Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods. Variables and outcomes definitions.

Variable	Definition
Critically ill patient	Any patient with a life-threatening impairment of the cardiovascular, respiratory or neurological system requiring in-hospital intubation.
Primary reason for intubation	The most relevant clinical alteration leading the clinician to proceed with tracheal intubation.
Cardiovascular instability[a]	Clinical features of circulatory shock with hypotension (or need of vasopressors use) and/or signs of organ hypoperfusion.
Respiratory failure	Clinical features of respiratory distress associated with impaired gas exchange
Neurological impairment	Reduced level of consciousness with signs of hypoventilation, airway obstruction or impaired upper airways reflexes.
Airway obstruction	Narrowing or occlusion of airways with impaired airflow driven by anatomic alterations or foreign bodies
Rapid sequence induction	Administration of rapid-onset induction agents and muscle relaxant with no ventilation between induction and laryngoscopy
Laryngoscopy attempt	Each introduction of the laryngoscope in patient's mouth.
Duration of the intubation procedure	Difference between time of tracheal intubation confirmation and first laryngoscopy start
Difficult tracheal intubation	Procedure requiring > 2 laryngoscopy attempts
Number of operators	Number of operators on the scene potentially qualified to perform an intubation attempt
Daytime procedure	Procedures performed from 8:00 am to 7:59 pm
Nighttime procedure	Procedures performed between 8:00 pm and 7:59 am
Cardiac arrhythmia	Occurrence of any supraventricular or ventricular arrhythmia within 30 minutes from the start of tracheal intubation
Cannot intubate cannot oxygenate (CICO)	Impossibility to achieve a successful tracheal intubation and adequate patient's oxygenation.
Emergency front of neck airway (FONA)	Emergency need for invasive access to the patient's airways to provide adequate oxygenation (e.g. cricothyroidotomy, percutaneous tracheostomy, surgical tracheostomy).
Aspiration	Inhalation of oropharyngeal or gastric contents into the larynx and the respiratory tract within the first 24 hours after intubation according to clinical and/or radiographic findings
Esophageal intubation	Accidental placement of the tracheal tube into the esophagus
Pneumomediastinum/pneumothorax	Detection of air collection into the mediastinum or pleural space as the consequence of airway instrumentation

Airway injury	Any detectable and clinically relevant injury attributable to tracheal intubation procedure (e.g bleeding, tracheal or bronchial tear or laceration)
Dental injury	Any notable change in patient's dentition as the consequence of airway instrumentation.

eMethods. Data quality control.

We held several live web-based meetings during which principal investigators provided training on the protocol, answered study related queries and provided support for issues arising during data collection in the electronic case report form (eCRF). At the time of data entry, the eCRF automatically generated queries in case of missing, outlying or contradictory values and response was required before marking record as complete. Three monitors manually screened all complete CRFs for consistency of clinical data (e.g. reported indication for tracheal intubation and actual pre-intubation clinical condition) and for erroneous values and they sent a request of verification to each local investigator. A second check for missing and outlying values was performed before the statistical analysis. We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement guidelines for observational cohort studies.

eTable 1. Outcomes of patients' undergoing reintubations

Variable	Value	Missing
N° of patients undergoing reintubation	94	0
Major intubation related complication, No. (%)	42 (44.7)	0 (0.0)
Cardiovascular instability, No. (%)	32 (36.8)	7 (7.5)
Systolic blood pressure < 65 mmHg	2 (2.2)	1 (1.1)
Systolic blood pressure < 90 mmHg for > 30 minutes,	3 (3.2)	1 (1.1)
New need/increase of vasopressors	32 (34.0)	0 (0.0)
Fluid bolus > 15 ml/Kg	2 (2.3)	7 (7.5)
Cardiac arrest, No. (%)	2 (2.1)	0 (0.0)
With return of spontaneous circulation	2 (100.0)	0 (0.0)
Reason:		
Hypoxia	1 (50.0)	0 (0.0)
Thrombosis (coronary or pulmonary)	1 (50.0)	0 (0.0)
Severe hypoxia (lowest SpO_2 < 80%), No. (%)	12 (12.9)	1 (1.1)
Secondary complications, No. (%)		
New onset cardiac arrhythmia	1 (1.1)	0 (0.0)
Atrial fibrillation	1 (100.0)	0 (0.0)
Aspiration of gastric contents, No. (%)	2 (2.2)	1 (1.1)
Airway injury, No. (%)	2 (2.2)	1 (1.1)
Laryngeal laceration	1 (50.0)	0 (0.0)
Other	1 (50.0)	0 (0.0)
Pneumothorax, No. (%)	3 (3.2)	1 (1.1)
Pneumomediastinum, No. (%)	1 (1.1)	1 (1.1)

eTable 2. Patients' characteristics, reason for intubation and procedure description in patients with and without peri-intubation major adverse events

Variable	All (N = 2964)	Major adverse events (N =1340)	No major adverse events (N = 1624)	P-value
Age, median (IQR), y	63.0 (49.0-74.0)	65.0 (52.0-75.0)	61.0 (45.0-73.0)	<.001
Women, No. (%)	1107 (37.4)	513 (38.3)	594 (36.6)	.359
Weight, median (IQR), kg	71.2 (60.0-84.0)	72.2 (61.0-84.0)	70.0 (60.0-84.0)	.198
BMI, median (IQR), kg/m^2	25.4 (22.5-29.4)	25.5 (22.4-29.4)	25.2 (22.5-29.0)	.307
SOFA score[a], median (IQR)	7.0 (4.8-10.0)	8.0 (5.0-11.0)	6.0 (4.0-9.0)	<.001
Respiratory infection during previous 30 days, No. (%)	288 (9.7)	145 (10.8)	143 (8.8)	.075
Chronic disease, No. (%)				
Arterial hypertension	1185 (40.0)	558 (41.6)	627 (38.6)	.101
Diabetes	719 (24.3)	333 (24.9)	386 (23.8)	.521
COPD	445 (15.0)	220 (16.4)	225 (13.9)	.058
Ischemic heart disease	423 (14.3)	223 (16.6)	200 (12.3)	<.001
Chronic renal failure	408 (13.8)	221 (16.5)	187 (11.5)	<.001
Solid neoplasm	349 (11.8)	182 (13.6)	167 (10.3)	.007
Heart failure (NYHA classification III - IV)	264 (8.9)	151 (11.3)	113 (7.0)	<.001
Chronic liver failure	176 (5.9)	87 (6.5)	89 (5.5)	.279
Hematologic malignancy	152 (5.1)	91 (6.8)	61 (3.8)	<.001
OSAS	133 (4.5)	68 (5.1)	65 (4.0)	.189
Asthma	116 (3.9)	50 (3.7)	66 (4.1)	.712
Neuromuscolar disease	75 (2.5)	40 (3.0)	35 (2.2)	.189
Cardiac arrythmia	72 (2.4)	38 (2.8)	34 (2.1)	.235
Interstitial lung disease	61 (2.1)	32 (2.4)	29 (1.8)	.308
Other[b]	814/2806 (29.0)	375 (29.9)	439 (28.3)	.396
Radiologic finding, No. (%)				
Bilateral lung opacities	826 (27.9)	428 (31.9)	398 (24.5)	<.001
Pleural effusion	403 (13.6)	218 (16.3)	185 (11.4)	<.001
Unilateral lung opacities	364 (12.3)	181 (13.5)	183 (11.3)	.073
Other	266 (9.0)	116 (8.7)	150 (9.2)	.628
Ongoing respiratory support, No. (%)				<.001
Standard oxygen	1509 (61.8)	668 (57.4)	841 (65.8)	
Noninvasive ventilation	521 (21.3)	272 (23.4)	249 (19.5)	
High flow nasal cannula	313 (12.8)	177 (15.2)	136 (10.6)	
Continuous positive airway pressure	100 (4.1)	47 (4.0)	53 (4.1)	
PaO_2/FiO_2, median (IQR)	165.0 (100.0, 265.0)	147.5 (91.5-242.9)	182.0 (110.0-286.7)	<.001
SpO_2/FiO_2[c], median (IQR)	165.7 (105.6, 261.1)	150.0 (100.0-232.5)	188.5 (110.0-290.0)	<.001
Receiving vasopressor/inotropic support, No. (%)	769 (25.9)	455 (34.0)	314 (19.3)	<.001

Fluid bolus 30 min before intubation, No. (%)	1065 (37.7)	554 (43.1)	511 (33.1)	<.001
Systolic blood pressure, mean (SD), mmHg	126.3 (35.7)	116.0 (35.0)	135.0 (34.0)	<.001
Diastolic blood pressure, mean (SD), mmHg	70.0 (20.7)	64.0 (20.0)	75 (20.0)	<.001
Heart rate, mean (SD)	103.7 (26.2)	105.0 (27.0)	102.0 (25.0)	.003
Reason for intubation, No. (%)				<.001
Respiratory failure	1548 (52.3)	778 (58.2)	770 (47.4)	
Neurological impairment	902 (30.5)	295 (22.1)	607 (37.4)	
Cardiovascular instability	277 (9.4)	178 (13.3)	99 (6.1)	
Airway obstruction	137 (4.6)	50 (3.7)	87 (5.4)	
Emergent/Urgent procedure	29 (1.0)	9 (0.7)	20 (1.2)	
Other	67 (2.2)	27 (2.0)	40 (2.5)	
Degree of emergency[d], No. (%)				.295
Tracheal intubation required without any delay[e]	1536 (51.9)	680 (50.7)	856 (52.8)	
Tracheal intubation required in < 1 hr	1065 (35.9)	502 (37.5)	563 (34.7)	
Tracheal intubation required in ≥ 1 hr	361 (12.2)	158 (11.8)	203 (12.5)	
At least one anticipated anatomical difficult airways, No. (%)				<.001
Yes	1308 (44.1)	639 (47.7)	669 (41.2)	
No	1487 (50.2)	639 (47.7)	848 (52.2)	
Not performed	169 (5.7)	62 (4.6)	107 (6.6)	
Predictors of difficult airway management[f], No. (%)				
Obesity	430 (15.8)	217 (17.4)	213 (14.5)	.041
High risk of full stomach	419 (15.4)	218 (17.5)	201 (13.7)	.007
Short neck	376 (13.8)	197 (15.8)	179 (12.2)	.007
Reduced mouth opening (< 3 cm)	227 (8.4)	122 (9.8)	105 (7.1)	.015
Mallampati score III-IV	205 (7.5)	102 (8.2)	103 (7.0)	.272
Neck stiffness	160 (5.9)	79 (6.3)	81 (5.5)	.399
Beard	119 (4.4)	60 (4.8)	50 (4.0)	.352
Large tongue	111 (4.1)	50 (4.0)	61 (4.1)	.941
Need of cervical spine immobilization	80 (3.0)	32 (2.6)	48 (3.3)	.342
Retrognatia	57 (2.1)	26 (2.1)	31 (2.1)	.963
Facial trauma	41 (1.5)	17 (1.4)	24 (1.6)	.683
Past airway surgery/radiotherapy or untreated airway cancer	34 (1.3)	15 (1.2)	19 (1.3)	.976
Prognatism	13 (0.5)	7 (0.6)	6 (0.4)	.763
MACOCHA score[g] ≥ 3	426 (14.4)	222 (16.6)	204 (12.6)	.002
Preoxygenation method, No. (%)				<.001
Bag-valve mask	1847 (62.4)	835 (62.4)	1012 (62.4)	
Standard facemask	389 (13.2)	145 (10.8)	244 (15.1)	
Noninvasive ventilation	344 (11.6)	186 (13.9)	158 (9.8)	

