

Quality of life after intensive care: A systematic review of the literature

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Objectives: To evaluate quality of life at least 12 months after discharge from the intensive care unit of adult critically ill patients, to evaluate the methodology used to assess long-term quality of life, and to give an overview of factors influencing quality of life.

Data Sources: EMBASE-PubMed, MEDLINE (OVID), SCI/Web of Science, the Cochrane Library, Google Scholar, and personal files.

Data Extraction: Data extraction was performed independently and cross-checked by two reviewers using a predefined data extraction form. Eligible studies were published between 1999 and 2009 and assessed quality of life ≥ 12 months after intensive care unit discharge by means of the Medical Outcomes Study 36-Item Short Form Health Survey, the RAND 36-Item Health Survey, EuroQol-5D, and/or the Nottingham Health Profile in adult intensive care unit patients.

Data Synthesis: Fifty-three articles (10 multicenters) were included, with the majority of studies performed in Europe (68%). The Medical Outcomes Study 36-Item Short Form Health Survey was used in 55%, and the EuroQol-5D, the Nottingham Health Profile, the RAND 36-Item Health Survey, or a combination was used in 21%, 9%, 8%, or 8%, respectively. A response rate of $\geq 80\%$ was attained in 26

studies (49%). Critically ill patients had a lower quality of life than an age- and gender-matched population, but quality of life tended to improve over years. The worst reductions in quality of life were seen in cases of severe acute respiratory distress syndrome, prolonged mechanical ventilation, severe trauma, and severe sepsis. Study quality criteria, defined as a baseline quality of life assessment, the absence of major exclusion criteria, a description of nonresponders, and a comparison with a reference population were met in only four studies (8%). Results concerning the influence of severity of illness, comorbidity, preadmission quality of life, age, gender, or acquired complications were conflicting.

Conclusions: Quality of life differed on diagnostic category but, overall, critically ill patients had a lower quality of life than an age- and gender-matched population. A minority of studies met the predefined methodologic quality criteria. Results concerning the influence of the patients' characteristics and illnesses on long-term quality of life were conflicting. (Crit Care Med 2010; 38:2386–2400)

KEY WORDS: intensive care unit; quality of life; long-term outcome; critically ill patients; methodology; comorbidity

Because intensive care medicine by definition treats the most critically ill patients who have an inherent high risk of mortality, it seems logical that, for many years, the primary outcome parameter has been survival rate. Although this is without any doubt an important issue, survival and mortality rate also have the advantage of being unambiguous and easy to measure. Advances in diagnostic and therapeutic options enable more and more patients to survive critical illness. Although studies investigating survival rates of critically ill patients are widely performed, we also

have to question whether critical illness has any impact on an individual's (very) long-term (i.e., ≥ 12 months after intensive care unit [ICU] discharge) health status and quality of life (QOL). Therefore, next to survival or mortality rate, QOL has to be considered of equal importance as an outcome parameter.

Although QOL has been accepted to be valuable regarding outcome, it is not routinely included in studies, and research on this topic is still in its infancy. This has many reasons. Measuring QOL with specific questionnaires is more labor-intensive and time-consuming and will always be more ambiguous for interpretation than the "dead" or "alive" outcome parameters. Optimal follow-up periods for measuring QOL are not defined. Baseline assessment of QOL is difficult but of great value to examine the burden of the critical illness.

Only a few reviews of QOL after intensive care have been published (1–4). There has been no systematic review providing accurate and recent data on the burden of critical illness on a patients' long-term

QOL. Nevertheless, a better understanding of how intensive care affects the health and well-being of its survivors will help physicians when deciding on allocating therapeutic efforts in the future. Consequently, it is the purpose of this article to give a systematic review of the literature published in the past decade of QOL and influencing factors at least 1 yr after discharge from the ICU and of the methodology used. Finally, we hope to give better insights into long-term QOL and to make methodologic recommendations for further research on this topic.

MATERIALS AND METHODS

Data Sources, Search Strategy, Study Selection, and Data Extraction

A two-stage systematic review process of existing published original research articles was conducted. First, two authors (SGO, DMV) independently searched EMBASE-PubMed, MEDLINE (OVID), SCI/Web of Science, the

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Cochrane Library, and Google Scholar on January 9, 2010, using the medical subject headings or text key words “quality of life,” or “long-term outcome” cross-referenced with “intensive care,” “critical care,” “critically ill patients,” “ICU patients,” “critical care patients,” “ICU stay,” or “ICU.” Limitations were applied regarding language (English language), time (articles published between January 1, 1999 and December 31, 2009), age (older than 18 yrs), and humans. Personal files that were known to the authors and reference lists of relevant articles also were hand-searched. Outcomes articles including exclusively cardiac or thoracic aortic surgery patients, methodologic articles, literature reviews, case reports, editorials, and letters were excluded. Studies with <50 patients were also not included. If it was unclear whether patients were admitted to the ICU, then articles were excluded (5–7).

In stage two, all abstracts were evaluated independently by two authors (SGO, DMV) for the following methodologic criteria: 1) assessment of QOL by means of at least one of the following instruments: the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36), the RAND 36-Item Health Survey (RAND-36), EuroQol-5D (EQ-5D), and/or the Nottingham Health Profile (NHP); and 2) a follow-up period of ≥ 12 months after discharge from the ICU. Disagreements regarding eligibility were resolved by consensus.

Subsequently, identified articles were downloaded and screened electronically. For each eligible article, using a predefined categorization system, information was extracted on the authors, journal, year of publication, study design, inclusion period, initial study cohort, number of eligible patients for long-term QOL assessment, instrument(s) and method(s) used for QOL assessment, response rate, follow-up period, final conclusion concerning QOL, and factors determining QOL. Study quality was assessed using four important criteria, analogous to those used by Dowdy et al (1): 1) QOL assessment before ICU admission, 2) description of key inclusion or exclusion criteria, 3) description of nonresponders and comparison with those remaining in the study, and 4) adjustment for confounders such as age and gender. The aforementioned criteria were not used in decisions regarding inclusion or exclusion of eligible studies. Any discrepancies between both reviewers were resolved by discussion.

QOL Measurement Instruments

SF-36, RAND-36, EQ-5D, and NHP were considered because they are generic instruments commonly used in intensive care re-

search (8); they are well validated and have population norms in the literature (9–16).

The SF-36 questionnaire contains 36 items measuring eight multi-item domains: physical and social functioning, role limitations caused by physical or emotional problems, mental health, vitality, bodily pain, and general perception of health (9–13).

Arising from SF-36, the RAND-36 questionnaire was developed. Although the count system in the latter differs somewhat compared to SF-36, questions and final results are almost identical (14).

The EQ-5D is a short questionnaire consisting of three parts (15, 17–19). A descriptive system measures health in five domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each domain has three levels: no problems, moderate problems, or severe problems. Therefore, patients can be classified into 1 of 243 (3^5) possible health states. Each of these can be converted into one single summary index that can be used in health-economy studies. On a visual analog scale, patients can rate their overall health between 0 and 100. Although the EQ-5D is a well-known and well-validated instrument to measure QOL in general populations, it has been less well validated in the critically ill population (17–19), and it may provide less information and may be less discriminative than the SF-36 (20).

The NHP consist of a two-part questionnaire (16). The first one comprises 38 statements related to six domains: physical mobility, pain, sleep, energy, emotional reactions, and social isolation. The second part lists seven activities of daily life: occupation, housework, social activity, home life, sex life, hobbies, and holidays. The NHP has already been used to evaluate QOL in the critically ill population, especially in cardiac surgery patients (21). Nevertheless, internal consistency and sensitivity to change were better for the SF-36 and RAND-36 than for the NHP (22–24).

