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REVIEW

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Cognitive impairment after intensive care unit admission: a systematic review

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Abstract *Purpose:* There is increasing evidence that critical illness and treatment in an intensive care unit (ICU) may result in significant long-term morbidity. The purpose of this systematic review was to summarize the current literature on long-term cognitive impairment in ICU survivors. *Methods:* PubMed/MEDLINE, CINAHL, Cochrane Library, PsycINFO and Embase were searched from January 1980 until July 2012 for relevant articles evaluating cognitive functioning after ICU admission. Publications with an adult population and a follow-up duration of at least 2 months were eligible for inclusion in the review. Studies in cardiac surgery patients or subjects with brain injury or cardiac arrest prior to ICU admission were excluded. The main outcome measure was cognitive functioning. *Results:* The search strategy identified 1,128 unique studies, of which 19 met the selection criteria and were included. Only one article compared neuropsychological test performance before and after ICU admission. The 19 studies that were selected reported a wide range of cognitive impairment in 4–62 % of the patients after a follow-up of 2–156 months. *Conclusion:* The results of most studies of the studies reviewed suggest that critical illness and ICU treatment are associated with long-term cognitive impairment. Due to the complexity of defining cognitive impairment, it is difficult to standardize definitions and to reach consensus on how to categorize neurocognitive dysfunction. Therefore, the magnitude of the problem is uncertain.

Keywords Cognition · Follow-up · Intensive care unit · Long-term cognitive impairment · Outcome

Introduction

The utilization of intensive care units (ICUs) has expanded rapidly over the past decades, with a concomitant increase in the proportion of patients surviving an episode of critical illness. This has resulted in a growing number of ICU survivors [1]. Results from previous studies suggest that ICU survivors may suffer from significant long-term morbidity [2]. An important long-term complication of critical illness and ICU treatment is cognitive impairment. Cognitive impairment is associated with a reduced quality of life, and it is a major determinant of societal healthcare costs and caregiving needs [3–5]. A large proportion of ICU patients consist of elderly people, and especially this population is prone to develop cognitive impairment [6]. However, it appears that younger, relatively healthy patients are also at risk for cognitive impairment following critical illness. Cognitive impairment often becomes apparent after ICU discharge, and intensivists may therefore not be aware of the occurrence

of this complication. In the last 2 years, a number of high-quality studies on this topic have been published [1, 5]. The aim of this systematic review was to summarize current evidence for long-term cognitive impairment in ICU survivors.

Methods

This systematic review was performed in accordance with the recent standards for systematic reviews published by the Institute of Medicine in March 2011 [7].

Search strategy

We conducted a search of PubMed/MEDLINE, CINAHL, Cochrane Library, PsycINFO and Embase from January 1980 through July 2012 using relevant search terms relating to cognition and ICU admission. The exact search strategy is described in Table 1. The reference lists from the selected articles were screened to identify additional articles. To assess the comprehensiveness of the search strategy, we tested the search-string with eight studies that we already had on file and which we considered relevant for this systematic review.

Study selection

Studies on cognitive functioning after ICU admission in adults as the primary or secondary endpoint were included in our review. The following studies/articles were excluded:

– reviews, case studies and animal studies, as well as articles published in languages other than English, Dutch, German or French;

