Dysphagia in Mechanically Ventilated ICU Patients (DYnAMICS): A Prospective Observational Trial

Joerg C. Schefold, MD[1]; David Berger, MD[1]; Patrick Zürcher, MD[1]; Michael Lensch[1]; Andrea Perren[2]; Stephan M. Jakob, MD, PhD[1]; Ilkka Parviainen, MD, PhD[3]; Jukka Takala, MD, PhD[1]

Objectives: Swallowing disorders may be associated with adverse clinical outcomes in patients following invasive mechanical ventilation. We investigated the incidence of dysphagia, its time course, and association with clinically relevant outcomes in extubated critically ill patients.

Design: Prospective observational trial with systematic dysphagia screening and follow-up until 90 days or death.

Settings: ICU of a tertiary care academic center.

Patients: One thousand three-hundred four admissions of mixed adult ICU patients (median age, 66.0 yr [interquartile range, 54.0–74.0]; Acute Physiology and Chronic Health Evaluation-II score, 19.0 [interquartile range, 14.0–24.0]) were screened for postextubation dysphagia. Primary ICU admissions ($n = 933$) were analyzed and followed up until 90 days or death. Patients from an independent academic center served as confirmatory cohort ($n = 220$).

Interventions: Bedside screening for dysphagia was performed within 3 hours after extubation by trained ICU nurses. Positive screening triggered confirmatory specialist bedside swallowing examinations and follow-up until hospital discharge.

Measurements and Main Results: Dysphagia screening was positive in 12.4% ($n = 116/933$) after extubation (18.3% of emergency and 4.9% of elective patients) and confirmed by specialists within 24 hours from positive screening in 87.3% ($n = 96/110$, $n = 6$ missing data). The dysphagia incidence at ICU discharge was 10.3% ($n = 96/933$) of which 60.4% ($n = 58/96$) remained positive until hospital discharge. Days on feeding tube, length of mechanical ventilation and ICU/hospital stay, and hospital mortality were higher in patients with dysphagia (all $p < 0.001$). The univariate hazard ratio for 90-day mortality for dysphagia was 3.74 (95% CI, 2.01–6.95; $p < 0.001$). After adjustment for disease severity and length of mechanical ventilation, dysphagia remained an independent predictor for 28-day and 90-day mortality (excess 90-d mortality 9.2%).

Conclusions: Dysphagia after extubation was common in ICU patients, sustained until hospital discharge in the majority of affected patients, and was an independent predictor of death. Dysphagia after mechanical ventilation may be an overlooked problem. Studies on underlying causes and therapeutic interventions seem warranted. (*Crit Care Med* 2017; XX:00–00)

Key Words: aspiration; deglutition disorder; muscular failure; sepsis; swallowing disorder

[1]Department of Intensive Care Medicine, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland.

[2]Department of Physiotherapy, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland.

[3]Department of Anesthesiology and Intensive Care, Kuopio University Hospital, Kuopio, Finland.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/ccmjournal).

Trial registration: NCT02333201, ClinicalTrials.gov.

Supported, in part, by Nestec, Vevey, Switzerland. Financial support was also received from the institutional scientific fund (Department of Intensive Care Medicine, Bern, Switzerland).

The Department of Intensive Care Medicine (to Drs. Schefold, Berger, Zürcher, Lensch, Jakob, and Takala) has/had research and development/consulting contracts with Orion Corporation, Abbott Nutrition International, B. Braun Medical AG, CSEM SA, Edwards Lifesciences Services GmbH/SA, Kenta Biotech, Maquet Critical Care AB, Omnicare Clinical Research AG, and Nestlé. Educational grants were received from Fresenius Kabi; GlaxoSmithKline; Merck, Sharp & Dohme; Lilly; Baxter; Astellas; AstraZeneca; B. Braun Medical AG, CSL Behring, Maquet, Novartis, Covidien, Nycomed, Pierre Fabre Pharma (Roba Pharma); and Pfizer, Orion Pharma. No personal financial gains resulted from respective development/ consulting contracts and/or educational grants. The remaining authors have disclosed that they do not have any potential conflicts of interest.

Drs. Schefold, Jakob, and Takala designed the study, supervised, analyzed data, drafted the article, and revised the article for important intellectual content. Drs. Berger, Zürcher, Lensch, Perren, and Parvianen collected and analyzed data, and revised the article for important intellectual content.

Address requests for reprints to: Joerg C. Schefold, MD, Department of Intensive Care Medicine, Inselspital, University Hospital of Bern, CH 3010 Bern, Switzerland. E-mail: joerg.schefold@insel.ch

DOI: 10.1097/CCM.0000000000002765

Swallowing disorders in critically ill patients may cause aspiration pneumonia, necessitate tracheostomy, and delay reinstitution of oral feeding. Previous reports suggest that presence of oropharyngeal dysphagia may impede recovery from critical illness (1–3), induce malnutrition/cachexia (4, 5), and prolong mechanical ventilation (MV) and ICU/hospital stay (6). In the general medical population, dysphagia is considered to impose a considerable burden on

public healthcare systems and was estimated to account for as much as 10 billion dollars of healthcare costs in the United States annually (7, 8).

The overall incidence of dysphagia in critically ill patients following MV is largely unknown. Previously, most retrospective studies in smaller heterogeneous cohorts or selected high-risk populations (e.g., in patients after diagnosed aspiration) without systematic screening have reported highly variable (3–62%) incidence (1, 2, 9–16). In addition, different timing of screening and lack of follow-up add to an incomplete understanding of the potential impact of dysphagia on the clinical course of ICU survivors (1, 2, 7, 9, 17). Given the fact that long-term impairment often results from critical illness (18–21), data on the incidence, evolution, and impact of dysphagia on clinical outcomes seem warranted (1, 2, 9).

The etiology of dysphagia after MV is unknown and considered multifactorial. Neurologic disease including neuromuscular weakness (e.g., ICU-acquired weakness), altered consciousness, reduced sensorium and motor response, use of sedative/analgesic drugs, direct oropharyngeal or laryngeal trauma (e.g., tube induced) (22, 23), increased gastrointestinal reflux, and prolonged MV may all contribute to development of dysphagia (1, 2, 9, 24–31).

