0.2-0.59) | 5.08(3.47-7.22) |
| 1.3 | 66(49-83) | 88(85-91) | 96(94-98) | 37(28-46) | 0.39(0.2-0.59) | 5.59(3.8-8.28) |
| 1.4 | 60(43-77) | 89(86-92) | 96(94-97) | 36(27-47) | 0.45(0.26-0.64) | 5.51(3.64-8.59) |
| 1.5 | 57(40-74) | 90(87-93) | 95(94-97) | 37(28-48) | 0.48(0.29-0.66) | 5.71(3.7-9.02) |
| 1.6 | 51(34-69) | 91(88-94) | 95(93-97) | 36(26-48) | 0.54(0.35-0.72) | 5.46(3.47-8.87) |
| 1.7 | 46(29-63) | 93(90-95) | 94(93-96) | 39(27-53) | 0.59(0.4-0.77) | 6.22(3.51-10.79) |
| 1.8 | 43(26-60) | 93(91-96) | 94(92-96) | 39(26-53) | 0.61(0.43-0.8) | 6.34(3.5-11.01) |
| 1.9 | 43(26-60) | 94(91-96) | 94(92-96) | 42(28-57) | 0.61(0.43-0.79) | 6.94(3.7-12.7) |
| 2.0 | 40(23-57) | 94(92-96) | 94(92-96) | 41(27-57) | 0.64(0.46-0.82) | 6.8(3.53-12.7) |
| 2.1 | 40(23-57) | 95(93-97) | 94(92-96) | 45(30-62) | 0.63(0.45-0.81) | 8(4.16-16.19) |
| 2.2 | 40(23-57) | 96(94-98) | 94(92-96) | 50(33-68) | 0.63(0.45-0.8) | 9.71(4.86-20.82) |
| 2.3 | 40(23-57) | 96(94-98) | 94(92-96) | 52(35-70) | 0.62(0.45-0.8) | 10.46(5.18-23.06) |
| 2.4 | 37(20-54) | 96(94-98) | 94(92-95) | 50(32-69) | 0.65(0.48-0.82) | 9.71(4.6-21.86) |
| 2.5 | 31(17-49) | 96(95-98) | 93(92-95) | 48(29-67) | 0.71(0.54-0.87) | 8.9(3.97-19.43) |

Sensitivity, specificity, negative and positive likelihood ratios are test characteristics that are independent of disease (AKI) prevalence. Negative and positive predictive values depend on disease (AKI) prevalence and should be adjusted for populations with significantly different AKI prevalence than in this study (9.3% of patients in the combined Sapphire-Topaz cohort had moderate-severe AKI within 12 hours, Figure 1 in the main manuscript).

**eFigure 1. Enhancement of clinical model with [TIMP-2]•[IGFBP7]**



Enhancement of clinical model by adding [TIMP-2]*•*[IGFBP7]. Risk assessment plots for the reference clinical model (dashed lines) and new model with [TIMP-2]*•*[IGFBP7] (solid lines) were calculated from the two models shown in Figure 4 of the main manuscript. Red lines represent 1-specificity versus the calculated risk for those without an event (KIDIGO 2 or 3 AKI within 12h or clinical adjudication); black lines represent sensitivity versus the calculated risk for those with an event. The larger difference between the solid black and red lines (new model with [TIMP-2]*•*[IGFBP7]) compared with the difference between the dashed black and red lines (reference clinical model) indicates that addition of [TIMP-2]*•*[IGFBP7] enhances the risk model. The NRI was two category at a risk cutoff equal to prevalence.