RESULTS

A total of 53 articles were finally included in the review. The articles were grouped according to diagnostic category. Studies concerning critically ill patients in general were separated based on follow-up period. Eleven articles concerning acute respiratory distress syndrome (ARDS) (25–35), three articles about prolonged mechanical ventilation (36–38), eight trauma studies (20, 39–45), six articles concerning cardiac arrest (46–51), six studies about elderly patients (52–57), two pancreatitis studies (58, 59), three sepsis studies (60–62), and four studies with various topics (63–66) were

included. There were four studies concerning outcome and QOL in general critically ill patients 1 yr after intensive care (19, 67–69) and six with longer follow-up periods (70–75). Table 1 gives an overview of the characteristics of these studies. All the studies were performed in large hospitals. Ten were multicenter studies (32–34, 40, 45, 48, 51, 57, 61, 66). Thirty-six were conducted in Europe (19, 20, 26–28, 35, 36, 41, 42, 44–46, 48, 49, 51–56, 59, 61–75), 13 were conducted in the United States (25, 29–31, 37–40, 43, 47, 50, 57, 58), and four were conducted in Canada (32–34, 60). Within Europe, the majority of studies were performed in Scandinavian countries (42, 44, 45, 51, 54, 59, 61, 64–67, 72–75), Germany (26–28, 35, 49, 71), and the Netherlands (20, 48, 55, 63).

Inclusion periods varied between <1 yr (61, 68, 70, 71) and ≥ 10 yrs (26–28, 35, 47, 50). All but three studies concerning critically ill patients in general had an inclusion period of 1 yr (19, 67, 69, 72–75). In three articles, the inclusion period was not further specified (32, 33, 40) (Table 1).

Table 2 gives an overview of QOL assessment after ICU discharge. The most frequently used QOL instrument was the SF-36 (55%), followed by the EQ-5D (21%), the NHP (9%), and the RAND-36 (8%). Four studies (8%) used a combination of QOL instruments: the SF-36 with the EQ-5D (19, 53), the RAND-36 with the EQ-5D (54), or the NHP with the Patrick's Perceived Quality of Life score, another QOL questionnaire (52).

Follow-up periods for QOL assessment varied between the included studies. Some had a strict follow-up period of 1 yr (29, 30, 37, 40, 41, 56, 67, 68), whereas others had large ranges within their follow-up time (26–28, 35, 43–47, 50, 52, 55, 58–60), and in one study, although at least 12 months, the follow-up period for QOL evaluation was not clearly defined (39). Twelve studies evaluated QOL at strict time points during the follow-up period (19, 31–34, 38, 51, 57, 66, 72, 74, 75). Median follow-up periods of ≥ 5 yrs were found in eight studies (26–28, 42, 48, 49, 71, 73). The Scandinavian area seemed to be particularly interested in research on QOL a long period after ICU discharge (42, 54, 59, 64, 65, 72–75).

QOL was assessed at follow-up by a mailed survey in 22 studies (42%) (20, 35, 36, 39, 45, 48, 49, 53, 54, 57, 59, 61, 67, 68, 63–66, 72–75), by telephone in 14 (26%) (19, 25, 32, 33, 40, 41, 44, 52, 55,

Table 1. Study characteristics

Reference	Country	Study Design	Inclusion Period	Patient Cohort	Eligible Patients for Long-Term QOL Assessment, N (%) ^a
ARDS					
Davidson et al, 1999 (25)	United States	Prospective, matched, controlled	January 1994–July 1996	102 sepsis or trauma-induced ARDS patients	80 (78%)
Schelling et al, 2000 (26)	Germany	Follow-up cohort	January 1985–January 1995	192 consecutive ARDS patients	119 (62%)
Rothenhäusler et al, 2001 (27)	Germany	Exploratory	January 1985–January 1995	192 consecutive ARDS patients	119 (62%)
Kapfhammer et al, 2004 (28)	Germany	Follow-up cohort	January 1985–January 1995	80 long-term ARDS survivors	80 (100%)
Hopkins et al, 1999 (29)	United States	Prospective	February 1994–July 1998	106 enrolled out of 274 ARDS patients	67 (63%)
Orme et al, 2003 (30)	United States	Prospective, cohort of a RCT	February 1994–December 1999	120 ARDS patients enrolled in high tidal volume vs. low tidal volume study	74 (62%)
Hopkins et al, 2005 (31)	United States	Longitudinal prospective, cohort of a RCT	February 1994–December 1999	120 ARDS patients enrolled in high tidal volume vs. low tidal volume study	74 (62%)
Heyland et al, 2005 (32)	Canada	Prospective, observational, multicenter	NA	221 ARDS patients enrolled in a phase III multicenter RCT	103 (47%)
Parker et al, 2006 (33)	Canada	Prospective, observational, multicenter	NA	221 ARDS patients enrolled in a phase III multicenter RCT	103 (47%)
Herridge et al, 2003 (34)	Canada	Longitudinal, multicenter	May 1998–May 2001	195 adult ARDS patients	109 (56%)
Deja et al, 2006 (35)	Germany	Prospective controlled	1991–2000	263 patients with severe ARDS	129 (49%)
Prolonged mechanical ventilation					
Combes et al, 2003 (36)	France	Prospective cohort	January 1995–June 1999	347 consecutive patients receiving mechanical ventilation for ≥ 14 d	99 (29%)
Chelluri et al, 2004 (37)	United States	Prospective, observational	June 1997–July 1999	817 patients receiving mechanical ventilation for ≥ 48 hrs	359 (44%)
Cox et al, 2009 (38)	United States	Prospective, observational	April 2006–April 2007	126 consecutive patients receiving mechanical ventilation ≥ 21 d or with a tracheotomy after ≥ 4 d of mechanical ventilation	90 (71%)
Trauma					
Miller et al, 2000 (39)	United States	Retrospective	January 1991–December 1997	115 severely injured patients spending ≥ 3 wks in the ICU	90 (78%)
Mackenzie et al, 2002 (40)	United States	Retrospective (hospital stay), prospective (QOL) multicenter	NA	Sample of 1587 patients registered in the Pennsylvania Trauma Outcomes Study	1587 (100%)
Dimopoulou et al, 2004 (41)	Greece	Prospective cohort	1999–2000	191 consecutive multiple trauma patients requiring mechanical ventilation	117 (61%)
Sluys et al, 2005 (42)	Sweden	Retrospective (patient cohort), prospective (QOL)	1996–1997	309 trauma patients	246 (80%)
Vles et al, 2005 (20)	The Netherlands	Prospective	January 1996–January 1999	295 severely injured patients (injury severity score ≥ 16)	196 (66%)
Jackson et al, 2007 (43)	United States	Retrospective	2003	97 trauma ICU survivors without intracranial hemorrhage	58 (60%)