Table 1 Search strategy

Database	Search filter	Retrieved
PubMed/Medline 1980 to 07/2012	{"Intensive Care"[Mesh] OR "Critical Illness"[Mesh] OR "Intensive Care Units"[Mesh] OR "Critical care"[Mesh] OR "Respiratory Distress Syndrome, Adult"[Mesh] OR "sepsis"[Mesh] OR "Intensive care"[title/abstract] OR "Critical illness"[title/abstract] OR "ICU"[title/abstract] OR "Critical care"[title/abstract] OR "Acute Respiratory Distress Syndrome"[title/abstract] OR "sepsis"[title/abstract]} AND {"cognition"[Mesh] OR "cognition"[title/abstract] OR cognitive[title/abstract] OR "neurocognitive"[title/abstract]}	603
EMBASE 1980 to 07/2012	{'intensive care':ab,ti OR 'intensive care unit':ab,ti OR 'critical illness':ab,ti OR 'critical care':ab,ti OR 'acute respiratory distress syndrome':ab,ti OR 'sepsis':ab,ti} AND {'cognition':ab,ti OR 'cognitive':ab,ti OR 'neurocognitive':ab,ti}	368
CINAHL 1980 to 07/2012	{TI ("Intensive Care" OR "Critical illness" OR "Intensive Care Unit" OR "Critical care" OR "ICU" OR "respiratory distress syndrome, adult" OR "sepsis") OR AB ("Intensive Care" OR "Critical illness" OR "Intensive Care Unit" OR "Critical care" OR "ICU" OR "respiratory distress syndrome, adult" OR "sepsis")} AND {TI ("Cognition" OR "Cognitive" OR "Neurocognitive") OR AB ("Cognition" OR "Cognitive" OR "Neurocognitive")}	393
PsycINFO 1980 to 07/2012	{("Intensive Care" or "Critical care" or "Critical illness" or "Intensive Care Unit" or "Acute respiratory distress syndrome" or "Sepsis").ti. or ("Intensive Care".ab. or "Critical care".ab. or "Critical illness".ab. or "Intensive Care Unit".ab. or "Acute respiratory distress syndrome".ab. or "Sepsis".ab.)} AND {(Cognition or Cognitive or Neurocognitive).ti. or Cognition.ab. or Cognitive.ab. or Neurocognitive.ab.}	284
Cochrane Library 1980 to 07/2012	{"Intensive Care" in Title, Abstract or Keywords or "Intensive Care Unit" in Title, Abstract or Keywords or "Critical care" in Title, Abstract or Keywords or "Critical illness" in Title, Abstract or Keywords or "Acute respiratory distress syndrome" in Title, Abstract or Keywords or "Sepsis" in Title, Abstract or Keywords"} AND {"Cognition" in Title, Abstract or Keywords and "Cognitive" in Title, Abstract or Keywords and "Neurocognitive" in Title, Abstract or Keywords}	116 non-reviews and non-groups
Total number of unique titles		1128

– investigations with a follow-up duration on cognitive functioning shorter than 2 months;
– studies on patients undergoing heart surgery and on those with cardiac arrest or brain injury prior to ICU admission;
– articles describing the same or an overlapping patient sample as that described in an article already included in the review; in this case, we only used the most recent article, which described both the new data and the data reported earlier.

The eligibility of each article that was found was independently evaluated on title, abstract and, if necessary, full text, by two reviewers using the above-mentioned selection criteria (AEW and AWvdK). If the two reviewers disagreed about the eligibility of an article, a third reviewer (AJCS) was consulted.

Data extraction

Both reviewers independently assessed the articles that were selected using a standardized data collection form to record the required data [Electronic Supplementary Material (ESM) 1]. The following characteristics were recorded: first author, year of publication, study design, study population with in- and exclusion criteria, number of enrolled participants and age at baseline, number of deceased subjects and loss-to-follow-up, measurement of baseline cognition and the neuropsychological tests used and the test results. Study quality was assessed based on four criteria: (1) availability of data on cognitive functioning at baseline; (2) use of neuropsychological tests to assess cognition; (3) description of inclusion and exclusion criteria; (4) adjustment for predictors which could interfere with the cognitive outcome, such as age and gender. These quality criteria were chosen because these are universally applicable (item 3 and 4) and specific for studies evaluating neurocognitive outcome (criteria 1 and 2).

Statistical analysis

The data of the included studies were not pooled because we expected considerable methodological differences between studies, especially with respect to the selection of neuropsychological tests, timing of assessment and definitions of cognitive impairment.

