Propofol, Ketamine and Etomidate as Induction Agents for Intubation and Outcomes in Critically Ill Patients: Supplemental Data

Table 1S-A – Patient demographics and ICU admission characteristics according to medication*

	Unweighted statistics						Weighted statistics					
	Propofol (n=962)	Ketamine (n=792)	Etomidate (n=919)	Std. Diff.‡			Propofol	Ketamine	Etomidate	Std. Diff.‡		
Age (y)	61.3 (15.8)	64.2 (15.4)	64.5 (16.0)	0.19	0.20	0.02	63.2 (15.7)	63.7 (15.5)	63.3 (15.9)	0.03	<.01	0.03
Sex												
Female	400 (42%)	321 (41%)	387 (42%)	0.02	0.01	0.03	(41%)	(46%)	(41%)	0.09	<.01	0.09
Male	562 (58%)	471 (59%)	532 (58%)	0.02	0.01	0.03	(59%)	(54%)	(59%)	0.09	<.01	0.09
BMI (kg/m²)	29.2 (8.5)	29.1 (8.1)	29.1 (8.2)	0.01	0.01	<.01	28.8 (8.2)	29.3 (8.3)	29.1 (8.1)	0.06	0.04	0.03
Readmission†	145 (15%)	124 (16%)	140 (15%)	0.02	<.01	0.01	(16%)	(15%)	(16%)	0.04	0.02	0.03
Invasive ventilation within 24 hours prior to intubation	25 (3%)	22 (3%)	29 (3%)	0.01	0.03	0.02	(3%)	(2%)	(4%)	0.02	0.06	0.07
Admission source												
Surgery/procedure	117 (12%)	72 (9%)	60 (7%)	0.10	0.19	0.10	(12%)	(12%)	(10%)	0.02	0.06	0.09
Direct admission ICU	181 (19%)	163 (21%)	188 (20%)	0.04	0.04	<.01	(20%)	(18%)	(20%)	0.04	<.01	0.05
Emergency department	170 (18%)	149 (19%)	230 (25%)	0.03	0.18	0.15	(19%)	(22%)	(20%)	0.07	0.03	0.04
Hospital floor	469 (49%)	386 (49%)	421 (46%)	<.01	0.06	0.06	(47%)	(45%)	(48%)	0.04	<.01	0.05
Transfer from another ICU	25 (3%)	22 (3%)	20 (2%)	0.01	0.03	0.04	(2%)	(3%)	(3%)	<.01	<.01	<.01
Admission ICU												
Cardiac surgical	76 (8%)	97 (12%)	22 (2%)	0.14	0.25	0.39	(7%)	(7%)	(7%)	<.01	0.01	<.01
Medical/Surgical/Transplant	217 (23%)	169 (21%)	114 (12%)	0.03	0.27	0.24	(19%)	(18%)	(19%)	<.01	<.01	0.01
Cardiac medical	33 (3%)	57 (7%)	98 (11%)	0.17	0.29	0.12	(7%)	(7%)	(7%)	<.01	<.01	<.01
Trauma/general surgical	21 (2%)	83 (10%)	183 (20%)	0.35	0.59	0.27	(11%)	(10%)	(11%)	0.03	0.02	0.01
Vascular/thoracic surgical	165 (17%)	53 (7%)	74 (8%)	0.33	0.28	0.05	(11%)	(11%)	(11%)	<.01	<.01	<.01