Table 1. —Continued

Reference	Country	Study Design	Inclusion Period	Patient Cohort	Eligible Patients for Long-Term QOL Assessment, N (%) ^a
Ulvik et al, 2008 (44)	Norway	Follow-up cohort	1998–2003	325 trauma patients	228 (70%)
Ringdal et al, 2009 (45)	Sweden	Exploratory multicenter	September 2001–August 2002	344 adult trauma survivors	344 (100%)
Cardiac arrest					
Saner et al, 2002 (46)	Switzerland	Retrospective case-control	1991–1996	439 OOHCA patients (of 1307 resuscitations)	50 (11%)
Bunch et al, 2003 (47)	United States	Prospective (cardiac arrest, survival, QOL)	November 1990–January 2001	145 OOHCA patients (of 200 resuscitations)	60 (41%)
Kuilman et al, 1999 (48)	The Netherlands	Retrospective, multicenter	1988–1994	441 OOHCA patients (of 898 resuscitations)	132 (30%)
Graf et al, 2008 (49)	Germany	Prospective cohort	January 1999–December 2000	354 consecutive patients with cardiac arrest	110 (31%)
Mahapatra et al, 2005 (50)	United States	Prospective (cardiac arrest, survival, QOL)	November 1990–January 2001	142 OOHCA patients (of 200 resuscitations)	60 (42%)
Lundgren-Nilsson et al, 2005 (51)	Sweden	Longitudinal multicenter	1996–1999	51 cardiac arrest survivors	51 (100%)
Elderly					
Montuclard et al, 2000 (52)	France	Prospective cohort	January 1993–August 1998	75 consecutive patients >70 yrs with ICU LOS \geq 30 d	30 (40%)
Merlani et al, 2007 (53)	Switzerland	Retrospective	January 1999–December 2000	141 consecutive patients \geq 70 yrs with abdominal pathologies	52 (37%)
Kaarlola et al, 2006 (54)	Finland	Cross-sectional survey	1995–2000	882 elderly (\geq 65 yrs), 1,827 controls (<65 yrs)	354 elderly (40%), 1,074 controls (59%)
de Rooij et al, 2008 (55)	The Netherlands	Retrospective cohort	January 1997–December 2002	578 consecutive patients \geq 80 yrs	231 (40%)
Garrouste-Orgeas et al, 2006 (56)	France	Prospective, observational	March 2002–November 2003	180 patients \geq 80 yrs triaged for ICU admission; 48 ICU admissions	28 (16%; only 9 ICU patients)
Kleinpell, 2003 (57)	United States	Longitudinal, prospective, multicenter	Period of 14 mos	883 patients \geq 45 yrs, ICU LOS \geq 24 hrs	284 (32%)
Pancreatitis					
Soran et al, 2000 (58)	United States	Retrospective	January 1992–December 1996	52 ICU patients with acute pancreatitis	39 (75%)
Halonen et al, 2003 (59)	Finland	Retrospective	January 1989–December 1997	283 consecutive patients with severe acute pancreatitis	174 (61%)
Sepsis					
Heyland et al, 2000 (60)	Canada	Cross-sectional survey	1993–1998	78 sepsis patients	30 (38%)
Karlsson et al, 2009 (61)	Finland	Prospective, observational, multicenter	November 2004–February 2005	470 severe sepsis patients	278 (59%)
Korošec et al, 2006 (62)	Slovenia	Observational	2003	164 patients (66 sepsis, 98 trauma)	78 patients (48%; 21 sepsis, 57 trauma)
Mixed ICU patients 1 yr after ICU					
Pettilä et al, 2000 (67)	Finland	Prospective, observational	1995	591 consecutive ICU patients	354 (60%)
Badia et al, 2001 (68)	Spain	Prospective cohort	October 1994–June 1995	523 consecutive patients (84 trauma, 239 scheduled surgery, 57 unscheduled surgery, 143 medical)	375 (69 trauma, 198 SS, 23 unscheduled surgery, 85 medical; 72%)
Cuthbertson et al, 2005 (19)	United Kingdom	Prospective cohort	May 2001–April 2002	423 consecutive ICU patients	300 (71%)
Stricker et al, 2005 (69)	Switzerland	Prospective, observational, case-control	September 1998–August 1999	173 patients with ICU LOS >7 d vs. 1,506 patients with ICU LOS \leq 7 d	116 with an ICU LOS >7 days (67%)

Table 1. —Continued

Reference	Country	Study Design	Inclusion Period	Patient Cohort	Eligible Patients for Long-Term QOL Assessment, N (%) ^a
Long-term QOL					
García Lizana et al, 2003 (70)	Belgium	Prospective, observational	June 25–September 10, 2000	202 consecutive admitted patients	118 (58%)
Graf et al, 2005 (71)	Germany	Prospective cohort	November 1997–February 1998	303 consecutive patients with ICU LOS >24 hrs	190 (63%)
Kaarlola et al, 2003 (72)	Finland	Prospective observational	1995	591 consecutive patients	169 (29%)
Flaatten and Kvåle, 2001 (73)	Norway	Retrospective (ICU stay), prospective (survival, QOL)	1987	219 ICU patients	88 (40%)
Kvåle and Flaatten, 2003 (74)	Norway	Prospective cohort	July 1999–August 2000	226 patients with ICU LOS >24 hrs discharged alive	226 (100%)
Kvåle and Flaatten, 2002 (75)	Norway	Prospective and retrospective cohort	1987 compared with 1997	219 patients with ICU LOS ≥24 hrs in 1987, 338 in 1997	88 (40%; 1987) 106 (31%; 1997)
Various diseases					
De Boer et al, 2000 (63)	The Netherlands	Prospective, observational	January 1993–May 1996	100 consecutive patients who underwent a transhiatal esophagectomy	35 (35%)
Ahlström et al, 2005 (64)	Finland	Cross-sectional cohort	1998–2002	703 patients receiving renal replacement therapy for acute kidney injury	229 (33%)
Ylipalosaari et al, 2007 (65)	Finland	Prospective	May 2002–June 2003	272 hospital survivors with ICU-LOS >48 hrs	187 (69%)
Orwelius et al, 2008 (66)	Sweden	Prospective, multicenter cohort	August 2000–November 2003	1,625 consecutive adult patients with ICU LOS >24 hrs	723 (44%)

QOL, quality of life; ARDS, acute respiratory distress syndrome; RCT, randomized controlled trial; NA, not available; ICU, intensive care unit; ISS, injury severity score; ICH, intracranial hemorrhage; OOHCA, out-of-hospital cardiac arrest; LOS, length of stay.

^aPercentage of initial patient cohort.

56, 58, 60, 62, 69), by face-to-face interviews in 12 (23%) (26–31, 34, 43, 46, 47, 50, 51), and by a combination of these methods in five studies (9%) (37, 38, 42, 70, 71). To gain the highest response rate possible, many studies sent reminder mails or phoned in the absence of any response by mail (20, 35, 39, 42, 45, 49, 53, 54, 57, 59, 65, 67, 68, 72–74). Nevertheless, there were three studies (6%) with a response rate of <50% (26, 27, 39), 24 studies (45%) with a response rate between 50% and 79% (19, 28, 32, 33, 35, 37, 38, 40, 41, 45, 49, 51, 53, 57, 58, 61, 62, 64–66, 69, 73–75), and 26 studies (49%) had a response rate of at least 80% of the eligible patient population for long-term outcome and QOL assessment (20, 25, 29, 30, 31, 34, 36, 42–44, 46–48, 50, 52, 54–56, 59, 60, 63, 67, 68, 70–72).

Four studies (8%) met all of the four predefined study quality criteria: assessment of QOL at baseline, no major exclusion criteria within the study population, description of the nonresponder group vs. the responder group, and comparison with an age- and gender-matched normal

population (19, 37, 53, 61) (Table 3). By omitting assessment of baseline QOL as quality criterion, the number of studies fulfilling the other three quality criteria increased to 21 (40%) (26–28, 32, 35, 36, 39, 40, 42, 45, 47, 49, 57, 59, 62, 64–66, 69, 72, 74). Only nine studies (17%) measured QOL before ICU (19, 37, 38, 44, 52, 53, 61, 68, 70), and in 27 articles (51%) (19, 26–28, 32, 35, 36, 37, 39, 40, 42, 44, 45, 47, 49, 53, 57, 59, 61, 62, 64–66, 69, 70, 72, 74), a description was given of the nonresponder group and compared with patients who responded to the QOL survey. All studies defined clearly which patients were included or excluded.