Systematic screening for dysphagia in the ICU is uncommon, and dysphagia screening methods mostly derive from stroke patients. Proposed diagnostic approaches for dysphagia include the bedside water swallow test (WST) (32), the fiberoptic endoscopic evaluation of swallowing (FEES), and videofluoroscopic swallowing studies (VFSS) (1, 2, 9, 32–36). VFSS and FEES are invasive, time-consuming, and complex procedures that require substantial resources (including transfer to a radiology suite in VFSS) and may not be readily available in most ICUs. Bedside WST examinations make systematic screening of dysphagia feasible in recently extubated critically ill patients (1, 9, 32).

We prospectively studied the incidence and evolution of dysphagia after MV and its association with clinical outcomes in a large cohort of adult multidisciplinary ICU patients.

MATERIALS AND METHODS

Trial Design and Patients, Inclusion/Exclusion Criteria

A prospective observational trial with systematic dysphagia screening (Dysphagia in Mechanically Ventilated ICU Patients [DYnAMICS]) was performed from April 2015 until October 2015 in a 900+ bed tertiary care academic medical center (Inselspital, Bern University Hospital, Switzerland). In this center, the Department of Intensive Care Medicine is the sole provider of intensive care medicine for adults. A second tertiary care academic center (Kuopio University Hospital, Finland) and its sole provider of intensive care medicine for adults (Department of Anesthesiology and Intensive Care; inclusion from October 2015 to December 2015) served as confirmatory cohort regarding incidence. All consecutive patients extubated/decannulated after MV were included. Prerequisites for extubation were stable gas exchange and hemodynamics on moderate pressure support and positive end-expiratory pressure, responsive to commands and presumably able to protect the airway. Initial bedside screening for dysphagia was performed within 3 hours of extubation unless any of the following exclusion criteria were met: 1) patients dying/on comfort therapy and 2) patients with recent esophageal injury and/or surgery (**Fig. 1**). Patients were followed up until 90 days, or death. The trial was performed in accordance with the "Declaration of Helsinki" and approved by the Kantonale Ethikkommission KEK, Bern, Switzerland, Nr. 314/2014 and Research Ethics Committee of the Northern Savo Hospital district, Finland.

Bedside Screening for Dysphagia, Confirmatory Examinations, and Diagnostic Criteria

Following physician-supervised repetitive training of ICU nurses, systematic standardized bedside dysphagia screening was performed within 3 hours of extubation. In brief, patients were checked for exclusion criteria and readiness to attempt swallowing (with one reassessment performed after 3 hr, if necessary; **Fig. E1**, Supplemental Digital Content 1, http://links.lww.com/CCM/C952). WSTs consisted of consecutive swallowing of three teaspoons of water (room temperature) followed by drinking half a glass (about 100 mL) of water (as suggested elsewhere [32, 37]). Coughing, choking, breathlessness, wet or gurgly voice, or any other symptom (e.g., water leaking out of mouth) suggestive of a swallowing disorder in any WST step were considered as WST failure. Failure in two screenings triggered examination by a dysphagia specialist (physiotherapist or speech language therapist [SLT]). WSTs could be replaced by specialist examinations on clinical indications (e.g., obvious severe dysphagia, Fig. 1). Dysphagia in screening is referred to as "screening positive," and dysphagia confirmed by specialists' examination as "confirmed dysphagia." In screening positive patients, a nil per os status (except for feeding via gastric tube; Fig. E1, Supplemental Digital Content 1, http://links.lww.com/CCM/C952) was prescribed until dysphagia specialist examinations were performed (≤ 24 hr). If ICU discharge occurred within 24 hours from positive screening, only one specialist assessment was performed and considered to represent the ICU discharge status. Patients with confirmed dysphagia were followed up (physiotherapist/SLT), and a final specialist assessment was performed less than or equal to 48 hours before hospital discharge. Dysphagia was treated by physiotherapist/SLT based on respective previous clinical assessments and the general principle of functional dysphagia therapy using 1) compensatory treatment procedures including postural changes (with mobilization, head and upright positioning), 2) adaptive measures including dietary texture modifications (liquid, nectar, pudding) and use of auxillary tools such as straw/spoon/glas, and 3) functional exercises for motor and sensomotor recovery with tongue and lip exercises, as suggested elsewhere (38). Functional outcomes and discharge destinations were recorded (Fig. E1, Supplemental Digital Content 1, http://links.lww.com/CCM/C952).