High flow nasal cannula	160 (5.4)	84 (6.3)	76 (4.7)	
Anesthesia breathing circuit	56 (1.9)	18 (1.3)	38 (2.3)	
Continuous positive airway pressure	51 (1.7)	21 (1.6)	30 (1.9)	
Venturi system	47 (1.6)	22 (1.6)	25 (1.5)	
Nasal cannula	47 (1.6)	22 (1.6)	25 (1.5)	
Other	19 (0.6)	6 (0.5)	13 (0.8)	
Apneic oxygenation[h], No. (%)	308 (10.4)	162 (12.1)	146 (9.0)	.007
Rapid sequence induction[i], No. (%)	1727 (62.2)	791 (63.5)	936 (61.1)	.219
Cricoid pressure, No. (%)	1120 (37.9)	519 (38.9)	601 (37.1)	.334
Induction agent, No. (%)				
Propofol	1230 (41.5)	523 (39.0)	707 (43.5)	.015
Midazolam	1079 (36.4)	487 (36.3)	592 (36.5)	.981
Etomidate	527 (17.8)	251 (18.7)	276 (17.0)	.237
Ketamine	421 (14.2)	217 (16.2)	204 (12.6)	.006
Muscle relaxant use, No. (%)	2095 (75.5)	935 (75.1)	1160 (75.8)	.717
Rocuronioum	1239 (41.8)	566 (42.2)	673 (41.4)	.688
Succinylcholine	646 (21.8)	272 (20.3)	374 (23.0)	.081
Other	191 (6.6)	84 (6.4)	107 (6.7)	.839
Opioid use, No. (%)	1415 (51.0)	630 (50.6)	785 (51.3)	.734
Elective method for laryngoscopy, No. (%)				.054
Direct laryngoscopy with Macintosh or Miller blade	2416 (81.5)	1082 (80.7)	1334 (82.2)	
Videolaryngoscopy	505 (17.1)	245 (18.3)	260 (16.0)	
First method used to confirm intubation, No. (%)				<.001
Auscultation	1711 (57.9)	736 (55.2)	975 (60.1)	
Waveform capnography[l]	758 (25.6)	372 (27.9)	386 (23.8)	
Colorimetric CO_2 detection[m]	222 (7.5)	107 (8.0)	115 (7.1)	
Capnometry[n]	138 (4.7)	68 (5.1)	70 (4.3)	
None	7 (0.2)	7 (0.5)	0 (0.0)	
Other[o]	120 (4.1)	44 (3.3)	76 (4.7)	

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; IQR, interquartile range; NYHA, New York Heart Association; SOFA, Sequential organ failure assessment.

[a]SOFA score was calculated with values last available before intubation. For all SOFA scores for which data points were missing, the corresponding value and omitted and the denominator adjusted accordingly.

[b]Other chronic disease includes seizure, stroke, endocrine disease, rheumatic disease, psychiatric disorder, immunosuppression.

[c]SpO_2/FiO_2 was reported only when SpO2 was $\leq 98\%$

[d]Degree of emergency was identified before intubation according to clinical judgment.

[e]Tracheal required without any delay indicates the need to proceed with intubation as soon as possible after patient presentation and assessment (e.g. within 5-10 minutes).

[f]Calculated on the 2716 patients on which all the predictors of difficult airway were evaluated.

[g]MACOCHA score is a predictive score of difficult intubation in intensive care unit. Its calculation includes the following items: Mallampati score III – IV (5 points), obstructive sleep apnea syndrome (2 points), reduced mobility of the cervical spine (1 point), limited mouth opening < 3 cm (1 point), coma (1 point), severe hypoxemia (1 point), non-anesthesiologist operator (1 point). It ranges from 0 (easy intubation) to 12 (very difficult intubation).

[h]Apneic oxygenation was defined as oxygen administration during laryngoscopy/fiberoscopy.

[i]Rapid sequence induction: rapid onset induction without positive pressure ventilation between induction and laryngoscopy.

[l]Waveform capnography: use of a monitor which provides the graphic measurement of exhaled CO_2 plotted against time.

[m]Colorimetric CO_2 detection: use of a device which employs a photochemical reaction to detect the presence of CO_2 in the exhaled air.

[n]Capnography: use of a monitor which provides only the absolute value of CO_2 concentration in the exhaled air.

[o]Other method used to confirm intubation includes chest x-ray and fiberoscopy.

eTable 3. Center, operator's characteristics and intubation setting.

Variable	All (N = 2964)	Major adverse events (N =1340)	No major adverse events (N = 1624)	P-value
Academic hospital, No. (%)	1998 (67.4)	906 (67.6)	1092 (67.2)	.861
Trauma center, No. (%)	1686 (56.9)	729 (54.4)	957 (58.9)	.015
N° of ICUs, median (IQR)	2.0 (1.0, 4.0)	2.0 (1.0, 4.0)	2.0 (1.0, 4.0)	.133
Total ICU beds, No. (%)				.094
< 10	252 (8.5)	126 (9.4)	126 (7.8)	
10-20	768 (25.9)	361 (26.9)	407 (25.1)	
> 20	1944 (65.6)	853 (63.7)	1091 (67.2)	
Frequency of emergency intubation/week, median (IQR)	7.0 (5.0, 10.0)	6.0 (5.0, 10.0)	7.0 (5.0, 10.0)	.053
Presence of a MET, No. (%)	2034 (68.6)	928 (69.3)	1106 (68.1)	.527
Application of an airway management protocol, No. (%) (n=2962)				.635
Yes	1510 (51.0)	695 (51.9)	815 (50.2)	
No	443 (15.0)	196 (14.6)	247 (15.2)	
Not available	1009 (34.0)	447 (33.4)	562 (34.6)	
Use of a checklist for airway management, No. (%) (n=2962)				.244
Yes	1494 (50.4)	660 (49.3)	834 (51.4)	
No	499 (16.9)	219 (16.4)	280 (17.2)	
Not available	969 (32.7)	459 (34.3)	510 (31.4)	
Airway trolley at the place of TI, No. (%) (n=2962)				.205
Yes	2212 (74.7)	991 (74.1)	1221 (75.2)	
No	532 (18.0)	236 (17.6)	296 (18.2)	
Not available	218 (7.3)	111 (8.3)	107 (6.6)	
Admission source, No. (%)				<.001
Out-of hospital admission/Emergency Department	1591 (55.6)	683 (52.5)	908 (58.1)	
Medical ward[a]	551 (19.2)	275 (21.1)	276 (17.7)	
Surgical ward[a]	247 (8.6)	138 (10.6)	109 (7.0)	
Operating room/recovery room	140 (4.9)	67 (5.1)	73 (4.7)	
ICU[b]	78 (2.7)	34 (2.6)	44 (2.8)	
Other[c]	258 (9.0)	105 (8.1)	153 (9.8)	
Daytime intubation, No. (%)	1887 (63.8)	838 (62.7)	1049 (64.6)	.300
Patient position, No. (%) (n=2961)				.001
Supine	1884 (63.6)	801 (59.8)	1083 (66.8)	
30-45° head-up position	642 (21.7)	333 (24.9)	309 (19.1)	
20° head-up position	284 (9.6)	130 (9.7)	154 (9.5)	
Beach chair	65 (2.2)	32 (2.4)	33 (2.0)	
Other[d]	86 (2.9)	43 (3.2)	43 (2.7)	
Total N° of operators, No. (%) (n=2959)				.210
1 operator	1567 (53.0)	698 (52.2)	869 (53.6)	
2-3 operators	1198 (40.5)	561 (41.9)	637 (39.3)	
>3 operators	194 (6.5)	79 (5.9)	115 (7.1)	
Operator performing the first attempt, No. (%) (n=2962)				.321
Resident	1536 (51.9)	701 (52.4)	835 (51.4)	
Staff physician/consultant	918 (31.0)	406 (30.3)	512 (31.5)	