Table 4 summarizes the major finding concerning long-term QOL per article. Long-term QOL varied between diagnostic categories. ARDS patients, patients after prolonged mechanical ventilation, severe trauma patients, and sepsis survivors showed significant impairments in long-term QOL (25–45, 60–62). Although physical aspects improved slowly over the years, mental and emotional conditions were stagnant or declined even further.

However, survivors of cardiac arrest, severe pancreatitis, esophagectomy, and acute kidney injury had a good QOL, which was comparable with or even better than that of an age- and gender-matched population (46–51, 58, 59, 63, 64). In the elderly, QOL was somewhat decreased, especially in the physical domains, but elderly patients generally adapted well to these limitations and perceived their QOL as good (27–32). One year after ICU, critically ill patients in general had a lower QOL, especially in physical domains, than an age- and gender-matched population (19, 67–69). However, a slow improvement to pre-morbid QOL levels could be found. The increase in QOL could be further seen several years after ICU, when QOL was quite comparable with that of the normal population (70–75).

Factors associated with reductions in QOL at least 1 yr after ICU discharge are also displayed in Table 4. In ARDS or patients with prolonged mechanical ventilation, ARDS and its sequelae influenced QOL by impairments in pulmonary

Table 2. Assessment of quality of life after ICU

Reference	QOL Assessment Instrument	Method of QOL Assessment	Response Rate, % (N of QOL Responders)	Follow-Up Period
Acute respiratory distress syndrome				
Davidson et al, 1999 (25)	SF-36	Telephone	96% (77)	Median 23 mos
Schelling et al, 2000 (26)	SF-36	Face-to-face	42% (50)	Median 5.5 yrs (range 1–10 yrs)
Rothenhäusler et al, 2001 (27)	SF-36	Face-to-face	39% (46)	Median 6 yrs (range 1–12 yrs)
Kapfhammer et al, 2004 (28)	SF-36	Face-to-face	58% (46)	Median 8 yrs (range 3–13 yrs)
Hopkins et al, 1999 (29)	SF-36	Face-to-face	82% (55)	1 yr
Orme et al, 2003 (30)	SF-36	Face-to-face	89% (66)	1 yr
Hopkins et al, 2005 (31)	SF-36	Face-to-face	84% (62)	1 and 2 yrs
Heyland et al, 2005 (32)	SF-36	Telephone	71% (73)	3, 6, 12 mos
Parker et al, 2006 (33)	SF-36	Telephone	71% (73)	3, 6, 12 mos
Herridge et al, 2003 (34)	SF-36	Face-to-face	80% (83) 3 mos 82% (82) 6 mos 86% (83) at 12 mos	3, 6, 12 mos
Deja et al, 2006 (35)	SF-36	Mail, telephone if no answer	50% (65)	57 ± 32 mos
Prolonged mechanical ventilation				
Combes et al, 2003 (36)	NHP	Mail	88% (87)	Average 3 yrs
Chelluri et al, 2004 (37)	SF-36	Telephone or face-to-face	64% (231) full interview 18% (65) mini-interview	1 yr
Cox et al, 2009 (38)	EQ-5D	Telephone or face-to-face	78% (70)	3, 12 mos
Trauma				
Miller et al, 2000 (39)	RAND-36	Mail, telephone if no answer	39% (35)	Unclear, mean of several years
Mackenzie et al, 2002 (40)	SF-36	telephone	78% (1230)	1 yr (range, 10–14 mos)
Dimopoulou et al, 2004 (41)	NHP	Telephone	74% (87)	1 yr
Sluys et al, 2005 (42)	SF-36	Mail or telephone, reminder mail	83% (205)	5 yrs
Vles et al, 2005 (20)	EQ-5D	Mail, telephone if no answer	85% (166)	Mean 41 mos
Jackson et al, 2007 (43)	SF-36	Face-to-face	100% (58)	12–24 mos
Ulvik et al, 2008 (44)	EQ-5D	Telephone	92% (210)	2–7 yrs (median 4 yrs)
Ringdal et al, 2009 (45)	SF-36	Mail, one written reminder, then telephone	69% (239)	6–18 mos
Cardiac arrest				
Saner et al, 2002 (46)	NHP	Face-to-face	100% (50)	Mean 31.7 mos (range, 5–68 mos)
Bunch et al, 2003 (47)	SF-36	Face-to-face	83% (50)	4.8 ± 3.0 yrs
Kuilman et al, 1999 (48)	EQ-5D	Mail	83% (109)	Mean 6.71 yrs
Graf et al, 2008 (49)	SF-36	Mail or telephone if no answer	74% (81)	5 yrs
Mahapatra et al, 2005 (50)	SF-36	Face-to-face	83% (50)	4.8 ± 3.0 yrs
Lundgren-Nilsson et al, 2005 (51)	NHP	Face-to-face	51% (26) at 1 yr	14 days, 45 days, 3 mos, 1 yr
Elderly				
Montuclard et al, 2000 (52)	Patrick's Perceived Quality of Life (1996) NHP (1998)	Telephone	93% (28) (first study) 95% (21) (second study)	557 ± 117 days for the first study, second 2 yrs later
Merlani et al, 2007 (53)	ED-5D, SF-36	Mail, telephone if no/incomplete answer	79% (41)	2 yrs
Kaarlola et al, 2006 (54)	EQ-5D, RAND-36	Mail, reminder mail	87% (307) elderly 77% (828) controls	Median 3 yrs for elderly median 4 yrs for controls
de Rooij et al, 2008 (55)	EQ-5D	Telephone	88% (204)	1 to 6 yrs, median 3.7 yrs
Garrouste-Orgeas et al, 2006 (56)	NHP	Telephone	100% (28)	1 yr
Kleinpell, 2003 (57)	SF-36	Mail, reminder mail, telephone if no answer	70% (199)	1, 3, 6, 12 mos
Pancreatitis				
Soran et al, 2000 (58)	SF-36	Telephone	54% (21)	Median 42 mos (range, 17–69 mos)
Halonen et al, 2003 (59)	RAND-36	Mail, reminder mail, or telephone	83% (145)	Median 61 mos (range, 19–127 mos)
Sepsis				
Heyland et al, 2000 (60)	SF-36	Telephone	100% (30) first interview 87% (26) second interview	16.6 ± 10.6 mos
Karlsson et al, 2009 (61)	EQ-5D	Mail	52% (252) QOL before 58% (156) long-term QOL	Median 17 mos

