Early Identification of Patients at Risk for Difficult Intubation in the Intensive Care Unit. Development and Validation of the MACOCHA Score in a Multicenter Cohort Study AT A GLANCE COMMENTARY Scientific Knowledge on the Subject

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Development and Validation of the MACOCHA Score in a Multicenter Cohort Study

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***Rationale*: Difficult intubation in the intensive care unit (ICU) is a challenging issue.**

***Objectives*: To develop and validate a simplified score for identifying patients with difficult intubation in the ICU and to report related complications.**

***Methods*: Data collected in a prospective multicenter study from 1,000 consecutive intubations from 42 ICUs were used to develop a simplified score of difficult intubation, which was then validated externally in 400 consecutive intubation procedures from 18 other ICUs and internally by bootstrap on 1,000 iterations.**

***Measurements and Main Results*: In multivariate analysis, the main predictors of difficult intubation (incidence = 11.3%) were related to patient (Mallampati score III or IV, obstructive sleep apnea syndrome, reduced mobility of cervical spine, limited mouth opening); pathology (severe hypoxia, coma); and operator (nonanesthesiologist). From the β parameter, a seven-item simplified score (MACOCHA score) was built, with an area under the curve (AUC) of 0.89 (95% confidence interval [CI], 0.85–0.94). In the validation cohort (prevalence of difficult intubation = 8%), the AUC was 0.86 (95% CI, 0.76–0.96), with a sensitivity of 73%, a specificity of 89%, a negative predictive value of 98%, and a positive predictive value of 36%. After internal validation by bootstrap, the AUC was 0.89 (95% CI, 0.86–0.93). Severe life-threatening events (severe hypoxia, collapse, cardiac arrest, or death) occurred in 38% of the 1,000 cases. Patients with difficult intubation (n = 113) had significantly higher severe life-threatening complications than those who had a nondifficult intubation (51% vs. 36%; $P < 0.0001$).**

***Conclusions*: Difficult intubation in the ICU is strongly associated with severe life-threatening complications. A simple score including seven clinical items discriminates difficult and nondifficult intubation in the ICU.**

Clinical trial registered with www.clinicaltrials.gov (NCT 01532063).

Keywords: difficult intubation; score; critical care; complications; mortality

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Risk factors for difficult intubation are well described in anesthesiology. However, in the intensive care unit (ICU), they have yet to be identified in prospective multicenter studies and no prediction score has been validated. Additionally, association between difficult intubation and related complications has not been studied in prospective studies.

What This Study Adds to the Field

Seven clinical items available in the ICU were identified as independent risk factors for difficult intubation and constituted the MACOCHA score. This study develops and validates a prediction score for difficult intubation in the ICU. This score demonstrated good performance in the original cohort, after external validation in a validation cohort and internal validation with bootstrap. Moreover, difficult intubation was strongly associated with moderate and severe life-threatening complications related to intubation.

* A complete list of members may be found before the beginning of the References.

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In the intensive care unit (ICU), intubation is a challenging issue (1–3) because it may be associated with life-threatening complications in up to one-third of cases (1, 2). Difficult intubation is known to be associated with life-threatening complications in the operating room (4) and in emergent conditions (5–7). Although several predictive risk factors and scores for difficult intubation were identified in anesthesia practice, to our knowledge none have been identified for ICU patients. Such patients differ from those undergoing elective surgery, with a high rate of acute respiratory or hemodynamic failure and with worse intubation conditions than in the operative room. Early identification of risk factors for difficult intubation could allow for anticipation and preparation of adequate material, use of an alternative intubation strategy, and call on additional assistance before intubation and thus reduce morbidity (5, 8).

Only retrospective studies (9, 10) have assessed the relationship between complications and difficult intubation. A study performed outside the operative room (9) reported that hypoxemia was sevenfold higher in case of difficult intubation in comparison with nondifficult intubation. Another study (10) in the emergency area showed that difficult intubation was associated with airway complication. Furthermore, the incidence of difficult intubation the ICU is highly variable across studies, ranging from 1 to 23%, depending on the center and the definition of difficult intubation (10–13).

The main objective of this study was to identify specific risk factors for difficult ICU intubation so as to develop and validate a simplified score predicting difficult intubation. This score was intended to include items that are clinically easily identifiable, applicable at bedside, and simple and clear to use. The secondary objectives were to assess the relationship between difficult intubation and complications and to establish the incidence of difficult intubation in a representative sample of ICU patients.

METHODS

Study Design and Population

A prospective, observational, multicenter study was conducted in 42 ICUs to develop a predictive model for difficult intubation (original cohort), and in 18 ICUs to validate the model (validation cohort). All adult patients consecutively intubated in the ICU were included. Exclusion criteria were pregnancy, refusal to participate after information was provided, or age younger than 18 years. See the online supplement for more information.

Ethics and Consent

Because of the observational, noninvasive design of this study, the need for written consent was waived. The local ethics committee, Comité de Protection des Personnes Sud-Mediterranée III, approved the study design (code UF:8819, register:2011-A001122-39). *See* the online supplement for more information.

Data Collection

Clinical parameters were prospectively assessed before, during, and after intubation procedures (*see* the online supplement and tables).