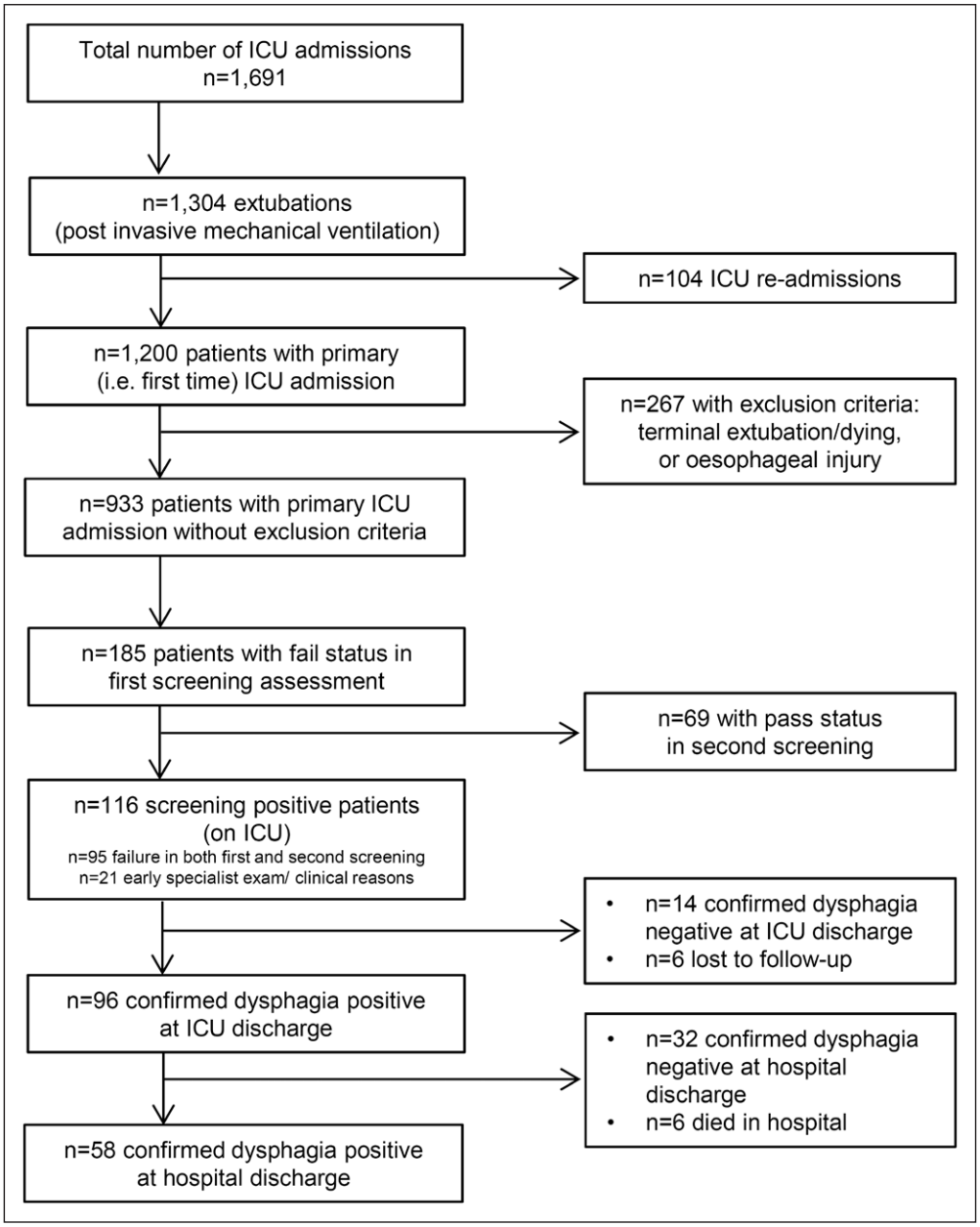

Figure 1. Trial flow chart.

Assessment of Disease Severity, and ICU Resource Use

For assessment of disease severity, baseline Acute Physiology and Chronic Health Evaluation (APACHE)-II scores (39) and Simplified Acute Physiology Score (SAPS)-II scores (40) were recorded. ICU resource use was assessed by analysis of the sum of Therapeutic Intervention Scoring System (TISS)-28 points (recorded once per shift over ICU stay) (41, 42). Total days on invasive MV, need for feeding tube, days on antibiotics/antimicrobials, days on vasopressors, and need for renal replacement therapy were recorded. Dysphagia severity was assessed using the following scoring systems: Bogenhausen Dysphagia Scores (BODS)-1/-2 and BODS sum score (impairment in saliva swallowing, oral intake) (38), National Outcomes Measurement System (NOMS): American Speech Language Hearing Association (1998–2008) and Dysphagia Outcome Severity Scale (DOSS) (therapeutic dependency/diet restrictions) (43). At ICU and hospital discharge, the Functional Independence Measure (44) and Medical Research Council sum score (45) less than 48 (yes/no; i.e., ICU-acquired weakness present or not) was recorded.

Statistical Analyses

Data were checked for normal distribution (Shapiro-Wilk test) with log transformation performed in an effort to reach normal distribution when indicated. Data are given as medians and 25–75th interquartile ranges (IQRs) or means ± SDs, as indicated. For between-group comparisons, rank-sum test (Mann-Whitney *U*) was used. For categorical data, Fisher exact test was used. Univariate followed by multivariate models including relevant clinical variables were used. Multivariate logistic regression was used to identify potential predisposing factors leading to dysphagia. For assessment of mortality prediction, Cox proportional hazards regression models were calculated. Patients were censored at time of loss to follow-up or at days 28 and 90, respectively. Log-rank *p* values (survival curves) and hazard ratios (HR) are given. Evolution of dysphagia severity was assessed by analysis of variance for repeated measures. Significance was assigned when the *p* value was less than 0.05. Statistical analysis was performed using MedCalc 16.4.3 Software (MedCalc, Mariakerke, Belgium).

RESULTS

Baseline Characterization of Study Cohort

A total of 1,304 admissions with 1,200 patients with first time ICU admission were assessed, and $n = 933$ individuals (56% emergency vs 44% elective patients, 61% postoperative patients, **Table 1**) were analyzed (Fig. 1). Emergency patients were younger and more severely ill (Table 1). Fifteen patients (1.6%) were decannulated from a tracheal tube. For

TABLE 1. Baseline Demographics of Extubated ICU Patients

Variables	Total Groups			
	All, *n* = 933	Dysphagia Screening Positive, *n* = 116	Dysphagia Screening Negative, *n* = 817	*p*
Age (yr), median (IQR)	65 (54–73.3)	64.5 (49.5–77.0)	65.0 (55.0–73.0)	0.83
Gender (male), *n* (%)	666 (71)	80 (69)	586 (72)	0.58
Weight (kg), median (IQR)	80.0 (70.0–90.0)	76.0 (69.8–86.0)	80.0 (70.0–90.0)	0.07
Body mass index, median (IQR)	26.2 (23.7–29.4)	25.7 (23.5–27.8)	26.3 (23.7–29.3)	0.07
APACHE-II score, median (IQR)	17 (13–23)	21 (17–25)	17 (13–22)	**< 0.001**
Simplified Acute Physiology Score-II score, median (IQR)	36 (28–46)	42.5 (34–55.5)	35 (28–45)	**< 0.001**
APACHE-IV admission diagnostic groups, *n* (%)				
Cardiovascular	556 (59.6)	34 (29.3)	522 (63.9)	**< 0.001**
Respiratory	52 (5.6)	6 (5.2)	46 (5.6)	1.0
Gastrointestinal	56 (6.0)	5 (4.3)	51 (6.2)	0.53
Neurologic	147 (15.8)	47 (40.5)	100 (12.2)	**< 0.001**
Trauma	71 (7.6)	17 (14.7)	54 (6.6)	**0.005**
Metabolic	2 (0.2)	0 (0)	2 (0.3)	
Hematologic	4 (0.4)	2 (1.7)	2 (0.3)	0.08
Urological	5 (0.5)	1 (0.9)	4 (0.5)	0.49
Diverse	31 (3.3)	2 (1.7)	29 (3.5)	0.41
Intoxication	9 (1.0)	2 (1.7)	7 (0.9)	0.31
Postoperative, *n* (%)	569 (61)	44 (38)	525 (64)	**< 0.001**
Emergency admission, *n* (%)	525 (56)	96 (83)	429 (53)	**< 0.001**

APACHE = Acute Physiology and Chronic Health Evaluation, IQR = interquartile range.