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	Unweighted statistics						Weighted statistics					
	Propofol (n=962)	Ketamine (n=792)	Etomidate (n=919)	Std. Diff.‡			Propofol	Ketamine	Etomidate	Std. Diff.‡		
Neuroscience	181 (19%)	6 (1%)	23 (3%)	0.64	0.55	0.11	(8%)	(9%)	(8%)	0.05	0.01	0.03
Medical ICU	269 (28%)	327 (41%)	405 (44%)	0.28	0.34	0.06	(37%)	(37%)	(37%)	<.01	<.01	<.01
ICU length of stay (h) §	5 (1, 23)	7 (2, 34)	6 (2, 29)	0.05	0.01	0.12	5 (1, 26)	7 (2, 34)	6 (2, 27)	<.01	0.03	0.07
Last MAP within 6 hours of intubation**	78 (22)	71 (25)	73 (25)	0.29	0.24	0.05	77 (22)	73 (24)	73 (25)	0.18	0.17	<.01
Acute physiology score (APS)	63.4 (20.3)	70.2 (20.6)	68.3 (20.8)	0.33	0.24	0.09	67.7 (21.1)	66.9 (20.6)	67.3 (20.5)	0.04	0.02	0.02
SOFA score	5.1 (3.4)	6.6 (4.0)	6.1 (3.8)	0.42	0.29	0.14	5.4 (3.4)	6.4 (4.1)	6.2 (3.9)	0.27	0.21	0.06
Respiratory	0 (0, 2)	2 (0, 2)	2 (0, 2)	0.27	0.30	0.04	1 (0, 2)	2 (0, 2)	2 (0, 2)	0.14	0.17	0.03
Coagulation	0 (0, 1)	0 (0, 2)	0 (0, 1)	0.16	0.02	0.18	0 (0, 1)	0 (0, 2)	0 (0, 1)	0.14	0.05	0.09
Liver	0 (0, 0)	0 (0, 0)	0 (0, 0)	0.19	0.12	0.08	0 (0, 0)	0 (0, 0)	0 (0, 0)	0.17	0.14	0.03
CV	1 (0, 1)	1 (1, 3)	1 (1, 1)	0.63	0.38	0.24	1 (0, 1)	1 (1, 3)	1 (1, 2)	0.58	0.36	0.23
CNS	0 (0, 1)	0 (0, 1)	0 (0, 1)	0.24	0.12	0.13	0 (0, 1)	0 (0, 1)	0 (0, 1)	0.27	0.08	0.19
Renal	0 (0, 3)	1 (0, 3)	1 (0, 3)	0.26	0.18	0.07	1 (0, 3)	1 (0, 3)	1 (0, 3)	0.06	0.03	0.03

* Continuous variables are summarized as mean (SD), categorical variables are summarized as n (%). Both weighted and unweighted cohorts are summarized. Data from a single imputation are summarized. Prior to imputation, data were complete for all characteristics except BMI (n=2,640), admission source (n=2,670), and APS (n=2,640).

‡ Standardized differences are from comparisons of Ketamine vs. Propofol, Etomidate vs. Propofol, and Etomidate vs. Ketamine respectively

† Readmission defined as any ICU admission other than the patient's first ICU admission during a single hospitalization

§ Hours in ICU prior to intubation

** Only available data is summarized (n=921, 763, and 867 for Propofol, Ketamine, and Etomidate groups respectively).

Table 1S-B: Severity Scores by single intravenous anesthetic agent used in all patients

Patients characteristics (All patients)	Overall (N=2,673)	Propofol (N=962)	Ketamine (N=792)	Etomidate (N=919)	P value
Age, year	63 (16; 63, 64)	61 (16; 60, 62)	64 (15; 63, 65) [*]	65 (16; 63, 66) [†]	<0.0001
Male	1565 (59)	562 (58)	471 (59)	532 (58)	0.7992
BMI, kg/m^2	29 (12; 29, 30)	30 (15; 29, 31)	29 (12; 29, 30)	29 (8; 29, 30)	0.9625
APACHE III	83 (28; 82, 84)	78 (26; 77, 80)	88 (29; 86, 90) [*]	85 (28; 83, 86) [†]	<0.0001
SOFA, day 1	8 (4; 8, 8)	7 (4; 7, 8)	9 (4; 8, 9) [*]	8 (4; 8, 8) [†£]	<0.0001

BMI: Body Mass Index, APACHE III: Acute Physiology And Chronic Health Evaluation III, SOFA: Sequential Organ Failure Assessment Score. Values are expressed as mean (standard deviation; 95% confidence interval). For comparisons between the three treatments, Kruskal Wallis test was used, or chi-square test as appropriate, with significance level set to 0.05. For each of the pairwise comparisons, statistical significance was defined by $p < 0.017$ after Bonferroni correction ([*]ketamine vs. propofol, [†]etomidate vs. propofol, [£]etomidate vs, ketamine).