Definition of Difficult Intubation and Complications

Difficult intubation was defined as three or more laryngoscopic attempts to place the endotracheal tube into the trachea or as lasting more than 10 minutes using conventional laryngoscopy (14). Severe life-threatening complications (1, 2) were defined as death; cardiac arrest; severe cardiovascular collapse, defined as systolic blood pressure less than 65 mm Hg recorded at least one time or less than 90 mm Hg that lasted 30 minutes despite 500–1,000 ml of fluid loading (crystalloids or colloids solutions) or requiring introduction of vasoactive support; or severe hypoxemia (decrease in oxygen saturation as measured by pulse oximetry <80% during attempts).

Mild to moderate complications (1, 2) were defined as esophageal intubation; aspiration of gastric contents (migration of stomach contents into the lung); supraventricular or ventricular arrhythmia (without pulseless rhythm) that required therapy; dangerous agitation (Richmond Agitation-Sedation Scale score > 3); or dental injury.

Statistical Analysis

See the online supplement for more information. The number of subjects needed was calculated to obtain composite criteria of difficult intubation with a sensitivity of 80 $\pm$ 10% based on a 9% incidence of difficult intubation, resulting in an estimated 700 intubation procedures. We decided to include 1,000 intubation procedures to develop the model in the original cohort, taking into account missing data, and 400 intubation procedures to externally validate the model in the validation cohort.

A logistic regression was used to identify risk factors for difficult intubation in the original cohort. A multivariate model was established to predict difficult intubation. Variables were selected if P value was less than 0.20 in the univariate analysis and a stepwise procedure was used to select the final model. To establish a simplified score, we gave a score to each of the variables included in the final prediction model in relation to each one's β parameter (regression coefficient) in that model (15). The discriminative ability of the score (sensitivity, specificity, positive predictive value, negative predictive value, positive and negative likelihood ratio) was estimated in both cohorts to externally validate the simplified score (15, 16), and receiver operating characteristic (ROC) curve was established to estimate the area under the curve (AUC) of the simplified score. We used the bootstrap to internally validate the simplified score by sampling with replacement for 1,000 iterations (17). A P value of less than or equal to 0.05 was considered statistically significant.

RESULTS

See the online supplement for more information. During the study period, 1,400 intubation procedures were studied in 1,360 patients. From September 1, 2011 to January 31, 2012, 1,000 intubation procedures performed in 972 patients from 42 centers were included in the original cohort. All the intubation procedures were included. Twenty-eight patients (0.28%) were intubated twice. The median (interquartile range) number of intubation procedures included by center was 15 (10–20). Then, from February 1, 2012 to April 1, 2012, 400 intubation procedures performed in 388 patients from 18 other centers were included in the validation cohort. Twelve patients were intubated twice. The median (interquartile range) number of intubation procedures included by center was 15 (11–28). The flow chart of the study is shown in Figure 1.

Incidence of difficult intubation was 11.3% (113 of 1,000 intubation procedures) in the original cohort and 8% (32 of 400 intubation procedures) in the validation cohort ($P = 0.07$).

Tables 1 and E1 show the characteristics of patients in original and validation cohorts according to the difficulty of intubation. In both cohorts, there were significantly more patients with body mass index (BMI) greater than or equal to 30 kg/m^2 in difficult intubation groups. In the original cohort, increased Simplified Acute Physiology Score II score and coma as a reason for intubation was significantly associated with difficult intubation.

The operator status and main variables obtained before intubation are reported in Tables 2 and E2 (*see* Table E2 in the online supplement). In the original cohort, preintubation saturation less than 80% was significantly associated with difficult intubation, whereas noninvasive ventilation (NIV) was associated with the absence of difficult intubation. The drugs used for intubation, in particular neuromuscular blockers, did not differ between groups (*see* Table E3). However, midazolam use was more frequent in case of difficult intubation. The main parameters observed before

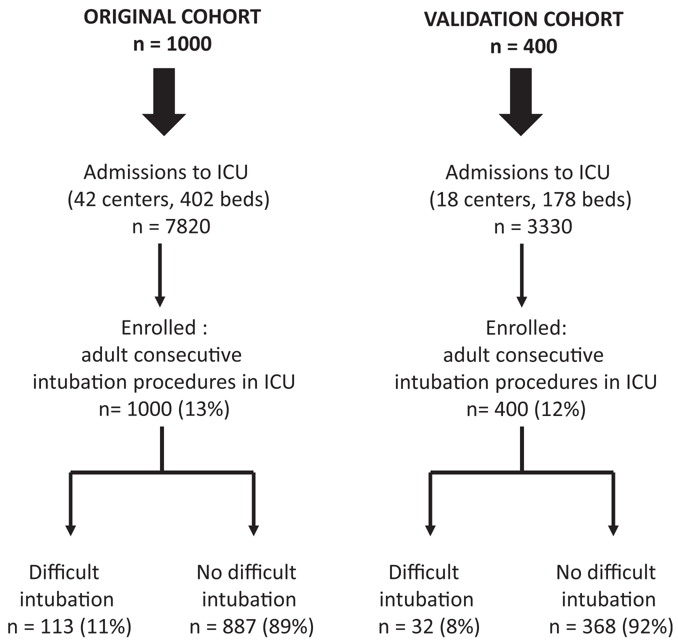

Figure 1. Patient flow diagram. ICU = intensive care unit.

