Evolution of Validated Biomarkers in Development of Post-Operative Acute Respiratory Distress Syndrome

Supplemental Appendix

Predictor variables – blood sample handling and analysis

At each time point, 6 cc's of blood were obtained from the patient's arterial (or central venous) catheter (following a 5 cc waste). The samples were collected and placed into EDTA anti-coagulated tubes. The samples were processed and plasma collected in cryogenic freezing tubes stored at -70-80^{o}C. Samples were subsequently transported to the Blood Systems Research Institute (San Francisco, CA) where all study assays were performed. Biomarker concentrations were analyzed using enzyme-linked immunosorbent assays (ELISAs). ELISAs were developed using customized multiplex arrays (R&D Systems, Minneapolis, USA). All samples were analyzed in duplicate.

Predictor variables – clinical data extraction and analysis

Key preoperative variables were recorded. These included demographics, medical conditions, preoperative American Society of Anesthesiologists (ASA) status (1), smoking and alcohol use as well as chronic medications. ARDS modifying clinical and health care delivery factors (blood product administration, intraoperative ventilator parameters, vital signs, vasopressor requirements, and fluid status) were also recorded. Postoperative outcome data were

extracted, including date and time of ICU admission (if required), severity of illness (as judged by the APACHE III score), date and time of ICU discharge, date of hospital discharge, ICU discharge status (alive vs. dead) and hospital discharge status (alive vs. dead). Ventilator free days (VFD) were defined as the number of days between successful weaning from mechanical ventilation and day 28 after study enrollment. Patients who died before day 28 were determined to have 0 VFD. For patients discharged before day 28, they were assumed to have no more days of mechanical ventilation (2). Data were extracted using customized, integrative relational research databases that contain a near-real time copy of clinical, administrative and environmental exposure data from the Electronic Medical Record (Peri-Operative Information Tool (POINT), the 'ICU Datamart' and the 'OR Datamart'), the Hospital Surgical Listing database, and the Mayo Clinic Life Sciences System (MCLSS) databases. All intraoperative variables were electronically captured using these existing institutional data capture tools. Manual chart review supplemented all electronic data retrieval. These retrieval strategies have been utilized and validated in prior studies by our group (3-6).

Matching cases to controls

ARDS cases were matched to non-ARDS cases based on age, sex, SLIP score and procedure. Matching required an exact match on procedure. Priority was then placed sequentially on SLIP score, sex and age. One ARDS case was matched to a single non-ARDS control given the procedure performed (pericardiectomy) was infrequently performed in the control group. All cases were matched to controls with good group balance (details outlined below).

	0 (N=51)	1 (N=26)	Total (N=77)	p value
Age at Surgery				0.6798
N	51	26	77	
Mean (SD)	62.5 (13.3)	63.3 (13.8)	62.8 (13.4)	
Median	63.1	69.0	63.2	
Q1, Q3	52.2, 73.7	50.5, 75.2	52.0, 74.1	
Range	(29.6-83.9)	(36.0-82.3)	(29.6-83.9)	
SLIP Score				0.9886
N	51	26	77	
Mean (SD)	36.9 (6.5)	37.6 (8.1)	37.2 (7.0)	
Median	34	35.5	34	
Q1, Q3	32.0, 40.0	32.0, 41.3	32.0, 40.5	
Range	(28.0-55.0)	(28.0-59.0)	(28.0-59.0)	
Sex				1.0000
Female	14 (27.4%)	6 (23.0%)	20 (26.0%)	
Male	37 (76.9%)	20 (72.5%)	57 (74.0%)	
Classification for Matching				1.0000
Aortic Vascular Only	22 (43.1%)	11 (42.3%)	33 (42.9%)	
CABG Only	8 (15.7%)	4 (15.4%)	12 (15.6%)	
CABG and Valve	2 (3.9%)	1 (3.9%)	3 (3.9%)	
CABG, Valve and Aortic Vascular	2 (3.9%)	1 (3.9%)	3 (3.9%)	
Esophageal	10 (19.6%)	5 (19.2%)	15 (19.5%)	
Pericardectomy	3 (5.9%)	2 (7.6%)	5 (6.5%)	
Thoracic - Lobectomy	2 (3.9%)	1 (3.9%)	3 (3.9%)	
Valve Only	2 (3.9%)	1 (3.9%)	3 (3.9%)	

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