Total group; data for emergency and elective subgroups are given in **Table E3** (Supplemental Digital Content 1, http://links.lww.com/CCM/C952). Mann-Whitney *U* or Fisher exact test. Acute Physiology and Chronic Health Evaluation-II and Simplified Acute Physiology Score-II scores at ICU admission are given. Boldface values indicate statistically significant results.

characteristics of the confirmatory cohort (*n* = 220), see **supplement** (Supplemental Digital Content 1, http://links.lww.com/CCM/C952).

Dysphagia Incidence, Results From Specialist Examinations, and Confirmatory Data

In total, 116 of 933 patients (12.4%) were screening positive for dysphagia (Fig. 1; 18.3% of emergency and 4.9% of elective patients). Specialist examinations (performed at median 0.76 (IQR, 0.37–1.0) days from positive screening) confirmed persisting dysphagia in 87.3% of cases (positive predictive value; *n* = 96/110, 10.4% of total population; missing data *n* = 6). Of patients discharged from the ICU with confirmed dysphagia, 90 patients survived the hospital stay and *n* = 58 of 90 (64.4%) did not recover from dysphagia until hospital discharge (Fig. 1). In the independent cohort (*n* = 220), confirmed dysphagia was noted in 11.4% following extubation (*n* = 25/218; 29.1% emergency vs 1.4% elective subgroups; *n* = 2 missing data).

Underlying Disease Characteristics in Dysphagia Patients

When grouped for APACHE-IV admission diagnostic groups, 75% of patients had a cardiovascular (*n* = 556/933; 59.6%) or a neurologic (*n* = 147/933; 15.8%) diagnosis (Table 1). At ICU discharge (*n* = 96), dysphagia was most common in patients admitted for neurologic disease (incidence rate 41%; *n* = 39), cardiovascular disease (29.2%; *n* = 28), trauma (15%; *n* = 14), and respiratory disease (6.3%; *n* = 6). When age, gender, baseline disease severity (APACHE-II or SAPS-II), admission status (elective vs emergency), admission diagnosis (neurologic vs nonneurologic), and length of MV were included in multivariate logistic regression models, APACHE-II score (odds ratio [OR], 1.05; 95% CI, 1.01–1.09), admission status (OR for emergency admission, 2.60; 95% CI, 1.47–4.59), and admission diagnosis (OR for neurologic disease, 3.46; 95% CI, 2.17–5.52), but not length of MV, were associated with a screening positive status (all $p < 0.01$).

Evolution of Dysphagia Severity and Recovery From Dysphagia

Over the ICU stay, dysphagia disease severity scores (BODS, NOMS, DOSS) remained unchanged (except in 14 patients recovering from dysphagia until ICU discharge). Dysphagia severity declined until hospital discharge ($p < 0.02$ for BODS, DOSS, NOMS scores in patients with complete datasets) (**Table E1**, Supplemental Digital Content 1, http://links.lww.com/CCM/C952). At hospital discharge, 33% of patients ($n = 32/96$) with confirmed dysphagia at ICU discharge had recovered. The recovery rate from dysphagia was highest in the cardiovascular diagnostic group (54%; $n = 15/28$) and lowest in neurologic patients (18%; $n = 7/39$). The OR for nonrecovery from dysphagia in neurologic (vs cardiovascular) patients was 5.27 (95% CI, 1.75–15.92; $p = 0.003$), and the OR for nonrecovery in emergency versus elective patients was 6.18 (95% CI, 1.92–19.89; $p = 0.002$).

Resource Use, Length of Stay, Readmission Rates, and Clinical Outcomes

Patients with dysphagia had longer invasive MV (all $p \leq 0.002$), use of feeding tube (all $p < 0.001$), antibiotic/antimicrobial therapy ($p \leq 0.04$), and more need for adrenaline ($p \leq 0.008$) (**Table 2**). Overall resource use (cumulative TISS-28 points, all $p < 0.001$), ICU and hospital length of stay (all $p \leq 0.008$), and all-cause hospital mortality rate (all $p \leq 0.02$) were higher in screening positive patients (Table 2). In respective patients, all-cause 28-day and 90-day mortality was increased by 6.6% and 9.2%, respectively (Table 2), with more frequent reintubations ($n = 34/116$; 29.3% vs 33/817; 4.0%; $p < 0.001$) and more ICU readmissions ($n = 20/116$; 17% vs 61/756; 7.5%; $p < 0.001$) observed. Patients with dysphagia were less likely to be discharged home (with/without receiving home care) (13.8% vs 29.0%; OR, 0.40 [95% CI, 0.23–0.69]; $p = 0.001$) and more likely discharged to other hospitals (including rehabilitation hospitals) (77.9% vs 67.3%; OR, 1.71; 95% CI, 1.07–2.73; $p = 0.03$). Hospital readmission rates within 14 days from hospital discharge in patients with versus without dysphagia did not differ (1.7% vs 0.9%; $p = 0.4$).