the intubation procedure are shown in Tables 3 and E4. In the original cohort, Guedel use, difficult mask ventilation, plastic laryngoscope blade, Mallampati score, previous documented difficult intubation, limited mouth opening, elevated neck circumference, reduced mobility of cervical spine, obstructive sleep apnea syndrome (OSAS), head and neck pathology, presence of teeth, snoring, and need to release the Sellick maneuver for intubation were significantly associated with difficult intubation. The nonanesthesiologist status of the operator was also associated with difficult intubation, whether an expert operator or not. No statistical interaction was found between nonanesthesiologist status and operator expertise ($P = 0.84$). Moreover, we performed a logistic regression to assess the risk factors of nonassessment of the Mallampati score in the original cohort (n = 234; 23%). The risk factors in the final multivariate model (*see* Table E5) were head and neck disease, limited mouth opening, the need to replace the endotracheal tube, and coma. Center effect was not significant in the final model. The main evaluated parameters and physiologic variables during the intubation procedure are presented in Table E6. In both cohorts, heart rate and oxygen saturation as measured by pulse oximetry during intubation were significantly decreased in difficult intubation groups. Components of the Intubation Difficulty Scale (IDS) score were also associated with difficult intubation.

In the final multivariate model constructed with the 694 intubation procedures and all available data, adjusted for age, the main predictors of difficult intubation were related to the patient (Mallampati score III or IV, OSAS, reduced mobility of cervical spine, limited mouth opening), the pathology (coma, severe hypoxia), and the operator (nonanesthesiologist) (Table 4). Center effect was assessed both as fixed and random effect, but was not significant in the final model. The goodness of fit, assessed by the Hosmer and Lemeshow test, was of 0.94. The AUC was at 0.90 (95% confidence interval [CI], 0.86–0.93).

The simplified score (MACOCHA score) built from the final model is described in Table 5, ranging from 0 to 12. The goodness of fit, assessed by the Hosmer and Lemeshow test, demonstrated no statistical evidence of lack of fit ($P = 0.20$) and the AUC was at 0.89 (95% CI, 0.85–0.94). When the score was applied to the validation cohort, the goodness of fit assessed

TABLE 1. PATIENT CHARACTERISTICS AND REASONS FOR ICU ADMISSION AND INTUBATION IN ORIGINAL AND VALIDATION COHORTS ACCORDING TO DIFFICULT INTUBATION

	Original Cohort				Validation Cohort			
	Total (*n = 1,000*)	Difficult Intubation (*n = 113*)	No Difficult Intubation (*n = 887*)	*P* Value	Total (*n = 400*)	Difficult Intubation (*n = 32*)	No Difficult Intubation (*n = 368*)	*P* Value
Age, yr	62 (51–73)	61 (51–68)	62 (51–73)	0.09	63 (48–74)	58 (45–69)	64 (49–74)	0.13
Sex, male	624/979 (64)	68/111 (61)	556/868 (64)	0.56	262/397 (66)	20/32 (63)	242/365 (66)	0.66
SAPS2	48 (36–62)	53 (38–66)	47 (36–61)	0.05	48 (36–61)	41 (31–56)	49 (36–62)	0.09
SOFA	6 (4–8)	6 (3–8)	6 (4–8)	0.77	5 (3–8)	5 (3–7)	5 (3–8)	0.58
Weight, kg	71 (60–85)	76 (63–90)	70 (60–85)	0.03	70 (60–80)	70 (64–83)	70 (60–80)	0.41
Height, cm	169 (160–175)	170 (160–175)	169 (160–175)	0.97	170 (163–175)	170 (160–175)	170 (163–175)	0.52
Body mass index, $\geqslant$30 kg/m^2	219/933 (23)	37/110 (34)	182/823 (22)	0.007	63/378 (17)	9/29 (31)	54/349 (15)	0.03
Medical type of admission	734 (73)	86 (76)	650 (73)	0.52	267 (67)	21 (66)	246 (67)	0.88
Reason for ICU admission								
Acute respiratory failure	455 (46)	45 (40)	410 (46)	0.20	209 (52)	18 (56)	191 (52)	0.64
Trauma	42 (4)	6 (5)	36 (41)	0.53	33 (8)	0 (0)	33 (9)	0.08
Postoperative	95 (10)	6 (5)	89 (10)	0.11	58 (15)	4 (13)	54 (15)	0.10
Cardiac arrest	24 (2)	2 (2)	22 (3)	1.00	10 (3)	2 (6)	8 (2)	0.18
Neurologic	250 (25)	37 (33)	213 (24)	0.04	68 (17)	4 (13)	54 (15)	0.48
Shock	264 (26)	33 (29)	231 (26)	0.47	105 (26)	11 (34)	94 (26)	0.28
Ascitic decompensation	29 (3)	3 (2)	26 (3)	1.00	2 (1)	0 (0)	2 (1)	1.00
Acute renal failure	95 (10)	9 (8)	86 (10)	0.55	29 (7)	4 (13)	25 (7)	0.27
Others	82 (8)	10 (9)	72 (8)	0.79	25 (6)	2 (6)	23 (6)	1.00
Reason for intubation								
Acute respiratory failure	632 (63)	63 (56)	569 (64)	0.08	253 (63)	20 (63)	233 (63)	0.93
Shock	138 (14)	13 (12)	125 (14)	0.45	74 (19)	9 (28)	65 (18)	0.16
Coma	252 (25)	39 (35)	213 (24)	0.02	73 (18)	9 (28)	66 (18)	0.16
Cardiac arrest	30 (3)	4 (4)	26 (3)	0.77	11 (3)	1 (3)	10 (3)	0.61
Replace the endotracheal tube	128 (13)	14 (12)	114 (13)	0.89	66 (17)	8 (25)	58 (16)	0.18
Others	72 (7)	8 (7)	64 (7)	0.96	38 (10)	2 (6)	36 (10)	0.75

Definition of abbreviations: ICU = intensive care unit; SAPS2 = Simplified Acute Physiologic Score; SOFA = Sequential Organ Failure Assessment.
Data are summarized as number (%) or median (interquartile range). One patient can have more than one reason for ICU admission or for intubation.