Fellow	411 (13.9)	195 (14.6)	216 (13.3)	
Medical student	77 (2.6)	27 (2.0)	50 (3.1)	
Other[e]	20 (0.6)	10 (0.7)	10 (0.6)	
Field of training of the operator performing the first attempt, No. (%) (n=2962)				.003
Anesthesia	1601 (54.0)	719 (53.7)	882 (54.3)	
Critical Care/Intensive Care	669 (22.6)	324 (24.2)	345 (21.3)	
Emergency Medicine	334 (11.3)	120 (9.0)	214 (13.2)	
Internal Medicine	136 (4.6)	65 (4.9)	71 (4.4)	
Pulmonary and Critical Care Medicine	107 (3.6)	58 (4.3)	49 (3.9)	
Other[f]	115 (3.9)	53 (4.0)	62 (3.8)	
N° of intubations/week of the operator of the 1st attempt, No. (%) (n=2959)				.075
≤ 1 intubations/week	763 (25.8)	367 (27.4)	396 (24.4)	
2-5 intubations/week	1275 (43.1)	586 (43.8)	689 (42.5)	
6-10 intubations/week	565 (19.1)	230 (17.2)	335 (20.7)	
11- 20 intubations/week	264 (8.9)	117 (8.8)	147 (9.1)	
>20 intubations/week	92 (3.1)	37 (2.8)	55 (3.4)	
Operator performing the successful attempt[g], No. (%) (n=256)				.330
Staff physician/consultant	145 (56.6)	80 (59.7)	65 (53.3)	
Resident	65 (25.4)	28 (20.9)	37 (30.3)	
Fellow	44 (17.2)	25 (18.7)	19 (15.6)	
Other	2 (0.8)	1 (0.7)	1 (0.8)	
Field of training of the operator performing the successful attempt[g], No. (%) (n=256)				.568
Anesthesia	133 (52.0)	71 (53.0)	62 (50.8)	
Critical Care/ Intensive Care	84 (32.8)	47 (35.1)	37 (30.3)	
Emergency Medicine	22 (8.6)	9 (6.7)	13 (10.7)	
Internal Medicine	7 (2.7)	3 (2.2)	4 (3.3)	
Pulmonary and Critical Care Medicine	7 (2.7)	0 (0.0)	3 (2.5)	
Other[f]	3 (1.2)	0 (0.0)	3 (2.4)	
N° of intubations/week of the operator of the successful attempt[c], No. (%) (n=256)				.584
≤ 1 intubations/week	58 (22.7)	32 (23.9)	26 (21.3)	
2-5 intubations/week	127 (49.6)	63 (47.0)	64 (52.5)	
6-10 intubations/week	38 (14.8)	20 (14.9)	18 (14.8)	
11- 20 intubations/week	21 (8.2)	14 (10.4)	7 (5.7)	
>20 intubations/week	12 (4.7)	5 (3.7)	7 (5.7)	
Laryngoscopy duration, minutes, median (IQR) (n=2947)	1.0 (1.0, 2.0)	1.0 (1.0, 3.0)	1.0 (1.0, 2.0)	.182

Abbreviations: IQR, interquartile range; ICU: intensive care unit; MET, medical emergency team; TI, tracheal intubation.

[a]For intubations performed in the intensive care unit.

[b]For intubations performed in medical or surgical wards; for intubations performed in ICU, this refer to other ICU of the same hospital.

[c]Other admission source include outpatient and other in-hospital areas.
[d]Other patient's position includes: ramp position, Trendelemburg (patient supine with feet elevated above the head level) and reverse-Trendelemburg (patient supine with head elevated above the feet level).
[e]Other operator performing the first attempt of intubation includes nurse and respiratory therapist.
[f]Other field of training for the operator performing intubation attempts includes: hematology/oncology, cardiology, pulmonary medicine and surgery.
[g]Calculated on the 256 patients with the operator performing the successful attempt different from the operator performing the first attempt.

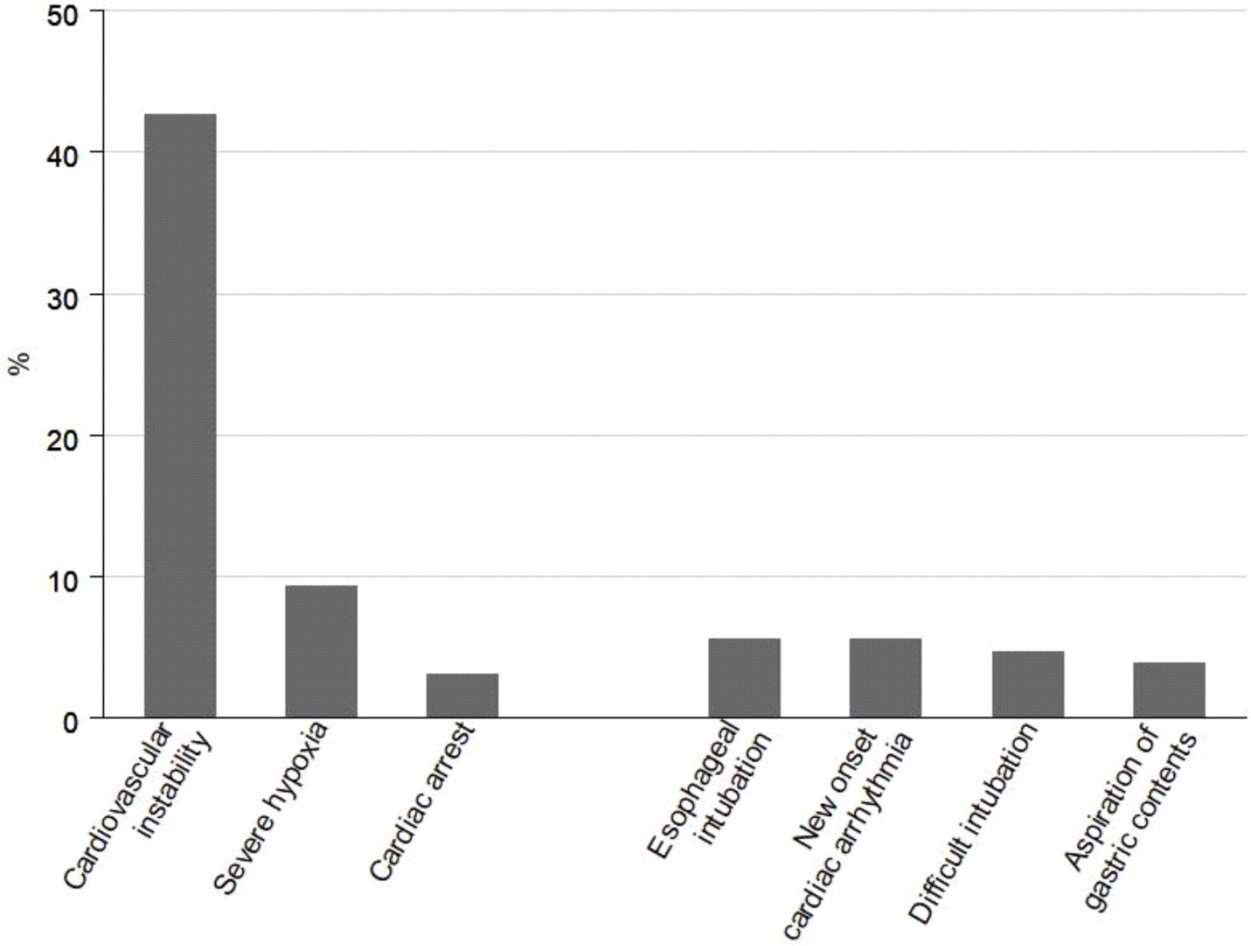
eTable 4. Outcomes distribution according to the geographical areas of participating centers.

Variable	Europe (N=1586)	North America (N=335)	South America (N=82)	Asia (N=816)	Africa (N=33)	Australia and New Zeeland (N=112)
Major intubation related complication, No. (%)	770 (48.5)	159 (47.5)	39 (47.6)	317 (38.8)	10 (30.3)	45 (40.2)
Cardiovascular instability, No. (%)	664 (44.9)	149 (47.5)	33 (41.8)	275 (36.1)	10 (45.5)	41 (42.3)
Systolic blood pressure < 65 mmHg	113 (7.2)	14 (4.2)	4 (4.9)	22 (2.7)	0 (0.0)	4 (3.6)
Systolic blood pressure < 90 mmHg for > 30 minutes,	147 (10.0)	33 (10.2)	6 (7.7)	57 (7.3)	6 (20.0)	3 (2.7)
New need/increase of vasopressors	603 (38.0)	132 (39.4)	33 (40.2)	243 (29.8)	5 (15.2)	37 (33.0)
Fluid bolus > 15 ml/Kg	81 (5.5)	25 (8.0)	2 (2.5)	37 (4.8)	2 (9.1)	4 (4.1)
Cardiac arrest, No. (%)	45 (2.8)	11 (3.3)	2 (2.4)	33 (4.0)	0 (0.0)	2 (1.8)
With return of spontaneous circulation	26 (57.8)	11 (100.0)	2 (100.0)	8 (24.2)	-	2 (100.0)
With death	19 (57.8)	0 (0.0)	0 (0.0)	25 (75.8)	-	0 (0.0)
Reason:						
Hypovolemia/hemodynamic instability	21 (46.7)	3 (30.0)	0 (0.0)	10 (30.3)	-	0 (0.0)
Hypoxia	12 (26.7)	3 (30.0)	2 (100.0)	5 (15.2)	-	1 (50.0)
Thrombosis (coronary or pulmonary)	4 (8.9)	0 (0.0)	0 (0.0)	15 (45.5)	-	0 (0.0)
Hypo/hyperkalemia	2 (4.4)	1 (10.0)	0 (0.0)	0 (0.0)	-	0 (0.0)
Toxins	2 (4.4)	0 (0.0)	0 (0.0)	0 (0.0)	-	0 (0.0)
Cardiac tamponade	2 (4.4)	0 (0.0)	0 (0.0)	1 (3.0)	-	0 (0.0)
Tension pneumothorax	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	-	1 (50.0)
Other	1 (2.2)	3 (30.0)	0 (0.0)	2 (6.1)	-	0 (0.0)
Severe hypoxia (lowest SpO_2 < 80%), No. (%)	169 (10.8)	20 (6.4)	9 (11.0)	63 (7.8)	3 (9.1)	8 (7.3)
Secondary complications, No. (%)						
New onset cardiac arrhythmia	90 (5.7)	18 (5.4)	6 (7.3)	44 (5.4)	6 (18.2)	3 (2.7)
Atrial fibrillation	30 (33.3)	6 (33.3)	0 (0.0)	10 (22.7)	1 (16.7)	1 (33.3)
Ventricular tachycardia	17 (18.9)	2 (11.1)	1 (16.7)	19 (43.2)	2 (33.3)	0 (0.0)
Bradycardia	24 (26.7)	4 (22.2)	2 (33.3)	5 (11.4)	1 (16.7)	2 (66.7)
Other	19 (21.1)	6 (33.3)	3 (50.0)	10 (22.7)	2 (33.3)	0 (0.0)
Aspiration of gastric contents, No. (%)	61 (3.8)	13 (3.9)	3 (3.7)	24 (2.9)	11 (33.3)	4 (3.6)
Dental injury, No. (%)	12 (0.8)	1 (0.3)	0 (0.0)	11 (1.3)	3 (9.1)	1 (0.9)
Airway injury, No. (%)	4 (0.3)	7 (2.1)	1 (1.2)	6 (0.7)	2 (6.1)	1 (0.9)
Tracheal laceration	1 (25.0)	1 (14.3)	0 (0.0)	2 (33.3)	0 (0.0)	1(100.0)
Bronchial laceration	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)
Laryngeal laceration	2 (50.0)	1 (14.3)	1 (100.0)	1 (16.7)	2 (100.0)	0 (0.0)
Other	1 (25.0)	5 (71.4)	0 (0.0)	2 (33.3)	0 (0.0)	0 (0.0)
Pneumothorax, No. (%)	12 (0.8)	5 (1.5)	1 (1.2)	3 (0.4)	1 (3.0)	0 (0.0)
Pneumomediastinum, No. (%)	4 (0.3)	3 (0.9)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)

