Current practice in nutritional support and its association with mortality in septic patients—Results from a national, prospective, multicenter study*

Gunnar Elke, MD; Dirk Schädler, MD; Christoph Engel, MD; Holger Bogatsch; Inez Frerichs, MD; Maximilian Ragaller, MD; Jens Scholz, MD; Frank M. Brunkhorst, MD; Markus Löffler, MD; Konrad Reinhart, MD; Norbert Weiler, MD; for the German Competence Network Sepsis (SepNet)

Objective: **To identify current clinical practice regarding nutrition and its association with morbidity and mortality in patients with severe sepsis or septic shock in Germany.**

Design: **Nationwide prospective, observational, cross-sectional, 1-day point-prevalence study.**

Setting: **The study included 454 intensive care units from a representative sample of 310 hospitals stratified by size.**

Patients: **Participants were 415 patients with severe sepsis or septic shock (according to criteria of the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference).**

Interventions: **None.**

Measurements and Main Results: **Data were collected by onsite audits of trained external study physicians during randomly scheduled visits during 1 yr. Valid data on nutrition were available for 399 of 415 patients. The data showed that 20.1% of patients received exclusively enteral nutrition, 35.1% exclusively parenteral nutrition, and 34.6% mixed nutrition (parenteral and enteral); 10.3% were not fed at all. Patients with gastrointestinal/intraabdominal infection, pancreatitis or neoplasm of the gastrointestinal tract, mechanical ventilation, or septic shock were less likely to receive exclusively enteral nutrition. Median Acute Physiology and Chronic Health Evaluation II and Sepsis-related Organ Failure Assessment scores were significantly different among the nutrition groups. Overall hospital mortality was 55.2%. Hospital mortality was significantly higher in patients receiving exclusively parenteral (62.3%) or mixed nutrition (57.1%) than in patients with exclusively enteral nutrition (38.9%) (p = .005). After adjustment for patient morbidity (Acute Physiology and Chronic Health Evaluation II score, presence of septic shock) and treatment factors (mechanical ventilation), multivariate analysis revealed that the presence of parenteral nutrition was significantly predictive of mortality (odds ratio, 2.09; 95% confidence interval, 1.29–3.37).**

Conclusions: **Patients with severe sepsis or septic shock in German intensive care units received preferentially parenteral or mixed nutrition. The use of parenteral nutrition was associated with an increased risk of death. (Crit Care Med 2008; 36:1762–1767)**

Key Words: sepsis; severe sepsis; septic shock; nutritional support; enteral nutrition; parenteral nutrition

Appropriate nutritional support is an important but challenging part of standard supportive care during critical illness. Patients with severe sepsis or septic shock commonly suffer from compromised gastrointestinal function, including enhanced intestinal permeability and reduced motility (1, 2). Underlying malnutrition is often encountered in these patients (3). Intestinal stimulation by enteral nutrients helps to maintain bowel integrity and decreases translocation, resulting in less infectious sequelae and decreased length of hospital stay (4–6). In clinical practice, surveys have revealed that nutritional support greatly varies depending on the intensive care unit (ICU) size and country (7, 8). A considerable number of patients do not receive adequate amounts of nutrients as a result of inappropriate prescription or delivery (9, 10).

This led to the development of clinical practice guidelines with preference for early enteral nutrition over parenteral nutrition in the average critically ill patient (11, 12). It has been shown that adoption of these guidelines in clinical practice decreased inefficient nutritional support and improved patient outcome (13–15).

Still, the debate about what type of nutrition is appropriate in critically ill patients continues with respect to the following two issues. First, it is unclear

***See also p. 1964.**

From the Department of Anesthesiology and Intensive Care Medicine, University Medical Center Schleswig-Holstein, Campus Kiel, Germany (GE, DS, IF, JS, NW); Institute of Medical Informatics, Statistics and Epidemiology, University of Leipzig, Germany (CE, HB, ML); Department of Anesthesiology and Intensive Care Medicine, University Hospital of the Technical University of Dresden, Germany (MR); and Department of Anesthesiology and Intensive Care Medicine, University Hospital of the Friedrich-Schiller-University of Jena, Germany (FMB, KR).

Supported, in part, by grant 01 KI 0106 from the Federal Ministry of Education and Research, Berlin, Germany (BMBF) and an unrestricted grant from Lilly Germany, Bad Homburg, Germany.