TABLE 2. OPERATOR STATUS AND MAIN VARIABLES OBTAINED BEFORE INTUBATION IN ORIGINAL AND VALIDATION COHORTS ACCORDING TO DIFFICULT INTUBATION

	Original Cohort				Validation Cohort			
	Total (*n* = 1,000)	Difficult Intubation (*n* = 113)	No Difficult Intubation (*n* = 887)	*P* Value	Total (*n* = 400)	Difficult Intubation (*n* = 32)	No Difficult Intubation (*n* = 368)	*P* Value
Daytime intubation	380/965 (39)	36 (33)	344 (40)	0.13	129 (34)	13 (43)	116 (33)	0.24
First intubation	643 (64)	67 (59)	576 (65)	0.24	250 (63)	15 (47)	235 (64)	0.06
Expert operator	370 (37)	45 (40)	325 (37)	0.57	178 (45)	10 (31)	162 (44)	0.11
Anesthesiologist	683 (68)	68 (60)	615 (69)	0.04	249 (62)	18 (56)	231 (63)	0.47
Number of operators				0.007				0.40
1	247/991 (25)	18/109 (17)	229/882 (26)		129/396 (33)	8/31 (26)	121/365 (33)	
2	630/991 (64)	70/109 (64)	560/882 (63)		226/396 (57)	18/31 (58)	208/365 (57)	
3	114/991 (12)	21/109 (19)	93/882 (11)		41/396 (10)	5/31 (16)	36/365 (10)	
Informed patient	619 (62)	61 (54)	558 (63)	0.07	276 (69)	23 (72)	253 (69)	0.71
Fluid loading before intubation				0.80				0.99
0	545 (55)	65 (58)	480 (54)		208 (52)	18 (56)	190 (52)	
<500 ml	165 (16)	15 (13)	150 (17)		35 (9)	2 (6)	33 (9)	
500–1000 ml	203 (20)	23 (20)	180 (20)		91 (23)	7 (22)	84 (23)	
>1,000 ml	87 (8)	10 (9)	77 (9)		66 (17)	5 (16)	61 (17)	
Nonperceived blood pressure	33 (3)	5 (4)	28 (3)	0.41	11 (3)	0 (0)	11 (3)	0.32
Emergency characteristic of intubation				0.26				0.86
Real emergency	445 (46)	47 (42)	398 (45)		142 (36)	11 (34)	131 (36)	
Relative emergency	464 (46)	51 (45)	413 (47)		218 (54)	19 (59)	199 (54)	
Deferred emergency	91 (9)	37 (27)	195 (17)		40 (10)	2 (6)	33 (9)	
Vasopressors use	210 (21)	22 (19)	188 (21)	0.67	78 (20)	4 (13)	74 (20)	0.30
SBP <90 mm Hg	239/908 (26)	27/103 (26)	212/805 (26)	0.98	113/372 (30)	11/31 (36)	102/341 (30)	0.52
Sp_{O_2} <80%	191/965 (20)	32/110 (29)	159/855 (19)	0.009	78/377 (21)	7/30 (23)	71/347 (20)	0.71
NIV	361 (36)	28 (25)	333 (38)	0.008	148 (37)	13 (41)	135 (37)	0.66
Full stomach	740 (74)	82 (73)	658 (74)	0.71	232 (58)	20 (63)	212 (58)	0.59

Definition of abbreviations: NIV = noninvasive ventilation; SBP = systolic blood pressure; Sp_{O_2} = oxygen saturation as measured by pulse oximetry.
Data are summarized as number (%) or median (interquartile range).
The emergency characteristic of intubation was categorized as follows: real emergency, intubation required without any delay; relative emergency, intubation required within 1 hour; deferred emergency, intubation required in more than 1 hour.

by Hosmer and Lemeshow test demonstrated no statistical evidence of lack of fit ($P = 0.28$) and the AUC was at 0.86 (95% CI, 0.76–0.96). ROC curves associated with the simplified score in the original and validation cohorts are respectively presented in Figures E1A and E1B, and the frequency of difficult intubation across the range of the score is presented in Figures 2A and 2B. In original and validation cohorts, using a cutoff of 3 or greater seems optimal in allowing a balance between excellent negative predictive value and good positive predictive value (*see* Tables E7A and E7B). In validation cohort, at the cutoff point of three determined by ROC analysis, positive and negative predictive values (95% CI) for difficult intubation were 36% and 98%, respectively, with a sensitivity of 73% and a specificity of 89%. After internal validation by bootstrap, the AUC of the simplified score was at 0.89 (95% CI, 0.86–0.93).