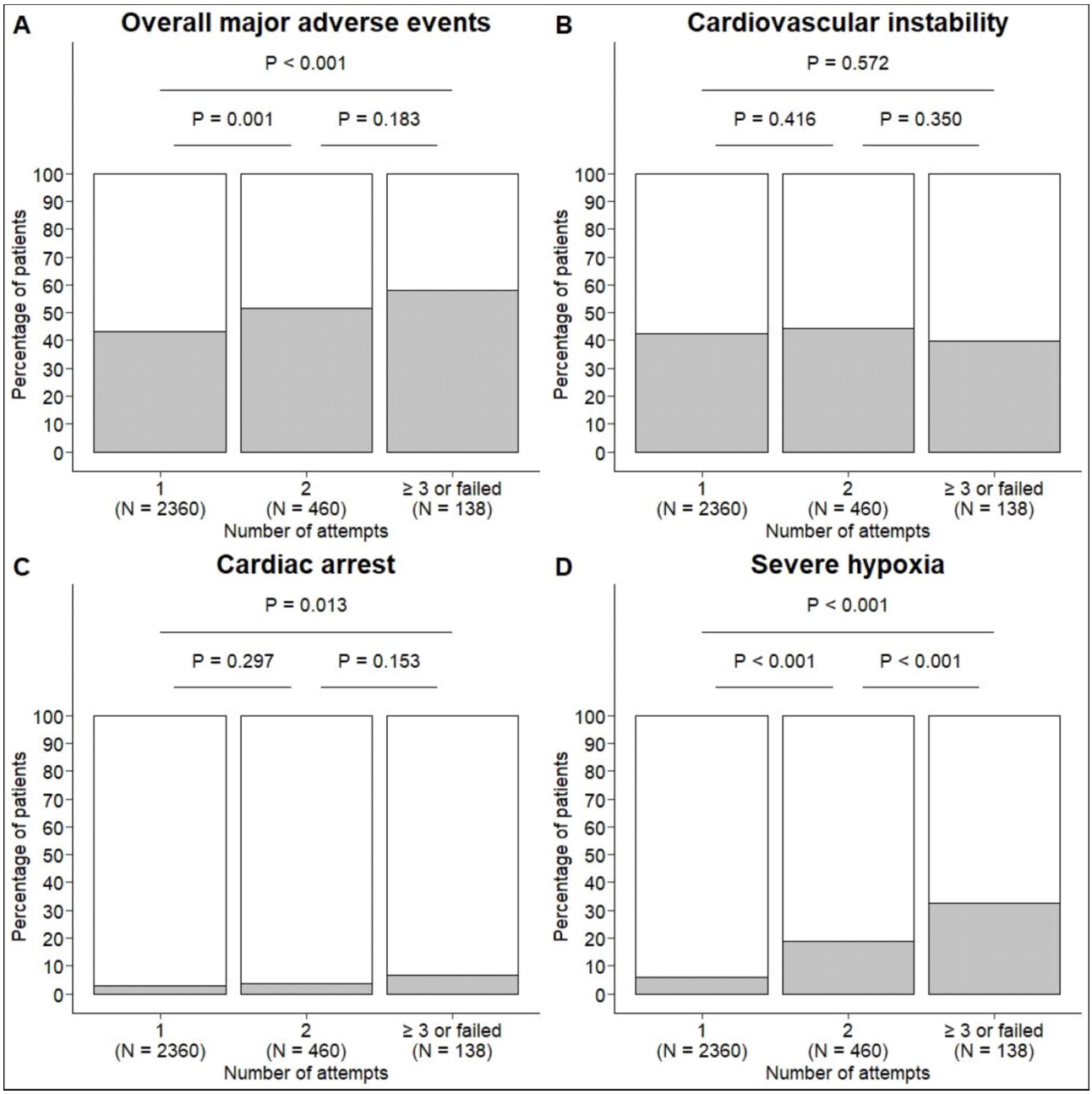
eTable 5. Missing values for the study outcomes.

Variable	Missing
Primary outcome (composite), No. (%)	0 (0.0)
Cardiovascular instability, No. (%)	211 (7.1)
Systolic blood pressure < 65 mmHg	11 (0.4)
Systolic blood pressure < 90 mmHg for > 30 minutes,	169 (5.7)
New need/increase of vasopressors	0 (0.0)
Fluid bolus > 15 ml/Kg	204 (6.9)
Cardiac arrest, No. (%)	0 (0.0)
Severe hypoxia (lowest SpO_2 < 80%), No. (%)	48 (1.6)
New onset cardiac arrhythmia	4 (0.1)
Aspiration of gastric contents, No. (%)	4 (0.1)
Esophageal intubation	5 (0.17)
Dental injury, No. (%)	4 (0.1)
Airway injury, No. (%)	5 (0.2)
Pneumothorax, No. (%)	1 (0.0)
Pneumomediastinum, No. (%)	4 (0.1)

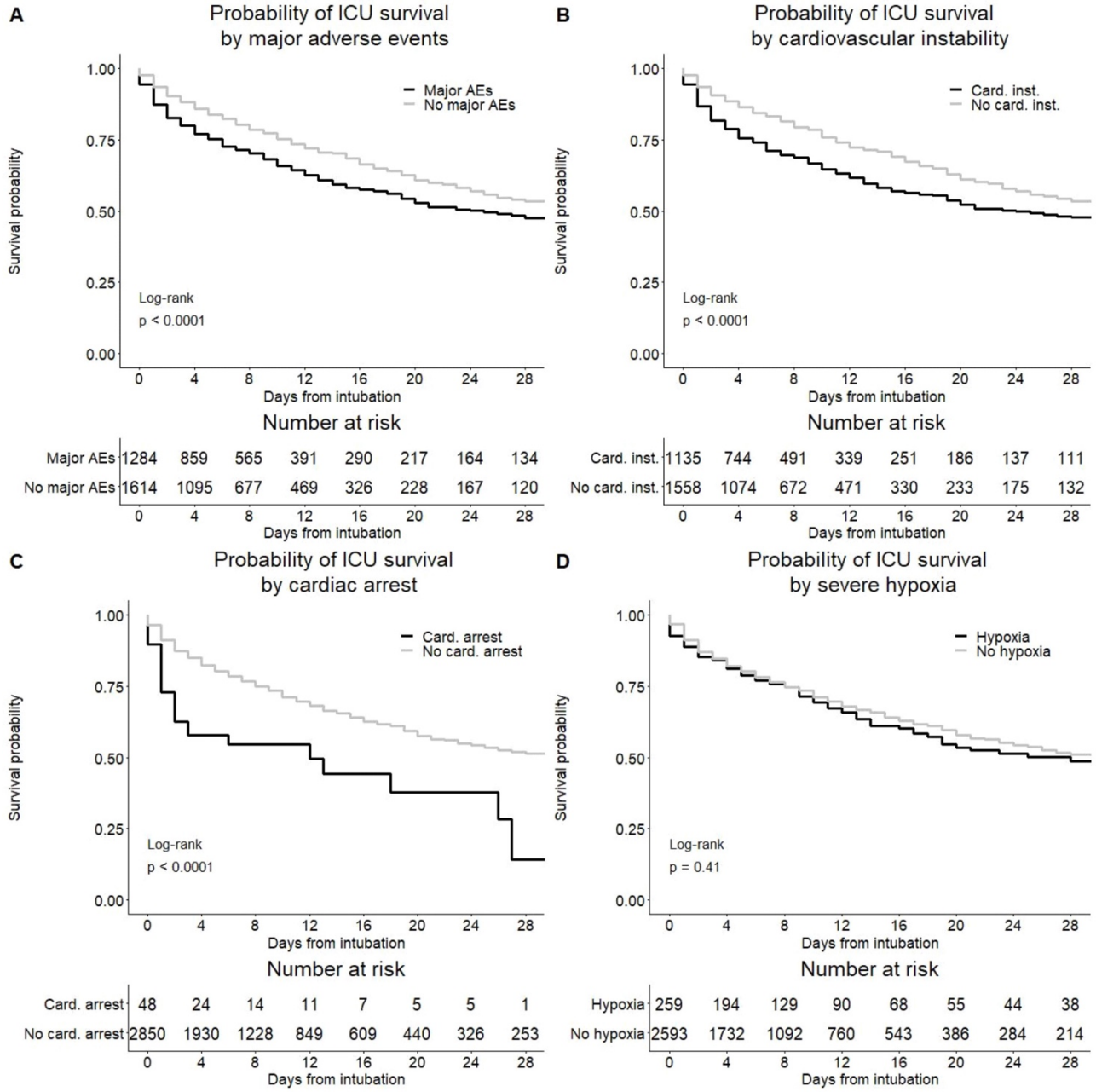
eFigure 1. Incidence of peri-intubation major adverse events and other peri-intubation events.



eFigure 2. Incidence of peri-intubation adverse events according to the number of attempts: A, overall major complications; B, cardiovascular instability; C, cardiac arrest and D, severe hypoxia.



eFigure 3. A, Kaplan-Meier survival curves by peri-intubation major adverse events. B, Kaplan-Meier survival curves by cardiovascular instability. C, Kaplan-Meier survival curves by cardiac arrest. D, Kaplan-Meier survival curves by severe hypoxia.



Abbreviations: AE, adverse events; card. arrest, cardiac arrest; card. inst., cardiovascular instability.

eTable 6. Multivariable analysis of organizational, operator and patient factors associated with major peri-intubation adverse events.