The authors have not disclosed any potential conflicts of interest.

For information regarding this article, E-mail: elke@anaesthesie.uni-kiel.de

DOI: 10.1097/CCM.0b013e318174dcf0

whether the route of nutrition has an influence on mortality in these patients. Second, studies regarding the efficacy of nutritional support in specific subgroups of critically ill patients are lacking. Because evidence for enteral nutrition in septic patients is based on conclusions drawn from studies in heterogeneous patient populations, the strength of this recommendation is low (grade C/E) (16, 17). In a recent meta-analysis, Simpson and Doig (18) showed that parenteral nutrition was associated with reduced mortality compared with delayed enteral nutrition (odds ratio [OR], 0.29; 95% confidence interval [CI], 0.12–0.70; p = .006). However, this effect could not be shown when parenteral nutrition was compared with early enteral nutrition (OR, 1.07; 95% CI, 0.39–2.95; p = .89). In another meta-analysis, Peter et al. (19) found that the use of enteral nutrition significantly reduced complication rates compared with parenteral nutrition without influencing mortality. Both studies included heterogeneous patient populations rather than selected subgroups of critically ill patients.

To describe the current clinical practice of nutritional support in patients with severe sepsis or septic shock and assess its potential association with mortality, we collected and systematically evaluated data with respect to nutrition policies within the framework of the representative survey titled "Epidemiology of Sepsis in Germany" (20).

MATERIALS AND METHODS

Study Design. The study was carried out by the German Competence Network Sepsis (SepNet), consisting of 18 academic clinical centers, a medical coordination center (University of Jena), and a center for biometry, data management, and telematics (University of Leipzig). The study was approved by the responsible institutional ethics committees and by the federal data protection commissioner. Data were collected prospectively on a cross-sectional (1-day) basis by on-site audits of trained external physicians in a representative random sample of German hospitals. Visits were randomly distributed over 1 yr (2003). Paper-based case report forms were used, which were entered into a central database (eResearch Network, eResearch Technology, Philadelphia, PA). A detailed description of the study design is outlined elsewhere (20). Hospitals were separated into five strata as follows: strata one to four included all nonuniversity hospitals with ≤200, 201–400, 401–600, and >600 beds, respectively, and stratum five included all university hospitals. All patients occupying an ICU bed between 6 am of the study day and 6 am of the following day were screened for the presence of infection, systemic inflammatory response syndrome, and organ dysfunction or septic shock based on modified consensus criteria of the American College of Chest Physicians and Society of Critical Care Medicine. Patients identified with severe sepsis or septic shock were then subjected to an extended documentation. This included demographic data (age, gender, weight, height), main diagnoses, comorbidities, and severity of illness (Acute Physiology and Chronic Health Evaluation [APACHE] II, Sepsis-related Organ Failure Assessment [SOFA] score) as well as diagnostic and therapeutic measures, including nutrition. Total length of ICU and hospital stay as well as hospital mortality was assessed by prospective follow-up after 3 months (by telephone or written inquiry).

Statistical Analysis. SPSS 11.0.1 (SPSS, Chicago, IL) was used for all data analyses. Categorical outcome data were reported as absolute or relative frequencies where appropriate. The effect on mortality was expressed with 95% confidence interval. The chi-square test and the Kruskal-Wallis H test were applied to compare categorical and continuous variables where appropriate.

We performed multivariate logistic regression analysis to identify independent predictors associated with the likelihood of receiving exclusively enteral nutrition. Besides patient morbidity (APACHE II and SOFA scores and presence of septic shock) and treatment factors (mechanical ventilation), we controlled for hospital size as well as length of ICU and hospital stay before study entry. We also adjusted for clinical diagnoses suspected to influence the route of nutritional support (enteral or parenteral). This applied to patients with: 1) gastrointestinal (GI) or intra-abdominal infection; 2) acute pancreatitis confirmed by either laboratory variables or computer tomography of the abdomen; or 3) neoplasm of the upper or lower GI tract.

Multivariate analysis was also used to analyze the association of the type of nutrition (enteral or parenteral) with mortality. In this analysis we adjusted for patient morbidity (APACHE II score, presence of septic shock, and renal dysfunction) as well as treatment factors (mechanical ventilation). Both analyses included only those factors that were found to be significantly predictive in a preceding univariate analysis ($p < .05$).