Table 2. —Continued

Reference	QOL Assessment Instrument	Method of QOL Assessment	Response Rate, % (N of QOL Responders)	Follow-Up Period
Korošec et al, 2006 (62)	EQ-5D	Telephone	50% (39)	2 yrs
Mixed ICU patients 1 yr after ICU				
Pettilä et al, 2000 (67)	RAND-36	Mail, reminder mail	87% (307)	1 yr
Badia et al, 2001 (68)	EQ-5D	Mail, telephone or face-to-face interview if no answer	89% (334)	1 yr
Cuthbertson et al, 2005 (19)	SF-36, also EQ-5D at 12 mos	Telephone	78% (233) 3 mos 67% (201) 6 mos 58% (173) 12 mos	3, 6, 12 mos
Stricker et al, 2005 (69)	SF-36	Telephone	65% (75)	12–18 mos
Long-term QOL				
García Lizana et al, 2003 (70)	EQ-5D	Mail or telephone	81% (96)	1, 5 yrs
Graf et al, 2005 (71)	SF-36	Mail or telephone	91% (173)	5 yrs
Kaarlola et al, 2003 (72)	RAND-36	Mail, reminder mail if no response	84 % (298) 1 yr 76 % (192) 6 yrs	1 yr and 6 yrs
Flaatten and Kvåle, 2001 (73)	SF-36	Mail, reminder mail if no response	58% (51)	12 yrs
Kvåle and Flaatten, 2003 (74)	SF-36	Mail, one reminder mail	56% (126) at 6 mos 79% (100) after 2 yrs	6 mos and 2 yrs
Kvåle and Flaatten, 2002 (75)	SF-36	Mail	58 % (51) in 1987 62 % (66) in 1997	3 yrs and 13 yrs
Various diseases				
De Boer et al, 2000 (63)	SF-36	Mail	100% (35)	Minimum of 2 yrs
Ahlström et al, 2005 (64)	EQ-5D	Mail	67% (153)	Median 2.4 yrs
Ylipalosaari et al, 2007 (65)	EQ-5D	Mail, telephone if no response	76% (142)	Median 22 mos
Orwelius et al, 2008 (66)	SF-36	Mail	69% (497) after 12 mos	6 and 12 mos

ICU, intensive care unit; QOL, quality of life; SF-36, Short-Form 36; NHP, Nottingham Health Profile; EQ-5D, EuroQol-5D.

functions, cognitive disorders, weakness, and post-traumatic stress disorders (25–35). In trauma patients, the injury severity, the degree of brain damage, and female gender dominated long-term QOL in a negative way (20, 41, 43, 44). However, in other studies the severity of illness played a less important role (71, 74). In a mixed ICU patient population, diagnostic category determined QOL (67, 68, 70). There were conflicting results regarding the influence of age on long-term QOL (19, 37, 42, 57, 59, 63, 67, 70, 74). Two studies found that poor preadmission QOL played a role in the reduction in QOL a long period after ICU discharge (19, 70).

DISCUSSION

It was the purpose of this review to give an overview of the literature of QOL at least 1 yr after discharge from the ICU, of the factors that determine QOL, and of the methodology used. Because of differences in study design, patient populations, QOL instruments, follow-up times, and response rates, it is impossible to make one overall conclusion. However, this review has some important findings.

First, long-term QOL depends largely on diagnostic category. Patients with severe ARDS, prolonged mechanical ventilation,

severe trauma, and severe sepsis appeared to have the worst reductions in QOL, which lasted a long time. Although physical aspects improved slowly over the years, mental and emotional aspects were stagnant or declined even further. Trauma patients were usually healthy and young before ICU admission. Their QOL often declined substantially after the trauma, both in physical and psychosocial dimensions, and delusional memories and the inability to return to work negatively influenced their perceived QOL (20, 41, 45). Survivors of cardiac arrest, elderly, patients with severe pancreatitis, patients after esophagectomy, or patients with acute kidney injury had good QOL or perceived it as even better than before illness. Acceptance of disability is, in general, higher among older patients, and it is even better if they have a good socioeconomic status (52). A high QOL despite the severity of illness or persisting symptoms may be explained by the fact that patients who are confronted with a life-threatening disease are faced with the necessity to acclimate to the disease, which may lower internal standards (63). Critically ill patients in general had a lower QOL than an age- and gender-matched population 1 yr after ICU discharge, but a slow improvement in QOL could be seen, and several years after ICU, QOL was quite comparable with that of the normal population.

The second finding was that factors that could be presumed to result in a poor QOL after ICU, such as age, prolonged mechanical ventilation, or a long ICU or hospital stay, are not indicators per se of reductions in QOL afterward (25, 27, 44). Other issues, such as cognitive impairments, sleep disturbances, post-traumatic stress disorder, the rehabilitation process, employment status, and cultural and payment differences, can influence QOL in a less tangible way than, for example, physical impairments after major trauma (26, 27, 35, 49, 52, 66).

Third, there were important methodologic differences between the included studies. Four of the 53 included studies met all four quality criteria. Only a minority of studies had a uniform follow-up time or measured QOL before ICU admission, and response rates to QOL surveys were generally low, which resulted in a limited interpretation of study results.

The ideal assessment of long-term QOL after critical care should use validated QOL instruments in large cohorts without major exclusions, with an extensive but reasonably long and uniform follow-up period, and with comparison with baseline evaluation before ICU stay (61). Future research on long-term QOL should focus on that. In this review, only

Table 3. Study quality criteria

Reference	QOL Before ICU	Key Inclusion or Exclusion Criteria	Description of Nonresponders	Age-/Gender-Matched General Population to Compare QOL
ARDS				
Davidson et al, 1999 (25)	No	ARDS survivors with severe head injuries were excluded	No	Matched with sepsis and trauma patients without ARDS
Schelling et al, 2000 (26)	No	Study population was a follow-up cohort of 80 long-term ARDS survivors and QOL responders in a study 3 yrs before	Yes	Age- and gender-matched control group of normal German subjects
Rothenhäusler et al, 2001 (27)	No	Only long-term ARDS survivors were included	Yes	Age- and gender-matched control group
Kapfhammer et al, 2004 (28)	No	Only long-term ARDS survivors were included	Yes	Standard values of the Short-Form 36 from volunteers of the West German population
Hopkins et al, 1999 (29)	No	168 ARDS patients were excluded for various reasons	No	Normative population data
Orme et al, 2003 (30)	No	Only long-term ARDS survivors were included	No	Normative population data
Hopkins et al, 2005 (31)	No	Long-term ARDS survivors were included	No	Normative population data
Heyland et al, 2005 (32)	No	Long-term ARDS survivors were included	Yes	Age- and gender-matched population derived from literature
Parker et al, 2006 (33)	No	Long-term ARDS survivors were included	No	Primary ARDS patients were compared to secondary ARDS patients
Herridge et al, 2003 (34)	No	Only severe ARDS patients were included Immobile patients, patients with a history of pulmonary resection or with a neurologic or psychiatric disease were excluded	No	Normal Canadian population
Deja et al, 2006 (35)	No	Only severe ARDS patients were included	Yes	Age- and gender-matched healthy German controls
Prolonged mechanical ventilation				
Combes et al, 2003 (36)	No	Only patients with prolonged mechanical ventilation (≥ 14 d) were included	Yes	Community-based age- and gender-matched controls
Chelluri et al, 2004 (37)	Yes	Patients with prolonged mechanical ventilation (≥ 48 hrs) were included	Yes	Samples of the U.S. population
Cox et al, 2009 (38)	Yes	Patients with ≥ 21 d mechanical ventilation or with tracheotomy after ≥ 4 d mechanical ventilation were included	No	U.K. population norms for persons aged 55–65 yrs
Trauma				
Miller et al, 2000 (39)	No	Only severely injured patients spending ≥ 3 wks in the ICU were included	Yes	General U.S. population
Mackenzie et al, 2002 (40)	No	Blunt trauma patients (18–59 yrs), with a hospital stay of ≥ 72 hrs were included. Drownings, electrocutions, burns, and hip or femoral neck fractures were excluded	Yes	Age- and gender-matched general population
Dimopoulou et al, 2004 (41)	No	Only mechanically ventilated polytrauma patients were included	No	No
Sluys et al, 2005 (42)	No	Blunt or penetrating trauma patients with an ISS of ≥ 9 were included; patients with psychiatric disorders or cognitive impairments were excluded	Yes	Swedish age- and gender-matched reference sample
Vles et al, 2005 (20)	No	Only patients with ISS ≥ 16 were included	No	Swedish reference database, corrected for age and gender
Jackson et al, 2007 (43)	No	Only trauma ICU survivors (ISS > 25) without intracranial hemorrhage were included	No	General U.S. population
Ulvik et al, 2008 (44)	Yes	Foreign trauma patients were excluded because of difficulties with follow-up	Yes	No
Ringdal et al, 2009 (45)	No	Nonsurvivors, attempted suicide, not resident in Sweden, intellectual impairment, and patients with unknown address were excluded	Yes	Age- and gender-matched reference sample drawn from the Swedish Short-Form 36 norm database

