

Outcome of Unilateral and Bilateral Hypoxaemic Respiratory Failure. Insights from the Lung Safe Study

Online supplement

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Table E1: Global and adjusted p-values for pairwise comparisons

	Global p-value	ARDS vs CHF	unilateral infiltrate vs ARDS
Age	<0.001	<0.001	0.277
Female gender	0.056	0.296	0.296
BMI	0.061	0.736	0.051
Illness Severity Indices			
SOFA Score	<0.001	0.376	<0.001
Non-pulmonary SOFA score	<0.001	0.146	0.001
Number of CXR quadrants	<0.001	<0.001	0.000
Bilateral opacities	<0.001	<0.001	0.000
PaCO ₂	0.003	0.005	0.165
pH	<0.001	0.657	<0.001
PaO ₂ /FiO ₂	<0.001	0.069	0.000
Worst PF in the 2 first days	<0.001	0.374	0.000
Initial Severity	<0.001	0.190	<0.001
Comorbidities			
Diabetes	0.009	0.010	0.999
COPD	0.001	0.030	0.023
Chronic Renal Failure	<0.001	<0.001	0.958
Immunosuppression	<0.001	<0.001	0.194
Chronic Cardiac Failure	<0.001	<0.001	0.924
Chronic Liver Failure	0.157	0.252	0.638
At least 1 comorbidity	0.004	0.003	0.968
“Cause of hypoxemia”			
Pneumonia	<0.001	<0.001	0.025
Non pulmonary Sepsis	<0.001	<0.001	0.049
Gastric aspiration	<0.001	0.002	0.009
Trauma	0.002	0.018	0.069
Pancreatitis	0.013	0.023	0.262
Pulmonary contusion	0.023	0.117	0.125
Pulmonary Vasculitis	0.356	0.589	0.589

Non cardiogenic Shock	0.001	0.002	0.096
Overdose	0.018	0.018	0.231
TRALI	0.412	0.976	0.662
CHF	<0.001	<0.001	0.003
COPD	<0.001	0.101	0.900
Asthma	0.101	<0.001	<0.001
No Cause identified	0.002	0.002	0.707
Ventilation Management			
VT	<0.001	<0.001	0.010
RR	<0.001	0.001	<0.001
PEEP	<0.001	<0.001	<0.001
FiO2	<0.001	0.668	<0.001
Plateau pressure	<0.001	0.061	<0.001
Driving pressure	<0.001	0.367	<0.001
PIP	<0.001	<0.001	<0.001
Minute ventilation	<0.001	0.008	0.002
Outcomes			
Duration of invasive MV	<0.001	<0.001	<0.001
VFD	<0.001	0.064	<0.001
ICU Length of Stay	<0.001	<0.001	0.007
Hospital Length of Stay	<0.001	<0.001	0.902
ICU mortality	<0.001	0.515	<0.001
Hospital mortality	<0.001	0.282	<0.001

Table E2: Use of adjunct treatments in the 3 groups

Var	ALL N=3176	unilateral infiltrate N=722	ARDS N=2193	CHF N=261	Global p-value	p-value unilat vs ARDS	p-value unilat vs CHF	p-value unilat vs CHF	N
Prone	186 (5.9%)	16 (2.2%)	167 (7.6%)	3 (1.1%)	<0.001	<0.001	0.418	<0.001	3176
ECMO	18 (0.6%)	0 (0.0%)	17 (0.8%)	1 (0.4%)	0.026	0.032	0.398	0.713	3176
NMBA	575 (18.1%)	87 (12.0%)	457 (20.8%)	31 (11.9%)	<0.001	<0.001	1.000	0.001	3176
Recruitment Maneuver	575 (18.1%)	90 (12.5%)	455 (20.7%)	30 (11.5%)	<0.001	<0.001	0.764	0.001	3176
Inhaled VD	191 (6.0%)	25 (3.5%)	152 (6.9%)	14 (5.4%)	0.003	0.003	0.367	0.411	3176
HFO	27 (0.9%)	2 (0.3%)	25 (1.1%)	0 (0.0%)	0.022	0.153	1.000	0.153	3176
Any Rescue treatment	1079 (34.0%)	178 (24.7%)	835 (38.1%)	66 (25.3%)	<0.001	<0.001	0.905	<0.001	3176