Association of Dysphagia With Clinical Outcomes

In univariate regression (**Table 3**), baseline disease severity (APACHE-II and SAPS-II scores, both $p \leq 0.001$), admission status (i.e., emergency vs elective) ($p = 0.002$), days

TABLE 2. Resource Use, Length of Stay, and Clinical Outcomes

Variables	Total Groups			
	All, $n = 933$	Dysphagia Screening Positive, $n = 116$	Dysphagia Screening Negative, $n = 817$	p
Days on invasive mechanical ventilation, median (IQR)	0.7 (0.5–1.3)	1.2 (0.6–3.3)	0.7 (0.5–1.1)	**< 0.001**
Days on feeding tube, median (IQR)	0.6 (0.4–2.3)	4.5 (1.7–6.8)	0.6 (0.3–1.5]	**< 0.001**
Days on nasogastric tube, median (IQR)	0.6 (0.4–2.0)	4.2 (1.6–6.4)	0.6 (0.3–1.4]	**< 0.001**
Days on antibiotics, median (IQR)	1.0 (0.0–2.0)	1.0 (1.0–4.5)	1.0 (0.0–2.0)	**0.04**
Days on antimicrobials, median (IQR)	1.0 (0.0–2.0)	1.0 (1.0–4.5)	1.0 (0.0–2.0)	**0.04**
Days on vasopressors, median (IQR)	0 (0–0.5)	0.005 (0–0.8)	0 (0–0.5)	0.35
Days on adrenaline, median (IQR), median (IQR)	0 (0–0)	0 (0–0.1)	0 (0–0)	**0.008**
Days on noradrenaline, median (IQR)	0 (0–0.3)	0 (0–0.5)	0 (0–0.3)	0.47
Patients on vasopressors, *n* (%)	494 (52.9)	64 (55.2)	431 (52.8)	0.7
Patients on renal replacement therapy, *n* (%)	47 (5.0)	12 (10.3)	35 (4.3)	**0.01**
Cumulative Therapeutic Intervention Scoring System-28 points, median (IQR)	124 (98–260)	344 (183–758)	119 (94–223)	**< 0.001**
ICU LOS total days, median (IQR)	1.0 (0.8–2.2)	2.9 (1.6–6.0)	0.9 (0.8–1.8)	**< 0.001**
ICU LOS until extubation, median (IQR)	0.5 (0.3–1.2)	1.2 (0.4–3.3)	0.5 (0.3–0.9)	**< 0.001**
ICU LOS after extubation, median (IQR)	0.5 (0.3–0.9)	1.1 (0.7–2.5)	0.5 (0.3–0.8)	**< 0.001**
Hospital LOS (d), median (IQR)	11.0 (8.0–17.6)	17.9 (7.8–24.9)	10.2 (8.0–15.8)	**< 0.001**
All-cause ICU mortality, *n* (%)	8 (0.9)	2 (1.7)	6 (0.7)	0.3
All-cause hospital mortality, *n* (%)	22 (2.4)	9 (7.8)	13 (1.6)	**0.001**
All-cause 28-day mortality, *n* (%)	35 (3.8)	11 (9.5)	24 (2.9)	**0.002**
All-cause 90-day mortality, *n* (%)	45 (4.8)	15 (12.9)	30 (3.7)	**< 0.001**

IQR = interquartile range, LOS= length of stay.

Total group; data for emergency and elective subgroups is given in **Table E4** (Supplemental Digital Content 1, http://links.lww.com/CCM/C952). Mann-Whitney *U* or Fisher exact test. Cumulative Therapeutic Intervention Scoring System-28 points are given for total ICU stay.

Boldface values indicate statistically significant results.

TABLE 3. Univariate and Multivariate Regression Models (28-d Mortality)

	Univariate Model (28 d Following ICU Admission)			Multivariate Model (28 d Following ICU Admission)		
Variables	**Hazard Ratio (95% CI)**	***p***	**Wald**	**Hazard Ratio (95% CI)**	***p***	**Wald**
Age (per 1 yr increase)	1.02 (0.99–1.05)	0.09	2.9	1.01 (0.99–1.04)	0.35	0.88
Gender (female)	1.51 (0.76–3.004)	0.24	1.4	1.27 (0.64–2.54)	0.5	0.46
Weight (per 1 kg increase)	0.98 (0.96–1.002)	0.07	3.3	–	–	–
Body mass index (per 1 step increase)	0.97 (0.90–1.05)	0.46	0.6	–	–	–
Acute Physiology and Chronic Health Evaluation-II score (per 1 increase)	1.09 (1.05–1.14)	**< 0.001**	15.6	1.07 (1.02–1.13)	**0.005**	8
Simplified Acute Physiology Score-II score (per 1 increase)	1.04 (1.02–1.06)	**< 0.001**	12.7	–	–	–
Cumulative Therapeutic Intervention Scoring System-28 points (per 10 increase)	1.004 (0.99–1.01)	0.11	2.6	–	–	–
Admission status (emergency group)	3.90 (1.62–9.40)	**0.002**	9.2	–	–	–
Dysphagia positivity on ICU (dysphagia group)	3.37 (1.65–6.87)	**< 0.001**	11.1	2.67 (1.29–5.51)	**0.008**	7
Days on invasive mechanical ventilation (per 1 increase)	1.05 (1.01–1.09)	**0.008**	7	1.05 (1.01–1.10)	**0.03**	4.6
Days on renal replacement therapy (per 1 increase)	1.03 (0.92–1.15)	0.65	0.2	–	–	–
Days on vasopressors (per 1 increase)	0.99 (0.87–1.13)	0.83	0.05	–	–	–
Days on antimicrobials (per 1 increase)	0.90 (0.78–1.04)	0.16	2	–	–	–
Days on antibiotics (per 1 increase)	0.89 (0.77–1.04)	0.14	2.2	–	–	–

Hazard ratios for (co-) variates for ICU patients after mechanical ventilation. Acute Physiology and Chronic Health Evaluation-II and Simplified Acute Physiology Score-II score at ICU admission. Overall model fitness: $p < 0.001$, $\chi^2 = 24.1$.