Some authors hypothesize that the risk of neurocognitive impairment is higher in patients with acute respiratory distress syndrome (ARDS) than in the general ICU population [4, 8]. Elderly ICU patients may also have an increased risk of cognitive impairment [6]. In the presentation of the selected studies, we therefore, distinguished studies with focus on ARDS and studies with focus on elderly patients. The other three ICU-population categories were: surgical, medical and general.

Results

The search-string (Table 1) yielded a total of 1,664 publications, of which 1,128 were unique. The defined search strategy did identify all eight studies that we already had on file and which we considered relevant for this systematic review. We excluded 1,094 articles based on title or abstract and evaluated 34 full-text articles (Fig. 1). There was disagreement on the eligibility of one article between the first two reviewers [5]. The study was of a high quality, especially because of the presence of baseline neuropsychological data, but the patient cohort did not exclusively comprise an ICU population. In consultation with the third reviewer, consensus was reached to exclude this study from the systematic review but to mention its results in the Discussion. Eventually, 19 articles met the selection criteria and were included. No extra titles were identified after screening the reference lists.

The included studies are shown in Tables 2 and 3. Table 2 summarizes the data of the 14 studies which extensively used neuropsychological testing to measure cognitive functioning, and Table 3 outlines five additional studies which used questionnaires or screening test data to assess cognitive performance. The number of subjects per study varied between 30 and 1,822. Most studies consisted of young, relatively healthy ICU survivors. Eleven studies had a study population with a mean age of 54 years or less. Four studies focused on the elderly or very elderly (>65, >75 and >80 years, respectively) [1, 9–11]. The patient populations of seven comprised ARDS patients. The studies had a follow-up duration varying from 2 months up to 13 years after ICU discharge.

Only one of the 19 articles met all four quality criteria, with the inclusion of a neuropsychological assessment prior to ICU admission [1]. Seven other investigations took an estimated premorbid cognitive functioning into account [8, 10–15]. Fourteen studies met the second quality criterion, which was the use of neuropsychological testing to assess cognitive functioning (Table 2) [1, 8, 12–23]. All 19 articles reported in- and exclusion criteria. The fourth quality criterion, i.e. adjustment for predictors (co-variables) which could interfere with the cognitive outcome, was met by 16 studies which compared the post-ICU test performance to normative age- and gender-matched population data [1, 8, 11–24]. One study used age- and gender-matched data from a population with long-standing illness for comparison [3]. In some studies