Table E3: Characteristics of survivors vs non-survivors (excluding CHF)

	ALL N=2904	Survivors N=1793	Deceased N=1111	p-value	N
Age	61±7	59±17	65±17	<0.001	2904
Female gender	1069 (37%)	656 (37%)	413 (37%)	0.780	2904
Weight	77.2±22.8	78.9±24.9	74.5±18.5	<0.001	2758
BMI	27.1±8.1	27.6±9.0	26.5±6.3	<0.001	2691
Illness Severity Indices					
SOFA Score	9.6 [7.0;12.0]	9.0 [6.0;12.0]	11.0 [8.0;14.0]	<0.001	2893
Non-pulmonary SOFA score	6.2 [4.0;9.0]	6.0 [3.8;8.0]	8.0 [5.0;11.0]	<0.001	2872
CXR quadrants involved				<0.001	2752
1	428 (16%)	300 (18%)	128 (12%)		
2	1090 (40%)	704 (42%)	386 (36%)		
3	505 (18%)	289 (17%)	216 (20%)		
4	729 (27%)	399 (24%)	330 (31%)		
Bilateral opacities	2184 (75%)	1302 (73%)	882 (79%)	<0.001	2904
PaCO ₂	46±15	46±14	46±16	0.980	2867
pH	7.33±0.12	7.35±0.11	7.30±0.14	<0.001	2867
PaO ₂ /FiO ₂	168±68	173±68	160±68	<0.001	2893
Initial Severity				<0.001	2904
Mild	988 (34.0)	663 (37%)	325 (29%)		
Moderate	1334 (46%)	817 (46%)	517 (47%)		
Severe	582 (20%)	313 (18%)	269 (24%)		
Comorbidities					
Diabetes	635 (22%)	372 (21%)	263 (24%)	0.071	2904
COPD	623 (22%)	385 (22%)	238 (21%)	1.000	2904
Chronic Renal Failure	277 (9.5%)	152 (8.5%)	125 (11%)	0.016	2904
Immunosuppression	582 (20.0%)	288 (16%)	294 (27%)	<0.001	2904
Chronic Cardiac Failure	280 (10%)	153 (9%)	127 (11%)	0.012	2904
Chronic Liver Failure	124 (4%)	43 (2%)	81 (7%)	<0.001	2904
At least 1 comorbidity	1701 (59%)	955 (53%)	746 (67%)	<0.001	2904
“Cause of hypoxemia” (more than 1 cause is possible)					
Pneumonia	1923 (66%)	1180 (66%)	743 (67%)	0.583	2904
Non pulmonary Sepsis	483 (17%)	259 (14%)	224 (20%)	<0.001	2904
Gastric aspiration	503 (17%)	309 (17%)	194 (18%)	0.914	2904
Trauma	150 (5%)	122 (7%)	28 (3%)	<0.001	2904
Pancreatitis	57 (2%)	29 (2%)	28 (3%)	0.117	2904
Pulmonary contusion	108 (4%)	86 (5%)	22 (2%)	<0.001	2904
Pulmonary Vasculitis	34 (1%)	14 (1%)	20 (2%)	0.021	2904
Non cardiogenic Shock	229 (8%)	114 (6%)	115 (10%)	<0.001	2904
Overdose	66 (2%)	54 (3%)	12 (1%)	0.001	2904
TRALI	122 (4%)	67 (4%)	55 (5%)	0.136	2904
CHF	399 (14%)	206 (12%)	193 (17%)	<0.001	2904
COPD	41 (1%)	29 (2%)	12 (1%)	0.303	2904
Asthma	399 (14%)	206 (12%)	193 (17%)	<0.001	2904
No Cause identified	127 (4%)	90 (5%)	37 (3%)	0.038	2904