APACHE II and SOFA scores were evaluated from documented physiologic and chronic disease variables as described elsewhere (21, 22). If a single variable was not documented, the corresponding subscore was set to zero.

RESULTS

ICU and Hospital Characteristics

The total study sample included 454 ICUs from 310 hospitals of the following categories: university hospitals (n = 10, 3.2%), university-affiliated hospitals (n = 106, 34.2%), general hospitals (n = 173, 55.8%), and others (n = 21, 6.8%). In total, 3,877 patients were screened for the presence of infection, systemic inflammatory response syndrome, and organ dysfunction or septic shock based on modified American College of Chest Physicians/Society of Critical Care Medicine consensus criteria. Among these patients, a total of 415 patients were found to have severe sepsis or septic shock.

Table 1 shows patient demographics along with information on hospital characteristics. Valid data about nutritional support were available for 399 of the 415 patients. Type of nutrition differed significantly with hospital size (p = .0006). University hospitals and hospitals in stratum 2 mostly used a combination of enteral and parenteral nutrition (52 of 100 patients or 21 of 51 patients, respectively); hospitals in strata 2 and 4 preferred the parenteral route (43 of 101 patients or 42 of 104 patients, respectively). Mean length of ICU and hospital stay before study entry was greatest for patients from university hospitals.

Patient Characteristics and Morbidity. Overall, 20.1% of patients received enteral nutrition, and 35.1% received only parenteral nutrition. Mixed parenteral and enteral nutrition was administered to 34.6% of patients, whereas 10.3% of the patients received no nutritional support at all. Median patient age was 67 yrs. Types of nutrition differed significantly with age: The oldest patients were encountered in the group receiving no nutrition.

Significant differences in severity of illness measures (APACHE II and SOFA scores), the presence of septic shock, and the number of patients receiving mechanical ventilation were found between the nutrition groups (Table 1).

We found that 68.7% of patients had no GI/intra-abdominal infection, pancreatitis, or neoplasm of the gastrointestinal tract. These patients were more often fed exclusively via the parenteral route (78 of 274 patients) or with mixed nutrition (102 of 274 patients).

Table 1. Patient demographics, morbidity, and hospital characteristics by types of nutritional support

Variable	Total n = 399 (100.0%)	Exclusively Enteral Nutrition n = 80 (20.1%)	Exclusively Parenteral Nutrition n = 140 (35.1%)	Mixed Nutrition n = 138 (34.6%)	No Nutrition n = 41 (10.3%)	p Value[a]
Age, median yrs; IQR	67; 53–74	71; 54–76	69; 57–74	62; 50–73	71; 60–78	.0128
Gender, n (%)						.9625
Male	233 (58.4)	47 (58.8)	80 (57.1)	81 (58.7)	25 (61.0)	
Female	163 (40.9)	32 (40.0)	60 (42.9)	55 (39.9)	16 (39.0)	
BMI, median; IQR	26; 23–29	26; 23–31	26; 22–29	26; 23–29	26; 22–30	.8861
APACHE II, median; IQR	19; 13–24	17; 12–23	21; 16–26	19; 13–23	21; 15–30	.0049
SOFA, median; IQR	8; 5–11	6; 4–10	9; 6–12	8; 6–11	8; 6–12	.0147
Septic shock, n (%)						<.0001[b]
No	202 (50.6)	60 (75.0)	55 (39.3)	69 (50.0)	18 (43.9)	
Yes	184 (46.1)	18 (22.5)	82 (58.6)	62 (44.9)	22 (53.7)	
Unknown	13 (3.3)	2 (2.5)	3 (2.1)	7 (5.1)	1 (2.4)	
Mechanical ventilation, n (%)	324 (81.2)	51 (63.8)	127 (90.7)	119 (86.2)	27 (65.9)	<.0001
Renal replacement, n (%)	82 (20.6)	10 (12.5)	30 (21.4)	35 (25.4)	7 (17.1)	.4583
GI/intra-abdominal diseases, n (%)						
No	274 (68.7)	71 (88.8)	78 (55.7)	102 (73.9)	23 (56.1)	<.0001[d]
Yes	125 (31.3)	9 (11.3)	62 (44.3)	36 (26.1)	18 (43.9)	<.0001
GI/intra-abdominal infection[c]	116 (29.1)	8 (10.0)	58 (41.4)	32 (23.2)	18 (43.9)	
Pancreatitis[c]	16 (4.0)	3 (3.8)	5 (3.6)	8 (5.8)	0 (0.0)	
Neoplasm of GI tract[c]	37 (9.3)	2 (2.5)	20 (14.3)	12 (8.7)	3 (7.3)	
Insulin dose, mean IU/24 hrs	34.7	27.3	32.0	46.4	18.8	.0002
Serum glucose concentration, mean mg/dL	181	178	179	186	178	.9602
LOS ICU, mean days	12.3	13.0	15.3	13.6	9.3	.706
LOS hospital, mean days	32.9	30.4	28.2	40.6	29.3	.0147
Stratum, n (%)[e]						.0006
1	43 (10.8)	10 (12.5)	12 (8.6)	15 (10.9)	6 (14.6)	
2	101 (25.3)	22 (27.5)	43 (30.7)	26 (18.8)	10 (24.4)	
3	51 (12.8)	6 (7.5)	14 (10.0)	21 (15.2)	10 (24.4)	
4	104 (26.1)	30 (37.5)	42 (30.0)	24 (17.4)	8 (19.5)	
5	100 (25.1)	12 (15.0)	29 (20.7)	52 (37.7)	7 (17.1)	
Specialty of ICU physician, n (%)						.6523
Surgical	145 (36.3)	27 (33.8)	50 (35.7)	53 (38.4)	15 (36.6)	
Medical	118 (29.6)	31 (38.8)	36 (25.7)	40 (29.0)	11 (26.8)	
Mixed	126 (31.6)	22 (27.5)	47 (33.6)	42 (30.4)	15 (36.6)	
Number of beds, median; IQR	12; 8–14	12; 9–14	11; 8–14	12; 9–14	10; 7–16	.7192
Hospital LOS before study entry, mean days	17.0	13.7	18.1	20.8	7.5	<.0001
ICU LOS before study entry, mean days	11.4	11.0	9.6	16.1	3.2	<.0001