When considering Mallampati score alone, the AUC was at 0.80 (95% CI, 0.74–0.86), significantly lower than the AUC of the MACOCHA score (0.89; 95% CI, 0.85–0.94; $P < 0.0001$) (*see* Figure E2). Furthermore, the Hosmer and Lemeshow test demonstrated statistical evidence of lack of fit with data when using Mallampati score alone ($P = 0.001$). Therefore, using MACOCHA score permitted detection of 11 additional difficult intubations that would not have been detected by Mallampati score alone. The relative sensitivity of Mallampati score to MACOCHA score was 82% (51 of 62). Indeed, with the Mallampati score alone, 51 of 82 difficult intubation procedures were predicted at a cutoff point of three (sensitivity of 62%), versus 62 of 82 at a cutoff point of three for the MACOCHA score (sensitivity of 76%) ($P = 0.002$). In the development cohort, overall complications occurred in 437 of 1,000 intubation procedures (43.7%), with 381 (38.1%) severe complications (26 cardiac arrests, 2.6%; five deaths, 0.5%; 274 severe collapses, 27.4%; 155 severe hypoxemia, 15.5%) and 112 (11.2%) moderate complications (15 agitations, 1.5%; 32 cardiac arrhythmias, 3.2%; 23 aspirations, 2.3%; 48 esophageal intubations, 4.8%; six dental injuries, 0.6%). Figures 3A and 3B show the detailed percentage of complications according to the difficulty of intubation. Patients with difficult intubation in both (original and validation) cohorts (Figures 3A and 3B) had significantly higher severe life-threatening complications than those who had nondifficult intubation.

Mortality was 299 (30%) of 982 in the original cohort and was 35 (32%) of 109 in the difficult intubation groups and 264 (30%) of 873 in the nondifficult intubation groups ($P = 0.69$).

DISCUSSION

This is the first study to identify risk factors of difficult intubation in a large multicenter cohort of ICU patients. We developed and validated internally and externally a score for difficult intubation in the ICU (MACOCHA score). This study shows that a simple model easily applicable in clinical practice predicts absence of difficult intubation in the ICU. This study also reveals a high rate of severe morbidity related to difficult intubation in the ICU.

Anticipating difficult intubation is a challenging issue: in the present study, the complications of intubation were higher when intubation was difficult (65% vs. 41% overall, 51% vs. 36% considering severe life-threatening complications). As underlined by a recent report, 25% of major airway events in Great Britain occur in the ICU, revealing a poor identification of patients at risk (5). Rates of complications in the present study were in the range of previous studies, with the incidence of severe complications varying with the definitions used, but generally ranging between 20% (9) and 50% (13). Additionally, airway complications in the report by Martin and coworkers (10) are comparable

TABLE 3. MAIN PARAMETERS IN ORIGINAL AND VALIDATION COHORTS ACCORDING TO DIFFICULT INTUBATION

	Original Cohort				Validation Cohort			
	Total (*n* = 1,000)	Difficult Intubation (*n* = 113)	No Difficult Intubation (*n* = 887)	*P* Value	Total (*n* = 400)	Difficult Intubation (*n* = 32)	No Difficult Intubation (*n* = 368)	*P* Value
Preoxygenation	946 (95)	106 (94)	840 (95)	0.69	374 (94)	31 (97)	343 (97)	0.71
Preoxygenation by NIV	407 (40)	37 (33)	370 (42)	0.07	158 (40)	14 (44)	144 (39)	0.61
Guedel use	94 (9)	17 (15)	77 (9)	0.03	35 (9)	6 (19)	29 (8)	0.05
Difficult mask ventilation	73/392 (19)	20/64 (31)	53/328 (16)	0.005	22/184 (12)	4/26 (15)	18/158 (11)	0.52
Laryngoscope blade				0.006				0.27
Plastic single-use	70/965 (7)	14/107 (13)	56/858 (7)		121/384 (31)	6/32 (19)	115/352 (33)	
Metal single-use	525/965 (54)	99/107 (88)	831/858 (94)		192/384 (50)	19/32 (59)	173/352 (49)	
Metal reusable	370/965 (38)	48/107 (45)	322/858 (38)		71/384 (19)	7/32 (22)	64/352 (18)	
Mallampati score				<0.000001				<0.000001
I	493/766 (64)	20/84 (24)	473/682 (69)		192/309 (62)	4/25 (16)	188/284 (66)	
II	180/766 (24)	11/84 (13)	169/682 (25)		77/309 (25)	3/25 (12)	74/284 (26)	
III	65/766 (8)	29/84 (35)	36/682 (5)		29/309 (9)	10/25 (40)	19/284 (7)	
IV	28/766 (4)	24/84 (29)	4/682 (1)		11/309 (4)	8/25 (32)	3/284 (1)	
Previous documented difficult intubation	23 (2)	9 (8)	14 (2)	0.0005	14 (4)	5 (16)	9 (3)	0.003
Limited mouth opening	120 (9)	25 (22)	67 (8)	<0.000001	28 (7)	6 (19)	22 (6)	0.02
Low thyromental distance	107 (11)	15 (13)	92 (10)	0.35	44 (11)	4 (13)	40 (11)	0.77
Elevated neck circumference	141 (14)	33 (29)	108 (12)	<0.000001	37 (9)	6 (19)	31 (8)	0.10
Reduced mobility of cervical spine	83 (8)	23 (20)	60 (7)	<0.000001	31 (8)	5 (16)	26 (7)	0.09
Obstructive apnea syndrome	78 (8)	33 (29)	45 (5)	<0.000001	20 (5)	8 (25)	12 (3)	0.00004
Head and neck disease	53 (5)	18 (16)	35 (4)	<0.000001	18 (5)	3 (9)	15 (4)	0.17
Beard	78 (8)	12 (11)	66 (7)	0.24	17 (4)	2 (6)	15 (4)	0.64
Toothless	283 (28)	21 (19)	262 (30)	0.01	87 (22)	9 (28)	78 (21)	0.36
Snoring	116 (12)	25 (22)	91 (10)	0.0002	28 (7)	5 (16)	23 (6)	0.06
Diabetes	177 (18)	21 (19)	156 (18)	0.79	48 (12)	6 (19)	42 (11)	0.25
Sellick maneuver	448 (45)	58 (51)	390 (44)	0.14	128 (32)	10 (31)	118 (32)	0.92
Need to release Sellick maneuver for intubation	105/448 (23)	29/58 (50)	76/390 (19)	<0.000001	18/128 (14)	4/10 (40)	14/118 (12)	<0.000001