Table 3. —Continued

Reference	QOL Before ICU	Key Inclusion or Exclusion Criteria	Description of Nonresponders	Age-/Gender-Matched General Population to Compare QOL
Cardiac arrest				
Saner et al, 2002 (46)	No	Patients with hypoxic brain damage, drug abusers, in hospital resuscitation, non-German-speaking, and <20 or >80 yrs were excluded	No	Healthy controls of similar age, gender, and socioeconomic status
Bunch et al, 2003 (47)	No	Only patients with OOHCA with ventricular fibrillation were included	Yes	Age- and gender-matched norms from a sample of the general U.S. population
Kuilman et al, 1999 (48)	No	Successfully resuscitated patients were included	No	No
Graf et al, 2008 (49)	No	Patients who received cardiopulmonary resuscitation for an in-hospital cardiac arrest or OOHCA were included	Yes	Healthy German population
Mahapatra et al, 2005 (50)	No	Only patients with an OOHCA with ventricular fibrillation were included	No	Age- and gender-matched norms from a sample of the general U.S. population
Lundgren-Nilsson et al, 2005 (51)	No	Only cardiac arrest survivors were included	No	Reference Swedish population
Elderly				
Montuclard et al, 2000 (52)	Yes	Consecutive patients >70 yrs with an ICU LOS \geq 30 d were included	No	General French population of mixed age and 76-yr-old Swedish urban citizens
Merlani et al, 2007 (53)	Yes	Patients aged \geq 70 yrs with abdominal pathologies were included	Yes	Age-matched population
Kaarlola et al, 2006 (54)	No	All consecutive patients admitted within the study period were included	No	Controls and an age- and gender-matched Finnish population
de Rooij et al, 2008 (55)	No	Consecutive patients aged \geq 80 yrs admitted within the study period were included	No	Age-matched British non-ICU general population
Garrouste-Orgeas et al, 2006 (56)	No	In 73% of patients aged \geq 80 yrs ICU admission was refused	No	Age- and gender-matched general French population
Kleinpell, 2003 (57)	No	Patients \geq 45 yrs with ICU LOS of \geq 24 hrs were included	Yes	General U.S. population
Pancreatitis				
Soran et al, 2000 (58)	No	Only acute pancreatitis patients were included	No	Age-matched normal control group
Halonen et al, 2003 (59)	No	Patients (majority needed ICU admission) with acute pancreatitis were included	Yes	Age- and gender-matched Finnish population
Sepsis				
Heyland et al, 2000 (60)	No	Patients with sepsis were included; patients with disabilities that would preclude a telephone interview were excluded	No	General U.S. population
Karlsson et al, 2009 (61)	Yes	All severe sepsis patients at admission or during ICU stay were included	Yes	Age- and gender-adjusted Finnish reference population
Korošec et al, 2006 (62)	No	Only sepsis and trauma patients were included	Yes	No
Mixed ICU patients 1 yr after ICU				
Pettilä et al, 2000 (67)	No	No major exclusion criteria	No	Age- and gender-matched general Finnish population
Badia et al, 2001 (68)	Yes	No major exclusion criteria	No	No
Cuthbertson et al, 2005 (19)	Yes	Patients who were not expected to survive ICU were excluded	Yes	Age- and gender-matched general U.K. population
Stricker et al, 2005 (69)	No	Surgical and trauma patients with ICU LOS >7 d and with ICU-LOS \leq 7 d were matched. Burn injuries were excluded	Yes	Age- and gender-matched sample of the German population
Long-term QOL				
García Lizana et al, 2003 (70)	Yes	ICU admissions for uncomplicated elective postoperative surgery were excluded	Yes	No
Graf et al, 2005 (71)	No	Patients with ICU LOS <24 hrs were excluded	No	Age-matched group of healthy Germans
Kaarlola et al, 2003 (72)	No	Patients who responded to both questionnaires in 1996 and 2001 were included	Yes	Age- and gender-matched Finnish population
Flaatten and Kvåle, 2001 (73)	No	Heart surgery and burn patients were not included	No	Age- and gender-matched general Norwegian population

Table 3. —Continued

Reference	QOL Before ICU	Key Inclusion or Exclusion Criteria	Description of Nonresponders	Age-/Gender-Matched General Population to Compare QOL
Kvåle and Flaatten, 2003 (74)	No	Heart surgery and burn patients were not included	Yes	Scores after 6 mos compared with scores after 2 yrs
Kvåle and Flaatten, 2002 (75)	No	Heart surgery and burn patients were not included	No	Age- and gender-matched control groups from the general Norwegian population
Various diseases				
De Boer et al, 2000 (63)	No	Only long-term survivors without tumor recurrence were included	No	Age-matched reference population
Ahlström et al, 2005 (64)	No	Only acute kidney injury patients needing renal replacement therapy were included	Yes	Age- and gender-matched population
Ylipalosaari et al, 2007 (65)	No	Only hospital survivors with ICU LOS >48 hrs were included	Yes	No
Orwelius et al, 2008 (66)	No	Only adult patients with ICU LOS >24 hrs and alive 6 mos after discharge were included	Yes	Random sample from the main intake area of the hospitals was used as a reference group

QOL, quality of life; ICU, intensive care unit; ARDS, acute respiratory distress syndrome; ISS, injury severity score; OOHCA, out-of-hospital cardiac arrest; LOS, length of stay.

studies that used at least one of four generic QOL instruments (SF-36, EQ-5D, RAND-36, NHP) were included. Generic instruments apply to a broad spectrum of populations and therefore are less responsive to changes in specific conditions as compared with specific QOL instruments (9). Although there is still no consensus about which tool should be used to measure QOL in critical care patients, SF-36 and EQ-5D are considered to be valid and reliable instruments for critically ill patients (10). The EQ-5D is validated for European populations (76, 77), but some still consider SF-36 or RAND-36 as the generic instrument of first choice in critically ill patients (19, 60, 67). Using use both EQ-5D and SF-36 together can be recommended (20).

One of the goals of QOL measures is differentiating between people with a better and a worse QOL and measuring how much QOL has changed over time (9). This change in QOL over time leads to an important and difficult issue in QOL studies. How long is “long” in long-term outcome, and when will functional outcome measures and questionnaires no longer give additional information? The follow-up intervals for QOL were very different in the included studies, which made it difficult to conclude which time course should be considered as the best to interpret the overall results and as sufficient to allow regaining the best achievable QOL (71). Between studies, there were large differences in timing, but also within the studies themselves

there were large differences; the follow-up intervals differed greatly, which was correctly considered as a limitation of study results (26, 27, 35, 36, 45–47, 50). A follow-up period of 1 yr is probably too short because physical limitations still tend to dominate over emotional problems (19, 30, 31, 35, 37, 41), and physical problems will not always be recovered (67). One year may also be too short to become accustomed to more restrictions in daily life (72). When follow-up periods extend to >1 yr, a tendency toward more emotional problems was found. It is generally accepted that the real burden of critical illness is seen up to 6 months after ICU discharge (32, 64), although it is possible that studies using 6 months as the first time point for data collection missed an earlier decline in QOL (19). Follow-up of 1 or 2 yrs will probably capture the most, and it may be the limit for improvement in most QOL dimensions, as seen after severe trauma (44, 68). Still, mental health will be affected for many more years (35, 70).