Ventilation Management					
VT	7.7±1.8	7.8±1.8	7.7±1.8	0.215	2758
RR	20±8	20±6.2	21±11	<0.001	2887
PEEP	8.0 [5.0;10.0]	8.0 [5.0;10.0]	8.0 [5.0;10.0]	0.405	2893
FiO2	0.6 [0.4;0.8]	0.5 [0.4;0.8]	0.6 [0.4;0.9]	<0.001	2893
Plateau pressure	23±6	22±6	24±6	<0.001	907
Driving pressure	15±6	14±5	16±6	<0.001	905
PIP	26±8	26±8	28±8	<0.001	2781
Minute ventilation	10.7±4.7	10.6±4.5	10.9±5.0	0.113	2839
Outcomes					
Duration of invasive MV	7.0 [4.0;14.0]	7.0 [4.0;14.0]	7.0 [3.0;15.0]	0.247	2753
VFD	14.0 [0.0;22.0]	21.0 [14.0;24.0]	0.0 [0.0;0.0]	<0.001	2753
ICU Length of Stay	10.0 [5.0;18.0]	11.0 [6.0;20.0]	8.0 [4.0;16.0]	<0.001	2904
Hospital Length of Stay	17.0 [8.0;32.0]	22.0 [13.0;40.0]	9.0 [4.0;19.0]	<0.001	2849
ICU mortality	962 (33%)	0 (0%)	962 (87%)	0.000	2904
Hospital mortality	1111 (38%)	0 (0%)	1111 (100.0%)	0.000	2904

Table E4: Multivariable analyses of factors associated with hospital death in patients with unilateral infiltrate or ARDS

	Model with Bilateral opacities				Model with number of quadrants		
	OR	95%CI	p-value		OR	95%CI	p-value
BILATERAL opacities	1.32	1.06; 1.64	<0.013		-	-	-
Number of quadrants (reference: 1 quadrant)	-	-	-				
2 quadrants	-	-	-		1.17	0.88; 1.56	0.284
3 quadrants	-	-	-		1.53	1.10; 2.11	0.011
4 quadrants	-	-	-		1.76	1.29; 2.41	<0.001
Age (for 1 year)	1.02	1.02; 1.03	<0.001		1.02	1.02; 1.03	<0.001
BMI (for 1 kg/m ²)	0.98	0.97; 1.00	0.011		0.98	0.97; 1.00	0.015
Medical admission	1.98	1.56; 2.51	<0.001		1.86	1.46; 2.38	<0.001
Trauma admission	1.84	1.10; 3.01	0.017		1.81	1.07; 3.00	0.024
Non-pulmonary SOFA	1.13	1.10; 1.16	<0.001		1.13	1.11; 1.16	<0.001
PF (for 10 mmHg decrease)	1.02	1.00; 1.03	0.028		1.01	0.99; 1.02	0.218
pH (for 0.01 increase)	0.98	0.97; 0.99	<0.001		0.98	0.98; 0.99	<0.001
RR (for 1/min)	1.02	1.01; 1.04	0.002		1.02	1.01; 1.04	0.003
PEEP (for 1cmH ₂ O)	0.94	0.91; 0.97	<0.001		0.94	0.91; 0.97	<0.001
PIP (for 1cmH ₂ O)	1.02	1.01; 1.03	0.002		1.02	1.01; 1.03	0.006
immunocompromised	2.19	1.76; 2.72	<0.001		2.19	1.75; 2.74	<0.001
Chronic liver Failure	2.54	1.60; 4.11	<0.001		2.52	1.57; 4.13	<0.001
Extra-pulmonary sepsis	1.32	1.04; 1.69	0.025		1.23	0.95; 1.58	0.109
Drug overdose	0.45	0.21; 0.90	0.031		0.40	0.18; 0.83	0.019
TRALI	1.60	1.03; 2.47	0.034		1.56	1.00; 2.42	0.005
Concomitant Cardiac Failure	1.34	1.04; 1.73	0.025		1.39	1.07; 1.81	0.013
Income area (reference High income Europe)							
Middle Income	1.58	1.26; 1.99	<0.001		1.71	1.35; 2.17	<0.001
High Income non Europe	0.62	0.49; 0.87	<0.001		0.59	0.47; 0.75	<0.001

Table E5: Multivariable analysis of variables associated with hospital mortality in patients with unilateral infiltrate