Definition of abbreviation: NIV = noninvasive ventilation.
Data are summarized as number (%) or median (interquartile range).

with our study (~4%). Likewise, rates of difficult ICU intubation ranged from 1% (13) to 23% (11) according to the definition used, around 10% on average (13, 18), which is consistent with our results. This large range of difficult ICU intubation rates may also be explained by the operator skill, which is not accounted for in the different definitions used (19).

In this study, we attempted to create a pragmatic, predictive difficult-intubation score. To our knowledge, it is the first time that such a predictive score (MACOCHA score) has been developed and validated in the ICU. The final model of the logistic regression in the original cohort is robust and presents very good characteristics, with very high AUC and excellent goodness of fit with data (20). The simplified score still presents very high AUC and matches well the observed data. By optimizing the discrimination threshold, the discriminative ability of the score is high. To reject difficult intubation with certainty, a cutoff of three or greater seems appropriate, allowing optimal negative predictive value (97% and 98% in the original and validation cohorts, respectively) and sensitivity (76% and 73% in the original and validation cohorts, respectively). However, the specificity (90% and 89%) and positive predictive values (48% and 36%) are lower, although improve with a threshold of four or greater (specificity of 93% and 92%, positive predictive value of 53% and 42%), whereas the negative predictive value remains very good (96% and 97%). At positivity thresholds of five or higher, sensitivity losses are pronounced whereas further specificity advances are marginal.

Because of the low prevalence of difficult intubation on average (8% in the validation cohort), positive predictive value is low despite a good specificity (20). Nevertheless, to reject difficult intubation with certainty, the main value of the score resides in the negative predictive value of the parameter. It is prudent to be prepared for a difficult intubation, even if the intubation is finally not difficult. We performed an external validation to show the generalizability of the model. External validation is necessary before implementing prediction models in clinical practice (21). Results are concordant between the original and validation cohorts, with very close discriminatory values. The internal validation by bootstrap confirmed those results.

The MACOCHA score has the advantage of being constituted with easily identifiable and clinically pertinent variables. Furthermore, the items used in the MACOCHA score are close to those identified in the operating room and include risk factors strongly associated with difficult intubation in multiple studies performed in anesthesiology (18, 22–25). Additionally, Hiremath and coworkers (26) showed that patients known to be difficult to intubate should be screened for sleep apnea, a strong risk factor of difficult intubation in our study. However,

TABLE 4. RESULTS OF MULTIVARIATE LOGISTIC REGRESSION FOR FINAL DIFFICULT INTUBATION PREDICTION MODEL FROM ORIGINAL COHORT (N = 694)

Variable	β Parameter	Odds Ratio (95% Confidence Interval)	*P* Value
Intercept	−2.83		
Mallampati score III or IV	2.87	17.67 (9.28–33.60)	<0.0001
Obstructive apnea syndrome	1.79	5.97 (2.68–13.23)	<0.0001
Reduced mobility of cervical spline	1.35	3.87 (1.58–9.52)	0.003
Limited mouth opening	1.17	3.21 (1.34–7.70)	0.009
Severe hypoxemia (<80%)	0.90	2.46 (1.23–4.92)	0.01
Coma	0.81	2.26 (1.16–4.39)	0.02
Nonanesthesiologist	0.71	2.03 (1.07–3.85)	0.03
Age	−0.02	0.98 (0.96–1.00)	0.02

The model has an area under the curve of 0.90.

TABLE 5. MACOCHA SCORE CALCULATION WORKSHEET

Factors	Points
Factors related to patient	
Mallampati score III or IV	5
Obstructive sleep apnea syndrome	2
Reduced mobility of cervical spine	1
Limited mouth opening <3 cm	1
Factors related to pathology	
Coma	1
Severe hypoxemia (<80%)	1
Factor related to operator	
Nonanesthesiologist	1
Total	12

Definition of abbreviation: MACOCHA = Mallampati score III or IV, Apnea syndrome (obstructive), Cervical spine limitation, Opening mouth <3 cm, Coma, Hypoxia, Anesthesiologist nontrained.

Coded from 0 to 12: 0 = easy; 12 = very difficult.

