Pneumonia After Cardiac Surgery: Experience of the NIH/CIHR Cardiothoracic Surgical Trials Network

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Online Supplementary Material

Supplemental Material

Appendix EI: Primary Endpoint Definition and Variables for Cox Regression

Appendix EII: CTSN Members

Appendix EI: Primary Endpoint Definition and Variables for Cox Regression

Definition of Pneumonia

To be classified as pneumonia, the following criteria must have been met (adapted from the CDC/NHSN guidelines for the clinical diagnosis of pneumonia):

1. At least one or more chest radiographs no earlier than two days post-surgery with at least 1 of the following: (a) new or progressive and persistent infiltrate, (b) consolidation, or (c) cavitation.
2. Patient has at least 1 of the following signs or symptoms: fever (>38°C) with no other recognized cause, leukopenia (<4,000 WBC/mm3) or leukocytosis (≥12,000 WBC/mm3), or altered mental status with no other recognized cause (for patients ≥ 70 years old) and at least 2 of the following: (a) new onset of purulent sputum or change in character or sputum or increased respiratory secretions or increased suctioning requirements, (b) new onset or worsening cough, or dyspnea, or tachypnea, (c) rales or bronchial breath sounds, (d) worsening gas exchange (e.g. oxygen desaturations, increased oxygen requirements, or increased ventilator demand)

Variables tested in the Stage 1 baseline risk model and their crude association with pneumonia

	# (%) Pneumonia	Unadjusted HR (95% CI)	P-value[†]
Demographics			
Age, (years)		1.02 (1.00, 1.03)	0.02
Gender		1.07 (0.73, 1.56)	0.73
Male	84 (2.4)		
Female	39 (2.3)		
Race		0.56 (0.38, 0.85)	0.01
White	92 (2.1)		
Non-White	31 (3.7)		
BMI, (kg/m^2)		1.00 (0.96, 1.03)	0.83
Insurance			0.59
Medicaid	8 (3.4)	1.79 (0.73, 4.38)	
Medicare	51 (2.6)	1.38 (0.74, 2.59)	
Government (Other)	12 (1.9)	1.00 (ref)	
Private	45 (2.1)	1.12 (0.59, 2.11)	
None/Self	7 (2.7)	1.41 (0.55, 3.59)	
Baseline Laboratories			
WBC, $x10^3/ml$		1.03 (0.99, 1.07)	0.19
Creatinine, mg/dL		1.14 (1.07, 1.22)	< 0.001

	# (%) Pneumonia	Unadjusted HR (95% CI)	P-value[†]
Hemoglobin, g/dL		0.80 (0.73, 0.88)	< 0.001
Cardiac morbidity			
Hypertension		1.60 (1.01, 2.54)	0.04
Yes	101 (2.6)		
No	22 (1.7)		
Heart failure		2.19 (1.53, 3.11)	< 0.001
Yes	58 (3.9)		
No	65 (1.8)		
Previous cardiac surgery		1.98 (1.35, 2.89)	< 0.001
Yes	38 (4.0)		
No	85 (2.0)		
Noncardiac morbidity			
Corticosteroids		2.82 (1.52, 5.21)	0.001
Yes	11 (6.3)		
No	112 (2.3)		
Diabetes[‡]		1.05 (0.69, 1.60)	0.81
Yes	29 (2.5)		
No	94 (2.4)		
History of Smoking			0.06
No	52 (1.9)	1.00 (ref)	
Current	23 (3.4)	1.76 (1.08, 2.88)	
Former	47 (2.7)	1.38 (0.93, 2.05)	
COPD		2.58 (1.75, 3.78)	< 0.001
Yes	37 (5.0)		
No	86 (1.9)		
Cerebrovascular Accident		1.06 (0.59, 1.88)	0.85
Yes	13 (2.5)		
No	110 (2.4)		