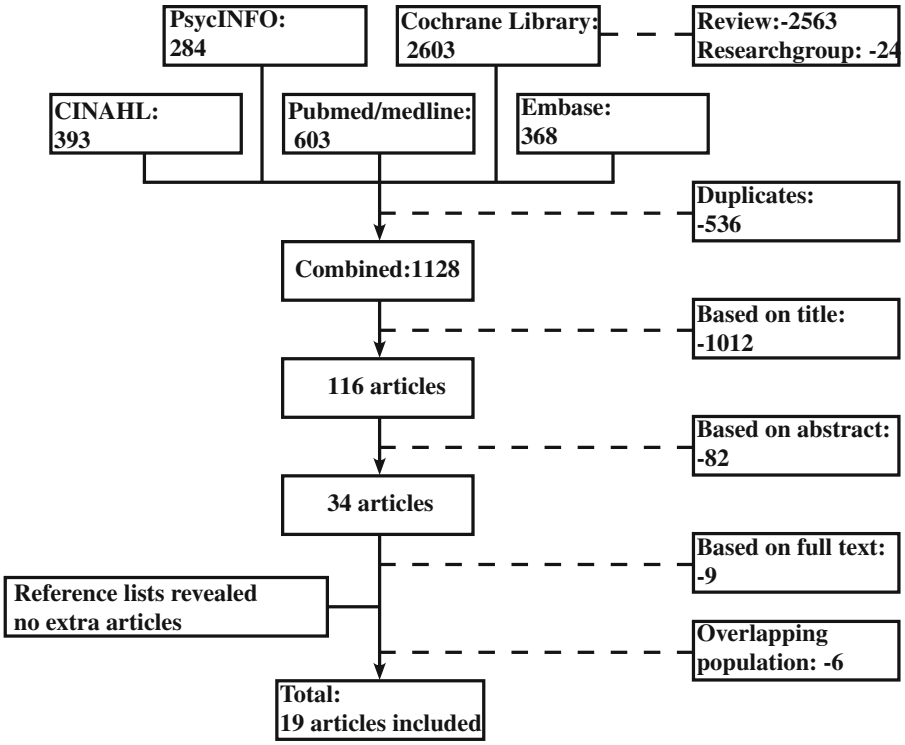

Fig. 1 Flowchart search and selection of literature

a correction was made for educational level [8, 11–15, 17–19], 11 studies made an adjustment for severity of illness during ICU admission [8, 9, 12–17, 21, 23, 24] and nine studies took the length of ICU admission into account [3, 9, 12, 15, 16, 19, 21, 23, 24].

Of the 19 articles reviewed, four reported a relatively good cognitive status amongst ICU survivors, which was defined as ≤10 % of patients with cognitive impairment [10, 16, 22] or a p value of >0.05 [11]. Absence of cognitive impairment was reported more often in studies with screening tests (2/5, 40 %; Table 3) than in investigations based on neuropsychological tests (2/13, 15 %; Table 2). In addition, in one of the studies which used neuropsychological tests half of the patients (N = 27) were excluded because they could not complete the cognitive testing [16]; if all these 27 patients had cognitive impairments, the rate of impairment would have been close to 100 %. The other 15 studies reported at least "mild" cognitive impairment in a larger proportion of ICU survivors. The studies with the screening test data reported impairment in 11–56 % of the population [3, 9, 24]. The investigations with neuropsychological testing showed impairment in 11–62 % of the examined population [1, 8, 12–15, 17–21]. Although the range of cognitive impairment was comparable, in general the studies with extensive neuropsychological testing reported a higher incidence of cognitive impairment than those with screening test data.

The incidence of cognitive impairment of ARDS survivors ranged from 4 to 56 % [8, 12, 15, 19, 22–24]. Within the general, medical and surgical ICU survivors the incidence of cognitive impairment ranged from 4 to 62 % [3, 13, 14, 16–18, 21]. Four studies assessed cognitive impairment in the elderly [1, 9–11], two of which, both based on screening test data, did not find significant cognitive impairment among their elderly subjects [10, 11]. The other two studies in elderly patients reported cognitive impairment varying from 17 to 56 % [1, 9].

The tested cognitive domains per article are shown in Table 4. Of the included studies, 14 tested for 'memory,' which was therefore the most tested domain. The domains of memory, attention, verbal fluency and executive functioning were most frequently impaired [12, 18–21, 24]. Two studies reported an association between a higher estimated premorbid IQ and less cognitive impairment [8, 13].

Seven studies measured cognitive functioning at multiple points in time after ICU admission [8, 12, 17, 21, 23, 24]. However, one study only reported the proportion of patients with cognitive impairment at the final assessment [23]. Two studies found no improvement of cognitive function during 1 to 2 years of follow-up [8, 12]. One article reported no improvement, even after 5 years of follow-up [24]. However, another study reported a return towards normal cognitive functioning by 9 months [21], and one study reported a decrease in severe impairment after 1 year [17].