IQR, interquartile range; BMI, body mass index; APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sepsis-related Organ Failure Assessment; GI, gastrointestinal; LOS, adjusted length of stay; ICU, intensive care unit. Sum of patient numbers within a variable may be lower than total column patient number due to missing data.

[a]Global tests for differences among types of nutritional support; [b]category "unknown" was excluded; [c]groups are not mutually exclusive; [d]yes vs. no; [e]strata 1–4 include all nonuniversity hospitals with ≤200, 201–400, 401–600, and >600 beds, respectively; stratum 5 includes all university hospitals.

Patients receiving a combination of enteral and parenteral nutrition required higher doses of insulin (mean 46.4 IU per 24 hrs) than patients in the other nutrition groups (p = .0002), while the maximum serum glucose concentration was not significantly different.

Length of hospital stay was significantly different among the nutrition groups, with the longest hospitalization time found in the patients with mixed nutrition (p = .0147).

The number of patients receiving immunonutrition, parenteral glutamine, or selenium was relatively small (3.9%, 4.3%, or 9.9% of the patients, respectively) and hence not further evaluated.

Predictors for Exclusively Enteral Nutrition. Independent predictors associated with the use of enteral nutrition are summarized in Table 2. Patients with mechanical ventilation (OR, 0.48; 95% CI, 0.26–0.91), a GI/intra-abdominal disease (OR, 0.24; 95% CI, 0.11–0.53), and the presence of septic shock (OR, 0.31; 95% CI, 0.16–0.61) were less likely to receive exclusively enteral nutrition. Hospital size or the length of hospital or ICU stay before study entry had no influence on the type of nutritional support.

Mortality. The overall hospital mortality was 55.2% (Table 3). Hospital mortality was significantly higher in patients receiving exclusively parenteral (62.3%) or mixed nutrition (57.1%) than in patients with exclusively enteral nutrition (38.9%) (p = .005).