Boldface values indicate statistically significant results. Dashes indicate data not included in model.

on MV ($p = 0.008$), and dysphagia status ($p < 0.001$) were associated with 28-day mortality. The univariate hazard for 28-day mortality was increased in patients with dysphagia (vs nonaffected patients; Table 3). In multivariate regression (Table 3), dysphagia was independently associated with 28-day mortality (HR, 2.67; 95% CI, 1.29–5.51; $p = 0.008$) after adjustment for age, gender, disease severity (APACHE-II score), and length of MV. When SAPS-II instead of APACHE-II scores, or admission status (emergency vs elective), or admission for neurologic/ nonneurologic disease (APACHE-IV admission category) was included in the model, dysphagia remained an independent predictor (not shown). The univariate HR for 90-day mortality was increased in the dysphagia group also (**Table E2**, Supplemental Digital Content 1, http://links.lww.com/CCM/C952). After adjustment, dysphagia (HR, 2.95; 95% CI, 1.57–5.53; $p < 0.001$) and APACHE-II score remained independent predictors of 90-day mortality (Table E2, Supplemental Digital Content 1, http://links.lww.com/CCM/C952; survival estimates following ICU admission [**Fig. 2**] and following extubation [**Fig. E2**, Supplemental Digital Content 1, http://links.lww.com/CCM/C952] are given).

DISCUSSION

Our main finding was a high incidence of dysphagia after extubation, its persistence until hospital discharge, and its association with clinically relevant adverse outcomes. The prospective large-scale approach applying systematic screening in a general ICU population may be regarded a strength of our analysis, and the high incidence was confirmed in an independent sample of comparable patients from another institution. Use of simple structured standardized bedside dysphagia screening by trained ICU nurses enabled systematic testing of all extubated patients, with the vast majority of screening positive cases being confirmed in prompt specialist examinations. Overall, the incidence was likely underestimated due to exclusion of 65 patients leaving our ICU alive with tracheostomy (no extubation/decannulation).

We observed that patients with postextubation dysphagia had longer tube feeding and MV, more antimicrobial drugs and ICU resources, increased ICU and hospital length of stay, and increased intrahospital-, 28-day-, and 90-day mortality. After adjustment for age, gender, length of MV, and baseline disease severity (APACHE-II or SAPS-II), or neurologic versus nonneurologic disease, dysphagia remained an independent predictor for 28-day

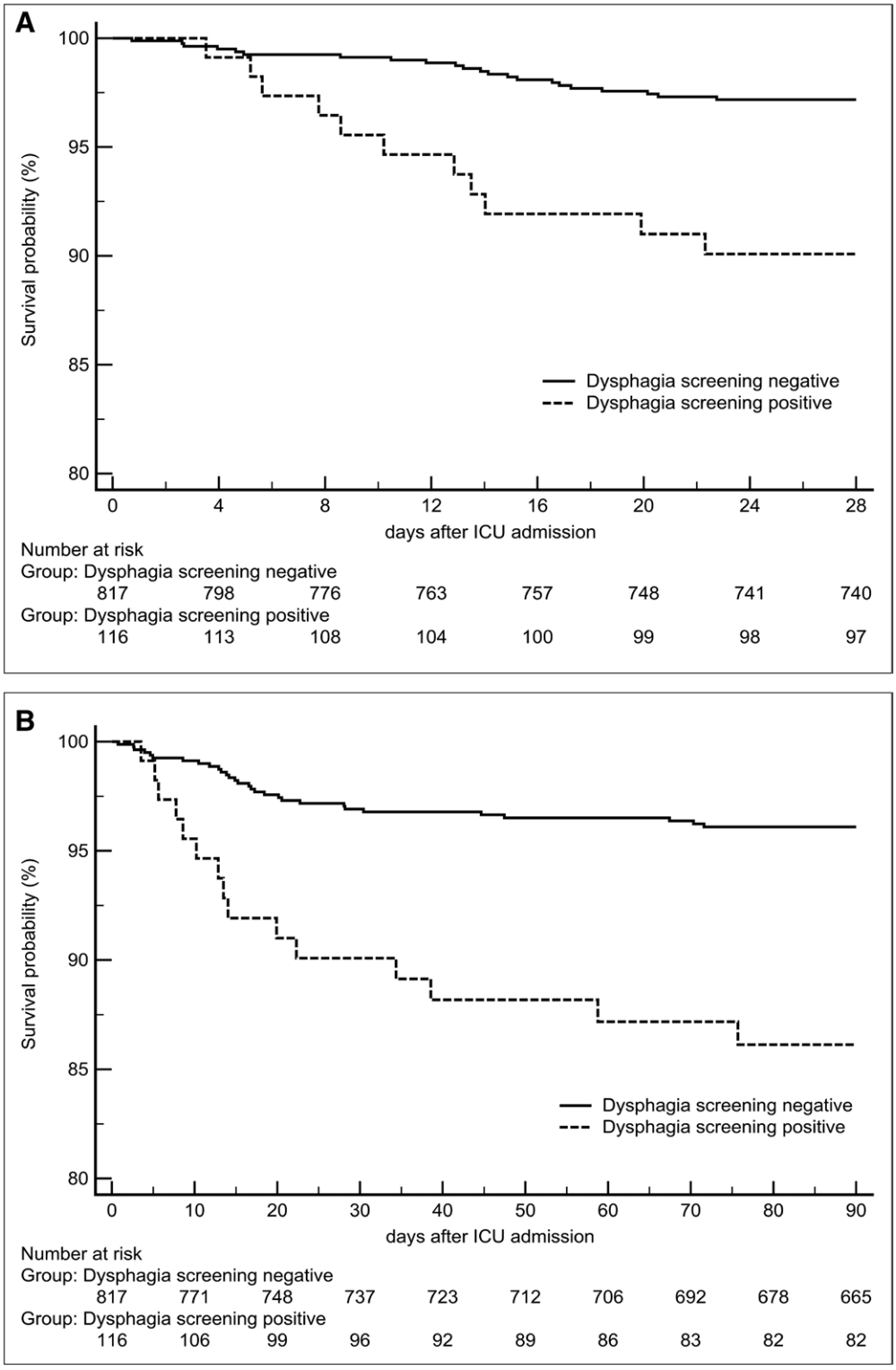

Figure 2. Survival estimates for (**A**) all-cause 28-d and (**B**) all-cause 90-d mortality in dysphagia screening positive/negative patients (days after ICU admission). Log-rank *p* value both $p < 0.001$. Numbers at risk are indicated. Survival estimates (28 and 90 d) from extubation are given in Fig E2 (Supplemental Digital Content 1, http://links.lww.com/CCM/C952).

and 90-day mortality. However, due to the observational nature of the trial, no cause-effect relationships can be concluded on.