Table 2 Summary of included studies which used neuropsychological tests

First author	Year of study	Design	Population	Baseline cognition.	*N*	Age at baseline (years)	Follow-up duration (months)	Deceased (*N*)	Loss to Follow-up (*N*)	Definition of cognitive impairment	Proportion of patients with cognitive impairment
Mikkelsen [23]	2012	Prosp. cohort	ARDS	No	213	49 (40–58)	12	22 (10 %)	53 (28 %)	≥2 SD below the population norm	41/75 (55 %)
Torgersen [16]	2011	Prosp. cohort	Surgical ICU	No	55	51 (16)	3	0 (0 %)	20 (36 %)	≥ 3 tests ≥1.5 SD or ≥ 2 tests ≥2 SD below the mean	4/35 (11 %)
							12	0 (0 %)	5 (14 %)	≥3 tests ≥1.5 SD or ≥2 tests ≥2 SD below the mean	3/30 (10 %)
Girard [17]	2010	Prosp. cohort	Medical ICU	No	126	61 (47–71)	3	27 (21 %)	9 (9 %)	2 tests ≥5 SD or 1 test ≥2 SD below the mean (mild)	13/76 (17 %)
										≥3 tests ≥1.5 SD or ≥2 tests >2 SD below the mean (severe)	47/76 (62 %)
							12	12 (15 %)	13 (17 %)	2 tests ≥1.5 SD or 1 test ≥2 SD below the mean (mild)	18/52 (35 %)
										≥3 tests ≥1.5 SD or ≥2 tests ≥2 SD below the mean (severe)	19/52 (36 %)
Ehlenbac [1]	2010	Prosp. cohort	Elderly	Yes	41	75 (7)	96 (49–119)	NR	NR	<86 on the CASI and diagnostic criteria for dementia at full standardized clinical examination	5/41 (12 %)
Duning [18]	2010	Retrosp. Case–Control	Surgical ICU	No	74	66 (1)	≥12	4 (7 %)	8 (11 %)	"Close below average" with matched healthy control subjects, mean over 74 subjects	10/17 tests
										"Far below average" with matched healthy control subjects, mean over 74 subjects	3/17 tests
Mikkelsen [19]	2008	Cross-sectional	ARDS	No	79	43 (13)	28 (35)	NR	NR	≥2 tests ≥1 SD or ≥1 test ≥1.5 SD below the population norm	44/79 (56 %)
Jackson [14]	2007	Retrosp. cohort	Surgical ICU[b]	No[a]	97	45 (14)	12–24	10 (10 %)	29 (33 %)	≥2 tests ≥1.5 SD or ≥1 test ≥2 SD below the mean	16/37 (43 %)
Larson [8]	2007	Prosp. cohort	ARDS	No[a]	74	45 (16)	12	3 (4 %)	5 (7 %)	≥2 tests >1.5 SD or 1 test >2 SD below the population norm	29/63 (46 %)
							24	2 (3 %)	2 (3 %)	≥2 tests >1.5 SD or 1 test >2 SD below the population norm	26/59 (44 %)
Jones [20]	2006	Prosp. cohort	General ICU	No	30	54 (18–78)	2	2 (7 %)	NR	Scores ≤25 percentile of matched control population for memory	5/16 (31 %)
										Scores ≤25 percentile of matched control population for problem solving	8/16 (50 %)

Table 2 continued

First author	Year of study	Design	Population	Baseline cognition.	*N*	Age at baseline (years)	Follow-up duration (months)	Deceased (*N*)	Loss to Follow-up (*N*)	Definition of cognitive impairment	Proportion of patients with cognitive impairment
Sukantarat [21]	2005	Prosp. cohort	General ICU	No	51	60 (26–82)	3	NR	6 (12 %)	1 test ≤ fifth percentile of normative data ≥2 test ≤ fifth percentile of normative data	28/51 (55 %), 18/51 (35 %)
							9			1 test ≤ fifth percentile of normative data ≥2 test ≤ fifth percentile of normative data	12/45 (27 %), 2/45 (4 %)
Hopkins [12]	2005	Prosp. cohort	ARDS	No[a]	74	46 (16)	12	3 (4 %)	5 (7 %)	≥2 tests >1.5 SD or 1 test 2 SD below the population norm	30/66 (45 %)
							24	2 (3 %)	2 (3 %)	≥2 tests >1.5 SD or 1 test ≥2 SD below the population norm	29/62 (47 %)
Kapfhammer [22]	2004	Retrosp. cohort	ARDS	No	80	37 (18 – 50)	96 (36 –156)	2 (3 %)	17 (21 %)	Norm value ≥5 are clinically relevant	4/46 (9 %)
Jackson [13]	2003	Prosp. cohort	Medical ICU	No[a]	275	53 (15)	6	119 (43 %)	116 (74 %)	≥2 tests >2 SD or ≥3 tests >1.5 SD below the population norm	11/34 (32 %)
Rothenhäusler [15]	2001	Retrosp. cohort	ARDS	No[a]	119	42 (15)	76,8 (38.4)	17 (14 %)	43 (42 %)	Norm value ≥5 are clinically relevant	11/46 (24 %)