Multivariate analysis revealed that the presence of parenteral nutrition was a significant independent predictor for mortality (OR, 2.09; 95% CI, 1.29–3.37). Furthermore, the APACHE II score (OR, 1.05; 95% CI, 1.02–1.09) and the presence of renal dysfunction (OR, 2.07; 95% CI, 1.30–3.31) were found to be signifi-

Table 2. Independent predictors for exclusively enteral nutrition

Variable	Univariate OR	Univariate p Value	Multivariate[a] OR[b]	Multivariate[a] 95% CI
Age	1.01	.149		
Gender	0.97	.895		
APACHE II	0.97	.081		
SOFA	0.91	.006	0.99	0.92–1.08
Septic shock	0.26	<.0001	0.31	0.16–0.61
Mechanical ventilation	0.31	<.0001	0.48	0.26–0.91
GI/intra-abdominal diseases[c]	0.22	<.0001	0.24	0.11–0.53
Stratum				
1[d]	1.00			
2	0.92	.846		
3	0.44	.146		
4	1.34	.489		
5	0.45	.092		
Hospital LOS before study	0.98	.088		
ICU LOS before study entry	0.99	.739		

OR, odds ratio; CI, confidence interval; APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sepsis-related Organ Failure Assessment; GI, gastrointestinal; ICU, intensive care unit; LOS, length of stay.

[a]Includes only variables that were significant in univariate analysis; [b]OR <1 indicates a lesser likelihood of receiving enteral nutrition; [c]GI/intra-abdominal diseases include gastrointestinal/intra-abdominal infection, pancreatitis, or neoplasm of the gastrointestinal tract; [d]reference category.

Table 3. Mortality

	No.	Mortality No.	Mortality %	Mortality 95% CI
Overall[a]	382	211	55.2	50.2–60.2
Nutritional support	374	205	54.8	49.8–59.8
Exclusively enteral	72	28	38.9	28.5–50.4
Exclusively parenteral	130	81	62.3	53.7–70.2
Mixed nutrition	133	76	57.1	48.7–65.2
No nutrition	39	20	51.3	36.2–66.1
Septic shock				
No	184	86	46.7	39.7–53.9
Yes	177	110	62.2	54.8–69.0
APACHE II (tertiles)[b]				
≤17	153	64	41.8	34.3–49.8
18–24	132	77	58.3	49.8–66.4
≥25	89	64	71.9	61.8–80.2

CI, confidence interval; APACHE, Acute Physiology and Chronic Health Evaluation. Of 415 patients with severe sepsis, 382 patients had valid follow-up information on mortality; 374 patients had valid mortality information in the subgroup nutrition.

[a]Of all patients with severe sepsis/septic shock; [b]odds ratio per point increase.

cant predictors for hospital mortality (Table 4).

DISCUSSION

This study is the first to present data about the practice of nutritional support in a large and representative sample of patients with severe sepsis or septic shock. Parenteral nutrition, either exclusively or in combination with enteral nutrition, was preferably used in this specific patient group, but overall nutritional support varied considerably with hospital size. Enteral nutrition was less frequently used in patients with mechanical ventilation, GI/intra-abdominal infection, pancreatitis, or neoplasm of the gastrointestinal tract as well as in patients with septic shock. Moreover, receiving parenteral nutrition was associated with an increased risk of death.

Prior surveys reported a privileged use of the enteral route in critically ill patients with a broad spectrum of different diseases, which is in accordance with evidence-based recommendations for nutrition (11, 12). Results of a questionnaire from 35 European countries showed that the enteral route was used preferably, ranging from 33% up to 92%, compared with parenteral nutrition (19% to 71%) or mixed nutrition (4% to 52%) (7). Nutritional support practices markedly depended on the country and ICU or hospital size (8, 23, 24). In Canada, the majority of patients (44.6%) received exclusively enteral nutrition, which was more likely in larger ICUs and in an academic setting (8). In contrast, half of our study population originated from larger hospitals (>600 beds and academic hospitals) and received predominantly parenteral nutrition. Neither the specialty of ICU physicians nor the ICU size had an influence on the type of nutrition in our study (Table 1). Considering the well-known deleterious effects of starvation or malnourishment (25), the number of patients receiving no nutrition (10.9%) was relatively high in our study. These patients were significantly older and more severely ill compared with patients receiving nutritional support.

The low percentage of enteral nutrition used in our study might be related to the presence of severe sepsis or septic shock. The recommendation for the preferential use of enteral nutrition in septic patients (compared with other critically ill patients) is weak (grade C/E) (16, 17). This might have promoted a rather arbitrary nutritional support management among ICU physicians.

In addition, the relatively low prescription rate of enteral nutrition in our study was influenced by three patient-related variables. Patients with mechanical ventilation, GI/intra-abdominal disease, or septic shock were less likely to receive nutritional support via the enteral route.