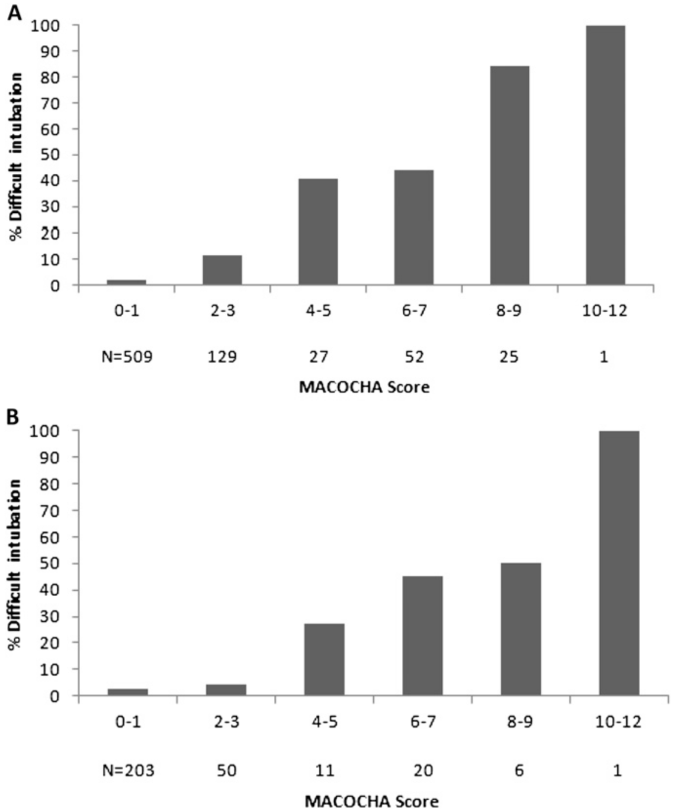

Figure 2. (*A*) Frequency of difficult intubation in original cohort according to the MACOCHA score. Frequency of difficult intubation with different MACOCHA score values. N = number of patients in the study who had particular MACOCHA score values. (*B*) Frequency of difficult intubation in validation cohort according to the MACOCHA score. Frequency of difficult intubation with different MACOCHA score values. N = number of patients in the study who had particular MACOCHA score values.

Mallampati score alone was less effective than MACOCHA score to predict difficult intubation. Two factors specific to ICU patients were recognized in this study and are included in the score: severe hypoxemia before intubation and coma (Glasgow score <8 as a reason for intubation). Severe hypoxemia as a risk factor can be explained by a shortness of time to be adequately prepared for the intubation and perhaps by increased stress for physicians performing the procedure. Likewise, patients intubated for coma often present increased oropharyngeal secretions, limiting view of the glottis.

Moreover, the simplified score contains a factor related to the operator: a formal anesthetic training of at least 24 months. Considering the link between anesthesiology formation and difficult intubation (1), previous studies were not powered enough to show this association. A recent study (13) performed in Scotland, where almost all operators had a formal anesthetic training greater than 24 months, revealed a very low rate of difficult intubation and complications, in accordance with our study. In previous studies, the presence of two operators to perform the intubation was found as a protective factor for complications related to intubation (1, 27). In our opinion, the standard of care changed in France more than 8 years after these studies: the increased number of operators when difficult intubation occurred in the current study was more a consequence of difficult intubation. It is noteworthy that BMI was assessed as a risk factor for difficult intubation in univariate analysis but not in multivariate analysis. This might be explained by the important clinical overlap of BMI with other risk factors more associated with difficult intubation in the final model, such as Mallampati score, mouth opening, OSAS, or severe hypoxemia before intubation. For example, in the study by Holmberg and coworkers (28), BMI greater than 40 kg/m^2 in prehospital tracheal intubation was associated with difficult intubation, but other risk factors for difficult intubation were not assessed. In fact, this might mean that the risk factors associated with obesity, rather than obesity itself, are probably associated with difficult intubation in this study, as Lundstrøm and coworkers (23) revealed in the anesthesiology area, where high BMI was a weak predictor for difficult and failed tracheal intubation.

NIV failure was associated with a lower risk of difficult intubation in univariate analysis, but not in multivariate analysis. NIV before intubation has been demonstrated to prevent hypoxemia and was associated with less airway complications of intubation (2, 3). It is the first study to show that NIV is associated with a lower rate of difficult intubation, perhaps related to the greater duration before hypoxemia occurrence compared with other patients (3).

As expected, the patients with difficult intubation had a significantly higher IDS score (6 [4–8] vs. 1 [0–2]; $P < 0.0001$). It should be noted that IDS score is a surrogate of the difficulty of intubation *a posteriori* and not a predictive score, as the MACOCHA score validated in this study.

Capnography was used only in 46% of intubations, whereas it is recommended (8) to be always used after intubation to assess the endotracheal position of the tracheal tube. Recent studies also found a similar result, reporting capnography use between 25% (29) and 54% (13). Systematic use of capnography could reduce the rate of complications related to intubation (2).