Prosp. Prospective, *Retrosp.* retrospective, *ICU* intensive care unit, *ARDS* acute respiratory distress syndrome, *SD* standard deviation, *NR* not reported

[a] Analyses with use of estimated premorbid cognitive function

[b] With regard to trauma patients, we only used data from the subpopulation without traumatic brain injury

Table 3 Summary of included studies which used questionnaires or screening test data

First author	Years	Design	Population	Baseline cognition	(*N*)	Age at baseline (years)	Follow-up duration (months)	Deceased (*N*)	Loss to follow-up (*N*)	Used test(s)	Definition of cognitive impairment	Proportion of patients with cognitive impairment
Daubin [11]	2011	Prosp. cohort	Elderly	No[a]	100	79.3 (3.4)	3	61 (61 %)	1 (3 %)	Individual components of IADL	Score range: 0–4 (0 = not impaired, 4 = severe impaired)	2.9 ± 1.4 ($p = 0.62$)
Adhikari [24]	2011	Prosp. cohort	ARDS	No	109	42 (35–56)	22 (6–48)	13 (12 %)	18 (19 %)	MAC-S (ability and frequency of occurrence)	> 2 SD below population norms;	5/64 (8 %) and 5/61 (8 %)
											>1.5SD below population norms;	10/64 (16 %) and 11/61 (18 %)
											> 1SD below population norms	13/64 (20 %) and 11/61 (18 %)
							41 (33–52)[b]	8 (12 %)	6 (7 %)	MAC-S (ability and frequency of occurrence)	>2 SD below population norms;	2/46 (4 %) and 0/38 (0 %)
											>1.5 SD below population norms;	4/46 (9 %) and 4/38 (11 %)
											>1 SD below population norms	7/46 (15 %) and 4/38 (11 %)
Sacanella [10]	2011	Prosp. cohort	Elderly	No[a]	230	73.4 (5.5)	12	118 (51 %)	0 (0 %)	MMSE	MMSE <24	11/112 (10 %)
Timmers [3]	2010	Prosp. cohort	Surgical ICU	No	1822	61 (16)	96 (72–132)	936 (51 %)	288 (33 %)	EQ-6D	Scores 2 (moderate) or 3 (severe) (Reference group scored 8 % with impairment)	247/575 (43 %)
de Rooij [9]	2008	Retrosp. cohort	Elderly	No	578	85.4 (3.0)	44 (12–71)	347 (60 %)	71 (31 %)	IQCODE-SF	Score >3.9 (severe)	27/164 (17 %)
											Score between 3.1 and 3.8 (mild-to-moderate)	92/164 (56 %)

IADL Lawton Index of daily living, *MAC-S* memory assessment clinic self-rating scale, *IQCODE(-SF)* informant questionnaire on cognitive decline in the elderly (short form), *MMSE* mini-mental state examination, *EQ-6D* EuroQoL-6D

[a] Analyses with use of estimated premorbid cognitive function

[b] Follow-up duration after first measurement

Table 4 Tested cognitive domains

	First Author									
Cognitive domain	Mikkelsen [23]	Daubin [11]	Torgersen [16]	Adhikari [24]	Sacanella [10]	Timmers [3]	Girard [17]	Ehlenbach [1]	Duning [18]	De Rooij [9]
Global cognitive and intellectual functioning		x			x	x	x	x	x	x
Verbal fluency	x						x	x		
(Visuo)Spatial skills							x		x	
Attention and concentration							x	x	x	
Memory	x		x	x			x	x	x	
Executive functioning	x		x				x		x	
Psychomotor speed			x				x			
Abstraction/visual construction								x		