In view of current clinical practice guidelines, the presence of mechanical ventilation should not prevent ICU physicians from prescribing enteral nutrition (12).

Patients with GI/intra-abdominal diseases were assumed to have impaired GI tract function. However, these diseases *per se* do not reflect absolute contraindications to the initiation of enteral nutrition. For example, patients with acute pancreatitis should be fed preferentially via the enteral route (26). In the study by Barr et al. (14), surgical patients were especially less likely to receive enteral nutrition compared with medical patients, despite the fact that the former group had lower Simplified Acute Physi-

Table 4. Independent predictors for mortality

Variable	Univariate		Multivariate[a]	
	OR	*p* Value	OR	95% CI
Enteral nutrition	0.68	.065	1.13	0.84–1.51
Parenteral nutrition	1.97	.003	2.09	1.29–3.37
APACHE II	1.07	<.0001	1.05	1.02–1.09
Renal dysfunction[b]	2.91	<.0001	2.07	1.30–3.31
Insulin dose (IU/24 hrs)	1.00	.338		
Serum glucose concentration (mg/dL)	1.00	.145		
Age	1.01	.051	1.01	0.99–1.02
Gender	0.90	.609		
Mechanical ventilation	2.88	.083		
Septic shock	1.85	.004	1.54	0.97–2.44

OR, odds ratio; CI, confidence interval; APACHE, Acute Physiology and Chronic Health Evaluation.
[a]Includes only variables that were significant in the univariate analysis; [b]renal dysfunction was defined as urine output <0.5 mL/kg body weight in a time interval of ≥1 hr despite an adequate fluid substitution or an increase in serum creatinine more than twice the reference category.

ology Score II. The authors suggested that these patients were treated according to the traditional surgical approach of withholding enteral feeding in the early course of their ICU stay. This observation reflected a bias against the adequate use of enteral nutrition and may provide a reasonable explanation why patients with GI/ intra-abdominal diseases were less likely to receive enteral nutrition in our study.

De Jonghe et al. (9) reported that an inadequate prescription rate of enteral nutrition was influenced by the level of critical care required. In their study, the use of vasoactive drugs was independently associated with a low prescription rate of enteral nutrition. Thus, the more severely ill the patient, the less attention was paid to the indication of feeding in favor of other interventions. This agrees with our finding that patients with septic shock especially did not receive enteral nutrition, which may also reflect possible confounding by indication. However, we found no correlation between severity of illness measures (APACHE II and SOFA scores) and the likelihood of receiving enteral nutrition. Certainly, the most severely ill patients might have presented multifactorial intolerance to enteral feeding as another reasonable cause. If such conditions persist over a long period of time and patients do not tolerate adequate amounts of enteral nutrition, parenteral nutrition is the alternative to achieve desired amounts. Nevertheless, it is recommended that parenteral nutrition should not be initiated until all efforts to maximize enteral nutrition in these patients have been undertaken (11, 16).

Artinian et al. (27) retrospectively evaluated the effects of early vs. late enteral feeding on the outcome in a general medical ICU population. The tendency to provide early enteral feeding was more common in patients with a lower severity of illness in their study. Hence, the authors also raised concern whether the type of nutrition is simply a marker of disease state rather than an independent factor affecting outcome. The major result was that early enteral feeding significantly reduced ICU and hospital mortality, especially in the sickest patients. Regarding the high risk of death in patients with parenteral nutrition, we also questioned whether the parenteral route was independently associated with increased mortality. Besides adjusting for the age of the patient, we particularly adjusted for APACHE II score, septic shock, renal failure, and mechanical ventilation in the multivariate analysis. We also included insulin doses and serum glucose concentrations, as patients with mixed nutrition required significantly higher insulin doses to maintain comparable serum glucose concentrations and tended to stay longer in the hospital. This analysis revealed that parenteral nutrition was an independent risk factor for mortality in patients with severe sepsis or septic shock. APACHE II score and renal dysfunction were further independent risk factors, as previously reported by Engel et al (20). Neither maximal serum glucose concentration nor the administered amount of insulin was associated with mortality in our study, which is in contrast to what has been reported for postoperative critically ill patients (28).