	# (%) Pneumonia	Unadjusted HR (95% CI)	P-value[†]
Peripheral Vascular Disease		1.59 (0.97, 2.59)	0.06
Yes	19 (3.6)		
No	104 (2.2)		
Operative			
Surgery time, hours		1.44 (1.31, 1.58)	< 0.001
Bypass		1.10 (0.58, 2.11)	0.77
Yes	113 (2.4)		
No	10 (2.2)		
Circulatory Arrest		2.19 (1.21, 3.97)	0.01
Yes	12 (4.9)		
No	111 (2.3)		
Sternotomy		0.78 (0.46, 1.32)	0.35
Full	107 (2.5)		
Not Full	16 (1.9)		
Surgery Type			0.08
Elective	80 (2.1)	1.00 (ref)	
Urgent	38 (3.1)	1.50 (1.02, 2.20)	
Emergent	5 (3.6)	1.72 (0.70, 4.22)	
Procedure		4.99 (2.84, 8.78)	< 0.001
LVAD/Tx	13 (10.7)		
All Others	110 (2.2)		
Previous IABP		1.51 (0.55, 4.10)	0.42
Yes	4 (3.5)		
No	119 (2.4)		

Abbreviations: CABG, coronary artery bypass grafting; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HR, hazard ratio; LVAD/Tx, left ventricular assist device or heart transplant surgery.

†Based on competing risk model with time to pneumonia as outcome, baseline factors as covariates, and death as competing risk.

‡Insulin or oral medications.

Variables not used because of small cell counts: The sternum was not closed for 16 patients and only 1 of whom developed pneumonia.

Variables not used because of excessive missing data: Ejection fraction

Variables tested in the Stage 2 process of care model and their crude association with pneumonia

Management Practice	# (%) Pneumonia	Unadjusted HR (95% CI)	P Value[†]
Correct timing of preoperative antibiotics prior to surgery		0.76 (0.48-1.22)	0.26
Yes	102 (2.3)		
No	21 (3.0)		
Nasopharyngeal decontamination		0.80 (0.56-1.15)	0.24
Yes	51 (2.1)		
No	71 (2.6)		
Scrubbing of surgical site			0.01
No	5 (6.4)	1.00 (ref)	
Yes with chlorhexidine	106 (2.6)	0.39 (0.16-0.96)	
Yes without chlorhexidine	12 (1.3)	0.20 (0.07-0.55)	
Appropriate dosing of intraoperative antibiotics		0.47 (0.21-1.06)	0.07
Yes	117 (2.3)		
No	6 (4.9)		
Postoperative antibiotics duration			<0.001
≤24 hours	48 (1.8)	1.16 (0.75-1.79)	

Management Practice	# (%) Pneumonia	Unadjusted HR (95% CI)	P Value[†]
24-48 hours	34 (1.6)	1.00 (ref)	
>48 hours	41 (9.4)	6.09 (3.87-9.59)	
Second generation CEPH		0.68 (0.47, 0.98)	0.04
Yes	46 (1.9)		
No	77 (2.8)		
Ventilation			<0.001
≤24 hours	46 (1.1)	1.00 (ref)	
24 – 48 hours	32 (4.7)	4.25 (2.71, 6.68)	
> 48 hours	43 (11.1)	10.36 (6.84, 15.67)	
NG Tube		1.84 (1.15, 2.94)	0.01
Yes	102 (2.7)		
No	21 (1.5)		
Femoral line		3.58 (1.13-11.32)	0.03
Yes	3 (8.1)		
No	120 (2.3)		
More than 1 central line		2.39 (1.56-3.67)	<0.001
Yes	27 (4.9)		
No	96 (2.1)		
Glucose management		1.21 (0.85-1.73)	0.30
Hyperglycemic	58 (2.6)		
Non-hyperglycemic	63 (2.2)		
PRBC (unit)		1.30 (1.24, 1.36)	<0.001

Management Practice	# (%) Pneumonia	Unadjusted HR (95% CI)	P Value†
Platelet		2.13 (1.50, 3.04)	<0.001
Yes	60 (3.7)		
No	63 (1.8)		

Abbreviations: CI, confidence interval; CEPH, cephalosporin; HR, hazard ratio; NG, nasogastric tube; PRBC, packed red blood cells

†Based on competing risk model with time to pneumonia as outcome, management practices as covariates, and death as competing risk.