The most important problem of long-term follow-up times is that more patients will be lost to follow-up, which could lead to an important bias in results. Patients who do not respond can do so for many different reasons. They can consider QOL questionnaires trivial if they recovered well, they can have post-traumatic stress disorder and avoid seeking memories of their ICU treatment, they can be too ill to have the ability to respond, or they may have died before

completing the survey (35, 36, 54). As such, QOL responders may represent a sample of healthier patients (47, 58). Therefore, analyzes of responders vs. nonresponders concerning severity of illness scores, comorbidities, mortality, or age should be made (44). To avoid selection bias, every effort has to be made to target the highest response rate possible. In many studies, although it was time-consuming and labor-intensive to do so, patients who did not respond to the initial mailed survey or to a mailed reminder were phoned, which did not always guarantee a high response rate (35, 39, 73). A lost-to-follow-up rate of 20% is considered to be acceptable for QOL studies (19), but only 49% of the studies had a response rate of at least 80% of the eligible patient population for long-term outcome and QOL assessment. As a consequence, the number of patients with a reliable QOL assessment at least 1 yr after ICU discharge was low.

When QOL measures are used as discriminative instruments, possible confounders that could influence QOL should be eliminated. Therefore, QOL in ICU patients can be compared to an age- and gender-matched general population, which should be considered as the upper limits of what is achievable (75). In most studies, QOL responders were matched with a representative healthy population. The study findings can also be compared with an appropriate control group, eliminating the influence of specific health conditions (25, 62). More important,

Table 4. Major findings and factors influencing long-term QOL

Reference	Long-Term QOL: Major Finding	QOL: Influencing Factors
ARDS		
Davidson et al, 1999 (25)	ARDS survivors had a significant reduction in QOL; sepsis-induced ARDS patients had more severe reductions in QOL than trauma-induced ARDS patients	ARDS and its sequelae, not comorbid disease, severity of trauma or illness, duration of mechanical ventilation, or hospital stay
Schelling et al, 2000 (26)	Long-term ARDS survivors have a significant reduced QOL	Multiple pulmonary function impairments
Rothenhäusler et al, 2001 (27)	Long-term QOL was impaired	Cognitive deficits and disability
Kapfhammer et al, 2004 (28)	Long-term ARDS survivors had major impairments in long-term QOL	Posttraumatic stress disorder
Hopkins et al, 1999 (29)	After 1 yr, there was improvement for the physical but not for the emotional domains	Cognitive impairments
Orme et al, 2003 (30)	ARDS survivors, treated with high or low tidal volume ventilation, had a reduced QOL, which was related to physical rather than emotional concerns	Pulmonary function impairments
Hopkins et al, 2005 (31)	ARDS survivors had decreased QOL, with physical and emotional domains improving at 1 yr, but no additional change or decline at 2 yrs	Neurocognitive impairments, although these may represent morbidity from critical illness rather than be specific for ARDS
Heyland et al, 2005 (32)	ARDS survivors had a significantly lower QOL than age- and gender-matched controls; after 1 yr, there was an improvement in the physical domains, whereas the mental scores remained unchanged	Pulmonary function impairments, baseline comorbidities
Parker et al, 2006 (33)	Primary ARDS patients had significantly better QOL scores than patients with secondary ARDS	Primary vs. secondary ARDS; not ICU LOS, hospital LOS, duration of mechanical ventilation, comorbidity, lung function
Herridge et al, 2003 (34)	QOL improved over 1 yr after ICU discharge but remained lower than these of the control population	Functional disability attributable to muscle wasting, weakness, fatigue
Deja et al, 2006 (35)	QOL in patients with ARDS was significantly reduced in all dimensions	Posttraumatic stress disorder
Prolonged mechanical ventilation		
Combes et al, 2003 (36)	QOL was impaired but perceived as acceptable, with psychosocial aspects being better than physical performance	Worse QOL seen in ARDS survivors
Chelluri et al, 2004 (37)	QOL was impaired mainly on the physical and social domains but comparable on the mental health and emotional domains	Influence of age and chronic illness predominate the long-term outcome
Cox et al, 2009 (38)	One year after ICU discharge, the majority of patients had a poor QOL	NA
Trauma		
Miller et al, 2000 (39)	QOL was low, especially in the physical domains	NA
Mackenzie et al, 2002 (40)	1 yr after trauma, QOL was low, except for vitality and mental health	NA
Dimopoulou et al, 2004 (41)	QOL was impaired in physical functioning, working ability, and emotional well-being	Injury severity, degree of brain trauma
Sluys et al, 2005 (42)	5 yrs after trauma, QOL was low in all dimensions of the Short-Form 36	Age, surgical procedures, ICU and hospital LOS, in-hospital complications, inadequate information
Vles et al, 2005 (20)	QOL was low and one-quarter of those of working age were unable to return to work	Injury severity, female gender
Jackson et al, 2007 (43)	QOL was low	Cognitive impairments
Ulvik et al, 2008 (44)	More than 2 yrs postinjury, 74% reported impaired QOL, mostly caused by pain and discomfort, but only a minority had severe problems	Severity of illness and injury, time since trauma (pain), female gender, degree of brain trauma; not age
Ringdal et al, 2009 (45)	Trauma patients scored low on all Short-Form 36 domains	Delusional memories, comorbidity
Cardiac arrest		
Saner et al, 2002 (46)	Long-term QOL remained fulfilling with only a few changes in the psychosocial profile	Little impact of changes in psychosocial profile
Bunch et al, 2003 (47)	Except from a reduction in vitality, QOL was similar to that of the general population	NA
Kuilman et al, 1999 (48)	No difference in QOL between patients resuscitated by emergency personnel, physicians, or bystanders	NA
Graf et al, 2008 (49)	Patients who survive without severe neurologic disabilities may expect a good QOL	NA
Mahapatra et al, 2005 (50)	Long-term survival and QOL are equally favorable in both genders	NA
Lundgren-Nilsson et al, 2005 (51)	QOL improved over the year with values comparable to the reference population	Cognitive impairments