The extent to which the route of nutritional support may affect clinical outcome of critically ill patients and especially septic patients is still controversial (29, 30). Several meta-analyses have evaluated the effect of different nutrition therapies on mortality with respect to timing or route of nutrition (18, 19, 31, 32). A clear advantage of one route over the other in regard to mortality could not be demonstrated, but enteral nutrition was associated with reduced morbidity and length of ICU and hospital stay. One major concern is the inclusion of heterogeneous patient populations reflecting a mix of postsurgical, medical, or trauma patients. In a meta-analysis, Gramlich et al. (33) included one early study with a small number of septic patients (34) and confirmed the positive effects of enteral nutrition on morbidity. There is recent evidence that the underlying disease has an important effect on the outcome of a given nutritional regimen (35–37). Our data indicate that septic patients may respond differently not only to the composition but also to the route of nutrition. However, whether parenteral nutrition is a relevant cause for increased mortality in patients with severe sepsis or septic shock cannot be answered by an observational study design and remains to be shown in randomized controlled trials.

Limitations of our study are the lack of detailed information on caloric intake, the components of nutrition formulations used, the presence or absence of prior malnutrition, the timing of nutrition, and infectious complications related to different nutrition regimens. However, we feel that the strength of our study lies in the available data from a large homogeneous sample of septic patients collected by externally trained study physicians in a random sample of ICUs stratified by hospital size.

CONCLUSION

This representative survey revealed a high rate of parenteral nutrition in patients with severe sepsis or septic shock in German ICUs, which was associated with an increased mortality. Further randomized controlled trials on the benefits and risks of nutrition in this patient group are needed. In view of current recommendations, however, our results emphasize that more concern should be given to the clinical practice of nutritional support and that enteral nutrition should be provided even for the most severely ill patients.