	OR	95%CI	p-value
Age (for 1 year)	1.02	1.01; 1.03	<0.001
Medical admission	2.27	1.51; 3.44	<0.001
Non-pulmonary SOFA	1.19	1.13; 1.25	<0.001
pH (for 0.01 increase)	0.98	0.97; 1.00	0.020
PEEP (for 1cmH2O)	0.88	0.81; 0.95	0.001
Immunocompromised	2.10	1.36; 3.23	<0.001
Income area (reference High income Europe)			
Middle Income	1.94	1.23; 3.07	0.004
High Income non Europe	0.67	0.42; 1.06	0.091

Table E6: Multivariable analysis of variables associated with hospital mortality in patients with 2 quadrants involved

	Model for patients with 2 quadrants		
	OR	95%CI	p-value
BILATERAL opacities	1.13	0.76; 1.69	0.56
Age (for 1 year)	1.02	1.01; 1.03	<0.001
BMI (for 1 kg/m ²)	0.99	0.97; 1.01	0.404
Medical admission	2.42	1.67; 3.54	<0.001
Trauma admission	2.57	1.18; 5.40	0.015
Non-pulmonary SOFA	1.08	1.04; 1.13	<0.001
PF (for 10 mmHg decrease)	0.99	0.96; 1.01	0.310
pH (for 0.01 increase)	0.98	0.97; 0.99	0.003
RR (for 1/min)	1.03	1.01; 1.06	0.015
PEEP (for 1cmH ₂ O)	0.94	0.89; 1.00	0.050
PIP (for 1cmH ₂ O)	1.01	0.99; 1.03	0.200
immunocompromised	2.21	1.53; 3.21	<0.001
Chronic liver Failure	2.62	1.14; 6.47	0.026
Extra-pulm sepsis	1.96	1.32; 2.92	<0.001
Drug overdose	2.27	0.03; 0.98	0.080
TRALI	3.11	1.50; 6.47	0.002
Concomitant Cardiac Failure	1.50	1.00; 2.26	0.049
Income area (reference High income Europe)			
Middle Income	1.44	1.00; 2.06	0.049
High Income non Europe	0.67	0.45; 0.99	0.044

Table E7: Baseline and outcomes of unilateral infiltrate patients according to their evolution

	Never developed ARDS N=579	Did develop ARDS N=143	p- value	N
Age	61.6±17.5	64.0±16.1	0.126	722
Female gender	214 (37.0%)	40 (28.0%)	0.055	722
Weight	75.2±18.2	78.0±20.2	0.147	691
BMI	26.3±6.1	27.2±6.3	0.135	674
Obese	105 (19.5%)	31 (22.8%)	0.465	674
Comorbidities				
Diabetes	128 (22.1%)	30 (21.0%)	0.858	722
COPD	147 (25.4%)	32 (22.4%)	0.523	722
Chronic Renal Failure	56 (9.7%)	12 (8.4%)	0.757	722
Immunosuppression	111 (19.2%)	22 (15.4%)	0.355	722
Chronic Cardiac Failure	57 (9.8%)	14 (9.8%)	1.000	722
Chronic Liver Failure	23 (4.0%)	5 (3.5%)	0.982	722
At least 1 comorbidity	346 (59.8%)	79 (55.2%)	0.375	722
Risk factor for AHRF				
Pneumonia	271 (46.8%)	77 (53.8%)	0.157	722
Non pulmonary Sepsis	81 (14.0%)	22 (15.4%)	0.769	722
Gastric aspiration	124 (21.4%)	25 (17.5%)	0.355	722
Trauma	34 (5.9%)	13 (9.1%)	0.227	722
Pancreatitis	9 (1.6%)	1 (0.7%)	0.696	722
Pulmonary contusion	24 (4.1%)	10 (7.0%)	0.223	722
Pulmonary Vasculitis	5 (0.9%)	1 (0.7%)	1.000	722
Non cardiogenic Shock	38 (6.6%)	8 (5.6%)	0.815	722
Overdose	17 (2.9%)	4 (2.8%)	1.000	722
TRALI	17 (2.9%)	7 (4.9%)	0.294	722
No Risk Factor identified	58 (10.0%)	15 (10.5%)	0.990	722
Concomitant Cardiac Failure	61 (10.5%)	14 (9.8%)	0.914	722
Concomitant Asthma	8 (1.4%)	3 (2.1%)	0.463	722
Concomitant COPDE	81 (14.0%)	22 (15.4%)	0.769	722
Type of admission			0.336	722
Medical	399 (68.9%)	99 (69.2%)		
Postoperative(elective)	45 (7.8%)	6 (4.2%)		
Surgical	105 (18.1%)	27 (18.9%)		
Trauma	30 (5.2%)	11 (7.7%)		
SOFA	9.0 [6.0;12.0]	9.6 [7.0;12.0]	0.145	711
Non-pulmonary SOFA	6.0 [3.8;9.0]	6.2 [4.0;9.0]	0.247	709
HD SOFA	2.0±1.8	2.4±1.7	0.015	672
Renal SOFA	0.8±1.1	0.9±1.1	0.277	687
Nb quadrants involved			0.218	612
1	351 (72.7%)	86 (66.7%)		
2	132 (27.3%)	43 (33.3%)		
First day with bilateral opacities				
- 3		62 (43.3%)		
- 5		34 (23.7%)		
- 7		25 (17.4%)		