Variable	Major AEs, No./Total No. (%)	Absolute Difference (95% CI)[b]	Multivariable OR (95% CI)[a]	P-value
Age (years)	-	4.0 (2.0, 6.0)	1.012 (1.006, 1.019)	<.001
BMI				
Normal weight	546/1254 (43.5)	Reference	1 (Reference)	
Underweight	72/151 (47.7)	4.2 (-4.7, 12.9)	1.541 (0.947, 2.507)	.081
Overweight	403/895 (45.0)	1.5 (-2.9, 5.8)	0.963 (0.758, 1.225)	.761
Obese or severe obese	312/646 (48.3)	4.8 (-0.09, 9.6)	0.903 (0.691, 1.180)	.455
Heart failure				
No	1189/2700 (44.0)	Reference	1 (Reference)	
Yes	151/264 (57.2)	13.2 (6.7, 19.6)	1.523 (1.064, 2.182)	.022
Hematologic malignancy				
No	1249/2812 (44.4)	Reference	1 (Reference)	
Yes	91/152 (59.9)	15.5 (7.1, 23.8)	1.610 (1.013, 2.558)	.044
Systolic blood pressure (mmHg)	-	-18.9 (-21.4, -16.4)	0.991 (0.986, 0.995)	<.001
Diastolic blood pressure (mmHg)	-	-10.4 (-11.8, -8.9)	0.992 (0.983, 0.999)	.028
Heart rate	-	2.9 (1.0, 4.8)	1.006 (1.002, 1.010)	.006
Reason for intubation				
Neurological impairment	195/902 (32.7)	Reference	1 (Reference)	
Respiratory failure	778/1548 (50.3)	17.6 (13.5, 21.6)	1.111 (0.851, 1.450)	.438
Cardiovascular instability	178/277 (64.3)	31.6 (24.9, 38.2)	1.866 (1.218, 2.859)	.004
Other reason	86/233 (36.9)	4.2 (-3.0, 11.4)	1.104 (0.713, 1.710)	.658
Receiving vasopressor/inotropic support before intubation				
No	885/2195 (40.3)	Reference	1 (Reference)	
Yes	455/769 (59.2)	18.9 (14.7, 23.0)	0.919 (0.676, 1.251)	.593
Pleural effusion				
No	1122/2561 (43.8)	Reference	1 (Reference)	
Yes	218/403 (54.1)	10.3 (4.9, 15.7)	1.241 (0.930, 1.656)	.142
Patient position				
Supine	801/1884 (42.5)	Reference	1 (Reference)	
30-45° head-up position	333/642 (51.9)	9.4 (4.8, 13.9)	1.197 (0.902, 1.588)	.214
20° head-up position	130/284 (45.8)	3.3 (-3.2, 9.7)	1.137 (0.795, 1.627)	.482

Other position	75/151 (49.7)	7.2 (-1.5, 15.8)	1.139 (0.705, 1.842)	.595
Place of intubation				
ICU	968/1992 (48.6)	Reference	1 (Reference)	
Emergency department	231/623 (37.1)	-11.5 (-16.0, -7.0)	0.763 (0.568, 1.024)	.072
Ward	107/260 (41.2)	-7.4 (-14.0, -0.9)	0.726 (0.499, 1.056)	.094
Other place[c]	34/89 (38.2)	-10.4 (-21.3, 0.5)	0.547 (0.281, 1.064)	.075
Use of propofol				
No	817/1734 (47.1)	Reference	1 (Reference)	
Yes	523/1230 (42.5)	-4.6 (-8.3, -0.9)	1.142 (0.907, 1.438)	.259
Use of succinylcholine				
No	1068/2318 (46.1)	Reference	1 (Reference)	
Yes	272/646 (42.1)	-4.0 (-8.4, 0.4)	0.855 (0.652, 1.121)	.256
Full stomach				
No	1027/2297 (44.7)	Reference	1 (Reference)	
Yes	238/457 (52.1)	7.4 (2.2, 12.5)	1.392 (1.040, 1.863)	.026
First pass success				
No	317/598 (53.0)	Reference	1 (Reference)	
Yes	1020/2360 (43.2)	-9.8 (-14.4, -5.2)	0.587 (0.455, 0.758)	<.001
No of ICUs	-	-0.2 (-0.4, -0.0)	0.941 (0.881, 1.005)	.071
Total ICU beds				
< 10	126/252 (50.0)	Reference	1 (Reference)	
10-20	361/768 (47.0)	-3.0 (-10.4, 4.4)	0.776 (0.480, 1.253)	.299
> 20	853/1944 (43.9)	-6.1 (-12.9, 0.7)	0.877 (0.542, 1.419)	.593
Frequency of emergency intubations/week	-	-1.0 (-1.0, 0.0)	0.984 (0.963, 01.006)	.156
Field of training				
Other field	620/1361 (45.6)	Reference	1 (Reference)	
Anesthesia and Intensive Care	719/1601 (44.9)	-0.7 (-4.3, 3.0)	0.929 (0.732, 1.177)	.541
Adjusted SOFA	-	2.0 (1.2, 2.0)	1.015 (0.985, 1.047)	.325
MACOCHA score[d]				
< 3	1118/2538 (44.1)	Reference	1 (Reference)	
≥ 3	222/426 (52.1)	8.0 (2.8, 13.3)	1.234 (0.920, 1.657)	.160
SpO_2 at the end of preoxygenation	-	-1.0 (-2.0, -1.0)	0.994 (0.985, 1.004)	.247
Laryngoscopy				
Direct with Macintosh or Miller blade	1082/2416 (44.8)	Reference	1 (Reference)	
Videolaryngoscopy	245/505 (48.5)	3.7 (-1.2, 8.6)	1.358 (1.004, 1.838)	.047
Fluid bolus 30 min before intubation				

No	731/1762 (41.5)	Reference	1 (Reference)	
Yes	554/1065 (52.0)	10.5 (6.7, 14.4)	1.257 (1.005, 1.572)	.045
SpO_2 / FiO_2[c]	-	-38.5 (-48.7, -28.0)	0.998 (0.997, 0.999)	<.001

Abbreviations: AEs, adverse events; ICU, intensive care unit.
[a]Model performed with 2015 patients with complete variables and SpO2< 98%.
[b] 95% bootstrap confidence interval with 10000 replicates calculated on the difference of the median values and 95% confidence interval calculated on the difference of the mean values.
[c]With *other place* it was indicated in most cases cardiology, radiology, endoscopy and other interventional rooms.
[d]MACOCHA score is a predictive score of difficult intubations in intensive care unit. Its calculation includes the following items: Mallampati score III – IV (5 points), obstructive sleep apnea syndrome (2 points), reduced mobility of the cervical spine (1 point), limited mouth opening < 3 cm (1 point), coma (1 point), severe hypoxemia (1 point), non-anesthesiologist operator (1 point). It ranges from 0 (easy intubation) to 12 (very difficult intubation).

eTable 7. Multivarible analysis of patient and operator factors associated with first pass intubation failure.

Variable[a]	Multivariable OR (95% CI)	P-value
Short neck	1.310 (0.945, 1.816)	.105
Mallampati III-IV	1.553 (1.035, 2.332)	.034
Reduced mouth opening	2.273 (1.559, 3.314)	<.001
Retrognatia	1.813 (0.939, 3.503)	.076
Neck stiffness	2.011 (1.308, 3.092)	.001
Need of cervical spine immobilization	1.634 (0.879, 3.040)	.121
Beard	1.772 (1.123, 2.794)	.014
High risk of full stomach	1.397 (1.039, 1.878)	.027
Large tongue	1.500 (0.903, 2.494)	.117
Other difficulties	1.906 (1.128, 3.219)	.016
Prognatism	1.711 (0.444, 6.583)	.435
Facial trauma	0.674 (0.260, 1.747)	.417
Past surgery/radiotherapy[b]	6.830 (2.717, 17.170)	<.001
BMI		
Normal weight	1 (Reference)	
Underweight	0.670 (0.392, 1.147)	.144
Overweight	0.902 (0.698, 1.167)	.433
Obese or severe obese	1.055 (0.784, 1.418)	.725
Laryngoscopy		
Direct with Macintosh or Miller blade	1 (Reference)	
Videolaryngoscopy	0.597 (0.421, 0.847)	.004
Field of training		
Other field	1 (Reference)	
Anesthesia and Intensive Care	0.533 (0.411, 0.691)	<.001
Operator performing the first attempt		
Other operator	1 (Reference)	
Staff Physician/Consultant	0.525 (0.397, 0.694)	<.001
Place of intubation		
ICU	1 (Reference)	
Emergency department	1.045 (0.771, 1.416)	.779
Ward	1.110 (0.729, 1.689)	.627
Other place	0.686 (0.311, 1.513)	.350
Degree of emergency of intubation		
No delay	1 (Reference)	
< 1 hour	1.276 (1.002, 1.626)	.049
≥ 1 hour	1.007 (0.703, 1.442)	.971

[a]Model performed with 2659 patients with complete variables.

[b]Surgery or radiotherapy performed on neck/airways.

eTable 8. Adjusted ICU mortality.[a]

Variable	Multivariable OR (95% CI)	P-value
Major adverse events	**1.517 (1.262, 1.825)**	**<.001**
Age (years)	1.025 (1.018, 1.031)	<.001
Sex		
Female	1 (Reference)	
Male	0.973 (0.807, 1.172)	.773
Heart failure	1.322 (0.963, 1.816)	.085
Hematologic malignancy	3.281 (2.223, 4.842)	<.001
Ischemic heart disease	1.162 (0.895, 1.510)	.260
Solid neoplasm	1.656 (1.262, 2.174)	<.001
SOFA[a]	1.136 (1.111, 1.162)	<.001

Abbreviations: SOFA, sequential organ failure assessment.

[a]Model performed with 2899 patients with complete variables (mixed model with a random intercept for the site)

[b]SOFA score was calculated with values last available before intubation. For all SOFA scores for which data points were missing, the corresponding value and omitted and the denominator adjusted accordingly.

eTable 9. Adjusted mortality at 28 days after intubation.[a]

Variable	Multivariable OR (95% CI)	P-value
Major adverse events	**1.438 (1.191, 1.735)**	**<.001**
Age (years)	1.023 (1.017, 1.029)	<.001
Sex		
Female	1 (Reference)	
Male	0.974 (0.805, 1.178)	.784
Heart failure	1.381 (1.002, 1.902)	.049
Hematologic malignancy	3.175 (2.155, 4.677)	<.001
Ischemic heart disease	1.188 (0.911, 1.548)	.204
Solid neoplasm	1.732 (1.315, 2.282)	<.001
SOFA score[a]	1.136 (1.111, 1.162)	<.001

Abbreviations: SOFA, sequential organ failure assessment.