Several limitations of our analysis deserve discussion. First, we present observations rather than cause-effect relationships. Hence, potential risk factors for dysphagia can be considered, but no conclusions on mechanisms can be made. Second, all swallowing examinations, even when performed by dysphagia specialists, have problems with sensitivity/specificity, and there are no universally accepted bedside screening tools for dysphagia. Ideally, confirmation of dysphagia in screening positive individuals using instrumental assessment with FEES or VFSS would have allowed better specificity. We decided against the use of these confirmatory methods on logistic reasons, for example, transport to radiology suite for VFSS and availability of trained operators for FEES, and the relative invasiveness of both VFSS and FEES in recently extubated patients. Our choice to use the WST as a pragmatic bedside screening tool followed by comprehensive specialist clinical examinations in screening positive cases thus is a compromise between feasibility and specificity. Several other investigators including a recent systematic review and meta-analysis support the use of the WST in dysphagia screening (1, 2, 9, 17, 32). Third, although about 90% of screening positive cases were confirmed to have dysphagia within a maximum time interval of 24 hours (positive predictive value 87.3%), the bedside screening procedure may have missed some dysphagia patients. Since only patients who tested positive in screening were further evaluated for dysphagia, we cannot provide the negative predictive value of the bedside screening approach. Nevertheless, the strong association between clinically relevant outcomes and dysphagia in this study supports the use of this pragmatic screening approach. Fourth, our statistical models include disease severity (scores) which potentially introduces some colinearity. Despite this, adjustment for disease severity was considered inevitable.

Further, one might argue that dysphagia could simply be a consequence of disease severity. Although disease severity was identified as a potential contributing factor to dysphagia in explorative analyses, dysphagia remained an independent predictor of all-cause, 28-day-, and 90-day mortality, when disease severity (APACHE-II or SAPS-II score), length of MV, admission status (e.g., emergency vs elective) (Table 3), and/or admission category (e.g., neurologic vs nonneurologic) were adjusted for. Thus, dysphagia may additionally worsen the outcome of affected patients. Although we are unaware of the exact causes for dysphagia, it seems tempting to speculate that future interventions for dysphagia might provide highest clinical benefits in patients with advanced disease severity. Fifth, the confirmatory cohort and the main cohort were somewhat different in regard to the distribution of emergency and elective admissions and underlying diagnoses (see supplement, Supplemental Digital Content 1, http://links.lww.com/CCM/C952). Nevertheless, the main findings were very similar indeed.

The increased number of neurologic patients with dysphagia suggests that some cases can most likely be attributed to specific diseases, for example, stroke or injury, whereas in the majority, no specific cause could be identified. Similar patterns of increased dysphagia incidence were found in the total cohort of patients and in those without neurologic reason for ICU admission after more than 2 days of intubation/MV (**Fig. E3**, Supplemental Digital Content 1, http://links.lww.com/CCM/C952). This association between duration of intubation/MV and subsequent development of dysphagia suggest that mechanical effects induced by the endotracheal tube should be evaluated as a potential cause of dysphagia in subsequent analyses. Other potential mechanisms include use of drugs that may interfere with swallowing, for example, analgesic/sedative drugs. However, the overall short duration of MV in our trial suggests that exposure to these drugs was short, and hence unlikely to be a major contributor to dysphagia. Even about 5% of elective patients with rather short times of MV were dysphagia positive, which may help to gain insight to underlying causes.

CONCLUSIONS

In conclusion, prospective systematic screening for dysphagia after extubation followed by early specialist confirmation demonstrated a high incidence of dysphagia. Patients with higher disease severity, emergency admission, and/or underlying neurologic disease were at increased risk for dysphagia. Dysphagia detected in the ICU persisted in the majority of affected patients throughout the hospital stay and was itself associated with increased morbidity and mortality. Dysphagia after MV thus seems an overlooked health problem that is associated with adverse clinical outcomes. Studies on underlying reasons and therapeutic interventions seem warranted.

ACKNOWLEDGMENTS

We thank all nurses and nursing specialists, all ICU staff, research nurses, and physiotherapists/speech language therapists for their dedicated care and support of DYnAMICS. We also thank senior statistician Dr. Andreas Limacher, CTU Bern, University of Bern, Switzerland, for expert statistical advice.