	First Author									
Cognitive domain	Mikkelsen [19]	Jackson [14]	Jones [20]	Larson [8]	Sukantarat [21]	Hopkins [12]	Kapfhammer [22]	Jackson [13]	Rothenhausler [15]	
Global cognitive and intellectual functioning	x		x	x	x	x				
Verbal fluency	x	x		x				x		
(Visuo)Spatial skills		x		x		x				
Attention and concentration	x	x		x		x	x		x	
Memory	x	x	x	x		x	x	x	x	
Executive functioning	x	x		x	x	x		x		
Psychomotor speed		x		x		x				
Abstraction/visual construction								x		

Discussion

In this review, we systematically assessed publications on cognitive impairment after admission to a general ICU. The 19 studies that met the selection criteria reported a wide range of cognitive impairment in 4–62 % of the patients after a follow-up of 2–156 months. Compared to studies which used neuropsychological testing, lower percentages of patients with cognitive impairment were reported in studies which only used screening test data. We found no difference in the risk of cognitive impairment between studies involving only ARDS patients and those which also included other ICU patients. In addition, we did not find a higher risk of cognitive impairment in studies in elderly patients, although three of the studies assessed only used screening test data.

The pathophysiology of cognitive impairment after ICU admission is believed to be multifactorial [13, 21]. The most frequently reported explanation for an abrupt decrease in cognitive functioning after ICU admission is that patients with multi-organ failure may also develop brain damage [13, 25]. Severe sepsis can lead to a neuro-inflammatory response, resulting in increased levels of cytokines in the brain [25, 26]. Elevated cytokine levels are associated with impaired memory in healthy volunteers [27], and neuro-inflammation is associated with the development of Alzheimer's disease [28]. Long-term cognitive impairment in patients may therefore represent a maladaptive version of cytokine-induced disease [26]. Other possible causes are hypoxemia and hypotension, which have been related to cognitive impairment in numerous investigations [12, 13]. Sedatives and analgesics are used extensively in the ICU, and some studies suggest that this may also play a causal role in the development of long-term cognitive impairment [13]. Both hyperglycemia and hypoglycaemia as well as fluctuations in blood glucose are also associated with poor cognitive outcomes [18, 29]. An association between delirium and long-term cognitive impairment has been reported, but the underlying cause remains to be elucidated [17, 30].

The focus of this review was on long-term cognitive impairment. We excluded those studies with a follow-up duration of less than 2 months. An early cognitive assessment may reflect residual pain, the effects of analgesic and sedative drugs and/or residual delirium [12, 16]. The results of studies that measured cognition immediately after ICU admission and also at various time points during a long-term follow-up indicate that the incidence of cognitive impairment is high after ICU discharge but improves during the first few months after discharge [12].

Even with the use of strict selection criteria, it was difficult to compare the reviewed studies and, therefore, it was impossible to present pooled data. Among the reviewed studies which reported the results of neuropsychological testing, there was a substantial variation in the definition of impairment, sample size and timing of assessment. In addition, medical practices in the ICU have substantially changed during the past decade, and these practical changes may also affect cognitive outcomes. However, we were unable to observe such an effect over time because all studies included in this review were published in the last 10 years.