Variable not used because of small cell counts:

1. Elevation of head of bed: Among the 18 patients who did not have elevation of head of bed, only 1 developed pneumonia.
2. Aspiration of secretions: Among the 201 patients who did not have aspiration of secretions, only 1 developed pneumonia.

3. **Appendix EII: CTSN Members**

The members of the Cardiothoracic Surgical Trials Network (CTSN) involved in this study were as follows:
National Heart, Lung and Blood Institute: Marissa A. Miller, Wendy C. Taddei-Peters, Dennis Buxton, Ron Caulder, Nancy L. Geller, David Gordon, Neal O. Jeffries, Albert Lee**;**
National Institute of Neurological Disorders and Stroke: Claudia S. Moy;
Canadian Institutes of Health Research: Ilana Kogan Gombos, Jennifer Ralph;
Network Chairs: *Christiana Care Health System*, Timothy J. Gardner, (Chair); *Brigham and Women's Hospital*, Patrick T. O'Gara, (Co-Chair);
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Core Clinical Site Investigators: *Cleveland Clinic Foundation*, Eugene H. Blackstone (PI), A. Marc Gillinov, Pamela Lackner, Leoma Berroteran, Diana Dolney, Suzanne Fleming, Roberta Palumbo, Christine Whitman, Kathy Sankovic, Denise Kosty Sweeney; *NHLBI Clinical Research Scholars*: Gregory Pattakos, Pamela A. Clarke; *Columbia University*, Michael Argenziano (PI), Mathew Williams, Lyn Goldsmith, Craig R. Smith, Yoshifumi Naka, Allan Stewart, Allan Schwartz; Daniel Bell, Danielle Van Patten; *Duke University*, Peter K. Smith (PI), Stacey Welsh, John H. Alexander, Carmelo A. Milano, Donald D. Glower, Joseph P. Mathew, J. Kevin Harrison; *NHLBI Clinical Research Scholars:* Mark F. Berry, Cyrus J. Parsa, Betty C. Tong, Judson B. Williams; *East Carolina Heart Institute*, T. Bruce Ferguson (PI), Alan P. Kypson, Evelio Rodriguez, Malissa Harris, Brenda Akers, Allison O'Neal; *Emory University*, John D. Puskas (PI), Vinod H. Thourani, Robert Guyton, Jefferson Baer, Kim Baio, Alexis A. Neill; *Montefiore-Einstein Heart Center, New York, NY*, Robert E. Michler (PI), David A. D'Alessandro, Joseph J. DeRose, Jr., Daniel J. Goldstein, Ricardo Bello, William Jakobleff, Mario Garcia, Cynthia Taub, Daniel Spevak, Roger Swayze; *Montreal Heart Institute*, Louis P. Perrault (PI), Arsène-Joseph Basmadjian, Denis Bouchard, Michel Carrier, Raymond Cartier, Michel Pellerin, Jean François Tanguay, Ismael El-Hamamsy, André Denault, Jonathan Lacharité, Sophie Robichaud; *NIH Heart Center at Suburban Hospital*, Keith A. Horvath (PI), Philip C. Corcoran, Michael P. Siegenthaler, Mandy Murphy, Margaret Iraola, Ann Greenberg; *University of Pennsylvania*, Michael A. Acker (PI), Y. Joseph Woo, Mary Lou Mayer; *University of Virginia*, Irving L. Kron (PI), Gorav Ailawadi, Karen Johnston, John M. Dent, John Kern, Jessica Keim Sandra Burks, Kim Gahring;
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Medical Monitors: James C. Fang, Wayne Richenbacher;
Overall Event Adjudication Committee: Vivek Rao (Chair); Karen L. Furie, Rachel Miller, Sean Pinney, William C. Roberts;
Infection Event Adjudication Committee: Rachel Miller (Chair); Shirish Huprikar, Marilyn Levi.