[a]Model performed with 2899 patients with complete variables (mixed model with a random intercept for the site)

[b]SOFA score was calculated with values last available before intubation. For all SOFA scores for which data points were missing, the corresponding value and omitted and the denominator adjusted accordingly.

eAppendix 1. List of endorsing Scientific Societies/Networks endorsing the study (alphabetical order):

- Australian and New Zealand Intensive Care Society Clinical Trials Group (ANZICS CTG)
- Dutch Society of Intensive Care (NVIC)
- European Airway Management Society (EAMS)
- European Society of Intensive Care Medicine (ESICM)
- Hellenic Society of Cardiopulmonary Resuscitation
- Indian Society of Critical Care Medicine (ISCCM)
- Irish Critical Care – Clinical Trials Network (ICC - CTN)
- Protective Ventilation (Prove) Network
- Russian Federation of Anesthesiologists and Reanimatologists (FAR)
- Società Italiana Anestesia Analgesia Rianimazione e Terapia Intensiva (SIAARTI) – Gruppo di Studio Vie Aeree
- Society of Critical Care Medicine (SCCM) – Discovery Critical Care Research Network

eAppendix 2: National Coordinators of INTUBE Study.

Australia and New Zeland: David Brewster; **Canada:** Matteo Parotto; **France:** Jean Bapstiste Lascarrou; **Germany**: Kristaps Bokums; **Greece:** Athanasios Chalkias **; India**: Sheila Nainan Myatra **Ireland:** John Laffey; **Italy:** Vincenzo Russotto; **Libya**: Muhammed Elhadi; **Poland**: Konstanty Szułdrzyński; **Russia**: Alexander Andreenko; **Sweden:** Christina Agvald Öhman; **United Kingdom**: Luigi Camporota, Andy Higgs; **US:** Philippe Bauer.

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Statisticians: Elena Tassistro (University of Milan – Bicocca, Monza, Italy), Laura Antolini University of Milan – Bicocca, Monza, Italy).

Site investigators by country

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CHILE

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INDIA

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eAppendix 4. Study protocol

INternational observational study To Understand the impact and BEst practices of airway management in critically ill patients

Study acronym identifier: INTUBE

Trial registration: clinicaltrials.gov Identifier: NCT03616054

Steering committee:

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Rationale

Tracheal intubation in critically ill patients is a potentially life-threatening procedure and approximately one-third of intubations are complicated by severe hypoxia, cardiovascular collapse and cardiac arrest [1,2]. Critically ill are prone to severe complications as the consequence of the underlying acute respiratory failure or hemodynamic instability, reduced oxygen stores and increased oxygen consumption [1,3]. Moreover, the rate of difficult airway management may be higher in the intensive care unit (ICU) and in the Emergency Department, prolonging the apnea time and the risk of desaturation [4]. Finally, operator's skills, procedures, devices and drugs, among others, may influence airway management success and patient's outcome [5]. Despite the high risk of the procedure, different interventions lack high-quality evidence and we hypothesize that a heterogeneous practice among different centers and geographical areas may be found [6,7].
The primary aim of our study is to evaluate the incidence of intubation-related adverse events in critically ill patients. Secondary aim is to evaluate current clinical practices on airway management in the in-hospital critical care setting.

METHODS

Study design
Prospective observational multi–center international cohort study.

Recruitment

We aim at recruiting for participation both academic and non-academic hospitals worldwide. We launched a website: www.intubestudy.com where we will publish study information and documents (e.g. protocol, case report form, national coordinator list) which will be available for potentially interested investigators. From the website, it will be possible to complete a form for center and local coordinator(s) data collection. The project will be presented and a call for centers will be announced during international meetings of intensive care. We will also apply for receiving the endorsement of international scientific societies in order to promote and enhance participation to this study.

Inclusion criteria
We will include all adult (≥ 18 years old) critically ill patients undergoing intubation during the period of observation. We will consider all in-hospital intubations. We will define critically ill those patients with a life-threatening condition requiring intubation for either respiratory failure or airway protection.

Exclusion Criteria
• Intubation performed in the out-of-hospital setting
• Intubation in patients with cardiac arrest
• Intubation performed only for anesthesia (during either diagnostic/endoscopic or surgical procedures)

Primary outcome
At least one of the following (composite outcome):
• Severe hypoxemia (SpO_2 < 80%) occurring within 30 minutes from intubation
• Cardiac arrest occurring within 30 minutes from intubation
• Cardiovascular collapse (at least one of the following), occurring within 30 minutes from intubation:
- Systolic blood pressure < 65 mmHg recorded 1 time
- Systolic blood pressure < 90 mmHg for > 30 minutes
- New need of vasopressors/their increase and/or fluid bolus > 15 ml/kg to maintain the target blood pressure.

Secondary outcomes
• Difficult intubation (> 2 laryngoscopy attempts)
• Cannot intubate cannot oxygenate scenario (CICO)
• Emergency front of neck airway (FONA)
• Cardiac arrhythmia occurring within 30 minutes from intubation
• Aspiration of gastric contents (time frame: 24 hours)
• Esophageal intubation
• Pneumothorax/pneumo-mediastinum (time frame: 24 hours)
• Dental injury (time frame: 24 hours)
• Airways injury (time frame: 24 hours)
• Mortality at ICU-discharge

Data collection

We will collect the following information:
• Informed consent and admission data
• Demographic and clinical characteristics
• Monitoring applied during the procedure
• Reason for intubation/re-intubation
• Ongoing respiratory support before intubation (standard nasal cannula, high-flow nasal cannula, facemask O_2, Venturi system, CPAP, noninvasive positive pressure ventilation)
• Patient's parameters and gas exchange (last available before preoxygenation start): (arterial pressure, heart rate, SpO_2, vasopressor use, need of fluids administration and total volume, blood gas analysis, GCS, urine output, electrolytes, creatinine and bilirubin levels)
• Chest X-ray findings (if available)
• Operator's specialty, training level and number of tracheal intubations performed in a week (for both the operator performing the first and the operator of the successful attempt of intubation, if different)
• Characteristics of intubation (anticipated difficult airway management, degree of emergency)
• Intubation procedure (position during preoxygenation, rapid sequence induction)
• Preoxygenation method and use of apneic oxygenation
• SpO_2 at the end of preoxygenation
• Drugs used for induction (molecules and dosages)
• Elective method for laryngoscopy
• Method used for the successful attempt
• Method used for adequate tube placement confirmation
• Duration of laryngoscopy
• Total number of attempts, laryngoscopy view, failed intubation and rescue strategy
• Lowest SpO_2 registered during the procedure, lowest systolic and diastolic blood pressures within 30 minutes from intubation, new start of vasopressors/inotropes or their increase within 30 minutes from intubation, cardiac arrest within 30 minutes from intubation)
• Any supraventricular/ventricular arrhythmia (within 30 minutes from intubation), aspiration of gastric contents (detected during the first 24 hours), esophageal intubation, dental injury (detected during the first 24 hours), airway injury and pneumothorax/pneumomediastinum (detected during the first 24 hours).
• Status at ICU discharge (dead, alive, transferred).

Local investigators are expected to transcribe all collected data into an electronic CRF (eCRF, Research Electronic Data Capture – RedCap). Each local investigator will be trained on how to use the eCRF and will receive a personalized username and password. Each patient will be coded through a patient identification number generated by the eCRF and no patient names or initials will be present on the paper CRF. Data will be handled confidentially and the paper CRF will be stored behind a lock at each local site. Any source of information which may allow to link a record with a patient will be destroyed at the end of the monitoring phase.

Sample size

Our aim is to collect data from at least 1000 major adverse events from airway management. The reported incidence of at least one major intubation-related complication (severe hypoxia, hemodynamic collapse, cardiac arrest) is approximately 28% [1]. Therefore, we plan to collect data from 3600 intubations. Intubation rate may vary from 0.5 to 2 tracheal intubations/day according to different centers (e.g. total hospital beds, number of ICUs and ICU beds) and local policies. In order to avoid over representation from centers with a higher admission rate, the total number of enrolled patients was limited to the first 20 consecutive cases during an 8-week observation period. A maximum time window of 8 weeks will be allowed for each center. Each center will select a start date for recruitment from 1 October to 31 July 2019. We plan to recruit at least 180 centers worldwide to achieve our sample goal.

Statistical analysis

We will report mean and standard deviation of normally distributed variables and we will compare them using the student T-test. We will report non-normally distributed variables as median and interquartile range, comparing them using the Mann-Whitney U test.
Categorical variables will be expressed as proportion and compared using the Chi-square or Fisher exact test as appropriate. We will perform a univariable analysis to identify variables associated with the composite outcome of major intubation-related complication and significant variables will be then used to construct a multivariable logistic model in order to identify independent variables. A two-sided p-value < 0.05 will be considered statistically significant.

Publication and authorship policy

The main results of INTUBE study will be published in a peer–reviewed international medical journal. Authorship policy will follow the International Committee of Medical Journal Editors (ICMJE) recommendations. Authorship will be considered based on contributions to recruitment of patients, data acquisition and cleaning, analysis and interpretation of the data, manuscript writing, submission of national/local grants AND final approval of the version to be published AND agreement to be accountable for all aspects of the work, in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Members of the Steering Committee will be part of the Writing Committee and listed as Authors. National Coordinators and particularly committed investigators fulfilling the previously exposed criteria will be part of the Writing Committee. Each center will designate a maximum of two local coordinators who will provide scientific and structural leadership in their centers. They will ensure that all local necessary ethical and regulatory approvals are obtained before start of patient inclusion. Local coordinators will guarantee the integrity of data collection and ensure timely completion of CRFs. Local coordinators will be listed as study collaborators.

Secondary analyses

After publication of the primary results, on request, the pooled dataset will be available for all investigators for secondary analyses, after judgment and approval of scientific quality and validity by the Steering Committee.
Before submission, the final version of all manuscripts related to the INTUBE study dataset must be approved by the Steering Committee. The members of the Writing Committee will be authors of the publications derived from the INTUBE study dataset.

eReferences

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eAppendix 5. Case report form.

