**Supplemental Digital Content**

**Supplemental Methods**

*Standardized anesthetic, surgical, and postoperative management*

General anesthesia was induced with propofol, fentanyl, and rocuronium and was maintained with isoflurane, fentanyl, and rocuronium. Patients were monitored with ECG, temperature, invasive blood pressure, pulse oximetry, central venous pressure, pulmonary artery pressure, and transesophageal echocardiography. Anticoagulation for cardiopulmonary bypass, when used, was achieved with 400 units/kg unfractionated IV heparin with a target activated coagulation time of longer than 400 seconds. Anticoagulation for off-pump coronary artery bypass (CABG) graft procedures was achieved with 150 units/kg unfractionated heparin and maintenance of activated clotting time greater than 300 seconds. Anticoagulation was reversed with IV protamine at the cessation of cardiopulmonary bypass or after revascularization for off-pump CABG. Packed red blood cells were transfused to maintain a hemoglobin concentration of 8 or 10 g/dL in the setting of ongoing hemorrhage. Patients were transported to the intensive care unit intubated, mechanically ventilated, and sedated with propofol. Postoperative care remained at the discretion of the intensivist. Extubation was considered when patients were normothermic, spontaneously breathing, conscious, and hemodynamically stable.

*Delirium assessment training*

Training consisted of independent review of the CAM-ICU Training Manual and CAM-ICU performance instructional videos, both located on icudelirium.org1; personal instruction from the principal investigator to each assessor of how to assess consciousness and perform the Confusion Assessment Method for the intensive care unit using the CAM-ICU flowsheet; direct observation of the principal investigator by each assessor of five Confusion Assessment Method for the intensive care unit patient assessments with additional instruction and discussion following each assessment; and direct observation of each assessor by the principal investigator of five Confusion Assessment Method for the intensive care unit patient assessments with additional instruction and discussion following each assessment. The principal investigator also performed a Confusion Assessment Method for the intensive care unit assessment on the five patient assessments used for assessor training to validate results. Inter-rater reliability for these assessments was 100%.

*F2-isoprostanes, isofurans, S100 calcium binding protein B, and ubiquitin C-terminal hydrolase L1 assay timing and quality control*

The Statin AKI Cardiac Surgery RCT enrolled patients from November 2009 to October 2014. F2-isoprostanes and isofurans assays were performed from 7/1/2010 through 3/8/2016 in sequential order. We include a quality control standard sample within every assay. These quality control samples are replaced every 2 years, and the quality control standards are stable during this time period (stable for at least 2 years). F2-isoprostanes and isofurans were measured within 2 years of collection. S100 calcium binding protein B and ubiquitin C-terminal hydrolase L1assays were performed from June 2016 through October 2016.

**Supplemental Table 1.** Original regression analysis (N=400) and sensitivity analysis in the subset of patients that underwent surgery with cardiopulmonary bypass (CPB; N=283).

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| Model | Independent variable | Delirium odds ratio  (95% CI) | P-value |
| Delirium | F­2-isoprostanes & isofurans | 3.5 (1.3 to 9.2) | 0.011 |
| Delirium CPB | F­2-isoprostanes & isofurans | 2.3 (0.7 to 7.5) | 0.156 |
| DeliriumS100B | F­2-isoprostanes & isofurans at S100 calcium binding protein B 10th percentile | 2.9 (0.7 to 12.3) | 0.151 |
|  | F­2-isoprostanes & isofurans at S100 calcium binding protein B 90th percentile | 4.2 (1.2 to 14.7) | 0.025 |
|  | S100 calcium binding protein B | 2.5 (1.1 to 5.6) | 0.042 |
|  | F­2-isoprostanes & isofurans x S100 calcium binding protein B interaction |  | 0.665 |
| DeliriumS100B CPB | F­2-isoprostanes & isofurans at S100 calcium binding protein B 10th percentile | 1.6 (0.3 to 9.6) | 0.337 |
|  | F­2-isoprostanes & isofurans at S100 calcium binding protein B 90th percentile | 2.8 (0.7 to 10.3) | 0.130 |
|  | S100 calcium binding protein B | 2.2 (0.9 to 5.2) | 0.101 |
|  | F­2-isoprostanes & isofurans x S100 calcium binding protein B interaction |  | 0.571 |
|  |  | UCHL1 ratio of geometric means (95% CI) |  |
| UCHL1 | F­2-isoprostanes & isofurans | 1.28 (1.00 to 1.64) | 0.020 |
| UCHL1 CPB | F­2-isoprostanes & isofurans | 1.35 (0.98 to 1.88) | 0.030 |
| UCHL1S100B | F­2-isoprostanes & isofurans at S100 calcium binding protein B 10th percentile | 1.02 (0.75 to 1.41) | 0.881 |
|  | F­2-isoprostanes & isofurans at S100 calcium binding protein B 90th percentile | 1.54 (1.09 to 2.18) | 0.014 |
|  | S100 calcium binding protein B | 1.30 (1.04 to 1.63) | 0.024 |
|  | F­2-isoprostanes & isofurans x S100 calcium binding protein B interaction |  | 0.049 |
| UCHL1S100B CPB | F­2-isoprostanes & isofurans at S100 calcium binding protein B 10th percentile | 1.21 (0.78 to 1.89) | 0.386 |
|  | F­2-isoprostanes & isofurans at S100 calcium binding protein B 90th percentile | 1.41 (1.94 to 2.12) | 0.096 |
|  | S100 calcium binding protein B | 1.37 (1.05 to 1.77) | <0.001 |
|  | F­2-isoprostanes & isofurans x S100 calcium binding protein B interaction |  | 0.183 |
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References

1. <https://www.icudelirium.org/medical-professionals/delirium/monitoring-delirium-in-the-icu>.