A major limitation of most of the studies reviewed is that a baseline assessment of cognitive status before ICU admission is lacking. Ideally, cognition should be measured before and after ICU admission because the real interest is not the absolute level of cognitive performance but rather the change in cognitive functioning. ICU admissions, however, are often not elective and, consequently, a baseline assessment is usually not available. Some studies estimated the baseline cognitive performance after ICU admission rather than testing it in advance. Adjustments were made for patients who showed signs of pre-existing cognitive impairment [8, 12–15]. Remarkably, there are two recent population-based studies with premorbid cognitive data [1, 5]. The first is a population-based longitudinal study of aging and dementia, designed to establish the incidence of both cognitive impairment and risk factors for cognitive decline [1]. Of the 2,929 subjects who underwent repeated neuropsychological testing, 41 were admitted to an ICU. The authors of this study concluded that those who were hospitalized for a critical illness had a greater likelihood of cognitive impairment, even after adjusting for premorbid cognitive screening scores and comorbidity. The rate of cognitive decline did not change after admission to the ICU compared with the normal rate of decline. Therefore, the authors suggested that critical illness may cause an abrupt loss of cognitive function rather than accelerate the decline in cognitive functioning [1]. The second study with premorbid cognitive data was conducted among patients who survived severe sepsis [5]. Baseline cognitive assessments were performed in 9,223 respondents, of whom 516 survived severe sepsis. This study was not included in the Results of this review because the study did not require that patients be treated in an ICU. Consultation with the authors of this study revealed that 43 % of the sepsis survivors were admitted to the ICU but that no subanalysis data on the ICU patients were available. The authors measured an increase from moderate to severe cognitive impairment among sepsis survivors. Before sepsis, 6.1 % of the eventual survivors showed moderate to severe cognitive impairment [5]; after severe sepsis, the prevalence increased to 16.7 %. These results led the authors to conclude that severe sepsis was independently associated with new cognitive impairment, which appeared to be substantial and persistent [5]. In the subgroup of the ICU patients, the risk of cognitive impairment was comparable to that of the whole study population (TJ Iwashyna, personal communication).

The effects of severity of illness on the risk for developing long-term cognitive impairment remain uncertain. Due to the small size of the patient groups, the availability of analyses in patient subgroups is limited. It is even more relevant to evaluate the effect of interventions that may reduce the risk of cognitive impairment. A possible intervention that could be evaluated in a randomized study is early mobilization [31]. Early mobilization has a positive effect on length of stay in the ICU and on physical independence after discharge [31, 32]; it also reduces depression in survivors of critical illness [32].

It remains uncertain whether a low performance on neuropsychological tests reflects an impairment in cognitive functioning related to critical illness and ICU admission, or whether it is perhaps merely a marker of patients with poor health and an increased risk of ICU admission. However, the two studies with premorbid cognitive data show that at least part of the measured cognitive impairment is related to the ICU admission and critical illness [1, 5]. There are similarities between recent studies on cognitive impairment after critical illness and ICU treatment and the slightly older studies on cognitive impairment after cardiac surgery [33–35]. It has become apparent in the field of cardiac surgery that it is extremely difficult to distinguish normal variation in test performance from true cognitive impairment [36, 37]. Consequently, in cardiac surgery, it is now accepted that the incidence of cognitive injury has long been overestimated because normal variations in test performance were formerly not always recognized [35, 38, 39]. However, cardiac surgical patients clearly differ from general ICU patients, and a comparison with the post-cardiac surgery literature might therefore be misleading. Additional research is still required to establish a reliable incidence of cognitive decline following ICU admission.

In conclusion, most of the studies reviewed here suggest that critical illness and ICU treatment are associated with long-term cognitive impairment. Due to the complexity of defining cognitive impairment, both the magnitude and severity of the problem are uncertain. It is therefore crucial that the definition of neurocognitive dysfunction is standardized. The pathophysiology of cognitive impairment after ICU admission is believed to be multi-factorial, and more research is needed to identify key risk factors. Previously identified risk factors for neurocognitive dysfunction are severity of illness, hypoxemia, hypotension, the use of sedatives and analgesics, hyper- and hypoglycaemia and the presence of a delirium. The aim of future studies should be to adjust for cognitive functioning before ICU admission, psychological co-morbidities and other possible confounders. Eventually these investigations may lead to improved long-term outcome after ICU admission.

Conflicts of interest None.

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