REFERENCES

1. Stechmiller JK, Treolar D, Allen N: Gut dysfunction in critically ill patients: A review of the literature. *Am J Crit Care* 1997; 6:204–209
2. Swank GM, Deitch EA: Role of the gut in multiple organ failure: Bacterial translocation and permeability changes. *World J Surg* 1996; 20:411–417
3. Hawker FH: How to feed patients with sepsis. *Curr Opin Crit Care* 2000; 6:247–252
4. Hadfield RJ, Sinclair DG, Houldsworth PE, et al: Effects of enteral and parenteral nutrition on gut mucosal permeability in the critically ill. *Am J Respir Crit Care Med* 1995; 152: 1545–1548
5. Wheeler AP, Bernard GR: Current concepts: Treating patients with severe sepsis. *N Engl J Med* 1999; 340:207–214
6. Heyland DK, MacDonald S, Keefe L, et al: Total parenteral nutrition in the critically ill patient: A meta-analysis. *JAMA* 1998; 280: 2013–2019
7. Preiser JC, Berre J, Carpentier Y, et al: Management of nutrition in European intensive care units: Results of a questionnaire. *Intensive Care Med* 1999; 25:95–101
8. Heyland DK, Schroter-Noppe D, Drover JW, et al: Nutrition support in the critical care setting: Current practice in Canadian ICUs—Opportunities for improvement? *JPEN J Parenter Enteral Nutr* 2003; 27:74–83
9. De Jonghe B, Appere-De-Vechi C, Fournier M, et al: A prospective survey of nutritional support practices in intensive care unit patients: What is prescribed? What is delivered? *Crit Care Med* 2001; 29:8–12
10. Krishnan JA, Parce PB, Martinez A, et al: Caloric intake in medical ICU patients: Consistency of care with guidelines and relationship to clinical outcomes. *Chest* 2003; 124: 297–305
11. Heyland DK, Dhaliwal R, Drover JW, et al: Canadian clinical practice guidelines for nutrition in mechanically ventilated, critically ill adult patients. *JPEN J Parenter Enteral Nutr* 2003; 27:355–373
12. Jolliet P, Pichard C, Biolo G, et al: Enteral nutrition in intensive care patients: A practical approach. *Intensive Care Med* 1998; 24: 848–859
13. Heyland DK, Dhaliwal R, Day A, et al: Validation of the Canadian clinical practice guidelines for nutrition support in mechanically ventilated, critically ill adult patients: Results of a prospective observational study. *Crit Care Med* 2004; 32:2260–2266
14. Barr J, Hecht M, Flavin KE, et al: Outcomes in critically ill patients before and after the implementation of an evidence-based nutritional management protocol. *Chest* 2004; 125:1446–1457
15. Martin CM, Doig GS, Heyland DK, et al: Multicentre, cluster-randomized clinical trial of algorithms for critical-care enteral and parenteral therapy (ACCEPT). *CMAJ* 2004; 170:197–204
16. Pérez J, Dellinger RP: International Sepsis Forum: Other supportive therapies in sepsis. *Intensive Care Med* 2001; 27:S116–S127
17. Reinhart K, Brunkhorst FM, Bone HG, et al: Diagnosis and therapy of sepsis: Guidelines of the German Sepsis Society Inc. and the German Interdisciplinary Society for Intensive and Emergency Medicine. *Internist* 2006; 47:356–373
18. Simpson F, Doig GS: Parenteral vs. enteral nutrition in the critically ill patient: A meta-analysis of trials using the intention to treat principle. *Intensive Care Med* 2005; 31:12–23
19. Peter JV, Moran JL, Phillips-Hughes J: A meta-analysis of treatment outcomes of early enteral versus early parenteral nutrition in hospitalized patients. *Crit Care Med* 2005; 33:213–220
20. Engel C, Brunkhorst FM, Bone HG, et al: Epidemiology of sepsis in Germany: Results of a national multicenter study. *Intensive Care Med* 2007; 33:606–618
21. Knaus WA, Draper EA, Wagner DP, et al: APACHE II: A severity of disease classification system. *Crit Care Med* 1985; 13: 818–829
22. Vincent JL, Moreno R, Takala J, et al: The SOFA (Sepsis-related organ failure assessment) score to describe organ dysfunction/failure. *Intensive Care Med* 1996; 22:707–710
23. Planas M: Artificial nutrition support in intensive care units in Spain. Nutritional and Metabolic Working Group of the Spanish Society of Intensive Care Medicine and Coronary Units (SEMIUC). *Intensive Care Med* 1995; 21:842–846
24. Hill SA, Nielsen MS, Lennard-Jones JE: Nutritional support in intensive care units in England and Wales. *Eur J Clin Nutr* 1995; 49:371–378
25. Middleton MH, Nazarenko G, Nivison-Smith I, et al: Prevalence of malnutrition and 12-month incidence of mortality in two Sydney teaching hospitals. *Intern Med J* 2001; 31: 455–461
26. Marik PE, Zaloga GP: Meta-analysis of parenteral nutrition versus enteral nutrition in patients with acute pancreatitis. *BMJ* 2004; 328:1407
27. Artinian V, Krayem H, DiGiovine B: Effects of early enteral feeding on the outcome of critically ill mechanically ventilated medical patients. *Chest* 2006; 129:960–967
28. Van den Berghe G, Wouters P, Weekers F, et al: Intensive insulin therapy in the surgical intensive care unit. *N Engl J Med* 2001; 345: 1359–1367
29. Heyland DK, Dhaliwal R: Early enteral nutrition vs. early parenteral nutrition: An irrelevant question for the critically ill? *Crit Care Med* 2005; 33:260–261
30. Bistrian BR, McCowen KC: Nutritional and metabolic support in the adult intensive care unit: Key controversies. *Crit Care Med* 2006; 34:1525–1531
31. Marik PE, Zaloga GP: Early enteral nutrition in acutely ill patients: A systematic review. *Crit Care Med* 2001; 29:2264–2270
32. Braunschweig CL, Levy P, Sheean PM, et al: Enteral compared with parenteral nutrition: A meta-analysis. *Am J Clin Nutr* 2001; 74: 534–542
33. Gramlich L, Kichian K, Pinilla J, et al: Does enteral nutrition compared with parenteral nutrition result in better outcomes in critically ill adult patients? A systematic review of the literature. *Nutrition* 2004; 20:843–848
34. Cerra FB, McPherson JP, Konstantinides FN, et al: Enteral nutrition does not prevent multiple organ failure syndrome (MOFS) after sepsis. *Surgery* 1988; 104:727–733
35. Heyland DK, Novak F, Drover JW, et al: Should immunonutrition become routine in critically ill patients; A systematic review of the evidence. *JAMA* 2001; 286:944–953
36. Novak F, Heyland DK, Avenell A, et al: Glutamine supplementation in serious illness: A systematic review of the evidence. *Crit Care Med* 2002; 30:2022–2029
37. Bertolini G, Iapichino G, Radrizzani D, et al: Early enteral immunonutrition in patients with severe sepsis: results of an interim analysis of a randomized multicentre clinical trial. *Intensive Care Med* 2003; 29:834–840