- 10		9 (6.3%)		
- 14		10 (7.0%)		
- 21		2 (1.4%)		
- 28		1 (0.7%)		
Ventilation and ABG				
PCO2	44.5±15.1	45.9±15.6	0.319	707
pH	7.35±0.12	7.33±0.11	0.047	707
FiO2	0.5 [0.4;0.6]	0.5 [0.4;0.8]	0.004	711
SpO2	97.0 [95.0;99.0]	97.0 [95.0;99.0]	0.705	489
PO2	79.2±50.0	84.8±49.2	0.226	711
VT	7.9±1.9	8.0±1.9	0.664	680
PF	191.9±62.9	182.6±67.0	0.138	711
Worst PF in the 2 first days	181.7±62.1	166.5±64.3	0.012	722
Initial Severity			0.031	722
Mild	278 (48.0%)	52 (36.4%)		
Moderate	243 (42.0%)	70 (49.0%)		
Severe	58 (10.0%)	21 (14.7%)		
Worst severity in the 2 first days			0.009	722
Mild	234 (40.4%)	43 (30.1%)		
Moderate	277 (47.8%)	71 (49.7%)		
Severe	68 (11.7%)	29 (20.3%)		
RR	19.1±5.6	19.0±5.4	0.814	711
PEEP	6.0 [5.0;8.0]	6.0 [5.0;8.0]	0.050	711
Plateau pressure	19.8±5.3	20.9±4.9	0.181	210
Driving pressure	12.9±5.0	13.7±4.6	0.291	210
PIP	24.2±7.6	26.9±9.0	0.002	676
Minute ventilation	10.11±4.40	10.55±4.46	0.292	701
Outcomes				
Duration of invasive MV	5.0 [3.0;10.0]	12.0 [8.0;20.0]	<0.001	677
VFD	20.0 [0.0;24.0]	5.5 [0.0;18.0]	<0.001	677
ICU LOS	8.0 [4.0;14.0]	16.0 [10.5;24.5]	<0.001	722
Hosp LOS	15.0 [8.0;28.2]	23.0 [14.0;42.0]	<0.001	705
ICU mortality	146 (25.2%)	42 (29.4%)	0.364	722
Hospital mortality	177 (30.7%)	52 (36.4%)	0.227	720

Table E8: Multivariable analysis of factors associated with evolution to ARDS in patients with initial unilateral infiltrate

	Model for patients with 2 quadrants		
	OR	95%CI	p-value
Age (for 1 year)	1.01	1.00; 1.01	0.073
Non-pulmonary SOFA	1.01	0.95; 1.06	0.837
PF (for 10 mmHg decrease)	1.01	0.98; 1.04	0.643
pH (for 0.01 increase)	0.99	0.97; 1.00	0.280
PIP (for 1cmH2O)	1.04	1.01; 1.06	0.002

Figure E1: Distribution of tidal volume vs plateau pressure on day 1 in patients with unilateral infiltrate or with ARDS