INternational observational study To Understand the impact and BEst practices of airway management in critically ill patients

Study acronym identifier: INTUBE

CASE REPORT FORM

SITE INFORMATION (to be completed only with screening of the 1st patient)

Centre ID number: _____
Local Principal Investigator's first name _____
Local Principal Investigator's last name_____
Local (2nd) Investigator's first name_____
Local (2nd) Investigator's last name_____

Type of hospital
☐ Academic/University
☐ Non academic
Is your hospital a trauma centre (i.e. referral centre for trauma in your geographical area)?
☐ YES
☐ NO
Is a Medical Emergency Team (MET) present in your hospital?
(A team alerted in case of deterioration of one or more vital sign)
☐ YES
☐ NO
Is a protocol for airway management in critically ill patients present in your hospital?
☐ YES
☐ NO
Is an emergency airway management checklist present in your hospital?
☐ YES
☐ NO
Is a difficult airway trolley routinely present in your hospital (at the intubation site)?
☐ YES
☐ NO
How many intensive care units (ICUs) do you have in your hospital? _____
How many (total) ICU beds do you have in your hospital? _____
How many endotracheal intubations in critically ill patients are approximately performed in your hospital (ICU, ED, ward areas) in a week? _____

SCREENING

Inclusion criteria

Is patient's age equal or higher than 18 years?

- ☐ YES
- ☐ NO

Is the patient critically ill?
(i.e. with a life-threatening condition requiring endotracheal intubation for cardio-respiratory failure and/or airway protection)

- ☐ YES
- ☐ NO

Was the patient intubated in hospital?

- ☐ YES
- ☐ NO

Exclusion criteria

Was the patient intubated ONLY for receiving general anethesia?
(e.g. general anesthesia for scheduled major surgery)

- ☐ YES
- ☐ NO

Was intubation performed for cardiac arrest?

- ☐ YES
- ☐ NO

If all the criteria were met, is the patient finally enrolled in the study?

- ☐ YES
- ☐ NO

    If NO, reasons for not enrolment:

    - ☐ Local investigator not present during the event
    - ☐ Treating physician’s decision
    - ☐ Lack of any form of required informed consent
    - ☐ Other, specify _____

1. ENROLLMENT

Patient's ID number: _____
Date of hospital admission: _____(DD)/_____(MM)/_____(YY)
Date of intubation: _____(DD)/_____(MM)/_____(YY)
Time of intubation: (HH:MM) _____: _____ am ☐ pm ☐
Informed consent required? YES ☐ NO ☐ (Choose no if waived by local EC)
If required, was consent obtained? YES ☐ NO ☐
If yes, date of informed consent: _____/_____/_____

2. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

Sex: M☐ F☐ Birth year:_____ Age: _____
Height: _____ inch ☐ cm ☐ Weight: _____ lbs ☐ Kg ☐
Comorbidities (check all that apply):
☐ Asthma
☐ COPD
☐ Diabetes Mellitus
☐ Solid neoplasm
☐ Metastatic ☐ Non-metastatic ☐ Unknown
☐ Hematologic malignancy
☐ Heart failure (NYHA III-IV)
☐ Ischemic heart disease
☐ Arterial hypertension
☐ Renal failure
☐ Chronic liver failure
☐ Neuromuscular disease
☐ OSAS (with use of nocturnal CPAP ☐; without use of nocturnal CPAP ☐)
☐ Interstitial lung disease
☐ Respiratory infection < 30 days ago
☐ Other, please specify_____
☐ None

3. INTUBATION SETTING

Place of intubation
☐ Intensive Care Unit (ICU)
☐ Emergency Department (ED)
☐ Ward areas
☐ Other, specify _____

Did you transfer the patient from another place to perform intubation?
YES ☐ NO ☐

For intubation performed in the ICU:
Admission source:
☐ Emergency Department (ED)
☐ Medical ward
☐ Surgical Ward
☐ Operating room/recovery room
☐ Other ICU from the same hospital
☐ Other hospital
☐ Other, please specify: _____

For intubation performed in the ED:
Admission source:
☐ Emergency Medical Service/Helicopter Emergency Medical Service
☐ Home (with private vehicle transport)
☐ Long-term care facility
☐ Other hospital
☐ Other, please specify: _____

For intubation performed in a ward:
Please specify if ☐ medical ward ☐ surgical ward
Admission source:
☐ Emergency Department
☐ Other ward
☐ Operating room
☐ ICU
☐ Other, please specify_____

Has the patient been previously intubated during THIS hospital admission?
☐ YES
☐ NO

MAIN Reason for new intubation (check the main reason):
☐ Respiratory failure
☐ Airway obstruction
☐ Cardiovascular instability
☐ Neurological impairment

☐ Other, specify _____

In case of reintubation:
Specify the date of extubation: _____/_____/_____
Extubation performed in operating room? ☐ YES ☐ NO
MAIN reason for reitubation (check the main reason):
☐ Respiratory failure
☐ Airway obstruction
☐ Cardiovascular instability
☐ Self – extubation
☐ Neurological impairment
☐ Inadequate reversal of neuromuscular block
☐ Other, specify _____

Degree of emergency of endotracheal intubation (ETI)
☐ Intubation required without any delay
☐ Intubation required in < 1 hour
☐ Intubation required in ≥ 1 hour

Anticipated ("anatomical") difficult airway management?
☐ YES
☐ NO
☐ Evaluation not performed

Predictors of difficult airway management
☐ Mallampati score III-IV
☐ Reduced mouth opening (< 3 cm)
☐ Short neck
☐ Neck stiffness
☐ Facial trauma
☐ Need of cervical spine immobilization
☐ High-risk of full stomach
☐ Prognathism (abnormal anterior position of the mandible)
☐ Retrognathia (abnormal posterior position of the mandible)
☐ Large tongue
☐ Beard
☐ Obesity
☐ Other, specify _____

4. PATIENT'S PARAMETERS BEFORE INTUBATION

Systolic blood pressure (last available before preoxygenation start):
_____mmHg

Diastolic blood pressure (last available before preoxygenation start):
_____mmHg

Heart rate (last available before preoxygenation start):_____/min

Respiratory rate (last available before preoxygenation start: _____/min

SpO_2 % (last available before preoxygenation start): _____%

Body temperature available (last available before preoxygenation start) ☐ YES ☐ NO
Body temperature: _____ ☐ °C ☐ °F

Need of vasopressor/inotrope support? (before preoxygenation start)
☐ YES ☐ NO
Specify all inotropes/vasopressors that apply:
☐ Norepinephrine; rate of infusion: _____mcg/Kg/min
☐ Epinephrine; rate of infusion: _____ mcg/Kg/min
☐ Dopamine; rate of infusion: _____ mcg/Kg/min
☐ Dobutamine; rate of infusion: _____ mcg/Kg/min
☐ Other; please specify:_____rate of infusion:_____ mcg/Kg/min
Fluid load administered in the last 30 minutes before intubation?
YES ☐ NO ☐
Specify total volume _____ ml

Arterial blood gas analysis available? (last available before preoxygenation start)?
YES ☐ NO ☐
Specify F_iO_2 % _____%
PaO_2 _____☐ mmHg ☐ kPa
$PaCO_2$ _____☐ mmHg ☐ kPa
PH _____
HCO_3^- (mEq/L - mmol/L)_____
Base excess (BE)_____
Lactate (mmol/L)_____

Ongoing respiratory support (e.g. O_2, CPAP, NIV BEFORE start of preoxygenation)?
YES ☐ NO ☐
Type of respiratory support
☐ Standard oxygen
☐ High flow nasal cannula (HFNC)
☐ Continuous positive airway pressure (CPAP)
☐ Noninvasive positive pressure ventilation (NPPV)

Is the patient receiving oxygen before intubation?
YES ☐ NO ☐

If yes, please specify the oxygen flow: _____L/min

And the delivery system:

☐ Nasal cannula

☐ High-flow nasal cannula (Specify total flow_____L/min; Specify FiO_2:_____%)

☐ Facemask

☐ with O_2 reservoir ☐ without O_2 reservoir

☐ Venturi system (Specify O_2 flow_____L/min; Specify FiO_2: _____%)

☐ Other, please specify _____

Is the patient receiving CPAP?
YES ☐ NO ☐

If yes, specify the CPAP level: _____cmH_2O

Specify the FiO2: _____%

Specify the interface:

☐ Helmet

☐ Oronasal

☐ Full face

☐ Nasal

☐ Other, please specify_____

Is the patient receiving NPPV?
YES ☐ NO ☐

If YES, please specify the pressure support administered: PS_____cmH_2O

Specify the PEEP level: _____ cmH_2O

Specify the FiO_2: _____%

Specify the interface:

☐ Helmet

☐ Oronasal

☐ Full face

☐ Nasal

☐ Other, please specify_____

Glasgow Coma Scale
Eye opening response: _____ (1-4)
Best verbal response: _____(1-5)
Best motor response: _____(1-6)

Laboratory data (last available before preoxygenation start)

White blood cell available?
YES ☐ NO ☐

If YES, specify _____ ($\times 10^3/\mu l$)

Platelet count available?
YES ☐ NO ☐

If YES, specify _____ ($\times 10^3/\mu l$)

Bilirubin level available?
YES ☐ NO ☐
If YES, specify _____ μmol/L☐ mg/dL☐
Creatinine level available?
YES ☐ NO ☐
If YES, specify _____μmol/L☐ mg/dL☐

BUN level available?
YES ☐ NO ☐
If YES, specify _____ μmol/L☐ mg/dL☐

Sodium level available?
YES ☐ NO ☐
If YES, specify _____mEq/L - mmol/L

Potassium level available?
YES ☐ NO ☐
If YES, specify _____mEq/L – mmol/L

Chest X-ray or CT scan available?
YES ☐ NO ☐
If YES, Chest X-ray or CT scan findings (check all that apply):
☐ Normal lung fields
☐ Pleural effusion
☐ Monolateral lung opacity
☐ Bilateral lung opacities
☐ Pulmonary contusion
☐ Rib fracture(s)
☐ Pneumothorax
☐ Hemothorax
☐ Other, please specify: _____

5. INTUBATION PROCEDURE

Preparation

Did you apply the protocol for airway management of critically ill patients of your hospital?
☐ YES
☐ NO
☐ Not available

Did you perform the emergency airway checklist of your institution?
☐ YES
☐ NO
☐ Not available

Was a difficult airway trolley present in your institution (at the intubation site)?
☐ YES
☐ NO
☐ Not available

Monitoring selected during the intubation procedure (check all that apply):
☐ ECG (3 or 5 leads)
☐ SpO_2
☐ Noninvasive blood pressure
☐ Invasive blood pressure
☐ Waveform capnography
☐ Capnometry
☐ Other _____

