

# 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  $\geq 12$  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

**B**ecause 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.,  $\geq 12$  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  $\geq 12$  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  $\geq 10$  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  $\geq 5$  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 (%) <sup>a</sup> |
|---|-----------------|--|-----------------------------|--|--|
| <b>ARDS</b>                             |                 |  |                             |  |  |
| 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%)  |
| <b>Prolonged mechanical ventilation</b> |                 |  |                             |  |  |
| Combes et al, 2003 (36)                 | France          | Prospective cohort   | January 1995–June 1999      | 347 consecutive patients receiving mechanical ventilation for $\geq 14$ d  | 99 (29%)   |
| Chelluri et al, 2004 (37)               | United States   | Prospective, observational                                   | June 1997–July 1999         | 817 patients receiving mechanical ventilation for $\geq 48$ hrs  | 359 (44%)  |
| Cox et al, 2009 (38)                    | United States   | Prospective, observational                                   | April 2006–April 2007       | 126 consecutive patients receiving mechanical ventilation $\geq 21$ d or with a tracheotomy after $\geq 4$ d of mechanical ventilation | 90 (71%)   |
| <b>Trauma</b>                           |                 |  |                             |  |  |
| Miller et al, 2000 (39)                 | United States   | Retrospective  | January 1991–December 1997  | 115 severely injured patients spending $\geq 3$ 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 $\geq 16$ )   | 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 (%) <sup>a</sup> |
|--|-----------------|---|-----------------------------|--|--|
| 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%)   |
| <b>Cardiac arrest</b>                    |                 |   |                             |  |  |
| 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%)  |
| <b>Elderly</b>                           |                 |   |                             |  |  |
| Montuclard et al, 2000 (52)              | France          | Prospective cohort                          | January 1993–August 1998    | 75 consecutive patients >70 yrs with ICU LOS ≥30 d   | 30 (40%)   |
| Merlani et al, 2007 (53)                 | Switzerland     | Retrospective                               | January 1999–December 2000  | 141 consecutive patients ≥70 yrs with abdominal pathologies                                      | 52 (37%)   |
| Kaarlola et al, 2006 (54)                | Finland         | Cross-sectional survey                      | 1995–2000                   | 882 elderly (≥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 ≥80 yrs   | 231 (40%)  |
| Garrouste-Orgeas et al, 2006 (56)        | France          | Prospective, observational                  | March 2002–November 2003    | 180 patients ≥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 ≥45 yrs, ICU LOS ≥ 24 hrs   | 284 (32%)  |
| <b>Pancreatitis</b>                      |                 |   |                             |  |  |
| Soran et al, 2000 (58)                   | United States   | Retrospective                               | January 1992–December 1996  | 52 ICU patients with acute pancreatitis  | 39 (75%)   |
| Halonon et al, 2003 (59)                 | Finland         | Retrospective                               | January 1989–December 1997  | 283 consecutive patients with severe acute pancreatitis  | 174 (61%)  |
| <b>Sepsis</b>                            |                 |   |                             |  |  |
| 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)                            |
| <b>Mixed ICU patients 1 yr after ICU</b> |                 |   |                             |  |  |
| 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 ≤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 (%) <sup>a</sup> |
|--------------------------------|-----------------|---|-----------------------------|--|--|
| <b>Long-term QOL</b>           |                 |   |                             |  |  |
| 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)                                     |
| <b>Various diseases</b>        |                 |   |                             |  |  |
| De Boer et al, 2000 (63)       | The Netherlands | Prospective, observational                            | January 1993–May 1996       | 100 consecutive patients who underwent a trans-hiatal 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%)  |
| Orweli 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.

<sup>a</sup>Percentage 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                                       |
|--|---|---|---|--|
| <b>Acute respiratory distress syndrome</b> |   |   |   |  |
| 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  |
| <b>Prolonged mechanical ventilation</b>    |   |   |   |  |
| 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  |
| <b>Trauma</b>                              |   |   |   |  |
| 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   |
| <b>Cardiac arrest</b>                      |   |   |   |  |
| 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                          |
| <b>Elderly</b>                             |   |   |   |  |
| 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  |
| <b>Pancreatitis</b>                        |   |   |   |  |
| 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)                      |
| <b>Sepsis</b>                              |   |   |   |  |
| 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                                       |
|---|----------------|---|------------------------------|---|
| <b>ARDS</b>                             |                |   |                              |   |
| 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<br>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   |
| <b>Prolonged mechanical ventilation</b> |                |   |                              |   |
| Combes et al, 2003 (36)                 | No             | Only patients with prolonged mechanical ventilation ( $\geq 14$ d) were included  | Yes                          | Community-based age- and gender-matched controls  |
| Chelluri et al, 2004 (37)               | Yes            | Patients with prolonged mechanical ventilation ( $\geq 48$ hrs) were included   | Yes                          | Samples of the U.S. population  |
| Cox et al, 2009 (38)                    | Yes            | Patients with $\geq 21$ d mechanical ventilation or with tracheotomy after $\geq 4$ d mechanical ventilation were included  | No                           | U.K. population norms for persons aged 55–65 yrs  |
| <b>Trauma</b>                           |                |   |                              |   |
| Miller et al, 2000 (39)                 | No             | Only severely injured patients spending $\geq 3$ 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 $\geq 72$ 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 $\geq 9$ 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 $\geq 16$ 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<br>Before<br>ICU | Key Inclusion or Exclusion Criteria  | Description of<br>Nonresponders | Age-/Gender-Matched General<br>Population to Compare QOL                    |
|--|----------------------|--|---------------------------------|---|
| <b>Cardiac arrest</b>                    |                      |  |                                 |   |
| 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  |
| <b>Elderly</b>                           |                      |  |                                 |   |
| 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   |
| <b>Pancreatitis</b>                      |                      |  |                                 |   |
| 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                                  |
| <b>Sepsis</b>                            |                      |  |                                 |   |
| 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  |
| <b>Mixed ICU patients 1 yr after ICU</b> |                      |  |                                 |   |
| 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                     |
| <b>Long-term QOL</b>                     |                      |  |                                 |   |
| 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<br>Before<br>ICU | Key Inclusion or Exclusion Criteria  | Description of<br>Nonresponders | Age-/Gender-Matched General<br>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, analyses 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   |
|---|--|--|
| <b>ARDS</b>                             |  |  |
| 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  |
| <b>Prolonged mechanical ventilation</b> |  |  |
| 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   |
| <b>Trauma</b>                           |  |  |
| 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   |
| <b>Cardiac arrest</b>                   |  |  |
| 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  |
|--|---|---|
| <b>Elderly</b>                           |   |   |
| 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   |
| <b>Pancreatitis</b>                      |   |   |
| 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                      |
| <b>Sepsis</b>                            |   |   |
| 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)   |
| <b>Mixed ICU patients 1 yr after ICU</b> |   |   |
| 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 premonitory 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   |
| <b>Long-term QOL</b>                     |   |   |
| 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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