Table 2S: Co- medications for intubation by single intravenous anesthetic agent used in patients non-intubated for cardiac arrest

Co-medications in intubated patients, N (% anesthetic agent)	Overall (N=2,598)	Propofol (N=944)	Ketamine (N=772)	Etomidate (N=882)	P Value
Other sedatives	**1,271 (49)**	**327 (35)**	**495 (64)** [*]	**449 (51)** [† £]	**<0.0001**
Midazolam	1,250 (48)	321 (34)	486 (63) [*]	443 (50) [† £]	<0.0001
Lorazepam	13 (<1)	5 (<1)	5 (<1)	3 (<1)	[§]0.6496
Dexmedetomidine	8 (<1)	1 (<1)	4 (50)	3 (<1)	[§]0.2670
Analgesics	**1,709 (66)**	**619 (66)**	**506 (66)**	**584 (66)**	**0.9461**
Fentanyl	1,696 (65)	613 (65)	504 (65)	579 (66)	0.9506
Morphine	13 (<1)	6 (<1)	2 (<1)	5 (<1)	[§]0.5374
Neuromuscular blocking agents	**2,091 (81)**	**765 (81)**	**656 (91)**	**670 (76)** [† £]	**<0.0001**
Succinylcholine	1,284 (49)	451 (48)	376 (49)	457 (52)	0.2017
Rocuronium	740 (28)	281 (30)	259 (34)	200 (23) [† £]	<0.0001

Vecuronium	60 (2)	28 (3)	21 (3)	11 (1)	0.0335
Atracurium	4 (<1)	3 (<1)	0 (0)	1 (<1)	§0.3984
Cisatracurium	3 (<1)	2 (<1)	0 (0)	1 (<1)	§0.7798
Topical	**97 (4)**	**46 (5)**	**38 (5)**	**13 (1)** [†£]	**<0.0001**
None	**83 (3)**	**38 (4)**	**15 (2)** [*]	**30 (4)**	**0.0464**

Co-medications may be multiple per patient. For comparisons between the three treatments, chi-square test of independence was used, or [§] Fisher's exact test as appropriate, with significance level set to 0.05. For each of the pairwise comparisons, chi-square test was used with statistical significance defined by p < 0.017 after Bonferroni correction ([*]ketamine vs. propofol, [†]etomidate vs. propofol, [£]etomidate vs ketamine).

Table 3S: Complications post -intubation by single intravenous anesthetic agent used in patients non-intubated for cardiac arrest

Complications after intubation N (% anesthetic agent)	Overall (N=2,598)	Propofol (N=944)	Ketamine (N=772)	Etomidate (N=882)	P Value
No immediate complication	2406 (93)	877 (93)	723 (94)	806 (91)	0.1936
Difficult airway	216 (8)	89 (9)	74 (10)	53 (6) [†£]	0.0095
Immediate oxygen desaturation (SpO$_2$<90%)	92 (4)	32 (3)	21 (3)	39 (4)	0.1662
Immediate witnessed aspiration	43 (2)	14 (1)	15 (2)	14 (2)	0.7446
Soft tissue injury with bleeding	37 (1)	13 (1)	14 (2)	10 (1)	0.5021
Immediate hypotension [$]	8 (<1)	4 (<1)	3 (<1)	1 (<1)	[§] 0.4498
Immediate cardiac arrest	5 (<1)	2 (<1)	2 (<1)	1 (<1)	[§] 0.8641
Cardiac arrest within 2 hours post intubation	60 (2)	9 (1)	25 (3) [*]	26 (3) [†]	0.0022
Cardiac arrest anytime post intubation	109 (4)	26 (3)	36 (5)	47 (5) [†]	0.0173
Sustained cardio-vascular collapse [**]	501 (19)	149 (16)	170 (22) [*]	182 (21) [†]	0.0023

Sustained severe hypoxia [&]	188 (7)	44 (5)	69 (9) [*]	75 (9) [†]	0.0006

[$]Immediate hypotension was defined by an immediate drop in systolic blood pressure ≤ 65 mmHg recorded at least once and/or a drop in systolic blood pressure $\leq$40 mmHg within the first 30 minutes following intubation, [**]Cardiovascular collapse was defined a systolic blood pressure ≤ 65 mmHg recorded at least once and/or $\leq$90 mmHg lasting 30 minutes despite fluid boluses (at least 500 mL crystalloid and/or colloid solutions and/or vasopressor requirement) between 30- and 120-minutes post intubation. [&]Severe hypoxia was defined as $SpO_2\leq$80% within 2 hours post intubation. For comparisons between the three treatments, chi--square test of independence between the three treatments was used, or [§]Fisher's exact test as appropriate, with significance level set to 0.05. For each of the pairwise comparisons, chi-square was used with statistical significance defined by $p < 0.017$ after Bonferroni correction test ([*]ketamine vs. propofol, [†]etomidate vs. propofol, [£]etomidate vs. ketamine).