Preoxygenation

Preoxygenation START time
(specify the precise time in terms of hours and minute, i.e. 10:32)
_____:_____ (HH:MM)

Patient position during preoxygenation
☐ Supine position
☐ Beach chair position
☐ 20° head-up position
☐ 30 – 45° head-up position
☐ Ramp position
☐ Trendelemburg position
☐ Reverse Trendelemburg position
☐ Other, please specify: _____

Elective method of preoxygenation
Device used for preoxygenation:
☐ Bag valve mask.
O_2 flow _____ L/min. O_2 reservoir available YES ☐ NO ☐

☐ Standard facemask

O_2 flow _____ L/min. O_2 reservoir available YES ☐ NO ☐

☐ Venturi mask

O_2 flow _____ L/min. FiO_2 _____%

☐ Nasal cannula (standard)

O_2 flow _____ L/min

☐ High-flow oxygen nasal cannula

Total flow _____L/min. FiO_2 _____%

☐ CPAP

CPAP level _____cmH_2O. FiO_2 _____%

Specify the interface:

☐ Helmet

☐ Oronasal

☐ Full face

☐ Nasal

☐ Other, please specify_____

☐ NPPV

PS _____cmH_2O. PEEP_____cmH_2O. FiO_2 _____%

Specify the interface:

☐ Helmet

☐ Oronasal

☐ Full face

☐ Nasal

☐ Other, please specify_____

☐ Other, please specify_____

O_2 _____L/min

Specify SpO_2 at the end of preoxygenation for the first attempt: _____%

Oxygen administration during laryngoscopy/fiberoscopy (apneic oxygenation)?

☐ YES ☐ NO

If YES, please specify the method:

☐ Standard nasal cannula

☐ High flow nasal cannula (HFNC)

☐ Facemask (with fiberoptic port)

☐ Helmet (with fiberoptic port)

☐ Other _____

Drugs

Rapid sequence induction applied? (avoidance of positive pressure ventilation between induction and laryngoscopy, rapid onset muscle relaxant use)

YES ☐ NO ☐

Drugs used (check all that apply):

☐ Awake intubation

☐ Lidocaine spray

☐ Propofol _____ mg

☐ Thiopental_____mg

☐ Midazolam _____ mg
☐ Ketamine _____ mg
☐ Etomidate _____ mg
☐ Succinilcoline _____ mg
☐ Rocuronium _____ mg
☐ Vecuronium _____ mg
☐ Cisatracurium _____ mg
☐ Fentanyl _____ ☐ mg ☐ μg
☐ Remifentanil _____ ☐mg ☐ μg
☐ Sufentanil _____ ☐mg ☐ μg
☐ Alfentanil _____☐ mg ☐ μg
☐ Morphine _____mg
☐ Others, please specify: _____

Laryngoscopy and endotracheal intubation

1st laryngoscopy START time
(specify the precise time in terms of hours and minute, i.e. 10:32)
_____:_____(HH:MM)

Cricoid pressure applied?
☐ YES ☐ NO

Elective method/device for laryngoscopy
☐ Direct laryngoscopy with Macintosh blade
☐ Direct laryngoscopy with Miller blade
☐ Videolaryngoscopy
    ☐ Macintosh – type blade ☐ Hyperangulated blade
☐ Fiberoptic
    ☐ standard ☐ through the CPAP/NIV interface ☐ through a supraglottic airway
    ☐Other, specify _____

Use of any intubation adjunct (e.g. bougie, stylet) for the first attempt
☐ YES ☐ NO
    If yes:
    ☐ Bougie
    ☐ Stylet
    ☐ Other, specify _____

Total number of laryngoscopy attempts _____
(laryngoscope in - laryngoscope out from patient's month)

Endotracheal intubation finally obtained? ☐ YES ☐ NO

Type of intubation ☐Orotracheal ☐ Nasotracheal

Esophageal intubation during at least 1 attempt? ☐ YES ☐ NO

Preoxygenation performed between multiple larygoscopic attempts? ☐ YES ☐ NO

Successful method/device for laryngoscopy
☐ Direct laryngoscopy with Macintosh blade
☐ Direct laryngoscopy with Miller blade
☐ Videolaryngoscopy
☐ Macintosh – type blade ☐ Hyperangulated blade
☐ Fiberoptic
☐ standard ☐ through the CPAP/NIV interface ☐ through a supraglottic airway
☐Other, specify _____

Use of any intubation adjuct (e.g. bougie, stylet) for the successful attempt
☐ YES ☐ NO
If yes:
☐ Bougie
☐ Stylet
☐ Other, specify _____

END of last laryngoscopy time (i.e confirmed endotracheal intubation)
(specify the precise time in terms of hours and minute, i.e. 10:32)
_____:_____(HH:MM)

Laryngoscopic view (Cormack - Lehane)
☐ I
☐ II
☐ III
☐ IV
Lowest SpO_2 % value registered during the whole procedure (1st or following attempts)
_____%

First method used to confirm endotracheal intubation:
☐ Waveform capnography
☐ Capnometry
☐ Colorimetric CO_2 detection
☐ Auscultation
☐ Chest X-ray
☐ Fiberoscopy
☐ None
☐ Other, please specify _____

What did happen after the failed intubation? (Specify the last event/intervention)
☐ Supraglottic airway insertion
☐ Cricothyroidotomy
☐ Percutaneous tracheostomy
☐ Surgical tracheostomy
☐ Cannot intubate cannot oxygenate scenario
☐ Other_____

Operator's training

Specify total number of operators involved in the procedure and qualified to perform of intubation
_____

Operator performing the 1st attempt
☐ Medical student
☐ Resident
☐ Fellow
☐ Staff physician/consultant
☐ Other _____

Specify the field of training of the operator performing the 1st attempt:
☐ Anesthesia and Intensive Care
☐ Critical Care/Intensive Care
☐ Emergency Medicine
☐ Internal Medicine
☐ Pulmonary Medicine
☐ Pulmonary and Critical Care Medicine
☐ Surgery
☐ Other _____

N° intubation(s)/week of the operator performing the 1st attempt:
☐ ≤ 1 intubation/week
☐ 2 -5 intubations/week
☐ 6 – 10 intubations/week
☐ 11 – 20 intubations/week
☐ > 20 intubations/week

Is the operator performing the successful attempt the same as the operator performing the 1st attempt?
☐ YES ☐ NO
Operator performing the successful attempt:
☐ Medical student
☐ Resident
☐ Fellow
☐ Staff physician/consultant
☐ Other _____

Specify the field of training of the operator performing the successful attempt:
☐ Anesthesia and Intensive Care
☐ Critical Care/Intensive Care
☐ Emergency Medicine
☐ Internal Medicine
☐ Pulmonary Medicine
☐ Pulmonary and Critical Care Medicine
☐ Surgery
☐ Other _____

N° intubation(s)/week of the operator performing the successful attempt:
☐ ≤ 1 intubation/week
☐ 2 -5 intubations/week
☐ 6 – 10 intubations/week
☐ 11 – 20 intubations/week
☐ > 20 intubations/week

6. OUTCOME OF INTUBATION

Lowest systolic blood pressure after intubation (within 30 minutes from the procedure) available?
☐ YES ☐ NO
If Yes _____ mmHg

Systolic blood pressure < 90 mmHg was present for more than 30 minutes?
☐ YES ☐ NO

Lowest diastolic blood pressure after intubation (within 30 minutes from the procedure) available?
☐ YES ☐ NO
If Yes _____ mmHg

Heart rate after intubation (within 30 minutes from the procedure) available?
☐ YES ☐ NO
If Yes _____ /min

Need of new/increase of vasopressors/inotropes after intubation?
☐ YES ☐ NO
Specify all inotropes/vasopressors that apply:
☐ Norepinephrine; rate of infusion: _____mcg/Kg/min
☐ Epinephrine; rate of infusion: _____ mcg/Kg/min
☐ Dopamine; rate of infusion: _____ mcg/Kg/min
☐ Dobutamine; rate of infusion: _____ mcg/Kg/min
☐ Other; please specify:_____rate of infusion:_____ mcg/Kg/min

Fluid bolus administered after intubation (within 30 minutes from the procedure)?
YES ☐ NO ☐
Total volume of administered fluid after intubation (within 30 minutes from the procedure) _____ ml

Arterial blood gas analysis available after the procedure? (within 1 hour)
YES ☐ NO ☐
Specify F_iO_2 % _____%
PEEP (cmH_2O)_____
PaO_2 _____☐ mmHg ☐ kPa
$PaCO_2$ _____☐ mmHg ☐ kPa
PH _____
HCO_3^- (mEq/L - mmol/L)_____
Base excess (BE)_____
Lactate (mmol/L)_____

Adverse events
New onset cardiac arrhythmia (within 30 minutes from intubation)?
YES ☐ NO ☐

If yes:
☐ Atrial fibrillation
☐ Ventricular tachycardia
☐ Other _____

Cardiac arrest (within 30 minutes from intubation)
YES ☐ NO ☐

If YES, ☐ with return of spontaneous circulation (ROSC) ☐ with death
Specify the supposed main reason for cardiac arrest development:
☐ Hypoxia
☐ Hypovolemia/Hemodynamic collapse
☐ Hypo/-hyperkalemia
☐ Tension pneumothorax
☐ Cardiac tamponade
☐ Thrombosis (coronary or pulmonary)
☐ Toxins
☐ Other _____

Aspiration of gastric contents (detected within 24 hrs from intubation)?
(Inhalation of gastric contents into the larynx and the respiratory tract)
YES ☐ NO ☐

Dental injury due to airway management?
(Any notable change to the patient's dentition attributable to the procedure of endotracheal intubation)
YES ☐ NO ☐

Airways injury due to airway management (detected within 24 hrs from intubation)?
(Any detectable/clinically relevant airways injury attributable to the endotracheal intubation procedure, e.g. bleeding, tracheal tear/laceration)
YES ☐ NO ☐

Specify the type of airways injury:
☐ Tracheal laceration
☐ Bronchial laceration
☐ Laryngeal laceration
☐ Other _____

Detection of pneumothorax within 24 hrs from intubation?
YES ☐ NO ☐

Detection of pneumo-mediastinum within 24 hrs from intubation?
YES ☐ NO ☐

7. STATUS AT ICU DISCHARGE

Date of ICU discharge _____:_____(HH:MM)

Status at ICU discharge

☐ Dead

☐ Alive

☐ Other _____