Table 4. —Continued

Reference	Long-Term QOL: Major Finding	QOL: Influencing Factors
Elderly		
Montuclard et al, 2000 (52)	After 1 yr, perceived QOL was good, especially emotional and social functioning	A moderate disability influenced QOL
Merlani et al, 2007 (53)	A high mortality and a decrease in QOL were observed for elderly patients with abdominal pathologies; these patients adapted well to their physical limitations	NA
Kaarlola et al, 2006 (54)	Aging decreased QOL mostly in the physical domains, but elderly patients had better values for mental health than the younger controls	Acceptance of disability is better with a good social network
de Rooij et al, 2008 (55)	QOL was significantly lower for usual activities; most patients were willing to receive ICU treatment again if necessary	NA
Garrouste-Orgeas et al, 2006 (56)	After 1 yr, QOL was poorer than in the general population; one-half of the survivors did not want further ICU admission if necessary	NA
Kleinpell, 2003 (57)	In the middle-aged and elderly patient group, Short-Form 36 scores remained below the general population norms but increased over time	Severity of illness rather than age
Pancreatitis		
Soran et al, 2000 (58)	Long-term QOL is good and comparable with an age-matched control population	NA
Halonen et al, 2003 (59)	Long-term QOL is good and comparable with an age-matched control population	Working status before acute pancreatitis, age; not follow-up time, cause, gender, ICU treatment, ICU LOS, multiple organ failure, operating status
Sepsis		
Heyland et al, 2000 (60)	The QOL of sepsis survivors is lower than that of the general population and comparable to QOL of patients with chronic disease or survivors of acute lung injury	NA
Karlsson et al, 2009 (61)	QOL in most patients was already lower before the episode of severe sepsis than in the general population, and it was even lower after the critical illness	NA
Korošec et al, 2006 (62)	Surgical ICU patients with sepsis have a higher mortality than trauma patients; however, QOL after 2 yrs is reduced to the same level in both groups	Anxiety and depression (trauma)
Mixed ICU patients 1 yr after ICU		
Pettilä et al, 2000 (67)	Survivors had a lower QOL than an age- and gender-matched general population; however, patients perceived their QOL as better or similar as before their ICU stay	Multiple organ failure, age, diagnostic category
Badia et al, 2001 (68)	Trauma patients experienced a worsening, unscheduled surgery and medical patients experienced a slight deterioration, and scheduled patients experienced a considerable improvement in QOL	Diagnostic category
Cuthbertson et al, 2005 (19)	Physical QOL increased to pre-morbid levels 1 yr after ICU discharge but physical scores remained below the population norms; mental scores were similar or higher than population norms; nonsurvivors had a lower QOL than survivors at all time points	Poor baseline situation; not prolonged ICU LOS, age, surgical or medical admissions
Stricker et al, 2005 (69)	When taking into account severity of illness, QOL 1 yr after ICU discharge is comparable between patients with short and long ICU stay; QOL remained lower than in a general population, mostly in physical aspects	Not prolonged ICU LOS
Long-term QOL		
García Lizana et al, 2003 (70)	38% felt their QOL was worse, 37% felt it to be similar, and 25% felt it was better than before their ICU admission; psychology domains were the most frequently affected	Previous QOL, prolonged hospital stay, ICU readmission, diagnostic category, Acute Physiology and Chronic Health Evaluation II score, age, female gender, organ failure
Graf et al, 2005 (71)	After 5 yrs, most patients lived independently and had a good QOL	Not severity of illness, morbidity, resource consumption, age, or gender
Kaarlola et al, 2003 (72)	Six years after ICU discharge, QOL was comparable with that of the general population; QOL revealed worse physical functioning, pain, and general health but improvement in the psychological domains	NA
Flaatten and Kvåle, 2001 (73)	QOL was acceptable but it was still lower than in the general population	NA

Table 4. —Continued

Reference	Long-Term QOL: Major Finding	QOL: Influencing Factors
Kvåle and Flaatten, 2003 (74)	There was an increase in QOL from 6 mos to 2 yrs in a mixed ICU population	Age; minor: severity of illness, ICU LOS
Kvåle and Flaatten, 2002 (75)	QOL was still reduced 3 and 13 yrs after ICU; QOL was more reduced in 1997 patients (3 yrs follow-up) than in 1987 patients (13 yrs follow-up)	NA
Various diseases		
De Boer et al, 2000 (63)	Although residual symptoms may persist, patients reported a similar or even better QOL (emotional well-being in particular) than an age-matched reference group	Prolonged hospital stay, age, fatigue, emotional aspects, not disease-specific symptoms
Ahlström et al, 2005 (64)	The long-term outcome and QOL of patients with acute kidney injury were poor but patients perceived their QOL as good	NA
Ylipalosaari et al, 2007 (65)	QOL was equally reduced in patients with or without ICU-acquired infection	Not ICU-acquired infection
Orwelius et al, 2008 (66)	QOL was reduced because of physical problems, bodily pain, general health, vitality, and mental health	Minor: sleep disturbances

QOL, quality of life; ARDS, acute respiratory distress syndrome; ICU, intensive care unit; LOS, length of stay; NA, not available.

long-term QOL should also be compared with QOL before ICU admission, to discriminate whether poor long-term QOL is a result of the severity of illness or is attributable to confounding factors or “background variables,” such as comorbid disease, poor preadmission QOL, age, gender, or acquired complications (44). Which factor will influence the most long-term QOL is a difficult question, and literature is definitively not conclusive about this issue (74). The long-term effect of a certain condition on QOL is cohort specific and may be the residua of any severe critical illness (34). It will also depend on the follow-up period and the tools used and will probably be a mixture of severity of illness, previous health status, premorbid QOL, age, gender, and diagnostic category.

Previous studies of QOL before ICU admission support the hypothesis that patients’ premorbid QOL has a large effect on QOL after critical illness (78, 79). It has been proved that pre-ICU QOL is low compared to that of the general population, indicating that ICU patients differ from the average population even before the onset of critical illness (10, 44, 80). Poor QOL before critical illness is also correlated with poor outcome (19, 81–84). Impaired QOL after ICU thus may reflect a poor baseline situation rather than being a function of intensive care (19, 67). Measuring QOL at baseline is difficult; in the majority of studies (83%), this was not performed. One-third of these studies considered this as a limitation (20, 25, 31, 36, 42, 43, 54–57, 62, 64, 65, 67). Most patients will not be able to complete questionnaires at time of ICU

admission and many studies asked patients or proxies a long period afterward how QOL was before admission (20, 44, 52, 53, 62). Recall bias can influence results of these QOL surveys. In retrospective studies, recall bias can also add some uncertainty to the study findings because QOL assessment is based on patient’s recall of memories from the ICU stay (45, 46). No baseline assessment of QOL because it would have been assessed retrospectively can be the reason for not measuring QOL prior to ICU admission (56).

Some authors considered that only patients could evaluate their own QOL (56), or they considered it a potential danger for bias if questionnaires were completed by proxies (67). However, the SF-36 and EQ-5D questionnaire completed by proxies can reliably assess the QOL of the critically ill patient on admission to the ICU (68, 81), although it is difficult to interview proxies when their relatives are critically ill (37). Proxies tend to underestimate the QOL of the patient, but differences are usually small (81).

There are some methodologic limitations in this review. First, only four generic QOL instruments were included, which are, however, commonly used in critically ill patients (8). This allowed us to compare among studies and make more comprehensive conclusions. Second, some studies had a low number of QOL responders and a nonuniform follow-up time, which limits the interpretation of study results. The findings of this review are also limited because of infrequent collection of QOL at baseline.

CONCLUSION

Future outcome evaluations should not be limited to “dead” or “alive” but should also incorporate QOL, even though this is much more complicated to investigate. Long-term QOL in critically ill patients depends largely on diagnostic category, with the worst reductions found in patients who survive severe ARDS, sepsis, trauma, and prolonged mechanical ventilation. For critically ill patients in general, a lower QOL compared to that of an age- and gender-matched healthy population was seen. However, evidence for poorer QOL after ICU is misleading when the previous health state of the patient is not taken into account. Baseline QOL assessment is necessary when investigating the influence of the critical illness and should be assessed on ICU admission to avoid recall bias. Follow-up periods should be kept strictly uniform, although there is no consensus regarding the most appropriate follow-up time. Measures to gain the highest response rate to avoid selection bias should be taken. Nevertheless, comparisons between responders and nonresponders should always be made.

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