REFERENCES

1. Macht M, White SD, Moss M: Swallowing dysfunction after critical illness. *Chest* 2014; 146:1681–1689
2. Macht M, Wimbish T, Bodine C, et al: ICU-acquired swallowing disorders. *Crit Care Med* 2013; 41:2396–2405
3. Skoretz SA, Yau TM, Ivanov J, et al: Dysphagia and associated risk factors following extubation in cardiovascular surgical patients. *Dysphagia* 2014; 29:647–654
4. Smithard DG, O'Neill PA, Parks C, et al: Complications and outcome after acute stroke. Does dysphagia matter? *Stroke* 1996; 27:1200–1204
5. Westergren A, Ohlsson O, Rahm Hallberg I: Eating difficulties, complications and nursing interventions during a period of three months after a stroke. *J Adv Nurs* 2001; 35:416–426
6. Macht M, King CJ, Wimbish T, et al: Post-extubation dysphagia is associated with longer hospitalization in survivors of critical illness with neurologic impairment. *Crit Care* 2013; 17:R119
7. Altman KW, Yu GP, Schaefer SD: Consequence of dysphagia in the hospitalized patient: Impact on prognosis and hospital resources. *Arch Otolaryngol Head Neck Surg* 2010; 136:784–789
8. Altman KW: Dysphagia evaluation and care in the hospital setting: The need for protocolization. *Otolaryngol Head Neck Surg* 2011; 145:895–898
9. Skoretz SA, Flowers HL, Martino R: The incidence of dysphagia following endotracheal intubation: A systematic review. *Chest* 2010; 137:665–673
10. Ferraris VA, Ferraris SP, Moritz DM, et al: Oropharyngeal dysphagia after cardiac operations. *Ann Thorac Surg* 2001; 71:1792–1795; discussion 1796
11. de Larminat V, Montravers P, Dureuil B, et al: Alteration in swallowing reflex after extubation in intensive care unit patients. *Crit Care Med* 1995; 23:486–490
12. Brodsky MB, Huang M, Shanholtz C, et al: Recovery from dysphagia symptoms after oral endotracheal intubation in acute respiratory distress syndrome survivors. A 5-year longitudinal study. *Ann Am Thorac Soc* 2017; 14:376–383
13. Brown CV, Hejl K, Mandaville AD, et al: Swallowing dysfunction after mechanical ventilation in trauma patients. *J Crit Care* 2011; 26:108.e9–108.e13
14. Moraes DP, Sassi FC, Mangilli LD, et al: Clinical prognostic indicators of dysphagia following prolonged orotracheal intubation in ICU patients. *Crit Care* 2013; 17:R243
15. Zielske J, Bohne S, Brunkhorst FM, et al: Acute and long-term dysphagia in critically ill patients with severe sepsis: Results of a prospective controlled observational study. *Eur Arch Otorhinolaryngol* 2014; 271:3085–3093
16. Brodsky MB, Gellar JE, Dinglas VD, et al: Duration of oral endotracheal intubation is associated with dysphagia symptoms in acute lung injury patients. *J Crit Care* 2014; 29:574–579
17. Macht M, Wimbish T, Clark BJ, et al: Postextubation dysphagia is persistent and associated with poor outcomes in survivors of critical illness. *Crit Care* 2011; 15:R231
18. Hopkins RO, Jackson JC: Long-term neurocognitive function after critical illness. *Chest* 2006; 130:869–878
19. Kahn JM, Benson NM, Appleby D, et al: Long-term acute care hospital utilization after critical illness. *JAMA* 2010; 303:2253–2259
20. Brummel NE, Balas MC, Morandi A, et al: Understanding and reducing disability in older adults following critical illness. *Crit Care Med* 2015; 43:1265–1275
21. Iwashyna TJ, Ely EW, Smith DM, et al: Long-term cognitive impairment and functional disability among survivors of severe sepsis. *JAMA* 2010; 304:1787–1794
22. Sue RD, Susanto I: Long-term complications of artificial airways. *Clin Chest Med* 2003; 24:457–471

23. Bishop MJ, Weymuller EA Jr, Fink BR: Laryngeal effects of prolonged intubation. *Anesth Analg* 1984; 63:335–342
24. Schefold JC, Bierbrauer J, Weber-Carstens S: Intensive care unit-acquired weakness (ICUAW) and muscle wasting in critically ill patients with severe sepsis and septic shock. *J Cachexia Sarcopenia Muscle* 2010; 1:147–157
25. Berger D, Bloechlinger S, von Haehling S, et al: Dysfunction of respiratory muscles in critically ill patients on the intensive care unit. *J Cachexia Sarcopenia Muscle* 2016; 7:403–412
26. Jolley SE, Bunnell AE, Hough CL: ICU-acquired weakness. *Chest* 2016; 150:1129–1140
27. Kim MJ, Park YH, Park YS, et al: Associations between prolonged intubation and developing post-extubation dysphagia and aspiration pneumonia in non-neurologic critically ill patients. *Ann Rehabil Med* 2015; 39:763–771
28. DeVita MA, Spierer-Rundback L: Swallowing disorders in patients with prolonged orotracheal intubation or tracheostomy tubes. *Crit Care Med* 1990; 18:1328–1330
29. El Solh A, Okada M, Bhat A, et al: Swallowing disorders post orotracheal intubation in the elderly. *Intensive Care Med* 2003; 29:1451–1455
30. Tolep K, Getch CL, Criner GJ: Swallowing dysfunction in patients receiving prolonged mechanical ventilation. *Chest* 1996; 109:167–172
31. Bordon A, Bokhari R, Sperry J, et al: Swallowing dysfunction after prolonged intubation: Analysis of risk factors in trauma patients. *Am J Surg* 2011; 202:679–682; discussion 682–683
32. Brodsky MB, Suiter DM, González-Fernández M, et al: Screening accuracy for aspiration using bedside water swallow tests: A systematic review and meta-analysis. *Chest* 2016; 150:148–163
33. DePippo KL, Holas MA, Reding MJ: Validation of the 3-oz water swallow test for aspiration following stroke. *Arch Neurol* 1992; 49:1259–1261
34. Daniels SK, Anderson JA, Willson PC: Valid items for screening dysphagia risk in patients with stroke: A systematic review. *Stroke* 2012; 43:892–897
35. Macht M, Wimbish T, Clark BJ, et al: Diagnosis and treatment of post-extubation dysphagia: Results from a national survey. *J Crit Care* 2012; 27:578–586
36. Brady S, Donzelli J: The modified barium swallow and the functional endoscopic evaluation of swallowing. *Otolaryngol Clin North Am* 2013; 46:1009–1022
37. Perry L: Screening swallowing function of patients with acute stroke. Part one: Identification, implementation and initial evaluation of a screening tool for use by nurses. *J Clin Nurs* 2001; 10:463–473
38. Bartolome G: Schluckstörungen: Diagnostik und Rehabilitation. München, Urban & Fischer Verlag/Elsevier GmbH, 2006
39. Knaus WA, Draper EA, Wagner DP, et al: APACHE II: A severity of disease classification system. *Crit Care Med* 1985; 13:818–829
40. Le Gall JR, Lemeshow S, Saulnier F: A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. *JAMA* 1993; 270:2957–2963
41. Miranda DR, de Rijk A, Schaufeli W: Simplified Therapeutic Intervention Scoring System: The TISS-28 items–results from a multicenter study. *Crit Care Med* 1996; 24:64–73
42. Moreno R, Morais P: Validation of the simplified therapeutic intervention scoring system on an independent database. *Intensive Care Med* 1997; 23:640–644
43. O'Neil KH, Purdy M, Falk J, et al: The dysphagia outcome and severity scale. *Dysphagia* 1999; 14:139–145
44. Linacre JM, Heinemann AW, Wright BD, et al: The structure and stability of the Functional Independence Measure. *Arch Phys Med Rehabil* 1994; 75:127–132
45. Medical-Research-Council: Aids to the investigation of the peripheral nervous system (War Memorandum No. 7). London, United Kingdom, Her Majesty's Stationary Office, Medical Research Councils, 1943