The study has some limitations. First, because data collection and intubation were sometimes performed by the same person, the degree of difficulty of intubation could have been overestimated or underestimated. Second, the Mallampati score was only available in 77% of the original cohort. The reasons for this might be an ignorance of the score by some operators. Moreover, Mallampati score is sometimes difficult to assess in an emergency context (30). This could be explained by the risk factors of nonassessment of Mallampati score determined in this study by multivariate logistic regression. Indeed, the need to replace the endotracheal tube is often done in emergency conditions, leaving no time to assess Mallampati score. More often, limited mouth opening, head and neck disease, or coma do not allow Mallampati score assessment. Accordingly, the modest bias induced by the lack of Mallampati score data does not influence the main results of the study. The main message remains that

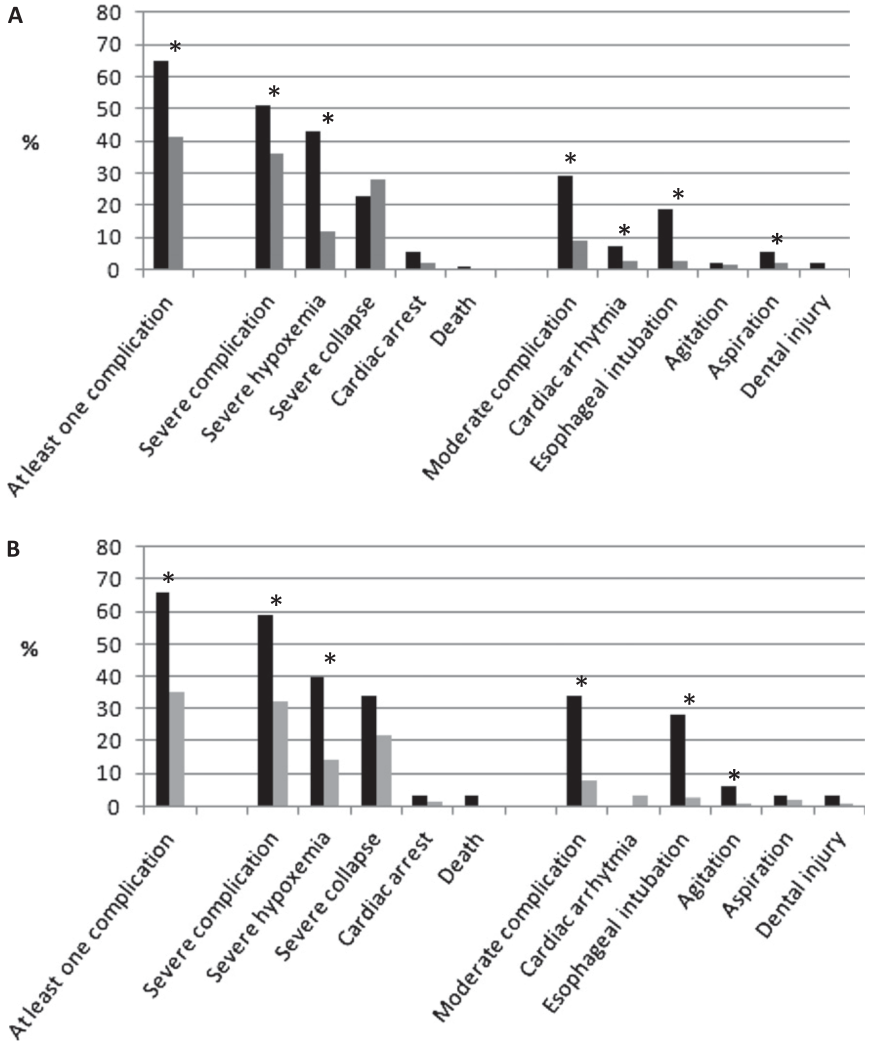

Figure 3. (*A*) Percentage of complications according to difficult intubation in original cohort. *Black* = difficult intubation; *gray* = no difficult intubation. *$P < 0.05$. (*B*) Percentage of complications according to difficult intubation in validation cohort. *Black* = difficult intubation; *gray* = no difficult intubation. *$P < 0.05$.

Mallampati scores should be evaluated as often as possible. In our study, Mallampati score was assessed in recumbent patients. Performance of Mallampati score with a recumbent patient is at least as good as in a sitting position, according to previous studies (31–34). The only situation where such an assessment is not possible is when the patient presents a much altered consciousness, which is also a risk factor for difficult intubation according to the current study. Besides, other missing data were very low. Third, it is a multicenter study, which is a strength because the result can be better extrapolated to the general population, and a limit because of unequal distribution intubation numbers among centers. However, the center effect was assessed and not retained. Fourth, the external validation was performed in French ICUs and not in other countries, which could limit the extrapolation of the results. Fifth, a statistical model for repeated data was not used despite several intubation procedures for a same patient included in the analysis. Yet, the number of patients who have been intubated at least twice was low in both cohorts (<1%). As a consequence, the bias is very limited. Sixth, neck circumference was estimated rather than measured. This parameter has to be considered with caution. Finally, intubation is a procedure that depends greatly on the intrinsic quality of the operator, which is hardly assessable in clinical studies.

To conclude, this is the first study to develop and validate a score predicting the difficulty of intubation procedure in the ICU with a high discriminative ability. The MACOCHA score is very easy to perform and to memorize. However, if the score does not predict a difficult intubation, one should remain vigilant because there is still a small possibility that it will be difficult. Mallampati score is the highest predictor of difficult intubation and should be evaluated as often as possible before intubation in the ICU. Complications of intubation are strongly associated with difficult intubation. Further studies are needed to appreciate if applying the MACOCHA score in daily practice helps to anticipate and further reduce complications of intubation.

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